CVI research programme emerging vector borne viral diseases

Rob Moormann

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(Zoonotic) viral diseases transmitted by insect vectors

- About 75% of the (re)-emerging viral diseases in man originate from an animal reservoir
- Increasing threat: Climate change, globalisation, migration
  Exotic ⟶ Endemic (BTV)
- Impact: more than 500 “vector-borne” viruses. *Toga-, Flavi-, Rhabdo-, Reo-, Bunyaviridae.* Of these about 100 are of veterinary and/or human importance.
- Lack of knowledge: Because of exotic character often little knowledge and experience with virus-vector combinations (in the Netherlands)
- Lack of effective and safe vaccines and diagnostics
- Part of new focal point of research of CVI-Wageningen UR and topic within “Kennisketen Infectieziekten Dier” (CVI-Wageningen UR, GD, FD)

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Selected emerging vector borne viral diseases

Viral disease	Insect vector	Affected species
Dengue fever	*Aedes aegypti*	man
Chikungunya fever	*Aedes albopictus*	man
West Nile fever	*Aedes sp.; Culex sp.*	horses/man
Rift Valley fever	*Aedes sp.; Culex sp.*	ruminants/man
Crimean Congo fever	*Hyalomma margin.*	ruminants/man
Bluetongue	*Culicoides sp.*	ruminants
African horsesickness	*Culicoides sp.*	horses

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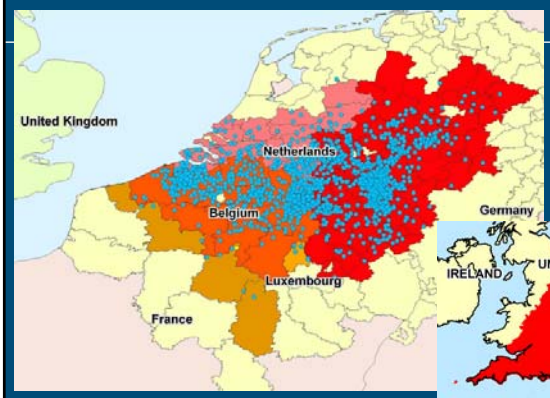
Spread of BTV 8



February 2007

May 2008

In Holland losses due to BT in 2007 amount to 81 million € (LTO)

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Rift Valley fever virus: Global distribution

Recent outbreaks

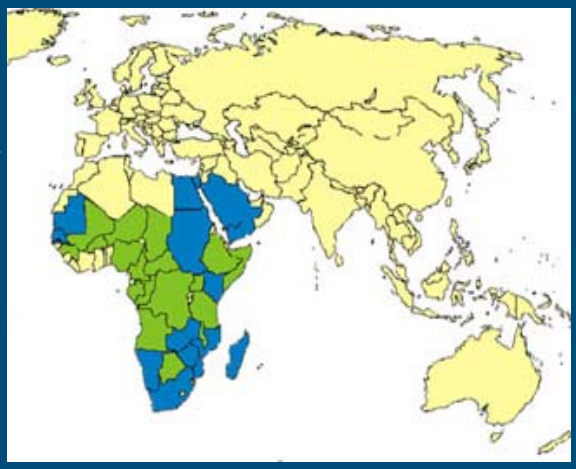
Kenia/Tanzania 1997-98
89,000 human cases, 487 deaths.
abortion storms in ruminants and camels.

Yemen + Saudi Arabia 2000
2210 human cases, 290 deaths.
20,000 abortions in sheep and goats.

Kenia/Tanzania/Somalia 2007
1062 human cases, 315 deaths.

Sudan/Madagascar 2007-2008
1116 human cases, 239 deaths.

South-Africa 2008
Ruminants: buffalo, sheep; abortions, deaths. Limited number of cases.



Endemic Epidemic

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Source: The EFSA Journal (2005) **238**, 1-128, and WHO (www.who.int)

Consequences for sheep/goat/cattle

- Mortality rate: (<1 wk of age) up to 90%
  (>1 wk of age) up to 30%
- Abortion may reach 100% (abortion storm)
- Economic consequences much bigger than those of BT; After RVFV epidemic in country or zone, export ban for at least 4 years (OIE article 2.2.14.2)

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Consequences for humans

- Mild disease:
  Influenza-like illness, recovery within 4-7 days
- More severe disease:
  Retinopathy, blindness, meningo-encephalitis hemorrhagic syndrome with jaundice, petechiae and death (<1-10%)
- Socio-economic impact high: quarantine measures, hospitals; secundary effects like tourism etc. (SARS 2003; 20 billion €)

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Control measures

Integrated approach

- Early warning: Modelling; Combination of geografic information (GIS) with pathogen-epidemiology; risk-assessment. CIb-RIVM, CVI-Wageningen UR, LEI-WageningenUR, Plant protection service (PD), FD-UU
- Surveillance: Diagnostics for animals CVI-Wageningen UR, GD; human CIb-RIVM
- Vector competence. Entomology-WU, CVI-Wageningen UR, PD, FD-UU, CIb-RIVM.
- Vaccine (DIVA) development; CVI-Wageningen UR-focal point; FD-UU, OVI-SA

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BTV: Epidemiology, surveillance, transmission, eradication

- Spatial transmission kernel estimated from BTV infected herds using GIS information; risk map for vector borne diseases. (R&D).
- Spatio-temporal risk factor analysis & risk modelling, and risk-based surveillance protocols. (Epizone).
- Vaccination against Bluetongue: level of immunological protection and possibilities for eradication (LNV)
  - Vector densities in relation to biting frequency.
  - Protection of (maternal) antibodies against BTV8 infection and transmission.
  - Extension of existing spatial and anima-vector transmission models (influence of transplacental transmission and temperature etc.)



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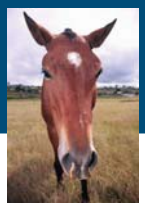
Modelling and Risk Assessment for RVFV and AHSV (QVERA)

- Risk analysis RVFV and AHSV: Analysis of risk of introduction of RVFV and AHSV via different routes (insects, import animal products, wild-life etc.) and definition of (most) effective preventive measures.
- Analysis of spread of RVFV and AHS after introduction in the Netherlands with a mathematical model.
- Analysis of possible control strategies for RVFV and AHSV and their efficacy with the a.m. mathematical model.
- Analysis of possible surveillance strategies for RVFV and AHS
- Cost analysis of a possible outbreak of AHS in the Netherlands.



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Surveillance/Diagnostics

- Participation of CVI in EU project ARBO-ZOONET. (WNV, RVFV, CCHFV)
  - Aim: Exchange of data, expertise, reagents, (reference) strains and diagnostic systems for surveillance (standardization).
- Coordination by CVI of EU coordination project Epizone. Strong network for BTV, exchange and standardization of BTV diagnostics (PCR, ELISA)
- Evaluation of infection models for BTV 8 in sheep and cattle (running). Generates samples for validation of tests.
- Development of infection models for AHSV in horses and RVFV in sheep. To be started in 2009.

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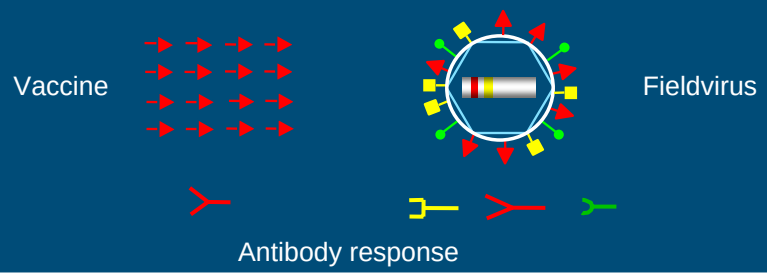
Vaccines

- Vaccines having DIVA properties.
  - Differentiating Infected from Vaccinated Animals
  - Vaccine in combination with diagnostic test
  - Allows for studying epidemiology of fieldvirus in a vaccinated population



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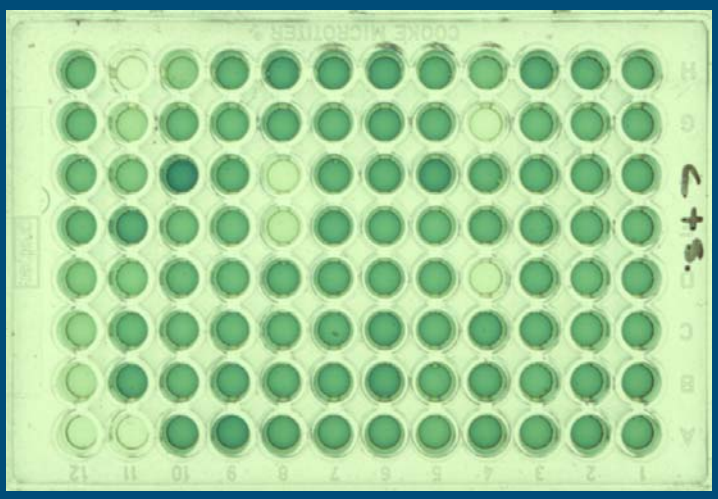
Example of E^{RNS} ELISA result



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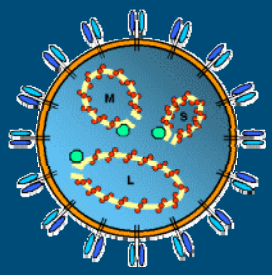
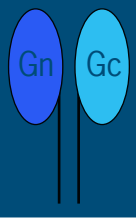
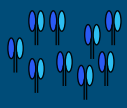
Approaches





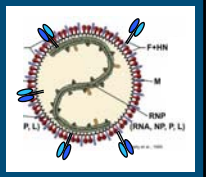
1: Subunit (RVFV) CVI-FD

(mammalian/insect cells)



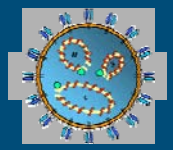
2: NDV vector (BTV, RVFV)

(reverse-genetics)



3: Modified live (BTV, RVFV)

(reverse-genetics)



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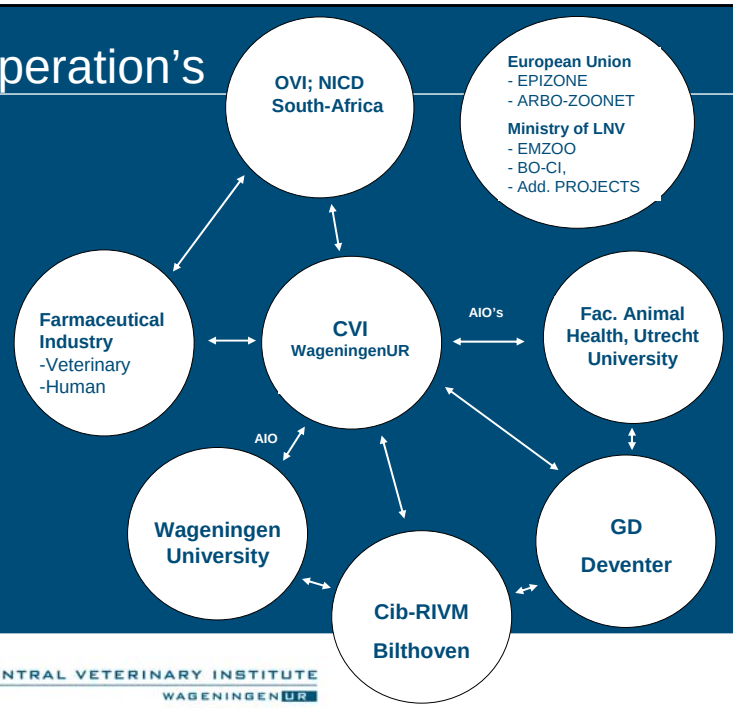
Cooperation's



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In summary

- CVI-Wageningen UR takes responsibility by investing in:
  - Knowledge generation on emerging vector borne (viral) diseases in general (focal point).
  - Development of effective and safe (DIVA) vaccines (RVFV, BTV).
  - Development of (DIVA) diagnostics (AHSV, WNV, RVFV, CCHFV)
  - Modelling studies
  - Facilities: BSL3 laboratories (before end 2008).

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Future

- Within 2-3 years validated diagnostics available for AHSV, WNV, RVFV, CCHFV. BTV already in place.
- Expectation: Suitable (DIVA) vaccines for RVFV and BTV in licensing procedures, or licensed depending on progress, 5 years from now.
- Start research on vaccine development for African Horse Sickness Virus.
- Have BSL4 facilities available to be able to do research on Crimean Congo Haemorrhagic fever virus. Tick borne, currently emerging in Turkey (41 casualties this year up till now out of 689 confirmed cases), and another growing threat to Western-Europe.

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Take home message

Prevention of zoonotic diseases in humans begins with eradication in animals

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