



## Hantaviruses in Africa



Peter T. Witkowski<sup>a,1</sup>, Boris Klempa<sup>a,b,1</sup>, Ndapewa L. Ithete<sup>c</sup>, Brita Auste<sup>a</sup>,  
John K.E. Mfunu<sup>d</sup>, Julia Hoveka<sup>d</sup>, Sonja Matthee<sup>e</sup>, Wolfgang Preiser<sup>c</sup>, Detlev H. Kruger<sup>a,\*</sup>

<sup>a</sup> Institute of Medical Virology, Helmut Ruska Building, Charité – University Medicine Berlin, Charitéplatz 1, D-10117 Berlin, Germany

<sup>b</sup> Institute of Virology, Academy of Sciences, Bratislava, Slovakia

<sup>c</sup> Division of Medical Virology, Faculty of Medicine and Health Sciences, Stellenbosch University, Tygerberg, South Africa

<sup>d</sup> Department of Biological Sciences, University of Namibia, Windhoek, Namibia

<sup>e</sup> Department of Conservation Ecology and Entomology, Stellenbosch University, Stellenbosch, South Africa

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### ABSTRACT

This paper summarizes the progress in the search for hantaviruses and hantavirus infections in Africa. After having collected molecular evidence of an indigenous African hantavirus in 2006, an intensive investigation for new hantaviruses has been started in small mammals. Various novel hantaviruses have been molecularly identified not only in rodents but also in shrews and bats. In addition, the first African hantavirus, Sangassou virus, has been isolated and functionally characterized in cell culture. Less is known about the ability of these hantaviruses to infect humans and to cause diseases. To date, no hantavirus genetic material could be amplified from patients' specimens collected in Africa. Serological studies in West Africa, based on a battery of screening and confirmatory assays, led to the detection of hantavirus antibodies in the human population and in patients with putative hantavirus disease. In addition to this overview, we present original data from seroepidemiological and field studies conducted in the Southern part of Africa. A human seroprevalence rate of 1.0% ( $n=1442$ ) was detected in the South African Cape Region whereas no molecular evidence for the presence of hantavirus was found in 2500 small animals trapped in South Africa and Namibia.

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## 1. Introduction

After the discovery of the Hantaan virus by Ho-Wang Lee and co-workers (Lee et al., 1978) it took nearly three decades before an indigenous hantavirus from Africa was demonstrated molecularly (Klempa et al., 2006) and subsequently also isolated in cell culture (Klempa et al., 2012). Thereafter, Africa became the scene of an intensive search for new hantaviruses and their reservoir hosts. This led not only to molecular proof of new hantaviruses but also to the identification of new hantavirus reservoir hosts – shrews and bats – in addition to rodents as the already established virus reservoir. This paper summarizes (i) the early attempts in hantavirus antibody detection in Africa, (ii) the progress achieved since the first molecular proof of an African hantavirus in 2006, and (iii) presents new data regarding hantavirus infections in South Africa and Namibia.

## 2. Early attempts in the search for hantavirus infections in Africa

Early diagnostic assays, immunofluorescence assays (IFA) and enzyme-linked immunoassays (EIA), were developed using the first known hantavirus, Hantaan virus (HTNV), and the subsequently isolated Seoul virus (SEOV) and Puumala virus (PUUV) as antigens. The establishment of appropriate techniques led to numerous investigations aimed to detect hantavirus antibodies in rodents (as the suspected reservoirs) as well as human beings in Africa.

Table 1a summarizes early data from screenings of small mammals for hantavirus antibodies. The estimated seroprevalence rates ranged from 2 to 22% and varied between geographical regions and animal species tested. In addition, the years and seasons when rodents were trapped may have influenced the results since it is known from other studies that the infection rate of reservoir animals fluctuates over time, with differences between years but also between seasons (Vaheri et al., 2013). Importantly, in practically all studies no confirmatory assays were used to substantiate the data of the primary antibody screening; only two sera found to be seropositive in IFA were confirmed by an independent assay (plaque reduction neutralization; LeDuc et al., 1986). Therefore, one can only speculate about the extent of possible false positive/negative results which might have biased the data.

\* Corresponding author. Tel.: +49 30 450525092.

E-mail address: [detlev.kruger@charite.de](mailto:detlev.kruger@charite.de) (D.H. Kruger).

<sup>1</sup> Contributed equally as first authors.

**Table 1a**  
Detection of hantavirus antibodies in African small mammals before 2006.

Location	Study object	Assay used	Antigen used	No. tested	Seroprevalence (%)	Confirmation by independent assay	Ref.
Senegal	Rodents	IFA	HTNV	401	11.5	No	Saluzzo et al. (1985)
Madagascar	Rats	IFA	HTNV	437	22	No	Rollin et al. (1985)
Madagascar	Rats	IFA	PUUV	437	11.7	No	Rollin et al. (1985)
Egypt	Rodents	IFA	HTNV	144	5.6	2 sera (by PRNT)	LeDuc et al. (1986)
Kenia	Rodents	IFA	HTNV	30	10	No	LeDuc et al. (1986)
CAR	Rodents	IFA	HTNV	353	2	No	Gonzalez et al. (1988)
Djibouti	Small mammals	IFA	HTNV	173	5.2	No	Rodier et al. (1993)
Egypt	Rodents	EIA	?	861	12.8	No	Baddour et al. (1996) (abstr.)
South Africa	Rodents	IFA	HTNV SEOV PUUV PHV	221	2.3	"Differential IFA", PRNT	Lee et al. (1999) (abstr.)

In more or less randomly selected human populations, seroprevalence rates were estimated to be between 0.2% and 17% (Table 1b). Antibody prevalences were not significantly higher in patients with chronic renal disease and not further classified renal dysfunction compared to the respective comparator populations (Gonzalez et al., 1988; Lee et al., 1999; Botros et al., 2004). This could be explained by the fact that hantavirus diseases are acute and, even in cases of acute fever and renal dysfunction, are only one of many possible etiological causes of renal disease. Since human beings in Africa are exposed to various infectious agents and their sera show some degree of antibody cross-reactivity (Everett et al., 2010), the findings of these

studies were limited by the lack of independent confirmatory assays.

Increasing hantavirus antibody titers were detected in a patient with high fever, slight conjunctival icterus, slight elevation of serum creatinine, *Plasmodium* infection, HIV infection, and hepatitis B infection. Seroreactivity was mainly directed against HTNV and to a lesser degree against SEOV or PUUV antigens (Coulaud et al., 1987). This is an interesting hint for the occurrence of a patient with hantavirus disease in Central Africa but, again, no independent confirmatory assays were used and it cannot be excluded that cross-reacting antibodies were detected in this multiple-infected patient (Table 1b).

**Table 1b**  
Detection of hantavirus antibodies in humans in Africa before 2006.

	Study object	Assay used	Antigen used	No. tested	Seroprevalence (%)	Confirmation by independent assay	Ref.
CAR	Humans	IFA	HTNV	87	1.2	No	Lee et al. (1981)
Gabon	Humans	IFA	HTNV	30	3.3	No	Lee et al. (1981)
Burkina Faso	Humans	IFA	HTNV	792	1	No	Gonzalez et al. (1984)
Benin	Humans	IFA	HTNV	603	3.3	No	Gonzalez et al. (1984)
CAR	Humans	IFA	HTNV	293	0.7	No	Gonzalez et al. (1984)
Gabon	Humans	IFA	HTNV	30	3.3	No	Gonzalez et al. (1984)
Senegal	Humans	IFA	HTNV	175	16.6	No	Saluzzo et al. (1985)
Nigeria	Humans	IFA	SEOV	668	1.2	No	Tomori et al. (1986)
Nigeria	Humans	IFA	HTNV	668	0.2	No	Tomori et al. (1986)
CAR	Patient with suspected HFRS	IFA	HTNV, SEOV, PUUV	1	n.a.	No	Coulaud et al. (1987)
Gabon	Humans	IFA	HTNV	213	8	No	Dupont et al. (1987)
Algeria	Humans	IFA	HTNV	168	1.8	No	Fleury et al. (1987)
Cameroon	Humans	IFA	HTNV	375	0.8	No	Fleury et al. (1987)
CAR	Patients with renal dysfunction	IFA	HTNV	305	4.6	No	Gonzalez et al. (1988)
CAR	Humans	IFA	HTNV	484	3.5	No	Gonzalez et al. (1988)
Mauritania	Humans	IFA	HTNV	956	0.3	No	Lepers et al. (1988)
Chad/Cameroon/Gabon/ Equat. Guinea	Humans	IFA	HTNV	2893	6.15	No	Gonzalez et al. (1989)
Egypt	Children (8–14 years)	EIA	HTNV	315	8.9	No	Corwin et al. (1992)
Egypt	Humans	EIA	HTNV	915	4	No	Corwin et al. (1993)
Djibouti	Humans	IFA	HTNV	212	3.3	No	Rodier et al. (1993)
Egypt	Humans	EIA	?	637	12.2	No	Baddour et al. (1996) (abstr.)
South Africa	Humans	IFA	HTNV SEOV PUUV PHV	1100	1.2	"Differential IFA", PRNT	Lee et al. (1999) (abstr.)
South Africa	Patients with fever and renal failure	IFA	HTNV SEOV PUUV PHV	318	0.9	"Differential IFA", PRNT	Lee et al. (1999) (abstr.)
Egypt	Humans	EIA	HTNV	695	1.0	No	Botros et al. (2004)
Egypt	Humans with chronic renal dis.	EIA	HTNV	350	1.4	No	Botros et al. (2004)

Abbreviations: CAR, Central African Republic; EIA, Enzyme-linked Immunosorbent Assay; HTNV, Hantaan virus; IFA, (indirect) Immunofluorescence Assay; n.a., not applicable; PHV, Prospect Hill virus; PRNT, Plaque Reduction Neutralization Assay; PUUV, Puumala virus; SEOV, Seoul virus.

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