

# Highly pathogenic avian influenza (HPAI) seriously suspected clinically: February 28<sup>th</sup> 2003



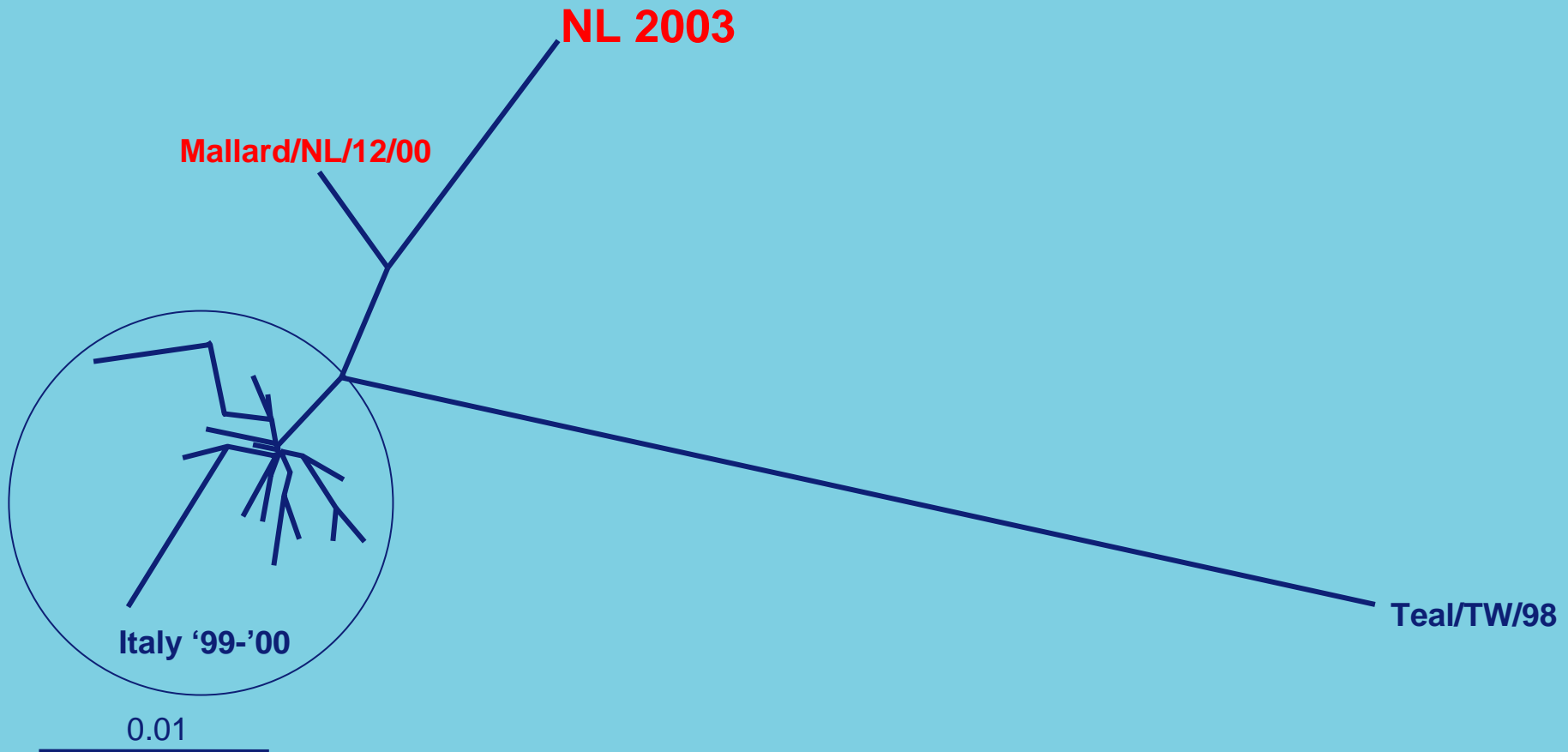
# H7N7 in The Netherlands

-Phylogeny of the HA gene -

Erasmus MC



Fouchier et al., PNAS 2003





A photograph showing two men in a slaughterhouse. The man on the right is wearing a full blue protective suit, a blue hairnet, and a white surgical mask. He is holding a plucked chicken. The man on the left is wearing a blue work jacket and is also holding a plucked chicken. The background shows industrial equipment and a concrete floor.

Protective measures for cullers and farmers:

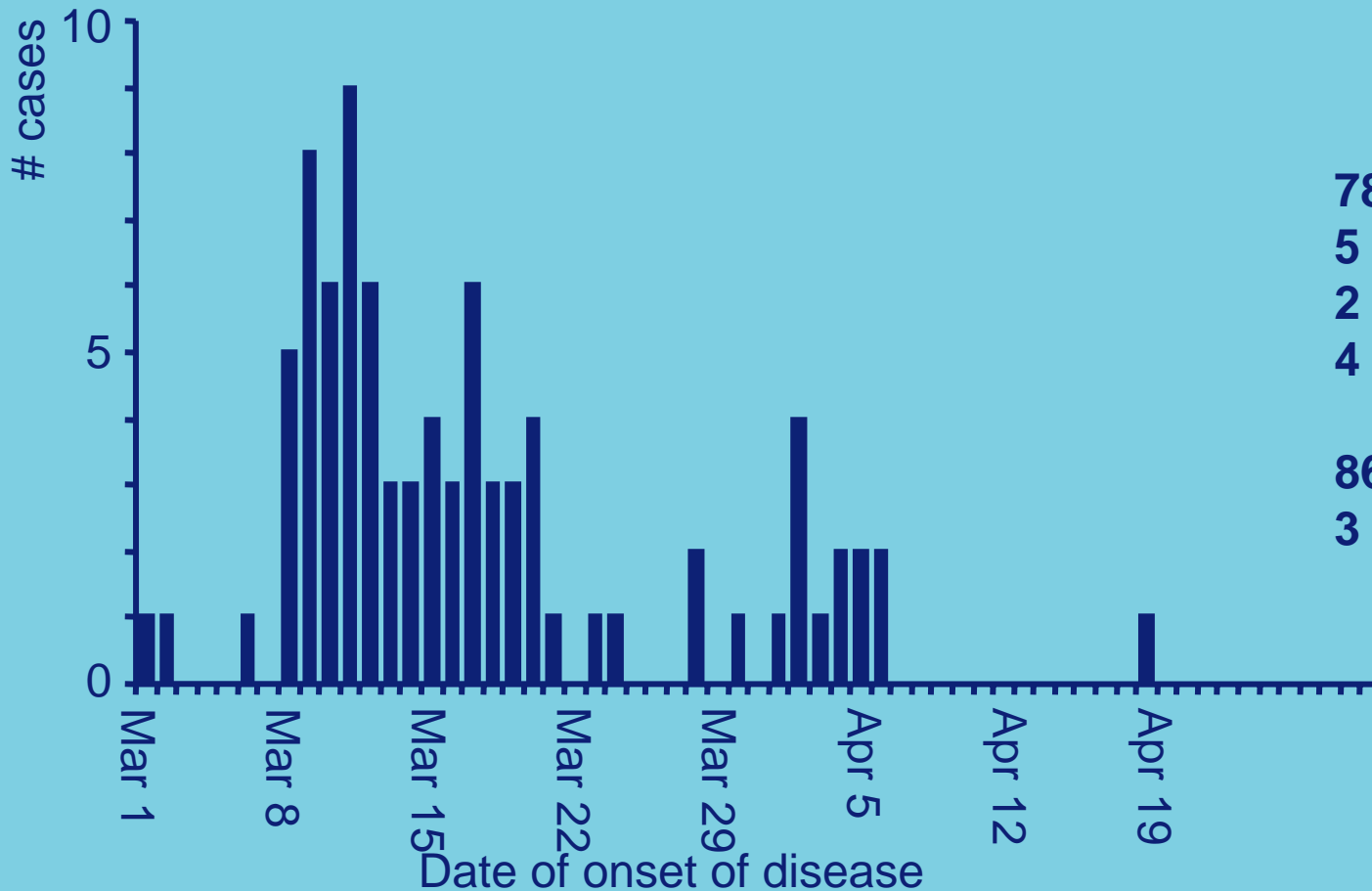
- *protective clothing/gloves/masks.....*
- *prophylactic treatment (oseltamivir)*
- *vaccination against epidemic flu (prevent reassortment)*

**COMPLIANCE?**



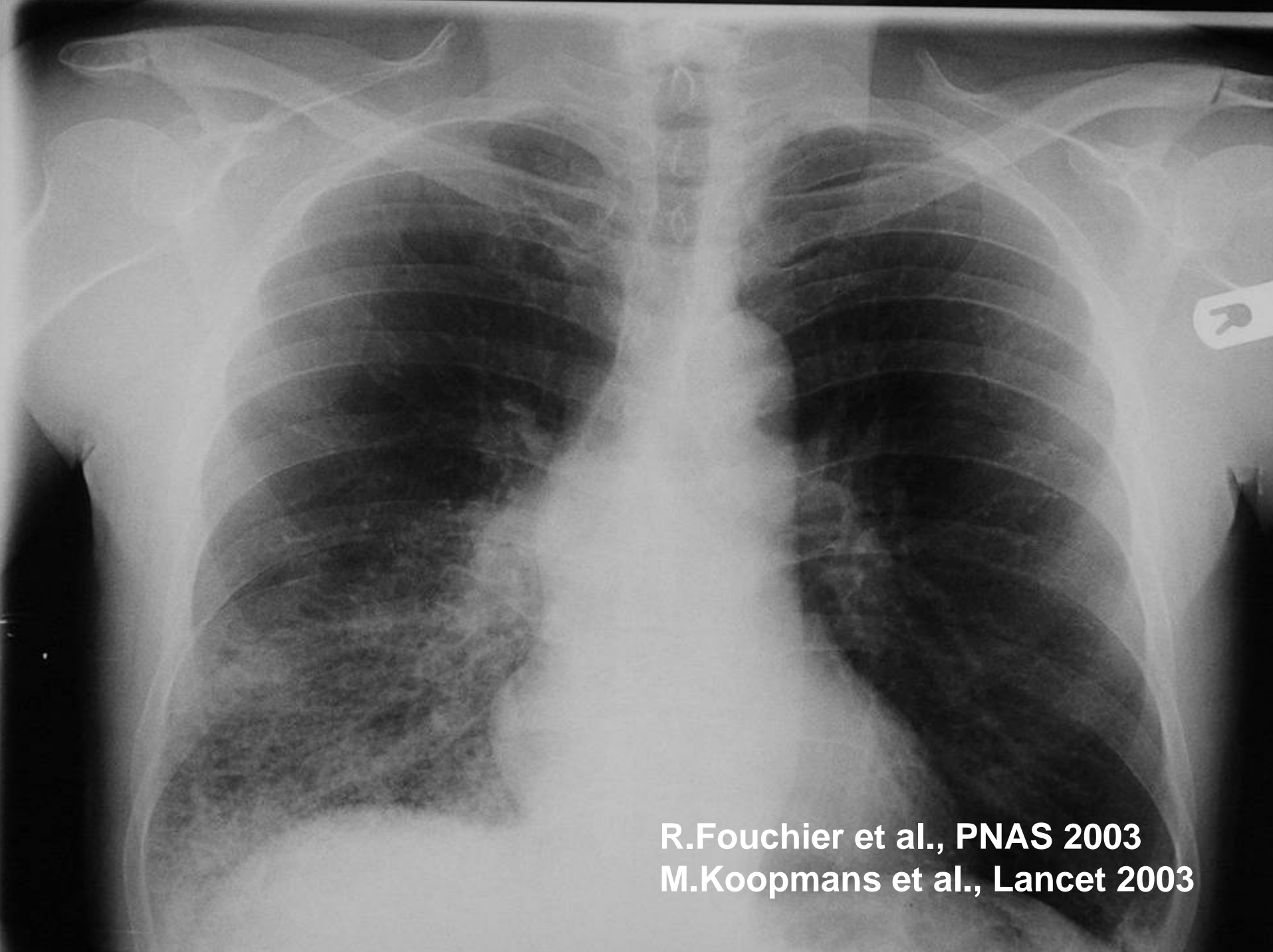
# H7N7 in The Netherlands

- Human cases -



78 conjunctivitis  
5 conjunctivitis + ILI  
2 ILI (1 fatal)  
4 no symptoms

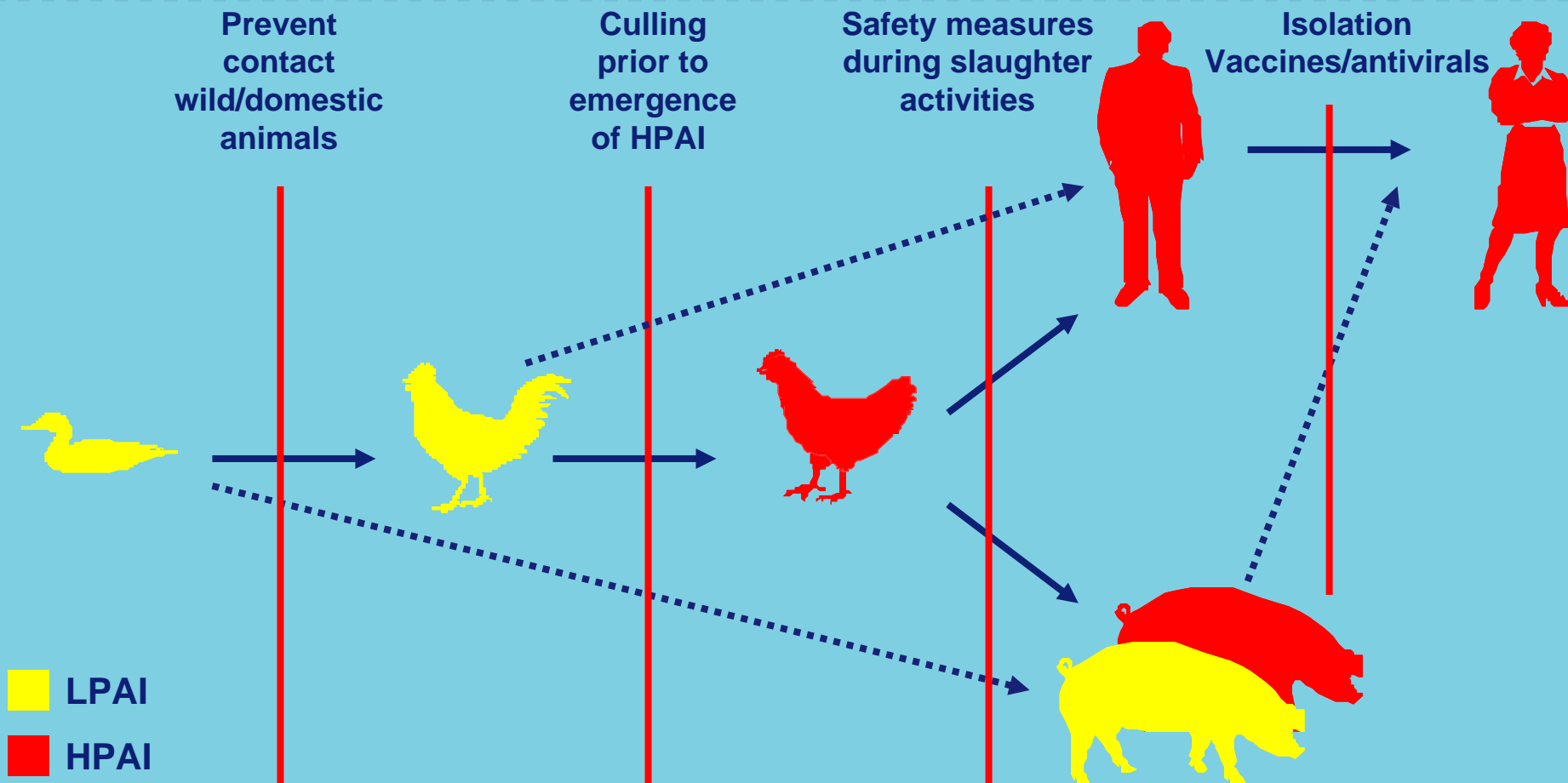
86 primary cases  
3 secondary cases



R.Fouchier et al., PNAS 2003  
M.Koopmans et al., Lancet 2003

# Avian influenza H7N7 infections in The Netherlands

- Chain of transmission and intervention strategies -



# INFLUENZA A VIRUS

## Recent zoonotic transmissions

Subtype	Country	Year	# Cases	# Deaths
H7N7	UK	1996	1	0
H5N1	Hongkong	1997	18	6
H9N2	SE-Asia	1999	>2	0
H5N1	Hongkong	2003	2?	1
H7N7	Netherlands	2003	89	1
H7N2	USA	2003	1	0
H7N3	Canada	2004	2	0
H5N1	SE-Asia	2004/5	>130	68*

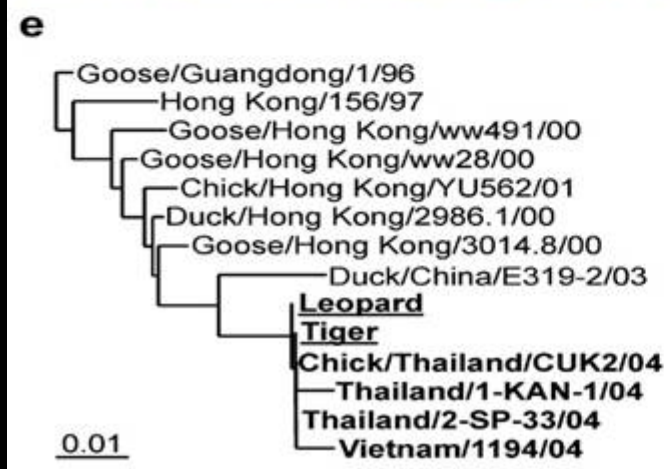
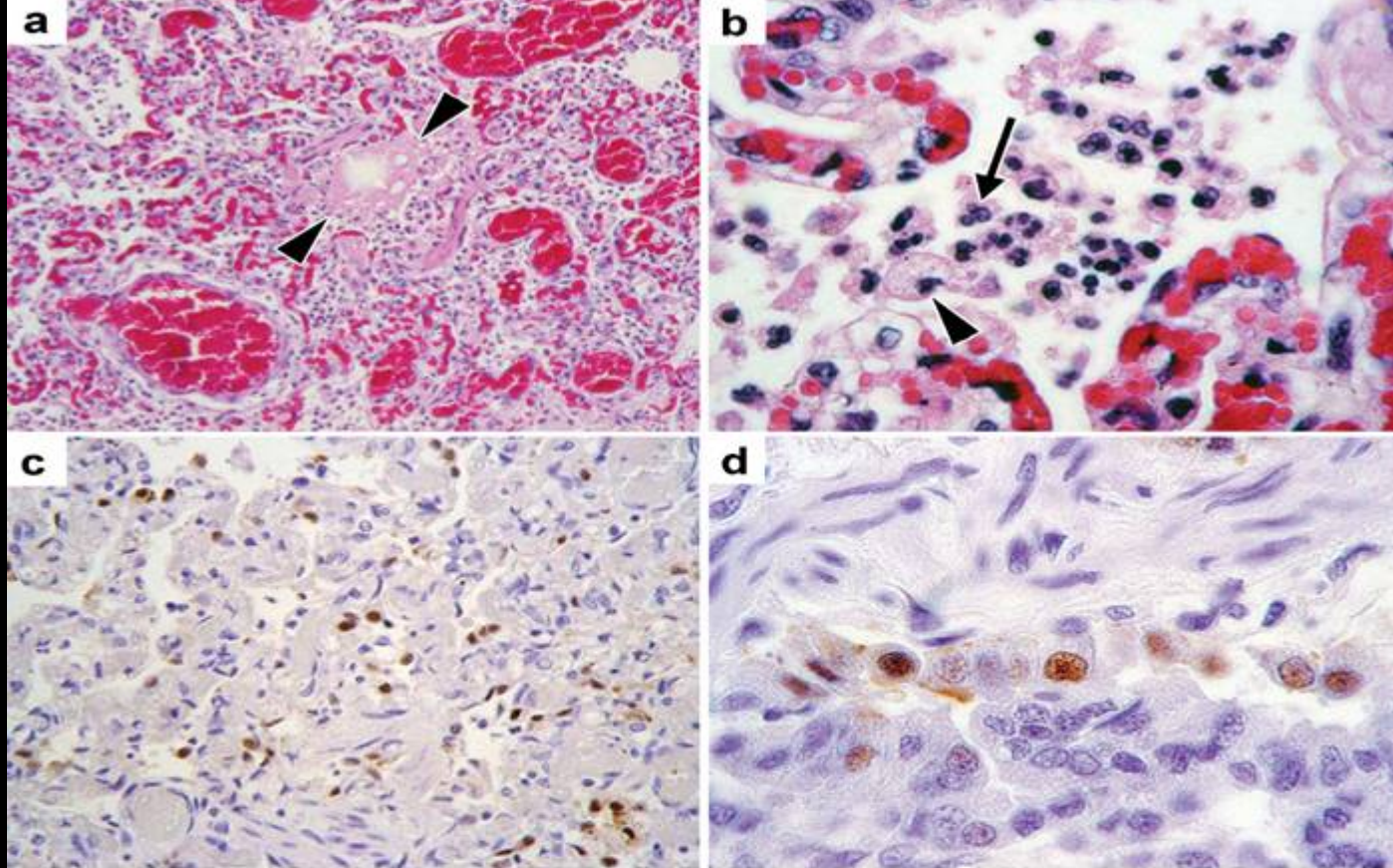
\*CFR ~ 50%



**Influenza A (H5N1) virus fatal for tigers and leopards** (*J.Keawcharoen et al.,EID, 2004*)

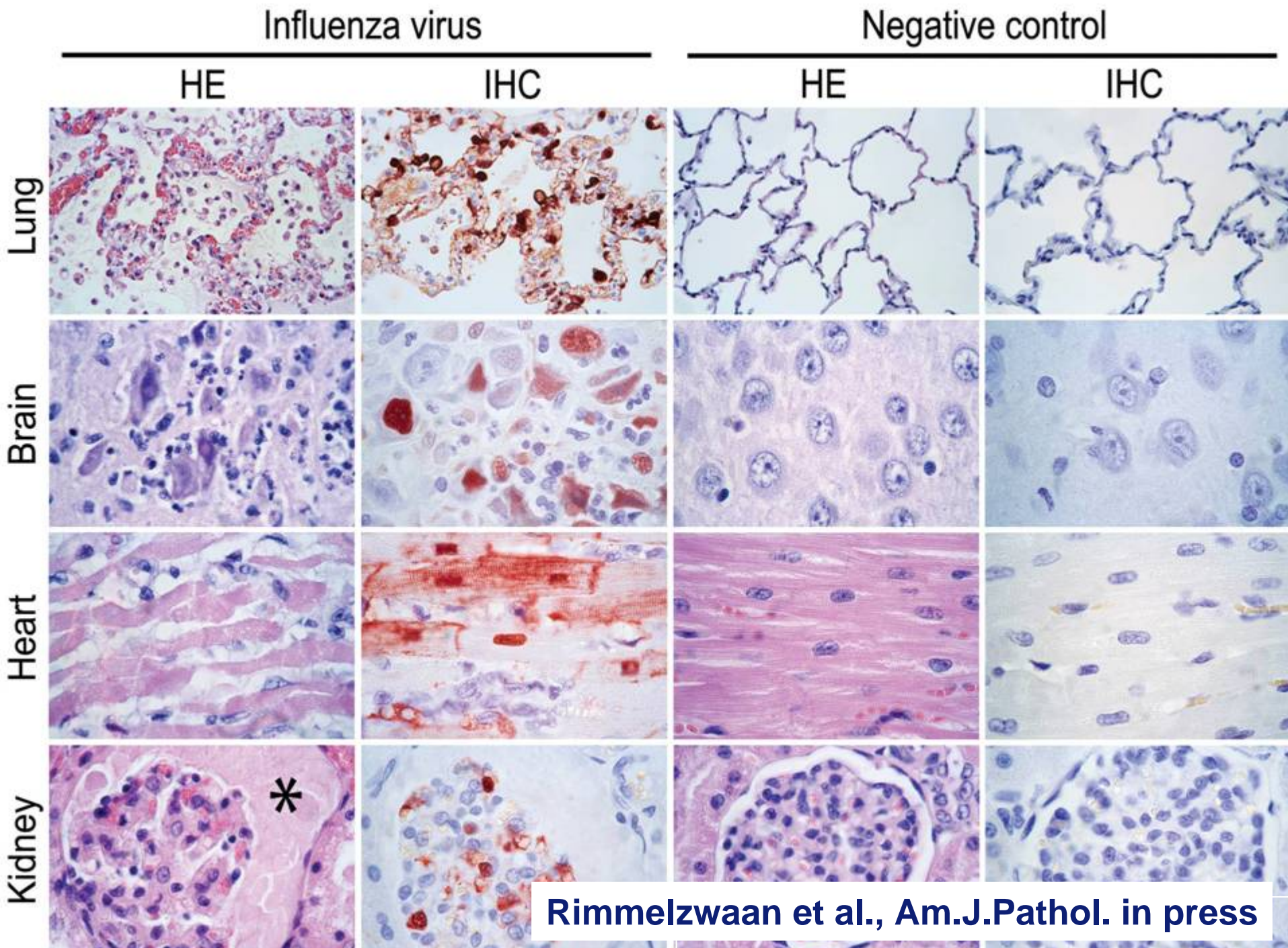
**Influenza A virus (H5N1) pathogenic for cats** (*Kuiken et al., Science,2004*)











# Westward spread of H5N1 virus April to October 2005





# SARS: A Global Threat!

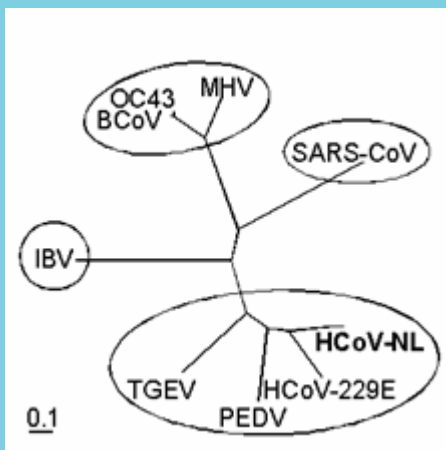


# HCoV-NL: a fourth coronavirus of humans

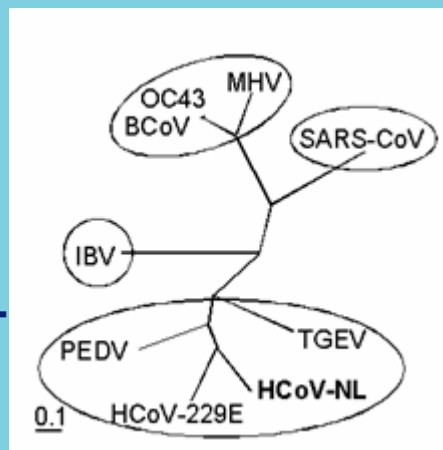
- phylogeny -

Fouchier et al., PNAS 2004

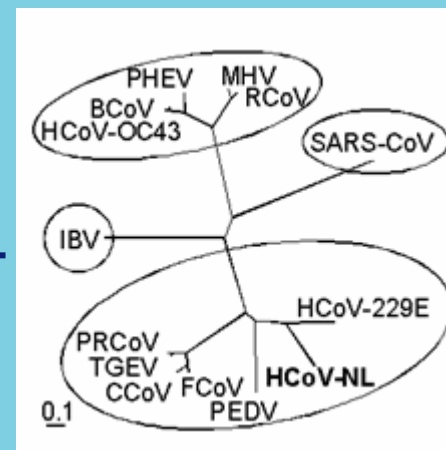
Full genome



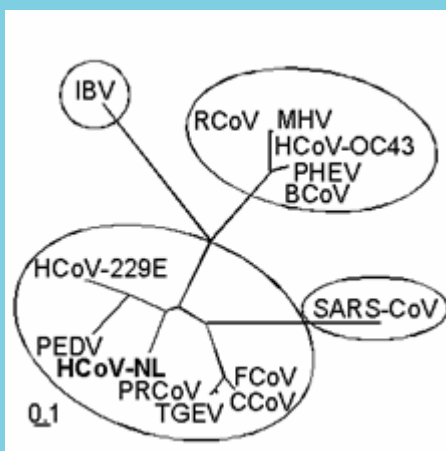
Replicase 1ab



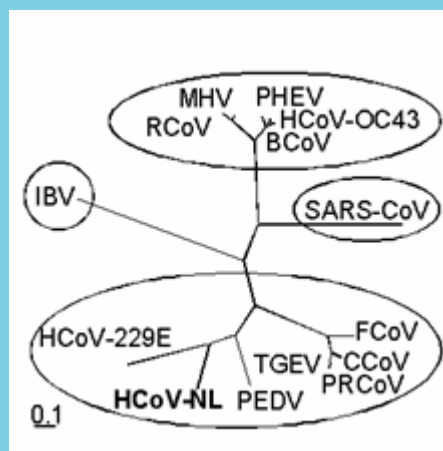
Spike



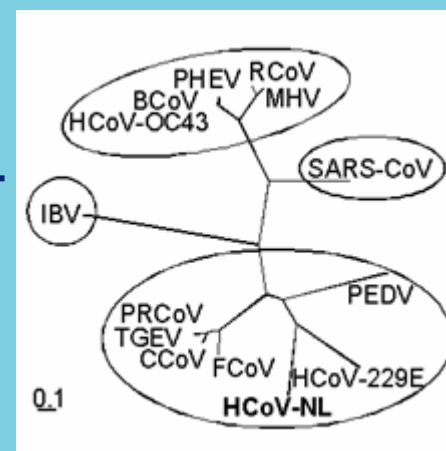
TM glycoprotein E



Matrix



Nucleocapsid



# SARS-CoV

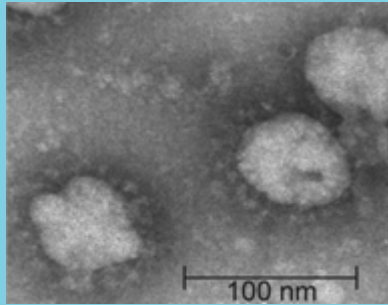
- Rivers' modified Koch's postulates -



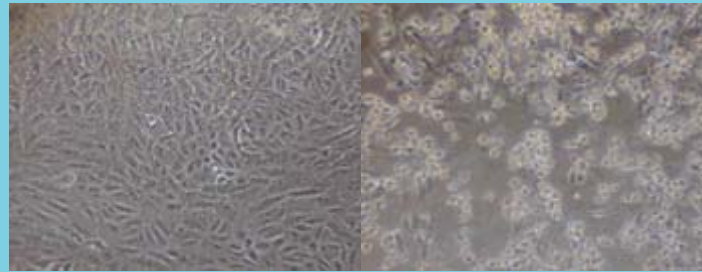
Erasmus MC  
*Erasmus*

Fouchier et al., Nature 2003  
Kuiken et al., Lancet 2003

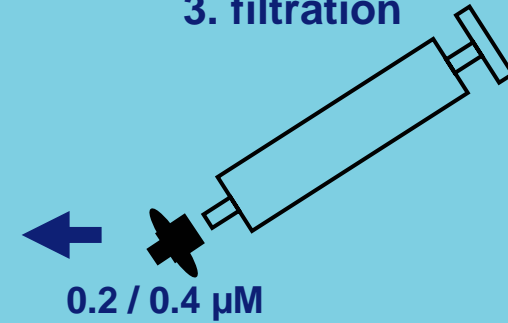
## 1. Virus isolation



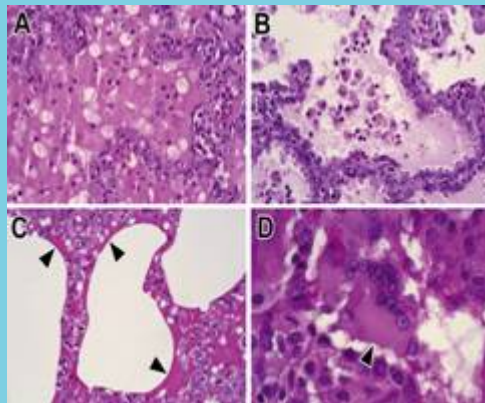
## 2. Virus propagation



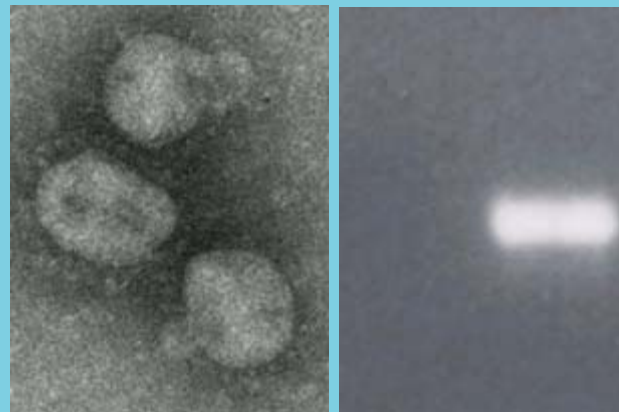
## 3. filtration



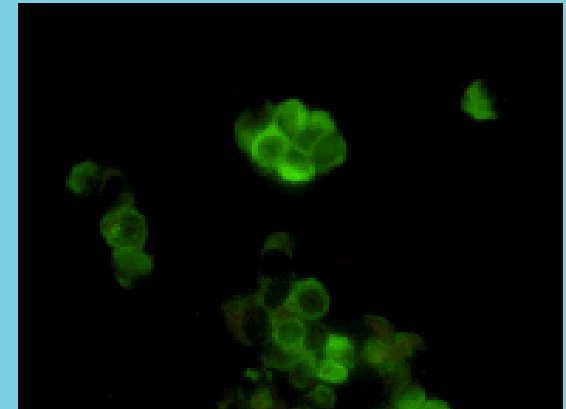
## 4. Disease in macaques



## 5. Re-isolation & PCR of virus



## 6. Specific immune response





**April 16, 2003**  
WHO Geneva

Conference of SARS  
etiology network

Official declaration of  
SARS-CoV as etiologic  
agent of SARS

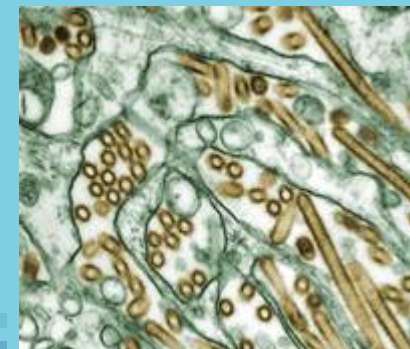
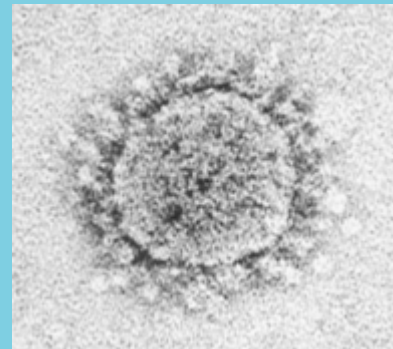
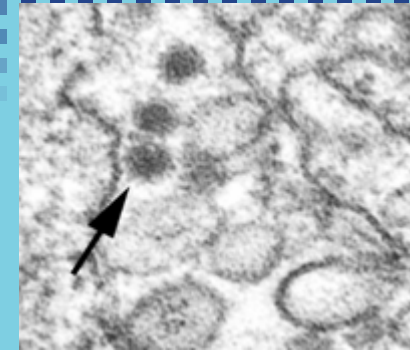
Short- and mid-term objectives:  
Clarification of transmission routes and natural history  
Establishment and evaluation of diagnostic tools





# Animals are source of virtually all newly emerging infections (Kuiken et al. 2005, Science)

- **Examples:**
  - **West Nile virus**: wild birds/mosquitoes
  - **SARS virus**: pteropid bats
  - **Influenza A virus**: free-living ducks
- **Emerging diseases have enormous impact on:**
  - Public health
  - Animal health/-welfare
  - Food supply
  - Economies
  - Environment (biodiversity)



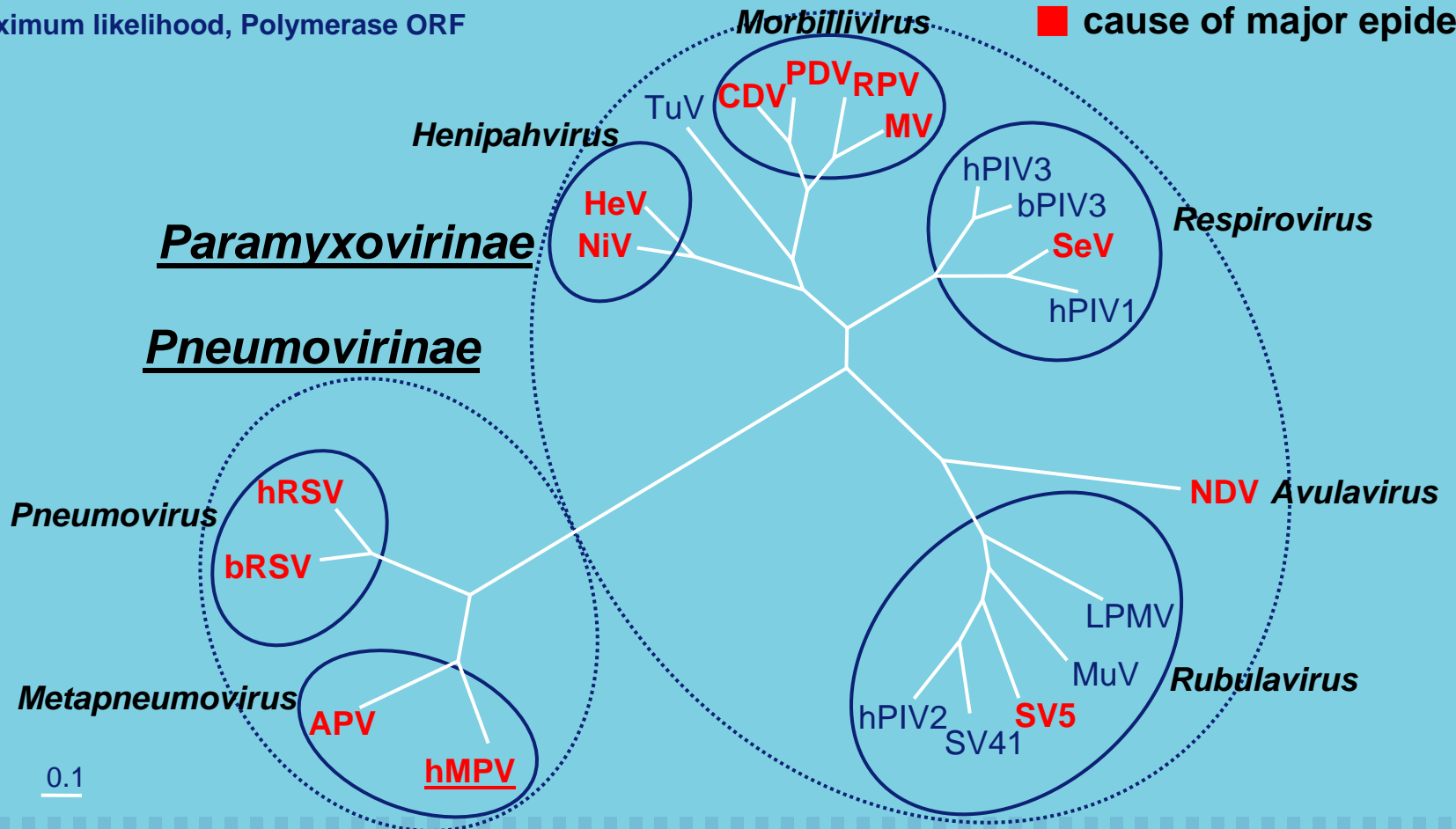
# Order *Mononegavirales*, family *Paramyxoviridae*

Erasmus MC



DNA Maximum likelihood, Polymerase ORF

■ cause of major epidemics



**Science October 2005**

# **Pathogen surveillance in animals: a key defense against emerging infections**

**T. Kuiken<sup>1</sup>, F. A. Leighton<sup>2</sup>, R. A. M. Fouchier<sup>1</sup>, J. W. LeDuc<sup>3</sup>, J. S. M. Peiris<sup>4</sup>, A. Schudel<sup>5</sup>, K. Stöhr<sup>6</sup>, A. D. M. E. Osterhaus<sup>1\*</sup>**

<sup>1</sup>Department of Virology, Erasmus MC, 3015 GE Rotterdam, The Netherlands

<sup>2</sup>Canadian Cooperative Wildlife Health Centre, University of Saskatchewan, Saskatoon, SK, S7N 5B4, Canada.

<sup>3</sup>National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333, USA.

<sup>4</sup>Department of Microbiology, University of Hong Kong, Hong Kong SAR, China.

<sup>5</sup>World Organization for Animal Health (OIE), Paris, France.

<sup>6</sup>World Health Organization, Department of Communicable Disease Surveillance and Response, Geneva, Switzerland.

# Rotterdam SARS and Flu studies

## Dept. Virology, Erasmus MC

Theo Bestebroer  
Bé Niemeyer  
Georgina Aron  
Robert Dias-d'Ullois  
Gerard van Doornum  
Martin Schutten  
Bert Niesters  
Vincent Munster  
Emmie de Wit  
Geert van Amerongen  
Bart Haagmans  
Byron Martina  
Thijs Kuiken  
Guus Rimmelzwaan  
Ron Fouchier  
Ab Osterhaus

## RIVM

Marion Koopmans  
Berry Wilbrink  
Adam Meijer  
Hans van der Nat  
Marina Conyn  
Arnold Bosman

## WHO & Members of the WHO SARS aetiology team

Centers for Disease Control & Prevention, Atlanta, USA  
Central Public Health Laboratory, London, UK  
Public Health Laboratory Centre, Hongkong, SAR China  
Prince of Wales Hospital, SAR China  
Queen Mary Hospital, SAR China  
Singapore General Hospital, Singapore  
Federal Laboratories for Health Canada, Winnipeg, Canada  
Health Canada, Ottawa, Canada  
Bernhard-Nocht Institute, Hamburg, Germany  
Institut Pasteur, Paris, France  
National Institute of Infectious Disease, Tokyo, Japan

## Various industrial partners

James Simon ViroNovative BV  
Frank Pistor Viroclinics BV

## Umeå University, Umeå, Sweden

Björn Olsen  
Anders Wallensten

## DLO, Lelystad

Guus Koch  
Arie Kant

## Virology Division

Utrecht University  
Berend Jan Bosch  
Peter Rottier

## Jeroen Bosch Hospital,

Peter Schneeberger  
Frans Rozendaal  
Jan Boekman  
Stiena Kemink



**Erasmus MC**  
Universitair Medisch Centrum Rotterdam



# Department of Virology

