Hantaviroses en Belgique :

Aspects cliniques et particularités épidémiologiques

Paul COLSON
Jan CLEMENT

CLINIQUE & MATERNITÉ SAINTE-ELISABETH
CHU Dinant Godinne UCL NAMUR

Déclaration de liens d'intérêt avec les industries de santé en rapport avec le thème de la présentation (loi du 04/03/2002) :

Intervenant : Nom/Prénom : **Colson Paul**

Titre : **Hantaviroses en Belgique :Aspects cliniques et particularités épidémiologiques**

L'orateur ne souhaite pas répondre ☐

- Consultant ou membre d'un conseil scientifique — ☐ **OUI** ☑ **NON**
- Conférencier ou auteur/rédacteur rémunéré d'articles ou documents — ☐ **OUI** ☑ **NON**
- Prise en charge de frais de voyage, d'hébergement ou d'inscription à des congrès ou autres manifestations — ☐ **OUI** ☑ **NON**
- Investigateur principal d'une recherche ou d'une étude clinique — ☐ **OUI** ☑ **NON**

Aspects cliniques

EPIDEMIE D'HANTAVIROSE DANS L'ENTRE-SAMBRE-ET-MEUSE 197

EPIDEMIE D'HANTAVIROSE DANS L'ENTRE-SAMBRE-ET-MEUSE

ANNEE 1992 - 1993

DONNEES CLINIQUES ET BIOLOGIQUES

P. Colson (1), Ph. Damoiseaux (2), J. Brisbois (1), E. Duvivier (3), P. Levecque (3), J.M. Roger (4), D-J. Bouilliez (5), P. Mc Kenna (6), J. Clement (6).

Clinical Course and Long-Term Outcome of Hantavirus-Associated Nephropathia Epidemica, Germany

Joerg Latus, Matthias Schwab, Evelina Tacconelli, Friedrich-Michael Pieper, Daniel Wegener, Juergen Dippon, Simon Müller, David Zakim, Stephan Segerer, Daniel Kitterer, Martin Priwitzer, Barbara Mezger, Birgit Walter-Frank, Angela Corea, Albrecht Wiedenmann, Stefan Brockmann, Christoph Pöhlmann, M. Dominik Alscher, and Niko Braun

Emerging Infectious Diseases January 2015

TABLEAU 2.
ANOMALIES CLINIQUES (% DE FRÉQUENCE) DANS LA NE EN ENTRE-SAMBRE-ET-MEUSE (E-S-M), EN EUROPE OCCIDENTALE (RÉF. 5) ET EN FINLANDE (RÉF. 11) - (RÉF. 12)

	E-S-M	France et Belgique	Finlande	
	1993-1994 n=55	1977-1987 n=76	< 1971 n=76	1982à1990 n=126
Fièvre	100%	100%	100%	
Douleur abdo. ou lombaire	80%	90%	82%	43% 54%
Nausées et/ou Vomissements	29%	24%	70%	58%
Diarrhées	14%	7%	12%	18%
Oedème MI	2%	5%	11%	9%
Diathèse hémor.	22%	17%	18%	10%
Céphalées	71%	83%	90%	62%
Myopie aiguë	24%	24%	12%	36%
Méningisme	11%	11%	5%	1%
Toux	24%	N.T.	N.T.	14%
Oligurie < 400 mL/24h	27%	68%	54%	34%

TABLEAU 3.
ANOMALIES BIOLOGIQUES (% DE FRÉQUENCE) DANS LA NE EN ENTRE-SAMBRE-ET-MEUSE (E-S-M), EN EUROPE OCCIDENTALE (RÉF. 5) ET EN FINLANDE (RÉF. 11) - (RÉF. 12)

	E-S-M	France et Belgique	Finlande	
	1993-1994 n=55	1977-1987 n=76	< 1971 n=76	1982à1990 n=126
Plaquettes <100000/µL	69%	58%	20%	75%
GB > 8000/µL	77%	79%	79%	50
LDH > 320 UI/L	69%	65%	71%	N.T.
GPT > 30 UI/L	46%	42%	40%	N.T.
gamma GT > 40 UI/L	28%	31%	52%	N.T.
Bili > 18 mmol/L (> 1 mg /100mL)	6%	7%	7%	N.T.
VS > 20 mm/h	85%	91%	90%	N.T.
CRP > 50 mg/L	86%	-	-	N.T.
CPK > 110 UI/L	0%	16%	27%	N.T.
Creat > 105 mmol/L (> 1.2 mg/100mL)	84%	100%	-	94%
Protéinurie	100%	94%	100%	94%
Hématurie microsc.	83%	68%	74%	58%

Acta Clinica Belgica 50-4, 1995

« Fièvre floue
Myopie transitoire
Thrombopénie
Activité exposante

Ne pas écarter le D si
+ atteinte pulm, digest, urinaire
+ hyperleucocytose »

Syndrome Pulmonaire Hantaviral Européen

Eur J Clin Microbiol Infect Dis (2013) 32:1341–1345
DOI 10.1007/s10096-013-1885-x

ARTICLE

Another case of "European hantavirus pulmonary syndrome" with severe lung, prior to kidney, involvement, and diagnosed by viral inclusions in lung macrophages

M. Gizzi · B. Delaere · B. Weynand · J. Clement · P. Maes · V. Vergote · L. Laenen · B. Hjelle · A. Verroken · A. Dive · I. Michaux · P. Evrard · D. Creytens · P. Bulpa

Fe 42 ans
Fièvre & hypoxémie
VNI - VM

Fig. 2 Chest computed tomography (CT) scan (day 8 POS) showing bilateral ground-glass pattern

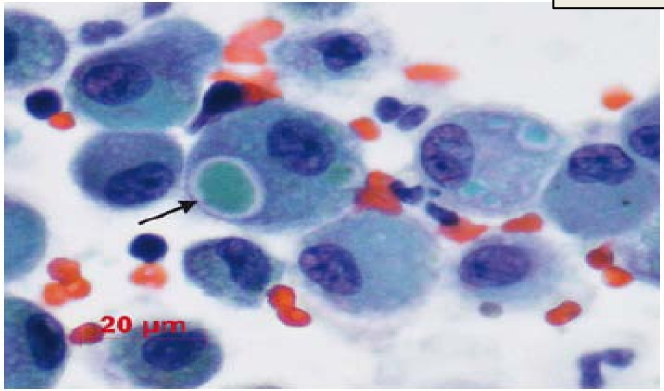


Fig. 3 Bronchoalveolar lavage (BAL) macrophages containing greenish cytoplasmic inclusions surrounded by a clear halo (*arrow*, Papanicolaou stain, magnification ×40)

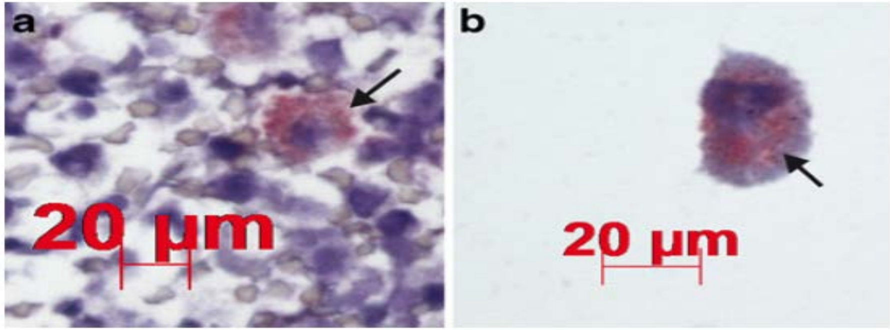


Fig. 4 a, b Macrophage inclusions stained positively with specific *Puumala virus* (PUUV) antibody [*arrow*, magnification ×60 (a), ×100 (b)]

1994

HANTAVIRUS PULMONARY SYNDROME IN NEW ENGLAND AND EUROPE

B-1120 Brussels, Belgium
J. Clement, M.D.
Military Hospital Queen Astrid

B-6460 Chimay, Belgium
P. Colson, M.D.
Centre de Santé des Fagnes

B-1120 Brussels, Belgium
P. McKenna, B.Sc., Ph.D.
Military Hospital Queen Astrid

Syndrome de Guillain-Barré

Case Report

Guillain-Barré syndrome associated with Puumula Hantavirus infection

G. Tassart[1], S. Balbeur[1], Th. Deltombe[2], M. Tintillier[1], Ch. Cuvelier[1]

[1]Service de médecine interne générale et néphrologie, Clinique et Maternité Sainte Elisabeth, Belgique, [2]CHU Mont-Godinne, Service de médecine physique et réadaptation, Belgique

We report the case of a 62-year-old man who developed Guillain-Barré syndrome (GBS) following Hantavirus infection. Only three similar cases have been described in the literature so far. GBS is an autoimmune disease characterized by progressive symmetrical weakness of lower limbs extending to upper limbs and face and low or absent tendon reflexes. Prompt diagnosis is mandatory as GBS is a potentially life threatening disorder and needs timely treatment to ensure fast recovery and fewer complications.

Hô 62 ans
Tr neuro-végét.
Parésie M.I.
LCR+ EMG+

We conclude that our patient had a predominantly sensory Guillain-Barré syndrome associated with hantavirus infection. Serious neurological complications during NE have been reported before[4,5] but to our knowledge this is only the second case of Guillain-Barré syndrome.

R A J Esselink, M N Gerding, P J A M Brouwers, H Solleveld, J G M Jordans, J Groen, A D M E Osterhaus

Departments of Neurology and Internal Medicine, PO Box 50000, 7500KA Enschede, Netherlands; and National Institute of Public Health and Environmental Protection, Bilthoven

Acta Clinica Belgica 2014 VOL. 69 NO. 5 371

Syndrome d'activation lympho-histiocytaire

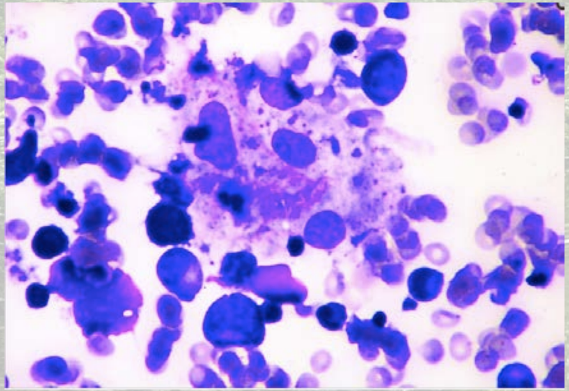
LETTRES

17 octobre 1998 / 27 / n° 31

La Presse Médicale → 1577

Syndrome hémophagocytaire et fièvre hémorragique avec syndrome rénal

V. Baty, H. Schuhmacher, C. Bourgoin, V. Latger, J. Buisine, T. May, Ph. Canton



Hô 62 ans

- **Fièvre**
- **Splénomégalie**
- ~~**Bi-/tricytopénies**~~ **(mais Plaq50.000)**
- **Hypertrigly 487mg/dl**
- **Ferritine 10.000ng/ml**
- **PM : Hémophagocytose**

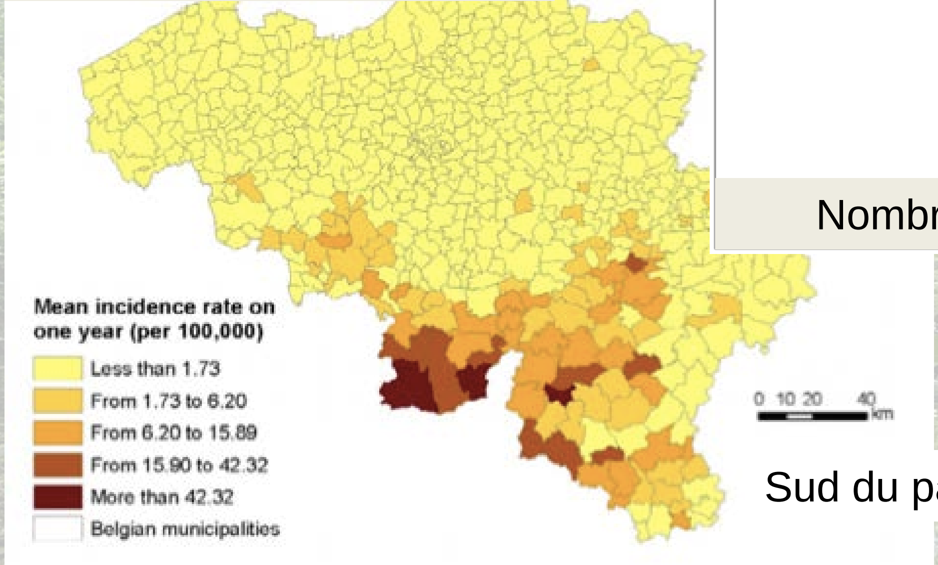
Hemorrhagic Fever with Renal Syndrome Presenting with Hemophagocytic Lymphohistiocytosis

Je-Jung Lee,* Ik-Joo Chung,* Dong-Hyeon Shin,* Sang-Hee Cho,* Duck Cho,* Dong-Wook Ryang,* Ali S. Khan,† and Hyeoung-Joon Kim*

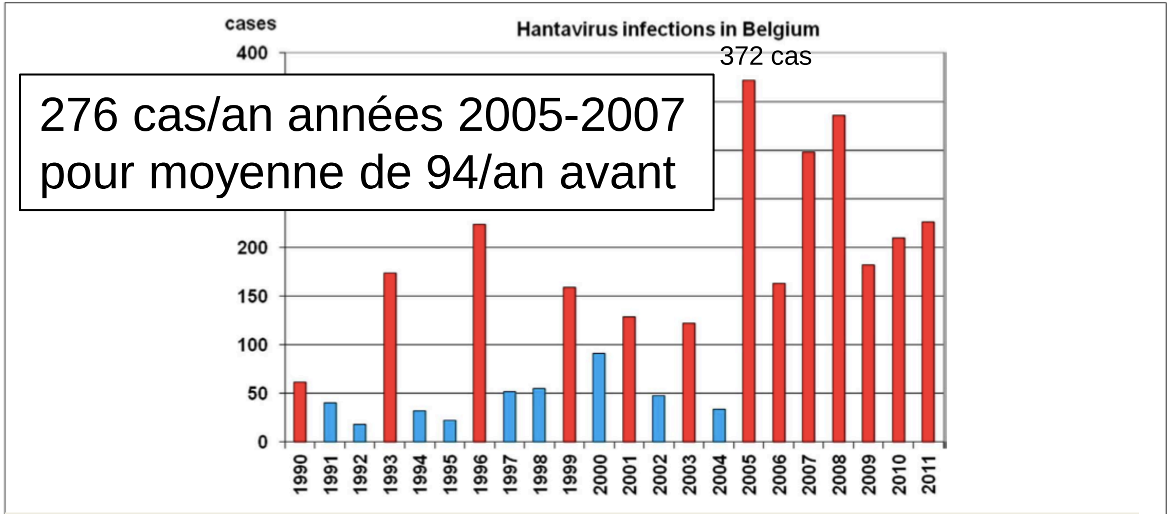
Epidémiologie:

En Belgique

Incidence annuelle moyenne
Sur les années 1994-2004
(par 100.000 habitants)



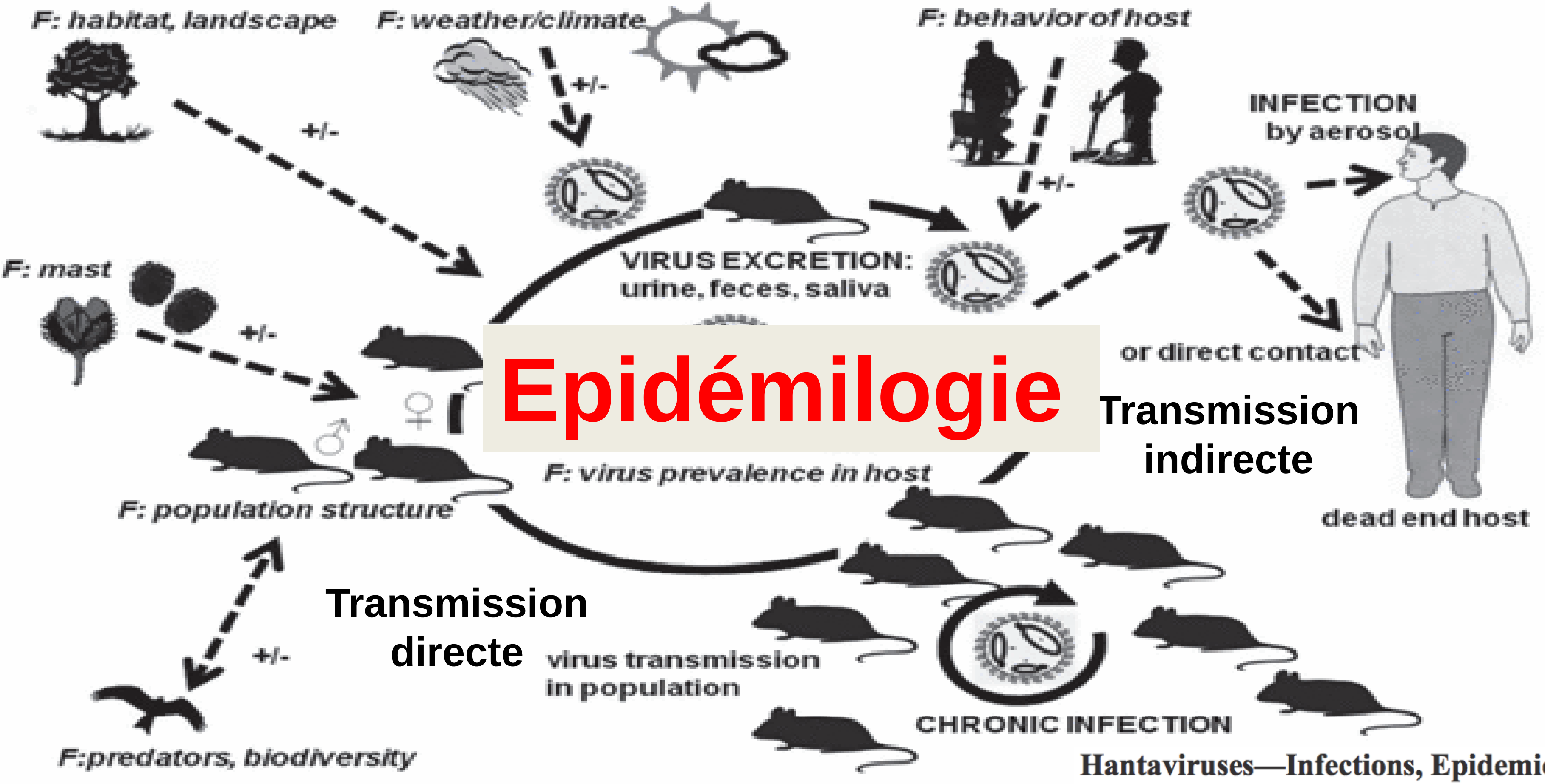
276 cas/an années 2005-2007
pour moyenne de 94/an avant



Nombre annuel de cas d’hantavirose en Belgique

Sud du pays et frontière franco-belge

Epidémilogie



Transmission indirecte

Transmission directe

Cycle de transmission de l'hantavirus

Hantaviruses—Infections, Epidemiology and Hosts

Sandra S. Essbauer and Ellen Krautkrämer

L'HOMME : Etudes cas/contrôles

A Case-Control Study after a Hantavirus Infection Outbreak in the South of Belgium: Who Is at Risk?

F. Van Loock, I. Thomas, J. Clement, S. Ghoos, and P. Colson

From the Scientific Institute of Public Health–Louis Pasteur (formerly the Institute of Hygiene and Epidemiology), Brussels; Department of Virology, University Hospitals of Leuven, Leuven; Military Epidemiology and Research Unit, Queen Astrid Military Hospital, Brussels; and "Centre de Santé des Fagnes," Chimay, Belgium

Facteurs humains

- Activités dérangeant les nids des rongeurs :
  - ⇒ Rénovation de maison, nettoyage
  - ⇒ Introduction dans des places closes occupées par les rongeurs.
- Activités plaçant l'homme en contact prolongé avec l'habitat du rongeur :
  - ⇒ Camping – dormir sur le sol, dans des huttes
  - ⇒ Exercices militaires
  - ⇒ Activités forestières (**bois de chauffage++)** - fermières

Exposition à risque	Nombre de patients (n = 103)
Emploi dans le secteur forestier	6
Agriculteur (autre que forestier)	8
Emploi dans le bâtiment	8
Manipulation de bois stocké	36
Ramassage de bois en forêt	16
Mise en suspension de poussière lors de loisir en extérieur	14
Jardinage, terrassement	34
Nettoyage, rénovation de local	28
Chasse	11
Contact avec des cadavres de rongeurs	4

Risque accru si fumeur (Vapalahti, Clement&Colson 2005)

LE RONGEUR : Ecologie

L'Environnement

LE RONGEUR : Ecologie

L'Environnement

Ecologie de l'hôte :

- Habitat = Forêt déciduales (+conifères) >< (Bocage avec haies*) (Guivier)
  - Sous-bois dense – qualité de la végétation (« verdeur ») (Linard).
  - A prédominance de hêtres.
  - Couche d'humus au sol (épines + résidus de feuilles).
  - Humidité du sol (Verhaegen)
  - Parcelles boisées de grandes tailles, non morcelées.

- Etude sérologique : 21.059 Belges en bonne santé, donneurs de sang.

=> 1,30% seropositifs PUUV IgG;

=> prévalence + élevée dans le sud (plus forestier).

**moindre qualité pour les ressources alimentaires*
+ grandes variations de t°, d'humidité, de radiations uv

LE RONGEUR : Ecologie

Le Climat

- Climat : relation avec le comportement
  - ➢ Hiver doux : début précoce de la saison de reproduction.
  - ➢ Hiver rigoureux :
    - le campagnol cherche un abri (se rapproche de l'habitat humain;
    - *(emploi accru de bois de chauffage);*
    - *(les excrétats sont plus longuement infectants) (Tersago).*
  - ➢ Augmentation de la densité de campagnols
    - si t° estivales élevées 2 ans auparavant;
    - si t° automnales élevées 1 an auparavant (=> masting) (Tersago).
  - ➢ Conséquences actuelles et futures du réchauffement climatique?

- Prédateurs :
  - ➢ Augmentation de la densité des mustélidés et des renards depuis 1980.

LE RONGEUR : Comportement

- Différence des genres :
  - ➢ Les mâles adultes présentent plus de blessures que les femelles et les jeunes.
  - ➢ Les mâles adultes sont plus souvent infectés que les femelles et les campagnols juvéniles (pour des raisons de comportement).
  - ➢ Les mâles adultes parcourent de grandes distances => possibilité d'introduire le virus dans des populations « virus free ».

- Population abondante :
  - ➢ En cas de densité importante de la population de campagnols, la dispersion des campagnols hors du nid est retardée (=>printemps).
    => disparition de l'immunité transmise par la mère lors de « l'exode »

LE RONGEUR : Comportement

Comportement de l’hôte combinée à l’écologie :

La « Mast hypothesis »

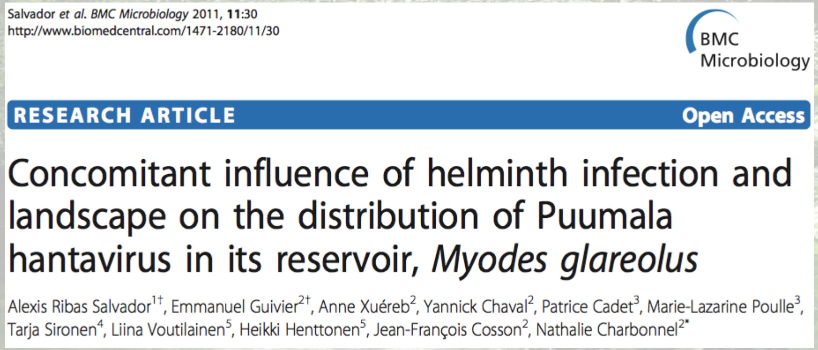
- **Alimentation abondante** (« Mast event »)
  (Faînes++ / Glands)
  - Augmentation des ressources.
  - Amélioration de la survie hivernale.
  - Début de la phase de reproduction + précoce et possibilité de deux portées (1ère : fin de l’hiver ou début du printemps).
    => densité ++ de rongeurs
    => animaux de la 1ère portée :
    - développement rapide
    - fertiles dès la première année

LE RONGEUR : Comportement

Comportement de l'hôte :

- Différence suite à l'infection :
  - ➢ La quantité de virus dispersé durant le premier mois de l'infection est nettement + importante que pendant la phase chronique ultérieure.

Et…



Salvador *et al. BMC Microbiology* 2011, **11**:30
http://www.biomedcentral.com/1471-2180/11/30

BMC Microbiology

RESEARCH ARTICLE **Open Access**

Concomitant influence of helminth infection and landscape on the distribution of Puumala hantavirus in its reservoir, *Myodes glareolus*

Alexis Ribas Salvador[1†], Emmanuel Guivier[2†], Anne Xuéreb[2], Yannick Chaval[2], Patrice Cadet[3], Marie-Lazarine Poulle[3], Tarja Sironen[4], Liina Voutilainen[5], Heikki Henttonen[5], Jean-François Cosson[2], Nathalie Charbonnel[2*]

➚
➚

➚ des cas infectés

- ➢ L'infection altère le profile de l'odeur de l'urine de son hôte et les campagnols de l'entourage sont capables de le détecter.

LE RONGEUR : La séroprévalence

Variations :

- Dépend de l'abondance des campagnols :
  - Surtout en phase non épidémique (Linard).
  - Facteurs climatiques :
    - ↗ si t° basse pendant l'hiver;
    - ↘ si précipitations++ l'automne précédent (Linard) l'hiver et le printemps.
- Dépend de l'âge :
  - Les jeunes sont protégés par les AC de la mère >30jours? (Verhaegen)
  - ↗ avec l'âge (Verhaegen – Augot). **?** avec le genre.
- Dépend du comportement :
  - Prévalence en relation avec maturité sexuelle/agressivité/mobilité (Escutenaire).

LE RONGEUR : La séroprévalence

Variations

- Dépend de la saison :
  - ➢ Séroconversion en automne et en hiver (Verhaegen – Escutenaire).
    - - Perte de l'immunité transmise par la mère
    - - Hivernage en groupe => ↗ rencontre avec un campagnol infecté;
  - ➢ Plus haute séroprévalence au printemps qu'en automne (Debly)

- Dépend de facteur immunogénétique.
  - ➢ Variabilité de susceptibilité du campagnol (Heyman 199?)

- Variations spatiales :
  - ➢ Belgique : Nord 1,79% en 2004 et 3,54% en 2005
    Sud 5,56%   12,30%

LE RONGEUR : La séroprévalence

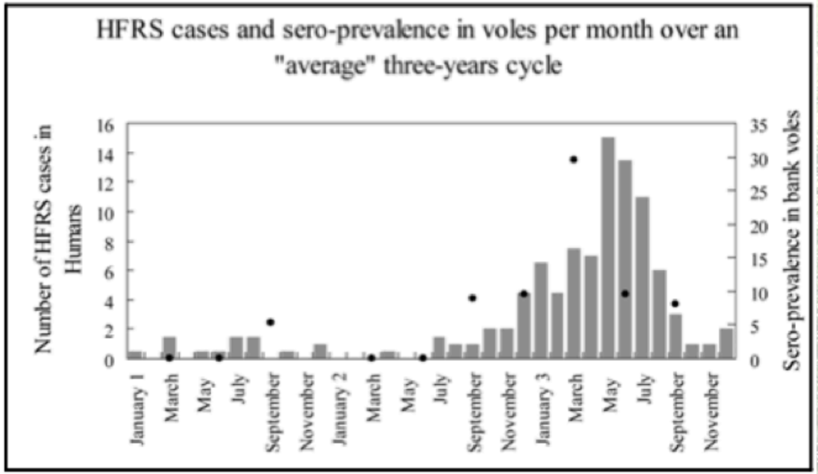


Figure 2. Temporal correspondence of reservoir contamination and of human cases of nephropathia epidemica over a typical 3-year cycle. Grey bars: the number of HFRS cases in humans per month for the Ardennes region (France) from 1991 to 1996; black points: observed hantavirus antibody prevalence in bank voles by trapping session in Elan forest over the same period. Right scale: percentage of seropositive voles in the trapped sample.

2002

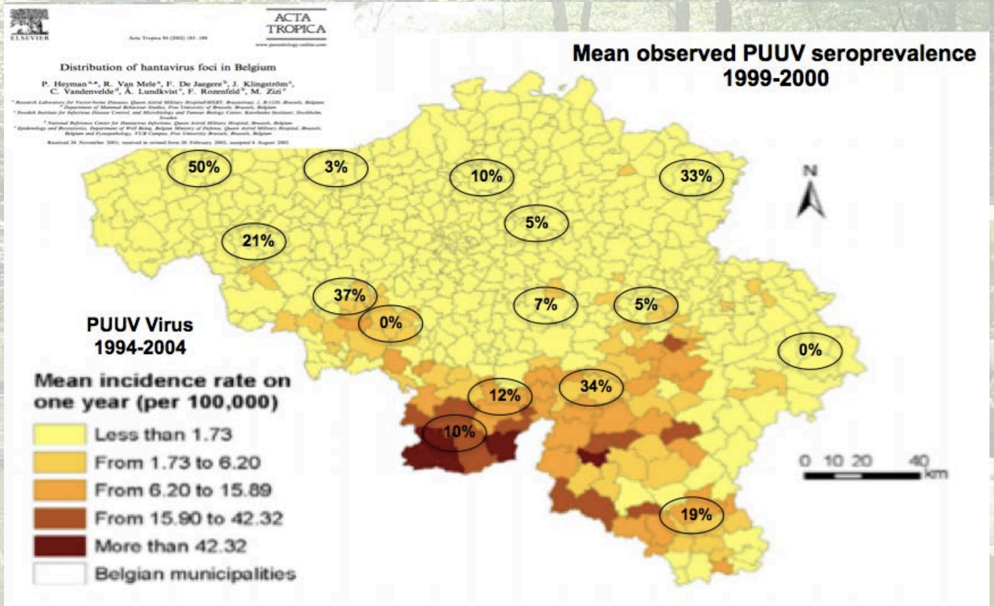
Puumala hantavirus Infection in Humans and in the Reservoir Host, Ardennes Region, France

F. Sauvage,* C. Penalba,† P. Vuillaume,‡ F. Boue,§ D. Coudrier,# D. Pontier,* and M. Artois**

We compared the occurrence of nephropathia epidemica cases, over a multi-annual population cycle, in northeastern France with the hantavirus serology for bank voles captured in the same area. We discuss hypotheses to explain the pattern of infection in both humans and rodents and their synchrony.

Emerging Infectious Diseases • Vol. 8, No. 12, December 2002 1309

Pas de relation linéaire entre prévalence et cas d'hantavirose



LE RONGEUR : Etude des années « épidémiques »

Etudes de « trapping » :
= Séropréalence sur 9 sites avant/pdt/après le pic de 2005.

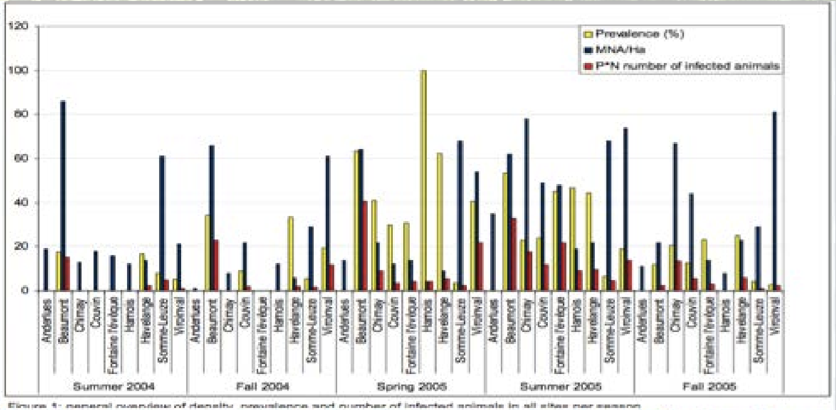
- Populations résiduelles dans les aires d'habitat préféré avec conditions de microclimat +.
  - Séroconversion automne 2004 – printemps 2005.
  - Abondance + grande dans zones forestières moins isolées.
    => les parcelles bien connectées sont plus recolonisées (Linard)

  - Abondance de campagnols stable entre 2004 mais
    - Prévalence moyenne de 5,56% en 2004 et 13,3% en 2005.
    - Importance du nombre de mâles sexuellement actifs en automne.
    - Nombreux campagnols PUUV-IgG+ localement n'impliquent pas d'office infection locale (cfr Augot).

LE RONGEUR : Etude des années « épidémiques »

Etudes de « trapping » :
= Séropréalence sur 9 sites
avant/pdt/après le pic de 2005.

	2004	2005	NE*
Beaumont	34%(137)	34%(77)	30
Chimay	0% (21)	28%(129)	120



Spatio-temporal variation of Puumala hantavirus infection in Western Europe (Belgium); an eco-epidemiological study.
Tersago K., Leirs H., Verhagen R.

2005

Année épidémique

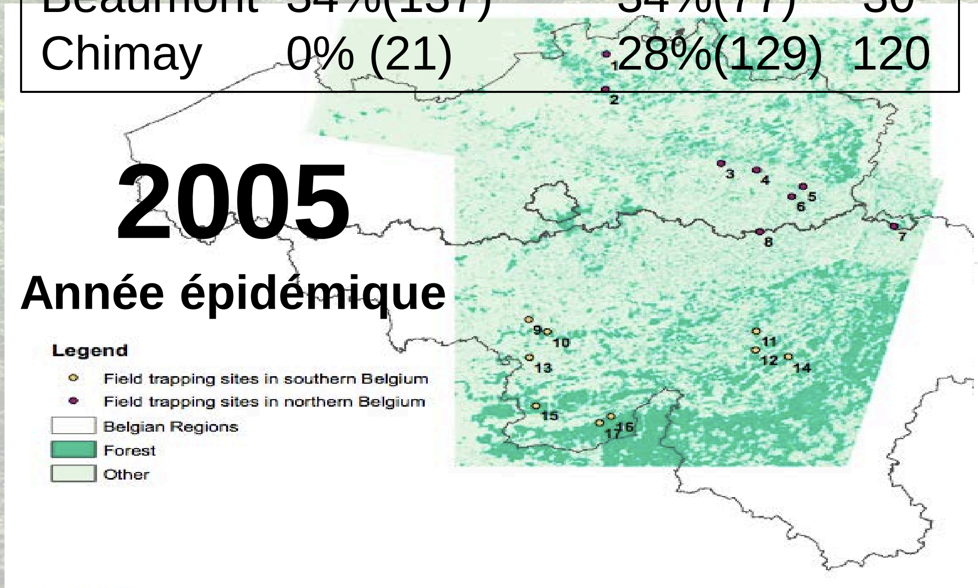


Figure 1
Study area: localization of field trapping sites and Landsat images.

International Journal of Health Geographics

BioMed Central

Research

Open Access

Environmental conditions and Puumala virus transmission in Belgium

Catherine Linard*[1], Katrien Tersago[2], Herwig Leirs[2,3] and Eric F Lambin[1]

Address: [1]Department of Geography, Université Catholique de Louvain, Place Pasteur 3, B-1348 Louvain-la-Neuve, Belgium, [2]Research group of Evolutionary Biology, University of Antwerp, B-2020 Antwerp, Belgium and [3]Danish Pest Infestation Laboratory, University of Aarhus, 2800 Kongens Lyngby, Denmark

Email: Catherine Linard* - Catherine.Linard@uclouvain.be; Katrien Tersago - Katrien.Tersago@ua.ac.be; Herwig Leirs - Herwig.Leirs@ua.ac.be; Eric F Lambin - Eric.Lambin@uclouvain.be

* Corresponding author

Published: 14 December 2007

International Journal of Health Geographics 2007, **6**:55 doi:10.1186/1476-072X-6-55

Received: 20 July 2007
Accepted: 14 December 2007

THE LANCET

Vol 343 • January 8, 1994

Spread of hantavirus infections in Europe

La « Mast hypothesis »

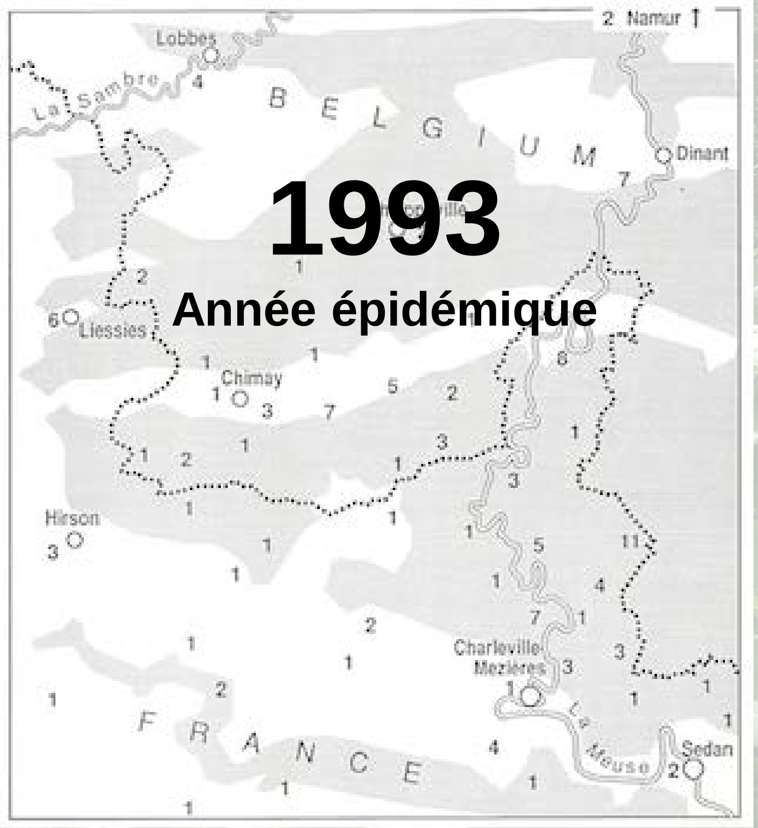
J Clement P Heyman P Colson P H P Groeneveld

THE MOUSE CONNECTION

In the epidemic region, i.e. mainly in the forested surroundings of Chimay, a conspicuously dense local population of the responsible vector the red bank vole (*Clethhrionomys glareolus*) was noted end 1992-begin 1993. Sighting of bank voles around the habitats or working areas was often reported by the NE patients (7,11). This increase in vole numbers can be due to a rare combination of ecological factors such as the mild '92-'93 Winter, the abundant Spring '93 rains and the extraordinary abundance in the forests of beechnuts, the staple food of the bank vole (3,11). We performed in '92 and '93 successive rodent trappings in the

Acta Clinica Belgica 50-1, 1995

In all regions, an abundance of indigenous rodents was noted in late 1992 and in the summer of 1993, when bank voles were often sighted by patients. This increase may be related to the unusual profusion of beechnuts (the staple food of this rodent)



1993

Année épidémique

LE RONGEUR : Etude des années « épidémiques »

Nephrol Dial Transplant (2010) 25: 1740–1746
doi: 10.1093/ndt/gfq122
Advance Access publication 17 March 2010

Beechnuts and outbreaks of nephropathia epidemica (NE): of mast, mice and men

Jan Clement[1], Piet Maes[1], Charles van Ypersele de Strihou[2], Guido van der Groen[3], José M. Barrios[4], Willem W. Verstraeten[4] and Marc van Ranst[1]

[1]Hantavirus Reference Centre, Laboratory of Clinical Virology, Rega Institute for Medical Research, Katholieke Universiteit Leuven, Minderbroedestraat, 10, 3000 Leuven, Belgium, [2]Nephrology, Catholic University of Louvain, Avenue Hippocrate, 1200 Brussels, Belgium, [3]Virology Unit, Institute of Tropical Medicine, Nationale Straat, 155, 2000 Antwerp, Belgium and [4]M3-BIORES, Biosystems Department, Katholieke Universiteit Leuven, Willem de Croylaan 34, 3001 Leuven, Belgium

Global Warming and Epidemic Trends of an Emerging Viral Disease in Western-Europe: The Nephropathia Epidemica Case

J. Clement et al.[1]
National Hantavirus Reference Centre, Clinical Virology, University Hospital Gasthuisberg & Rega Medical Research Institute, University of Leuven, Leuven, Belgium

La « Mast hypothesis »

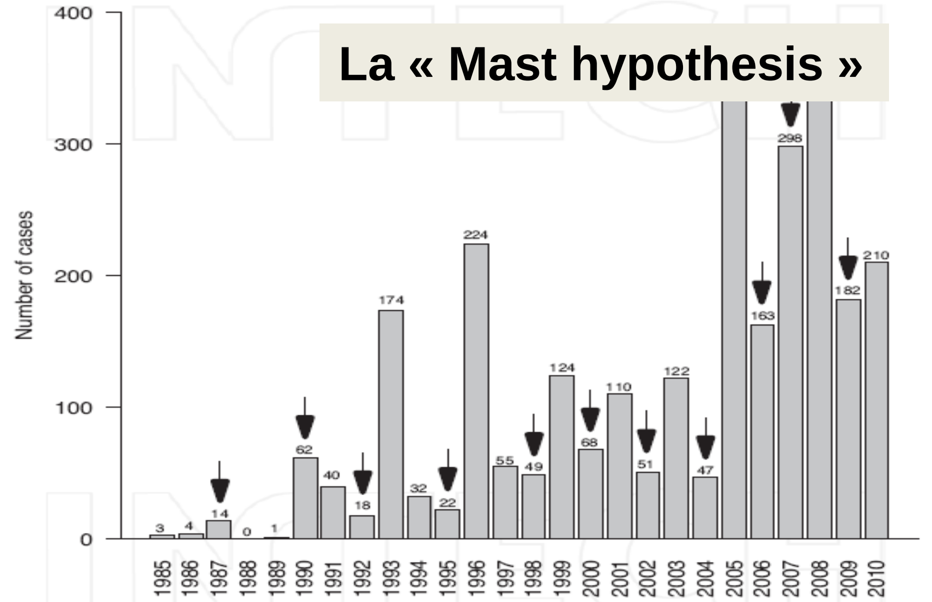
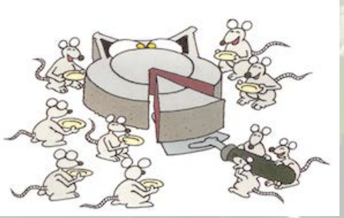


Fig. 1. Evolution of the number of NE cases officially registered in Belgium, 1985-2010. Black arrows indicate a "mast year". Note that from 1992 on, each mast year is followed by a NE peak. Moreover, since 2005, an almost continuous epidemic trend is maintained.

Rating		Year
Native oak	Beech	
+++	+++	1995
0	0	1996
0	0	1997
+++	++	1998
0	0	1999
+++	+++	2000
0	0	2001
0	+++	2002
0	0	2003
+++	+++	2004
0	0	2005
+	+++	2006
+++	+	2007
0	0	2008
+	+	2009



LE RONGEUR : Etude des années « épidémiques »

Pourquoi des années « épidémiques » ininterrompues depuis 2005?

CANICULE :
Été 2003 : t° 19.7°C / N 17°C

Automne 2006 : t° 13.9°C / N 10.4°C
Hiver 2006 : t° 6.6°C / N 3.1°C

2007 : pic de NE induit par automne chaud
+ effet fin 2007 d'un « masting » prononcé

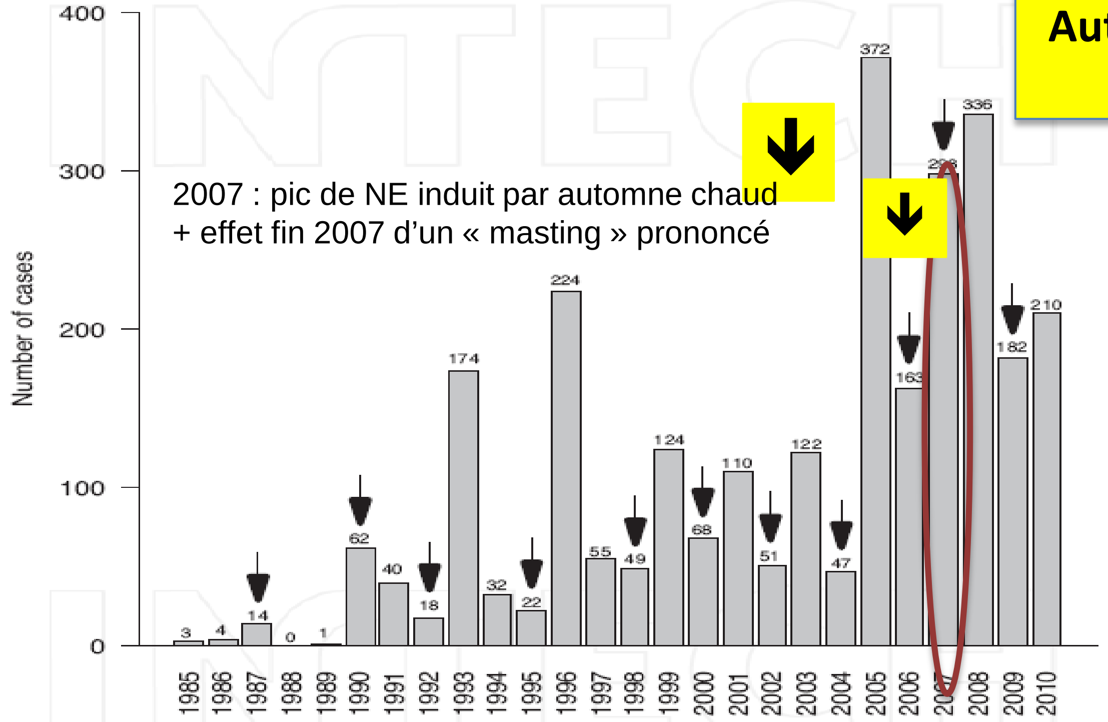
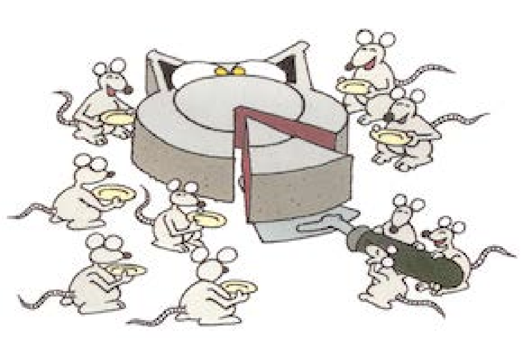


Fig. 1. Evolution of the number of NE cases officially registered in Belgium, 1985-2010. Black arrows indicate a "mast year". Note that from 1992 on, each mast year is followed by a NE peak. Moreover, since 2005, an almost continuous epidemic trend is maintained.

La « Mast hypothesis »
+
Influence du climat



LE RONGEUR : Etude des années « épidémiques »

Extension transfrontalière en Europe Occidentale (avec exceptions)

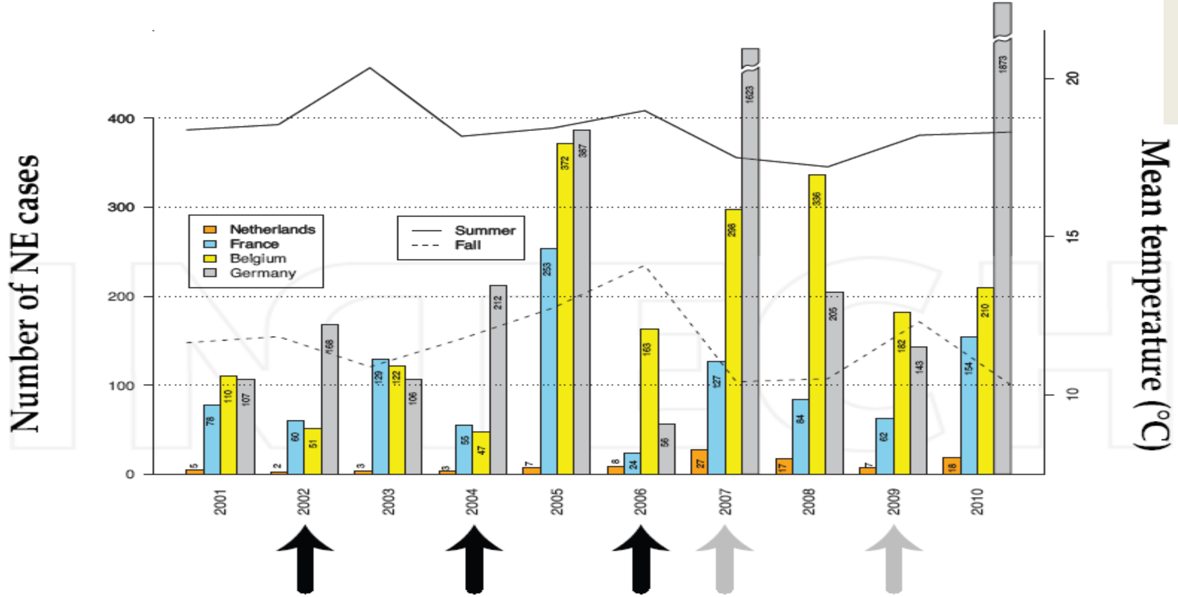
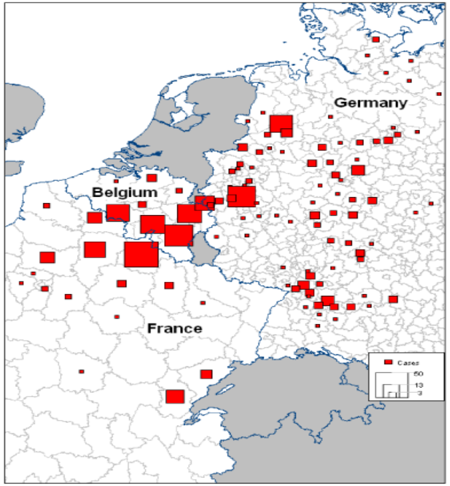


Fig. 4. NE cases in four W.-European countries. Black arrows indicate beech mast years in Belgium. The gray 2007 arrow indicates a heavy oak mast year. The gray 2009 arrow indicates a weak mast year in Belgium, but a heavy beech mast year in (South)-Germany. Note the high 2003 summer temperature, inducing the major joint 2005 NE peak in the four countries.



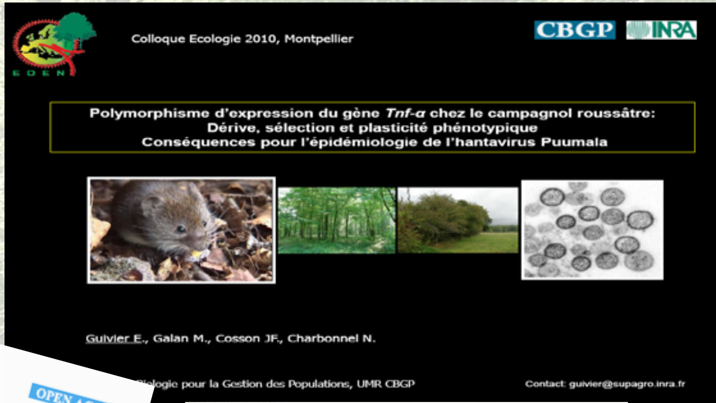
Mailles A, et al. Larger than usual increase in cases of hantavirus infections in Belgium, France and Germany, June 2005. Euro Surveill. 2005;10(29)

LE VIRUS : Ecologie

Le Virus

- Aspect génétique

… et l'homme



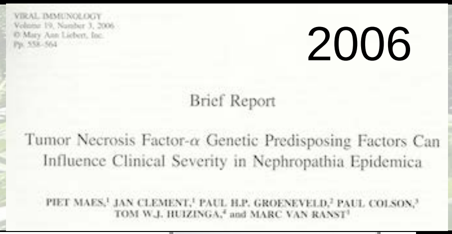
Viruses 2014, 6, 2214-2241; doi:10.3390/v6052214

OPEN ACCESS
viruses
ISSN 1999-4915
www.mdpi.com/journal/viruses

Review

Immunogenetic Factors Affecting Susceptibility of Humans and Rodents to Hantaviruses and the Clinical Course of Hantaviral Disease in Humans

Nathalie Charbonnel [1,*], Marie Pagès [1,2], Tarja Sironen [3], Heikki Henttonen [4], Olli Vapalahti [3,5,6], Jukka Mustonen [7,8] and Antti Vaheri [3,5]



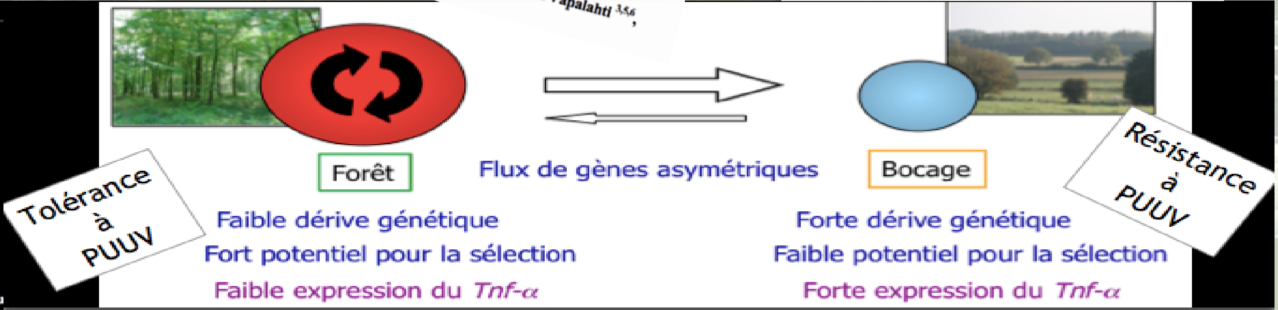
VIRAL IMMUNOLOGY
Volume 19, Number 3, 2006
© Mary Ann Liebert, Inc.
Pp. 558–564

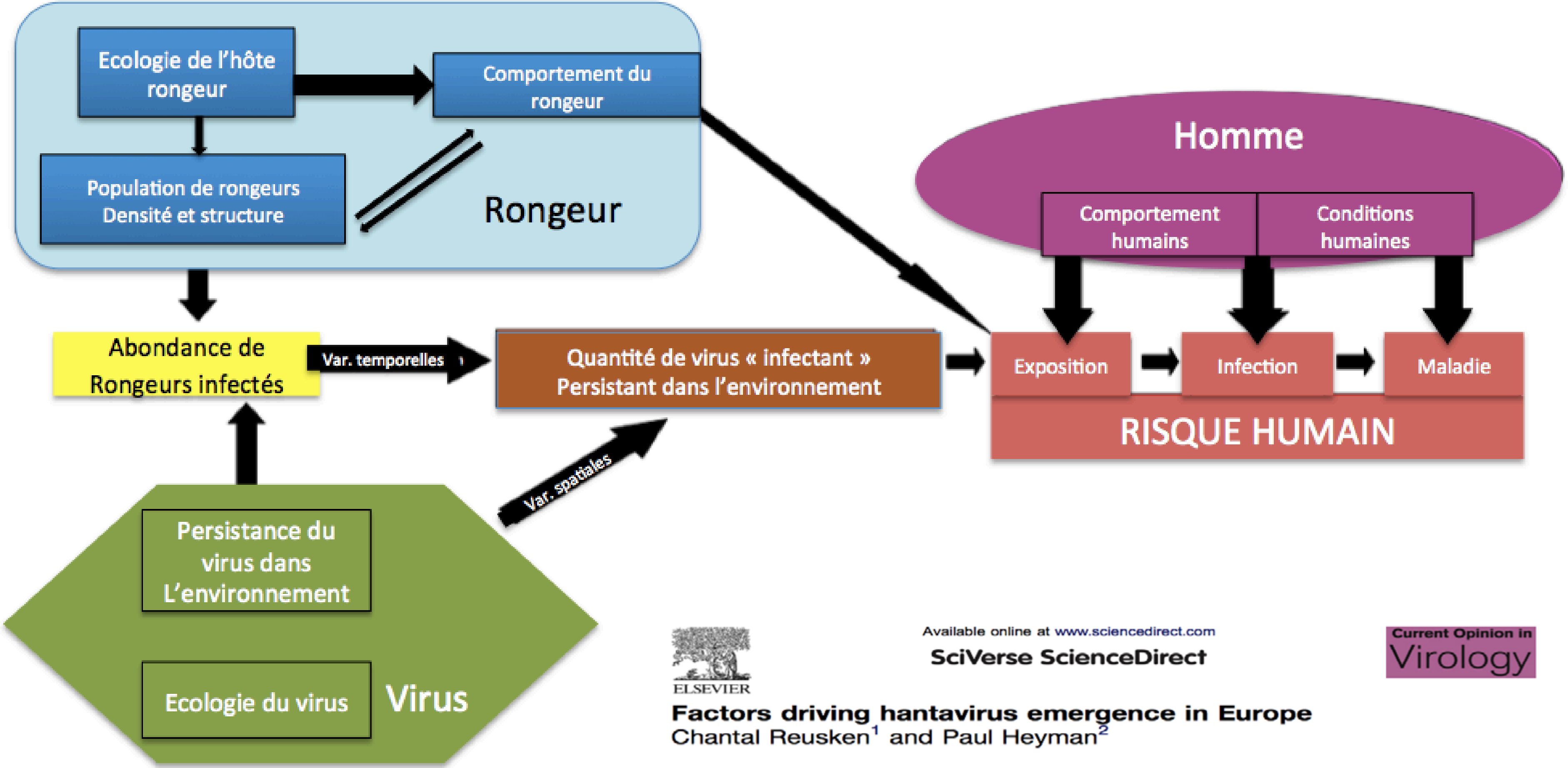
2006

Brief Report

Tumor Necrosis Factor-α Genetic Predisposing Factors Can Influence Clinical Severity in Nephropathia Epidemica

PIET MAES,[1] JAN CLEMENT,[1] PAUL H.P. GROENEVELD,[2] PAUL COLSON,[3] TOM W.J. HUIZINGA,[4] and MARC VAN RANST[1]





Available online at www.sciencedirect.com
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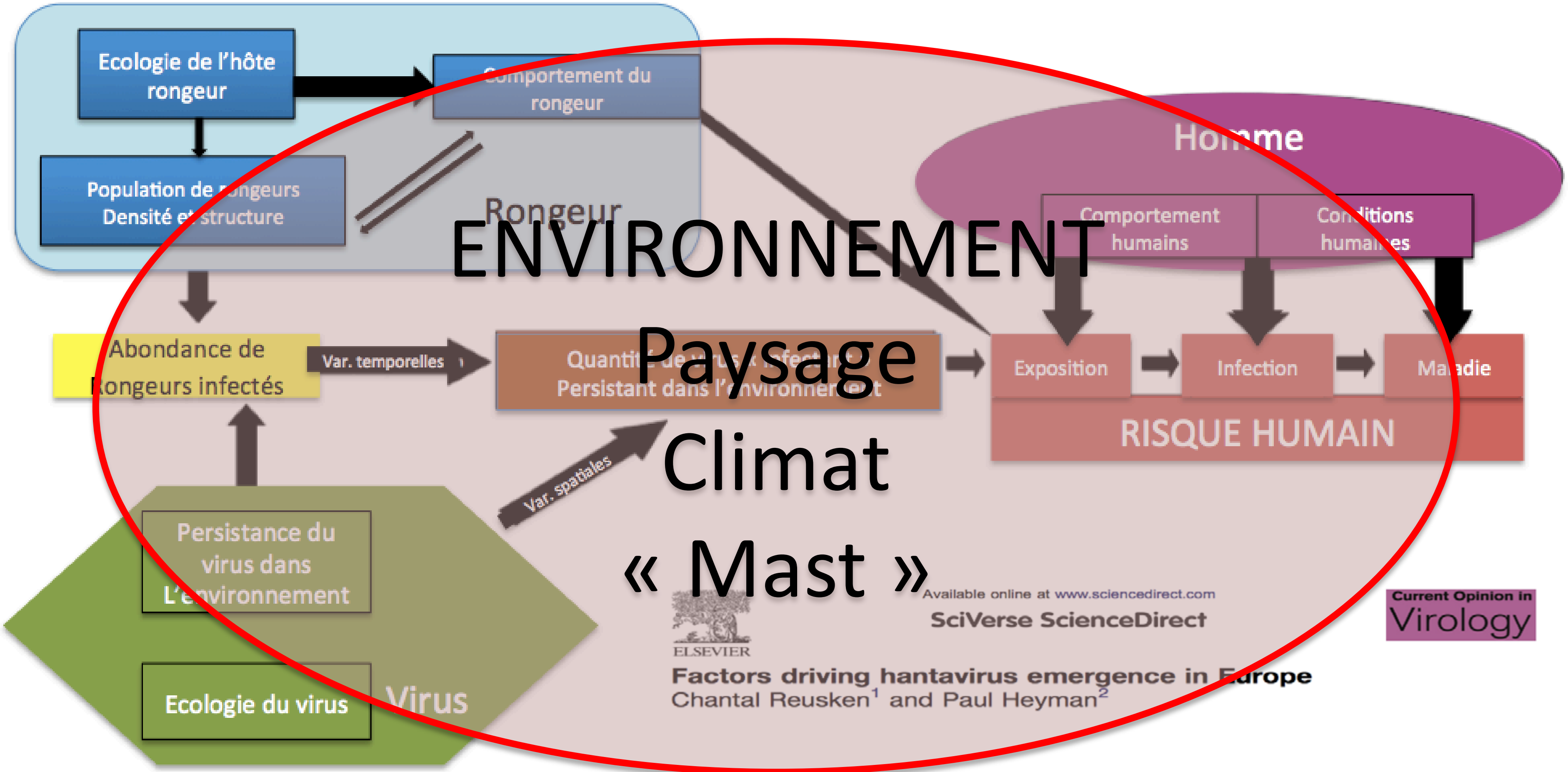
ELSEVIER
Current Opinion in Virology

Factors driving hantavirus emergence in Europe

Chantal Reusken[1] and Paul Heyman[2]


Ecologie de l'hôte rongeur
Comportement du rongeur
Population de rongeurs Densité et structure
Rongeur
ENVIRONNEMENT
Homme
Comportement humains
Conditions humaines
Abondance de Rongeurs infectés
Var. temporelles
Quantité de virus infectant Persistant dans l'environnement
Paysage
Exposition
Infection
Maladie
RISQUE HUMAIN
Climat
Var. spatiales
Persistance du virus dans L'environnement
« Mast »
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ELSEVIER
Current Opinion in Virology
Factors driving hantavirus emergence in Europe
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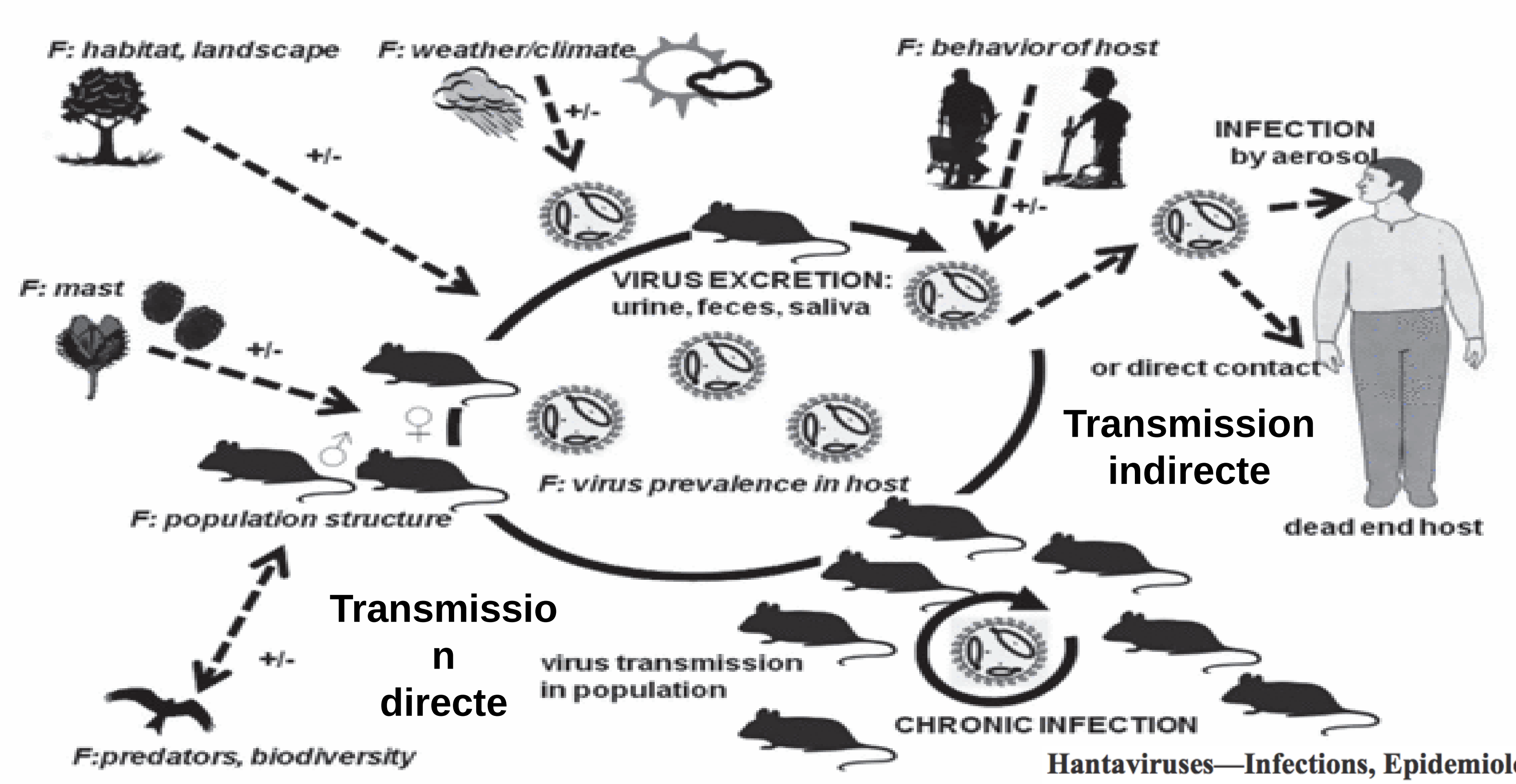
Ecologie du virus
Virus



Hantaviruses—Infections, Epidemiology and Hosts

Sandra S. Essbauer and Ellen Krautkrämer

Cycle de transmission de l'hantavirus

LE RECHAUFFEMENT CLIMATIQUE : Quelle influence?

Zoonoses and Public Health

ORIGINAL ARTICLE

Climate Variability and the Occurrence of Human Puumala Hantavirus Infections in Europe: A Systematic Review

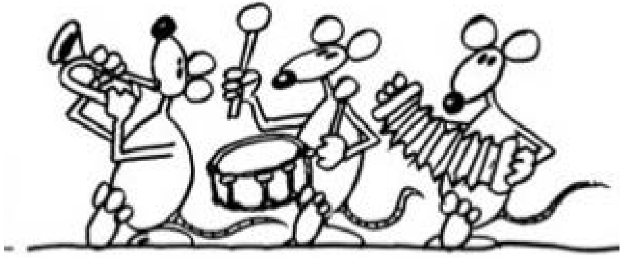
J. Roda Gracia[1,*], B. Schumann[2,3,*] and A. Seidler[1]

[1] Institute and Policlinic of Occupational and Social Medicine (IPAS), TU Dresden, Dresden, Germany
[2] Department of Public Health and Clinical Medicine, Umeå Centre for Global Health Research, Umeå University, Umeå, Sweden
[3] Centre for Population Studies, Ageing and Living Conditions Programme, Umeå University, Umeå, Sweden

Incidence de l'hantavirose ➚➚

Impacts

- We scrutinized the evidence for climate sensitivity of nephropathia epidemica (NE, vole fever), a haemorrhagic fever endemic in many European regions.
- In central Europe, higher temperature leads to higher NE incidences, while no clear impact of precipitation was found. In northern Europe, research evidence so far is insufficient.
- Due to global warming, public health has to prepare for a possible increase in nephropathia epidemica cases in Europe.



frontiers in PUBLIC HEALTH
ORIGINAL RESEARCH ARTICLE
published: 31 March 2015
doi: 10.3389/fpubh.2015.00054

Landscape and regional environmental analysis of the spatial distribution of hantavirus human cases in Europe

Caroline Brigitte Zeimes[1]*, Sophie Quoilin[2], Heikki Henttonen[3], Outi Lyytikäinen[4], Olli Vapalahti[5], Jean-Marc Reynes[6], Chantal Reusken[7,8], Arno N. Swart[8], Kirsti Vainio[9], Marika Hjertqvist[10] and Sophie O. Vanwambeke[1]

[1] Georges Lemaître Centre for Earth and Climate Research, Earth and Life Institute, Université Catholique de Louvain (UCL), Louvain-la-Neuve, Belgium
[2] Epidemiology Unit of Infectious Diseases, Scientific Institute of Public Health, Brussels, Belgium
[3] Natural Resources Institute Finland, Vantaa, Finland
[4] Infectious Disease Control Unit, Department of Infectious Diseases, National Institute for Health and Welfare, Helsinki, Finland
[5] Infectious Disease Control Unit, Department of Virology, University of Helsinki, Helsinki, Finland
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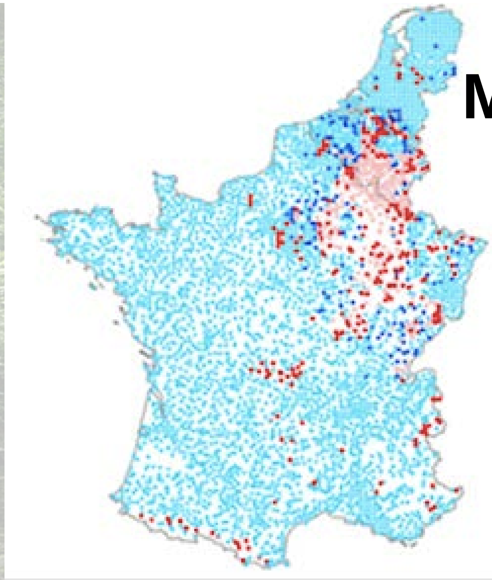
[7] Department of Viroscience, ErasmusMC, Rotterdam, Netherlands
[8] Centre for Infectious Disease Control, Rijksinstituut voor Volksgezondheid en Milieu (RIVM), Bilthoven, Netherlands
[9] Department of Virology, Norwegian Institute of Public Health, Oslo, Norway
[10] The Swedish Institute for Infectious Disease Control, Stockholm, Sweden

Variables	Bank voles	Virus	Human	Resolution	Units	Sources
Annual precipitation (8, 23)	X	X		1 km, 1950–2000	mm	Worldclim
Maximum temperature in summer (8)		X		1 km, 1950–2000	°C	Worldclim
Minimum temperature in winter (8, 9, 13, 19)	X	X	X	1 km, 1950–2000	°C	Worldclim
Snow cover (8, 14–18, 22)	X	X		0.05°, 2000–2008	Area percentage	MODIS
Proportion of forest	X			100 m	Area percentage	Corine 2006 (EEA)
Proportion of coniferous forest (25)	X			100 m	Area percentage	Corine 2006 (EEA)
Proportion of broadleaved forest (24)	X			100 m	Area percentage	Corine 2006 (EEA)
Proportion of mixed forest	X			100 m	Area percentage	Corine 2006 (EEA)
Forest contiguity index (6, 7)	X			100 m	None	Corine 2006 (EEA)
Built-up areas in forest ecotones (24, 27)	X		X	100 m	Area percentage	Corine 2006 (EEA)
Enhanced vegetation index (EVI) (28)	X			0.0083°, 2001–2012	None	MODIS
Number of green days (28)	X			0.005°, 2006–2010	Number of days	MODIS
Soil water index (SWI) (8, 23)	X	X		25 km, 2007–2010	None	TU-WIEN
Population proximity index (31)			X	0.0083°, 2005	Number of persons	Environment Research Group Oxford

Modèles pronostiques



False presences and absences

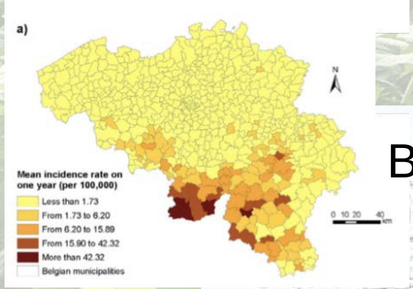
- Absence observed and predicted
- False presence
- False absence
- Presence observed and predicted

ORIGINAL ARTICLE

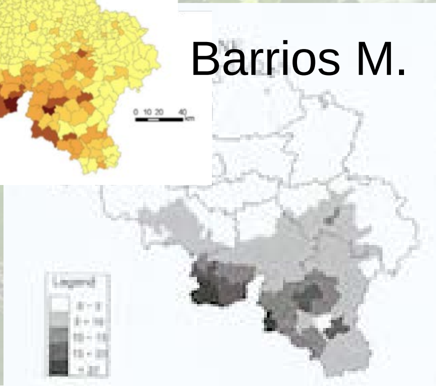
Model-Based Prediction of Nephropathia Epidemica Outbreaks Based on Climatological and Vegetation Data and Bank Vole Population Dynamics

S. Amirpour Haredasht[1], C. J. Taylor[2], P. Maes[3], W. W. Verstraeten[1,4,5], J. Clement[3], M. Barrios[1], K. Lagrou[6], M. Van Ranst[3], P. Coppin[1], D. Berckmans[1] and J.-M. Aerts[1]

[1] Measure, Model and Manage Bioresponses (M3-BIORES), Department of Biosystems, KU Leuven, Leuven, Belgium
[2] Department of Engineering, Lancaster University, Lancaster, UK
[3] National Reference Laboratory for Hantavirus Infections, Laboratory of Clinical Virology, Rega Institute, KU Leuven, Leuven, Belgium
[4] Royal Netherlands Meteorological Institute (KNMI), Climate Observations, De Bilt, The Netherlands
[5] Eindhoven University of Technology, Applied Physics, Eindhoven, The Netherlands
[6] Department of Experimental Laboratory Medicine, KU Leuven, Leuven, Belgium

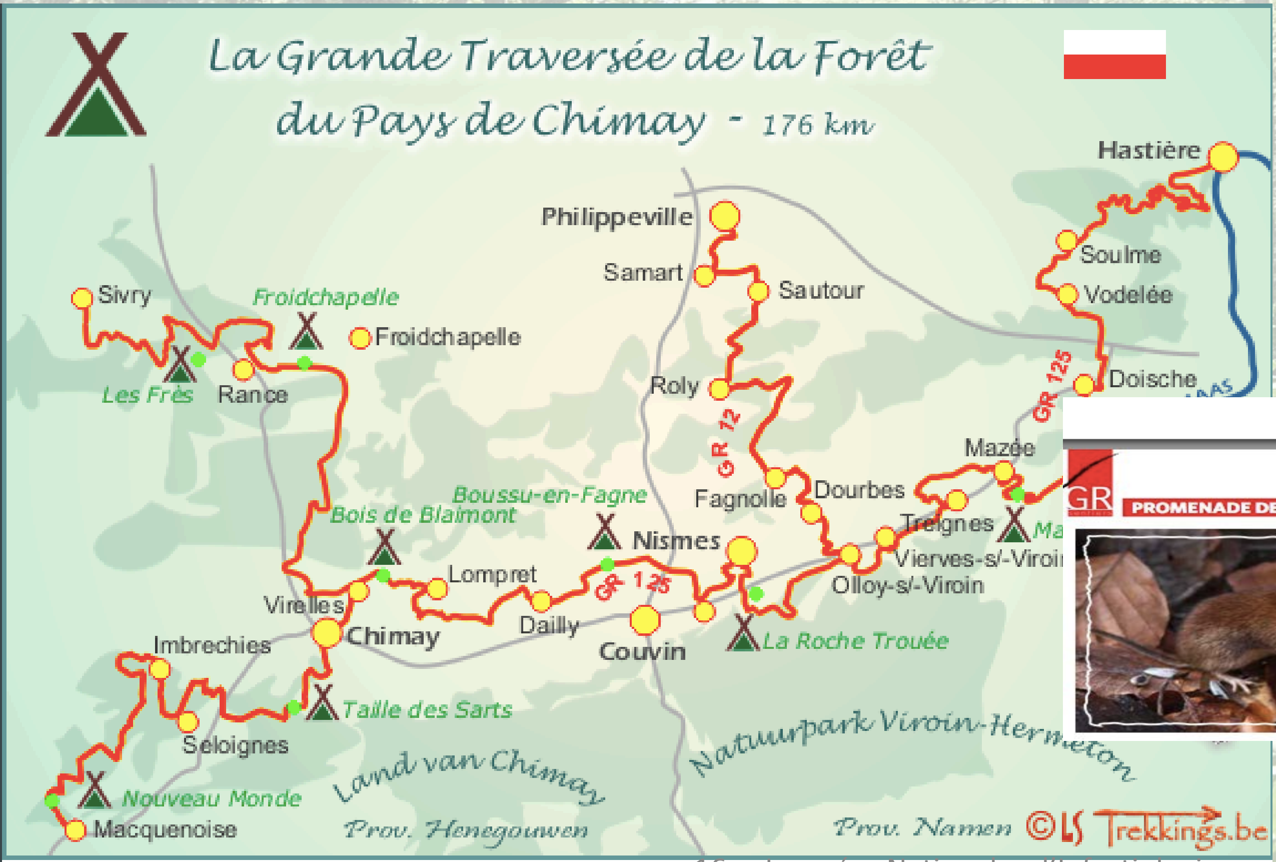


Barrios M.



Zoonoses and Public Health, 2013, 60, 461–477

Mais quels modèles pronostiques pour le promeneur? le forestier?




GR Sentiers • N°203 • Été 2014 • 27

PROMENADE DE SANTÉ

Prévenir l'hantavirose
Quelques conseils aux randonneurs

La MALADIE HANTAVIRALE : Peut-on prédire l'évolution de la maladie?

Outinen *et al. BMC Infectious Diseases* 2010, **10**:132
http://www.biomedcentral.com/1471-2334/10/132

BMC Infectious Diseases

RESEARCH ARTICLE — Open Access

The severity of Puumala hantavirus induced nephropathia epidemica can be better evaluated using plasma interleukin-6 than C-reactive protein determinations

Tuula K Outinen*[1], Satu M Mäkelä[1,2], Ilpo O Ala-Houhala[1,2], Heini SA Huhtala[3], Mikko Hurme[2], Antti S Paakkala[4], Ilkka H Pörsti[1,2], Jaana T Syrjänen[1,2] and Jukka T Mustonen[1,2]

Abstract

Background: Nephropathia epidemica (NE) is a Scandinavian type of hemorrhagic fever with renal syndrome caused by Puumala hantavirus. The clinical course of the disease varies greatly in severity. The aim of the present study was to evaluate whether plasma C-reactive protein (CRP) and interleukin (IL)-6 levels associate with the severity of NE.

Results: We found that high IL-6 associated with most variables reflecting the severity of the disease. When compared to patients with low IL-6, patients with high IL-6 had higher maximum blood leukocyte count (11.9 *vs* 9.0 × 10^9/l, P = 0.001) and urinary protein excretion (2.51 *vs* 1.68 g/day, P = 0.017), as well as a lower minimum blood platelet count (55 *vs* 80 × 10^9/l, P < 0.001), hematocrit (0.34 *vs* 0.38, P = ...

Background

Nephropathia epidemica (NE) is a Scandinavian type of hemorrhagic fever with renal syndrome. The causative agent, Puumala virus (PUUV), is a member of the genus *Hantavirus* in the family *Bunyaviridae* [1]. Other hantaviruses causing more severe forms of HFRS include Hantaan, Seoul, and Dobrava viruses [2]. Many hantaviruses in North and South America, e.g. Sin Nombre, Andes, and Black Creek Canal viruses, cause hantavirus pulmonary syndrome (HPS) [2]. The natural host of PUUV is the bank vole (*Myodes glareolus*) [3].

Nephropathia epidemica is prevalent in Finland, elsewhere in Scandinavia, in Western Russia, in the Balkan region and also in many parts of ... Approximately 1000 serologic ... infection are made in Finland ... seroprevalence in the Finnish population is 5%, implying that most infections are subclinical or undiagnosed [5].

... have been shown to influence the clinical picture [6,7]. It is clinically characterized by acute fever, headache, back and abdominal pains, myalgia, nausea, vomiting, and transient myopia, while hemorrhages are uncommon [8,9]. Renal involvement causes proteinuria, hematuria and oliguria, followed by polyuria [8,9]. A minority of patients needs transient dialysis treatment [8], but com-

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Full list of author information is available at the end of the article

Interleukine-6 plasma - urines

OPEN ACCESS Freely available online — PLOS | ONE

Thrombocytopenia as a Predictor of Severe Acute Kidney Injury in Patients with Hantaan Virus Infections

Meiliang Wang[1*¶], Jiuping Wang[2¶], Tianping Wang[2], Jing Li[2], Ling Hui[1,3], Xiaoqin Ha[1,3]

1 Center for Experimental Medicine, Lanzhou General Hospital, Lanzhou Military Command, Lanzhou, Gansu, China, 2 Department of Infectious Diseases, Tangdu Hospital, the Fourth Military Medical University, Xi'an, Shaanxi, China, 3 Gansu Key Laboratory of Stem Cell and Gene Therapy, Lanzhou, Gansu, China

Abstract

Background: Hematological abnormalities often occur several days before kidney injury in patients with hemorrhagic fever with renal syndrome (HFRS). We aimed to investigate the prevalence and prognostic value of the early hematological markers in patients with HFRS caused by Hantaan virus (HTNV) infection.

Methods: In a retrospective cohort study, we analyzed the case records of 112 patients with acute HTNV infection and evaluated the hematological markers for early prediction and risk stratification of HFRS patients with acute kidney injury (AKI).

Results: Of 112 patients analyzed, 66 (59%) developed severe AKI, defined as either receipt of acute dialysis or increased serum creatinine ≥354 µmol/L. The prognostic accuracy of hematological markers, as quantified by the area under the receiver-operating-characteristic curve (AUC), was highest with the nadir platelet count (AUC, 0.89; 95% CI, 0.83–0.95), as compared with the admission platelet count (AUC, 0.84; 95% CI, 0.77–0.92), and the admission and peak leukocyte counts. The nadir platelet count correlated moderately with the levels of peak blood urea nitrogen (r = −0.616) and serum creatinine (r = −0.589), the length of hospital stay (r = −0.599), and the number of dialysis sessions that each patient received during hospital stay (r = −0.625). By multivariate analysis, decreased nadir platelet count remained independently associated with the development of severe AKI (odds ratio, 27.57; 95% CI, 6.96–109.16; P < 0.0001).

Conclusions: Thrombocytopenia, rather than leukocytosis, is independently associated with subsequent severe AKI among patients with acute HTNV infection.

Introduction

Hemorrhagic fever with renal syndrome (HFRS) is a combination of fever, hemorrhage, thrombocytopenia and acute kidney injury (AKI), ... Currently, there is as yet no vaccine or specific antiviral therapy for HFRS. The treatment for patients with hantavirus infections is supportive care, including intermittent hemodialysis (IHD) and continuous renal replacement therapy (CRRT). Expected prognosis whether or when dialysis is started is of great importance to patients with severe HFRS and their clinicians, and for planning of

treatment guidelines. Most of the symptoms and signs currently used in classifying HFRS [1,2], such as oliguria, anuria and kidney injury, do not appear until the later stages of illness. Thrombocytopenia is an early, consistent process during hantavirus infection, and is a major diagnostic feature in patients with HFRS [3]. In a cohort of patients infected with PUUV, which causes a mild form of HFRS in Europe, previous study showed that low platelet count (<60×10^9/L) was significantly associated with the subsequent severe AKI [4]. This study used the platelet count obtained at the initial evaluation (1–9 days after symptom onset) to classify thrombocytopenia that may still be normal or have already returned to normal in some patients. Other attempts have provided a list of symptoms, signs, and hematological, biochemical or immunological parameters, that could be associated with severe HFRS [5–9], but how these parameters should be applied for clinical diagnosis is not apparent. To date, no prognostic models are available for patients with HTNV infection in Asia.

Acute hantavirus infection is a highly dynamic process, characterized by a short transient thrombocytopenia followed by mild-to-severe AKI [4]. We therefore assessed the extent to which

Thrombopénie?

Peut-on prédire l'évolution de la maladie?

Infection (2015) 43:83–87
DOI 10.1007/s15010-014-0699-9

BRIEF REPORT

Severe thrombocytopenia in hantavirus-induced nephropathia epidemica

J. Latus · D. Kitterer · S. Segerer · F. Artunc · M. D. Alscher · N. Braun

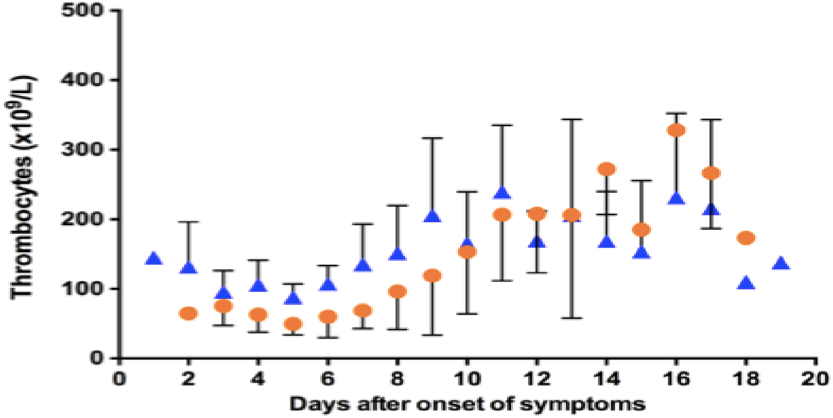


Fig. 1 Platelet nadir count was reached at day 5 (4–8) in both groups after the onset of symptoms. Thrombocyte levels were in the normal range in both groups 10 days after symptom onset

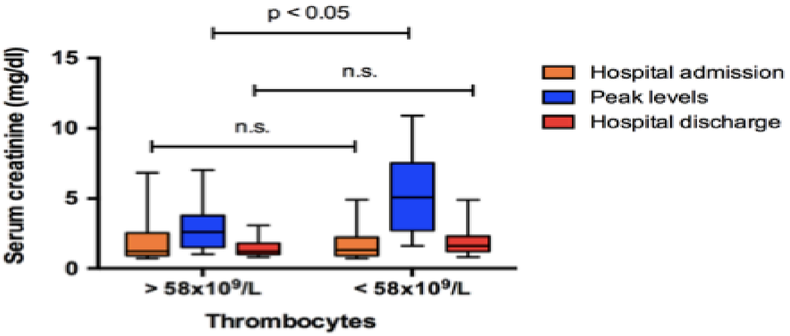


Fig. 2 Patients in the severe thrombocytopenia group had significantly higher creatinine peak levels during the acute course of nephropathia epidemica, whereas creatinine levels at admission to hospital and at discharge were not different between both groups. Creatinine peak levels were significantly higher than creatinine levels at hospital admission and hospital discharge in both groups. *Box* plots with median, interquartile range, minimum and maximum values are shown. *NS* Not significant

Peut-on prédire l'évolution de la maladie?

http://www.kidney-international.org

mini review

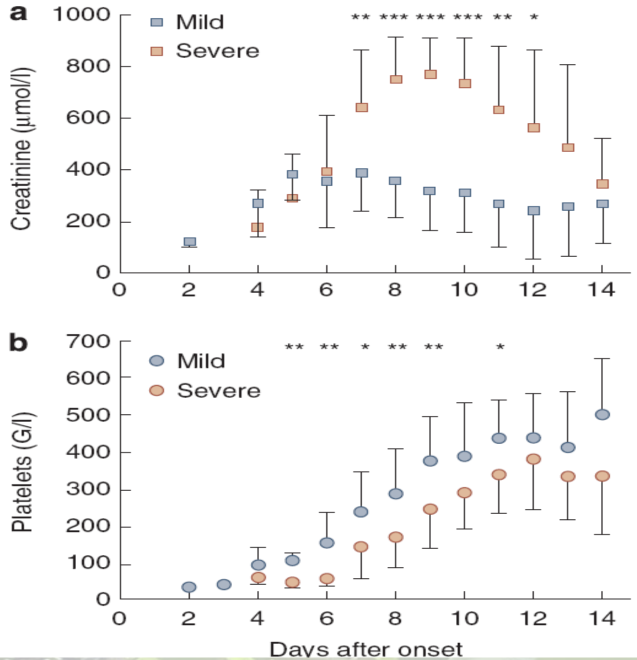
Hantavirus infection: an emerging infectious disease causing acute renal failure

Ellen Krautkrämer[1], Martin Zeier[1] and Alexander Plyusnin[2]

[1]Department of Nephrology, University of Heidelberg, Heidelberg, Germany and [2]Research Programs Unit, Infection Biology Research Program, Department of Virology, Haartman Institute, University of Helsinki, Helsinki, Finland

Au 5^e^-6^e^ jour, des plaquettes qui restent basses prédisent une évolution sévère.

« A low platelet count (<60G/L) precedes severe acute renal failure (creat>620µmol/l) »



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ANN MED

informa healthcare

Annals of Medicine, 2014; 46: 38–43

ISSN 0785-3890 print/ISSN 1365-2060 online
DOI: 10.3109/07853890.2013.862960

ORIGINAL ARTICLE

Plasma B-type natriuretic peptide (BNP) in acute Puumala hantavirus infection

Saara-Mari Rajaniemi[1,2], Nina Hautala[3], Tarja Sironen[4], Olli Vainio[1,2], Olli Vapalahti[4], Antti Vaheri[4], Olli Vuolteenaho[5], Heikki Ruskoaho[6,7], Heikki Kauma[8] & Timo Hautala[8]

[1]Institute of Diagnostics, Department of Medical Microbiology, University of Oulu, Oulu, Finland, [2]Clinical Microbiology Laboratory, Oulu University Hospital, Oulu, Finland, [3]Department of Ophthalmology, Oulu University Hospital, Oulu, Finland, [4]Department of Virology, Haartman Institute, University of Helsinki, Helsinki, Finland, [5]Department of Physiology, Institute of Biomedicine, University of Oulu, Oulu, Finland, [6]Department of Pharmacology and Toxicology, Institute of Biomedicine, University of Oulu, Oulu, Finland, [7]Division of Pharmacology and Toxicology, University of Helsinki, Helsinki, Finland, and [8]Department of Internal Medicine, Oulu University Hospital, Oulu, Finland

Merci!

Et merci à Philippe GELUCK


16es Journées Nationales d'Infectiologie,
Nancy du 10 au 12 juin 2015

D’autres pistes …

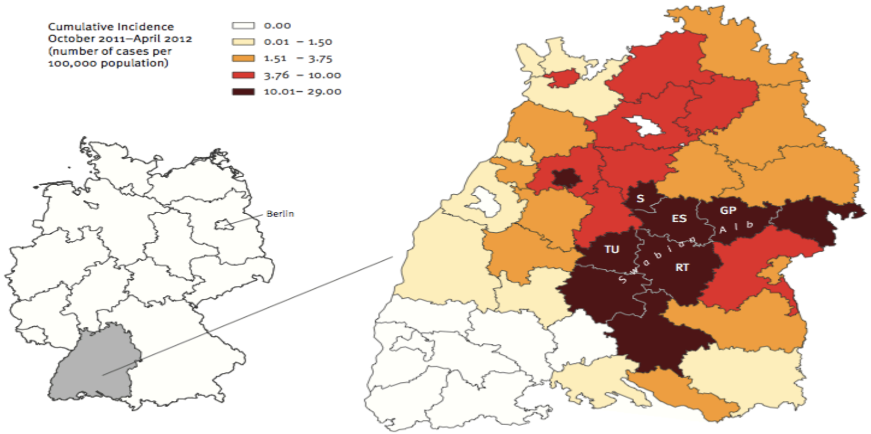
LE RONGEUR : Ecologie

Ecologie de l'hôte :

- Baden-Wurtenberg (population comparable à la Belgique) :

Figure 2

Geographical distribution of cases of hantavirus infection, by county and cumulative incidence, Baden-Württemberg, Germany, 3 October (reporting week 40) 2011–27 April (week 17) 2012 (n=580)



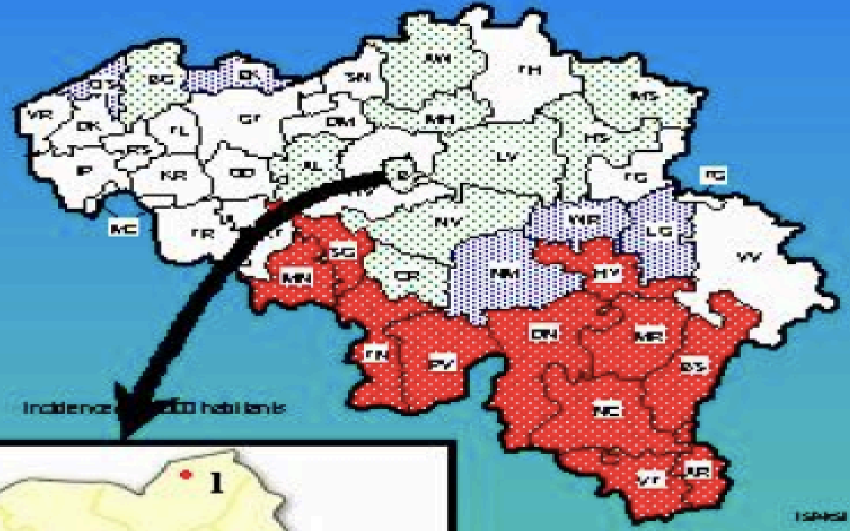
ES: Esslingen; GP: Göppingen; RT: Reutlingen; S: Stuttgart; TU: Tübingen.
Source: Robert Koch Institute [2], as of 16 May 2012.

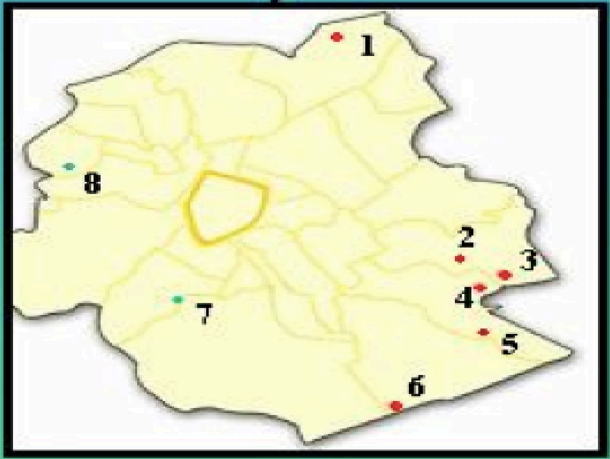
=> couverture forestière nettement plus importante;
=> incidence de NE 3,6x plus élevée que l'incidence belge;
=> les districts avec la + haute couverture en hêtres (15% ou +) ont l'incidence la plus haute en NE.

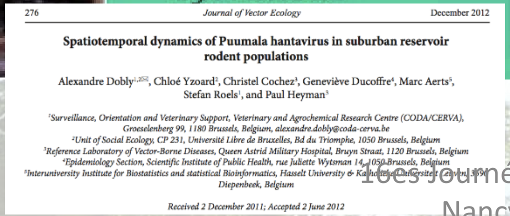
Norway rats
Rattus norvegicus

Bank voles
Clethrionomys glareolus

Wood mice
Apodemus sylvaticus







276 Journal of Vector Ecology December 2012

Spatiotemporal dynamics of Puumala hantavirus in suburban reservoir rodent populations

Alexandre Dobly[1,2✉], Chloé Yzoard[2], Christel Cochez[3], Geneviève Ducoffre[4], Marc Aerts[5], Stefan Roels[1], and Paul Heyman[3]

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[3]Reference Laboratory of Vector-Borne Diseases, Queen Astrid Military Hospital, Bruyn Straat, 1120 Brussels, Belgium
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Received 2 December 2011; Accepted 2 June 2012

Uncovering the mysteries of hantavirus infections

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Abstract | Hantaviruses are negative-sense single-stranded RNA viruses that infect many species of rodents, shrews, moles and bats. Infection in these reservoir hosts is almost asymptomatic, but some rodent-borne hantaviruses also infect humans, causing either haemorrhagic fever with renal syndrome (HFRS) or hantavirus cardiopulmonary syndrome (HCPS). In this Review, we discuss the basic molecular properties and cell biology of hantaviruses and offer an overview of virus-induced pathology, in particular vascular leakage and immunopathology.

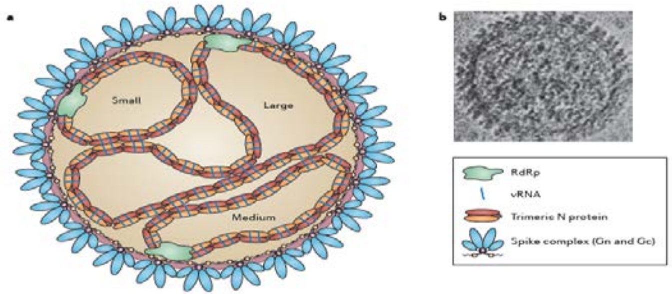

Figure 1 | **Hantavirus particles, genes and proteins.** **a** | Schematic representation of the hantavirus virion. The hantavirus particle contains the trisegmented viral RNA (vRNA) genome, comprising the small, medium and large ORFs. These are encapsidated by nucleocapsid (N) protein. The outer part of the virion consists of spikes comprising four units of each glycoprotein, Gn and Gc. The viral genome is replicated and transcribed by RNA-dependent RNA polymerase (RdRp). **b** | A hantavirus particle viewed by cryoelectron microscopy. The spike height is invariably 12 nm, and the median diameter of the virion is 135 nm. Part **b** image is courtesy of P. Laurinmäki and S. Butcher, University of Helsinki, Finland.

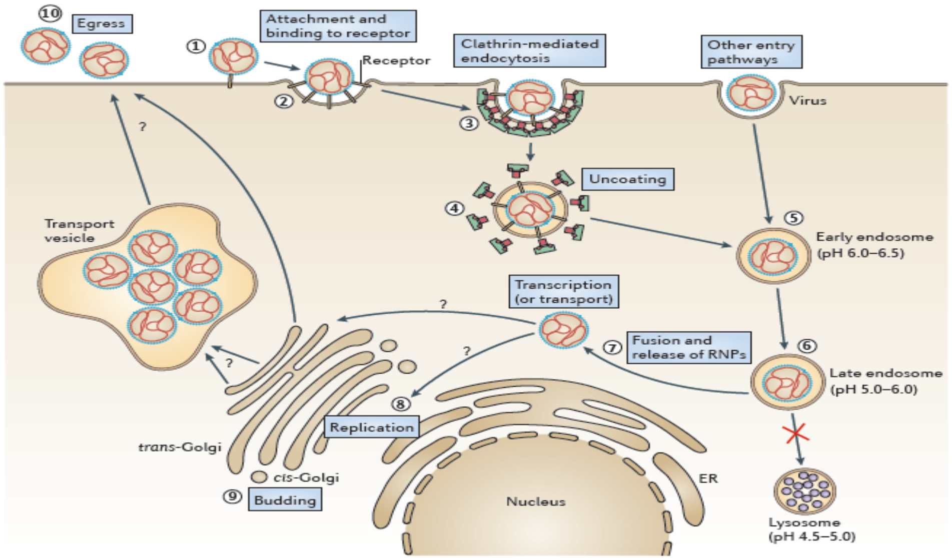

Figure 2 | **The life cycle and replication of hantaviruses.** The hantavirus virion attaches to a receptor on the cell surface (step 1). This binding event induces endocytosis signalling (step 2), after which the virion enters the cell in clathrin-coated vesicles (step 3). Other entry pathways have also been observed for some hantaviruses. In the case of clathrin-mediated endocytosis, the clathrin coat of the vesicle is disassembled (step 4), and the virion-harbouring vesicle enters the early endosome (step 5), which matures into a late endosome (step 6). Fusion between the viral and endosomal membranes is driven by acid-induced conformation changes in the viral fusion protein in the late endosome. This results in release of the viral ribonucleoproteins (RNPs) (step7). Initial transcription might take place at the site of release; alternatively, the RNPs might be transported to the ER–Golgi intermediate compartment (ERGIC) for transcription. It is also possible that the virus is directly transported to the Golgi complex from the late endosome, either before or after fusion. Viral replication is thought to occur in viral factories that might be located at the ERGIC or the *cis*-Golgi (step 8). The nascent viruses are thought to bud into the *cis*-Golgi (step 9), from where they are transported to the plasma membrane for release, presumably via recycling endosomes. The egress of progeny virions takes place at the plasma membrane (step 10).

[2]Nat RevMicrobiol, 11, 539-550

HANTAVIRUS DISEASE

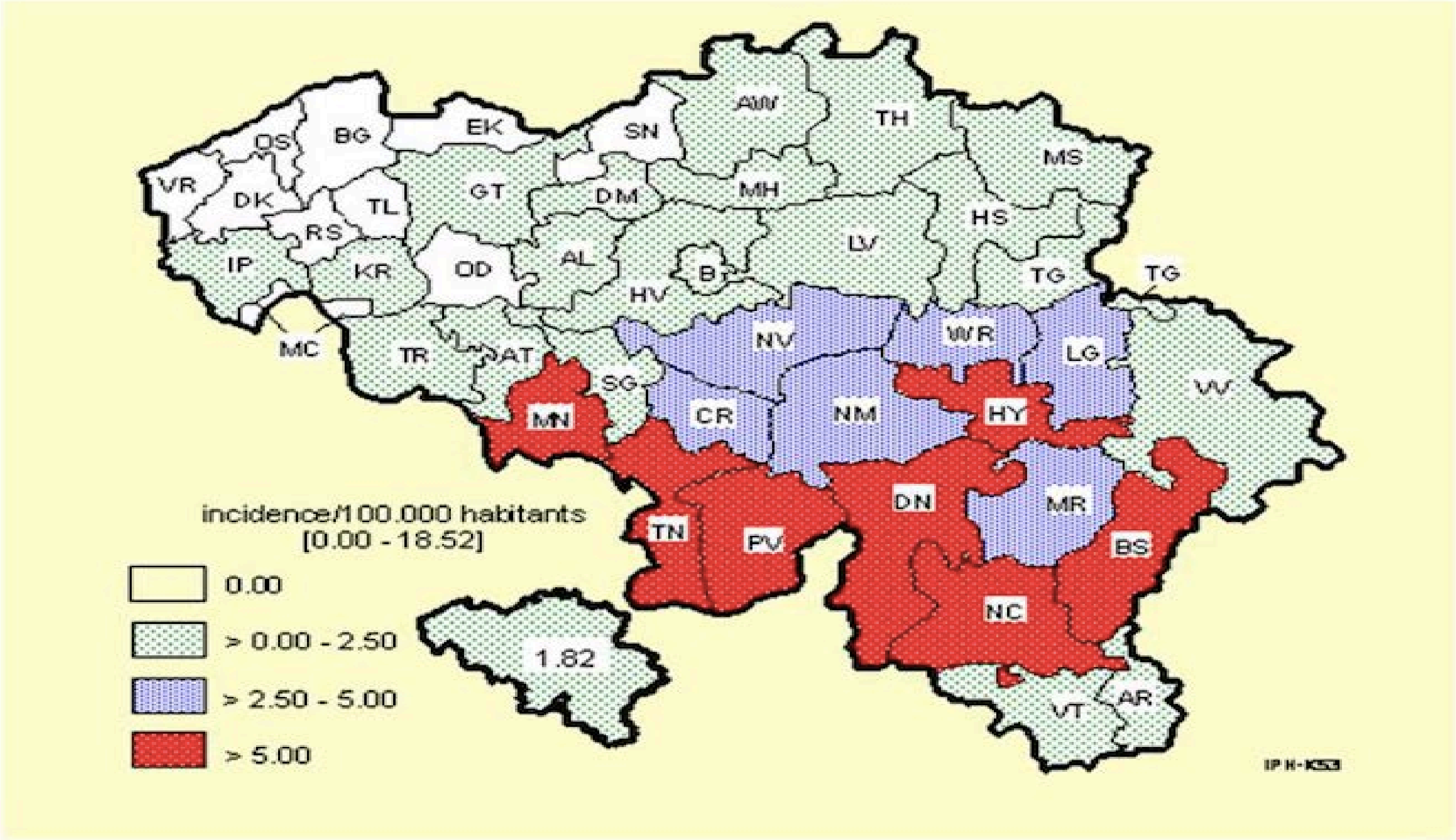

Figure 3 : Répartition par arrondissement de l'incidence (N/100000 habitants) de l'hantavirose en fonction du lieu de contamination (2011)

Sources : Laboratoires Vigies et Centre national de Référence

Fièvre hémorragique avec syndrome rénal révélant une leptospirose

An hemorrhagic fever with renal syndrome revealing a leptospirosis

La leptospirose et les infections à *Hantavirus* possèdent de nombreuses similitudes sur le plan clinique et paraclinique les rendant parfois difficile à distinguer.
Nous rapportons ici le cas d'un patient adressé dans notre service pour une insuffisance rénale aiguë oligo-anurique. Les données cliniques et paracliniques semblaient correspondre à une fièvre hémorragique avec syndrome rénal à virus Hanta alors que l'analyse sérologique a affirmé une leptospirose.

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Reçu le 30 août 2014
Accepté le 9 octobre 2014
Disponible sur internet le : 8 janvier 2015

http://dx.doi.org/10.1016/j.lpm.2014.10.007