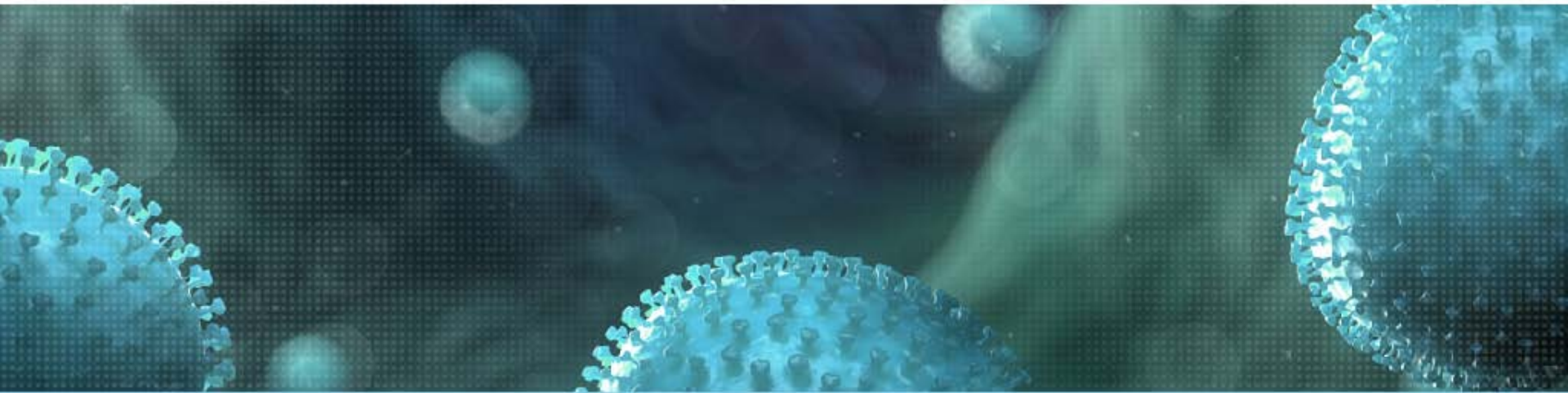


Erasmus MC



Viroscience lab

WHERE SKILLS MEET TO STUDY & PROTECT



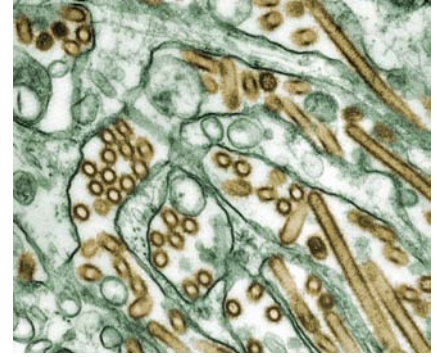
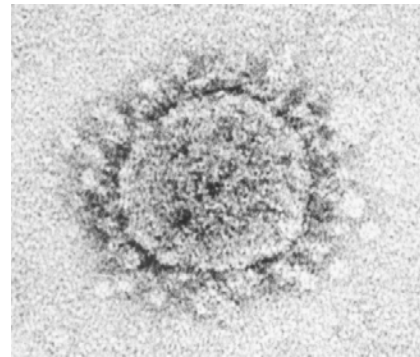
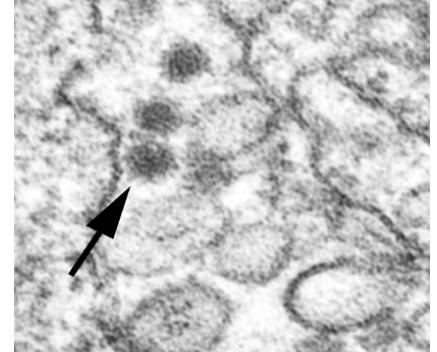
Barriers to and factors favoring emergence

Thijs Kuiken

Zoonoses and EIDs: biology meets anthropology, Paris, 10 & 11 June 2013

Many emerging infectious diseases originate from another host species

- (Wild) animals source of more than 70% of all EIDs (*Taylor et al. 2001, Philos Trans Roy Soc London Ser B*)
- Common property of most EIDs: ability to jump species barrier
- Important to understand how they do this



Definition host species barrier *(Kuiken et al. 2006, Science)*

“The interaction of factors that collectively limit
the transmission of an infection
from a donor host species to a recipient host species”

Species barrier approach of ANTIGONE project

Limited to reservoir



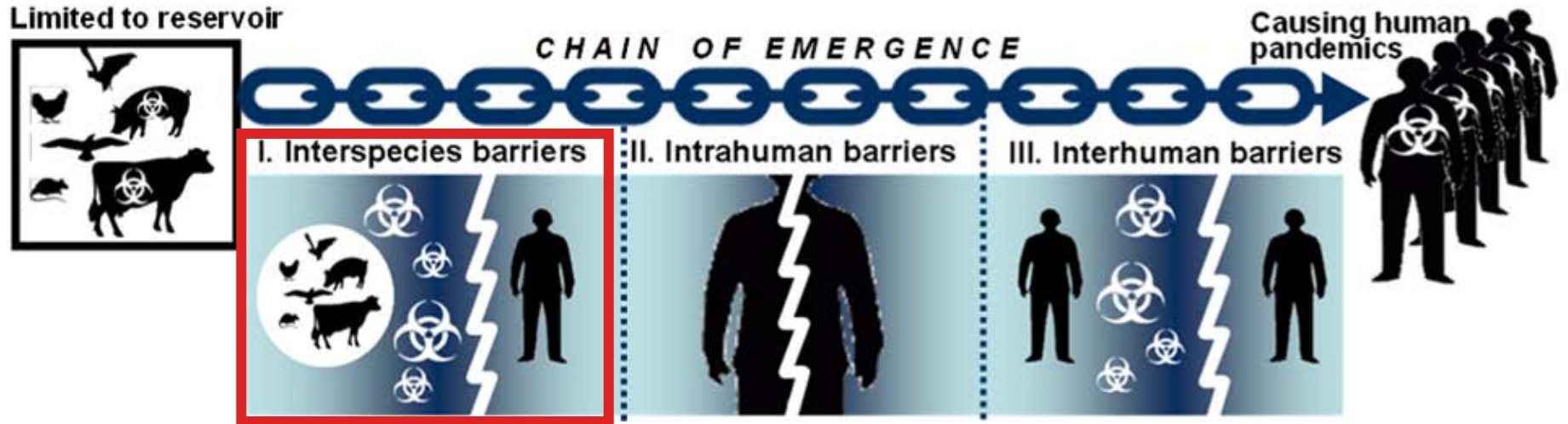
CHAIN OF EMERGENCE



Causing human pandemics



1. Interspecies barrier



The interspecies barriers encompass those that determine the level and nature of exposure to pathogens.

Interspecies barrier *(Kuiken et al. 2006, Science)*

- Geographical
 - Broken by international travel and trade



Kilpatrick et al. Lancet 2012

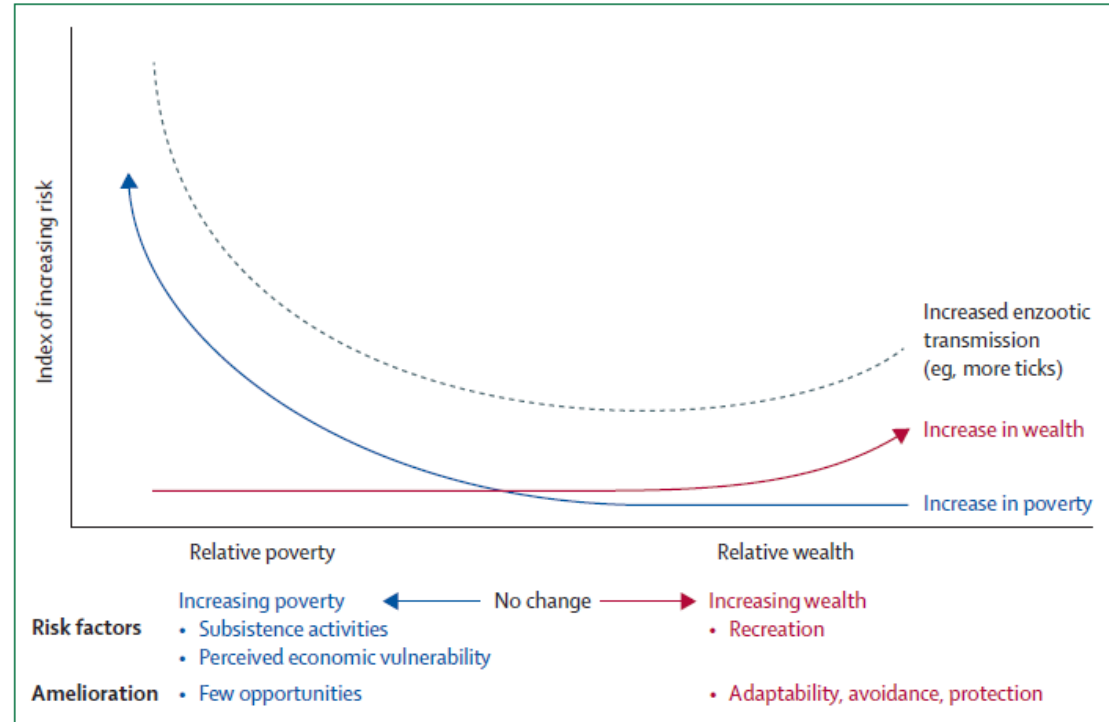
Interspecies barrier *(Kuiken et al. 2006, Science)*

- Geographical
 - Broken by international travel and trade
- Environmental/habitat use
 - Broken by incursion into wilderness areas



Interspecies barrier *(Kuiken et al. 2006, Science)*

- Geographical
 - Broken by international travel and trade
- Environmental/habitat use
 - Broken by incursion into wilderness areas
- Behavioural
 - Broken by increased human activities outdoors



Kilpatrick et al. Lancet 2012

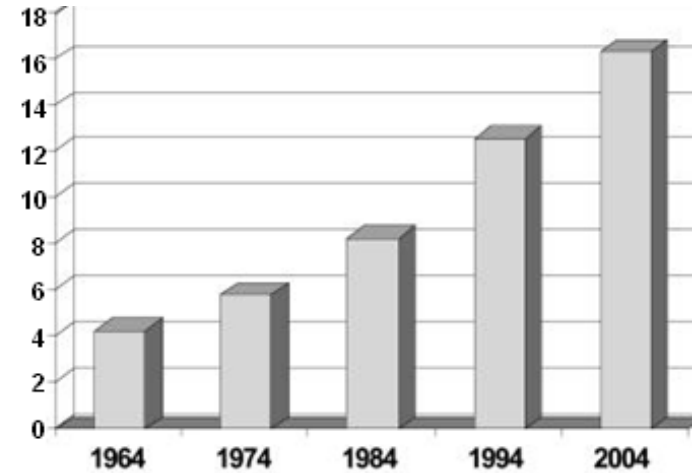
Interspecies barriers for influenza

- Donor species: wild birds
- *Barriers: geographical, habitat use*
- Intermediate species: poultry
- *Barriers: habitat use, behaviour*
- Recipient species: human beings



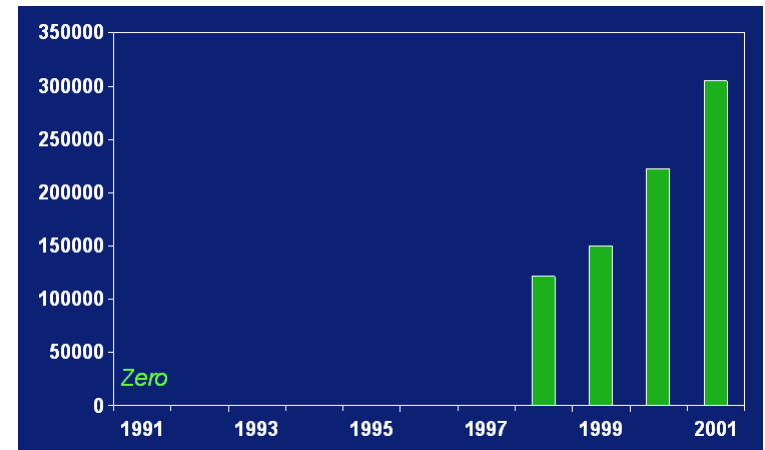
Factors associated with breakdown of interspecies barrier

- Increased poultry production



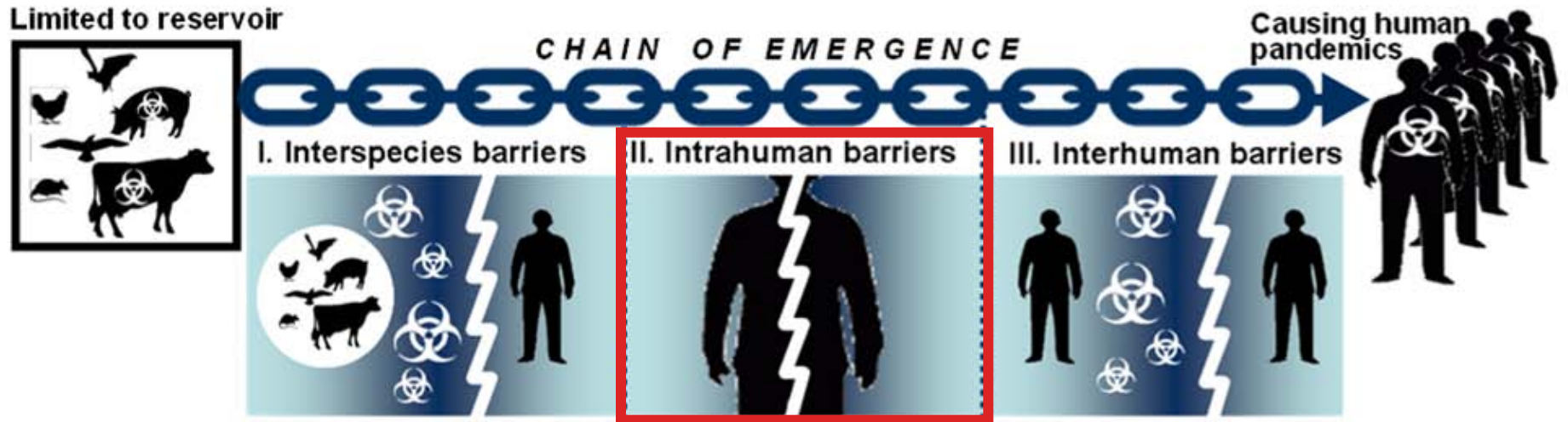
Annual global production of poultry (billions)

- Increased range poultry production



Annual NL production of range poultry

2. Intrahuman barrier



The intrahuman barriers determine the ability of a zoonotic pathogen to (1) gain access to the appropriate tissue, (2) replicate in the appropriate cell type, (3) deal appropriately with the host immune response, and (4) be excreted from the infected human host.

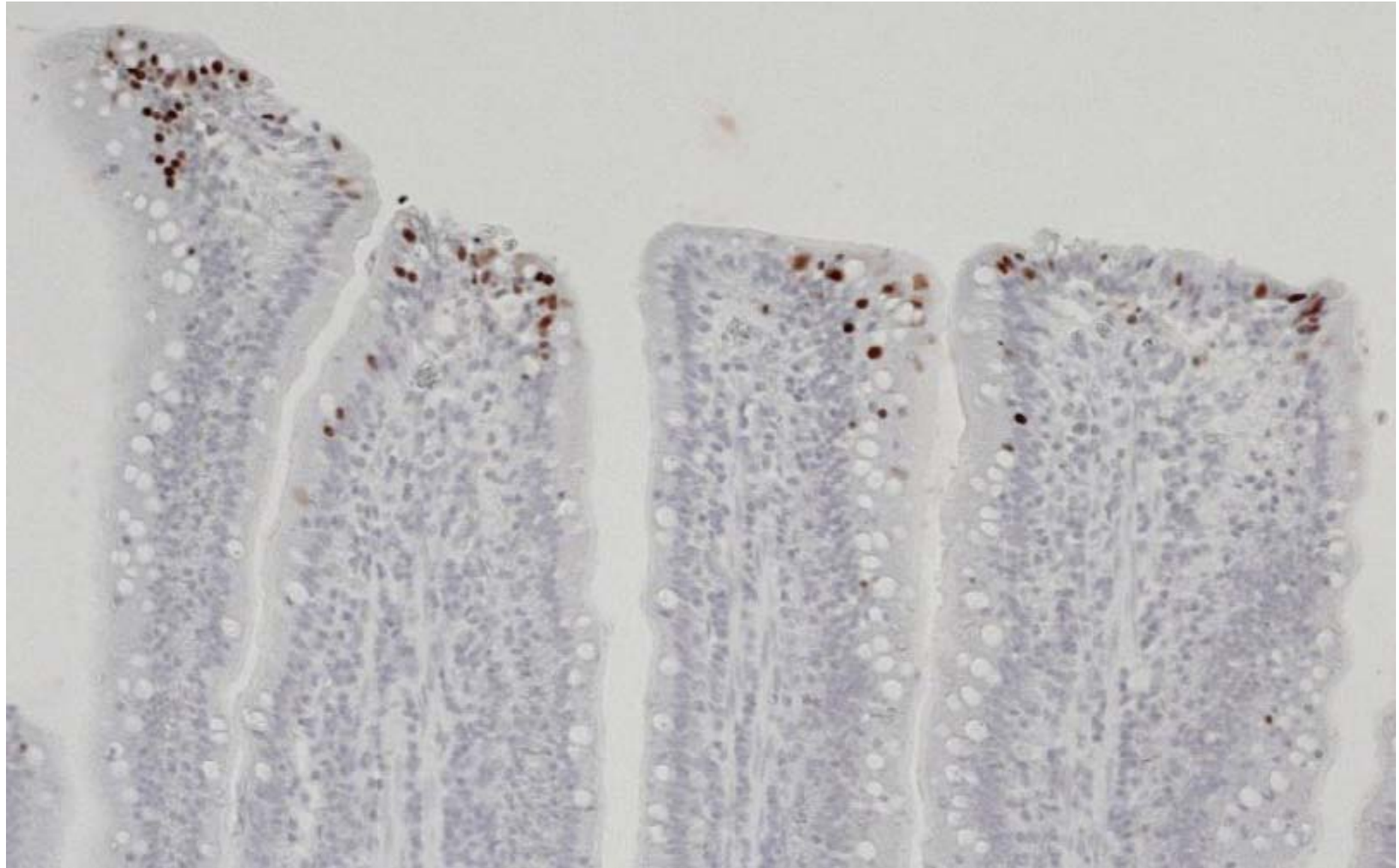
Influenza virus in ducks: intestinal infection



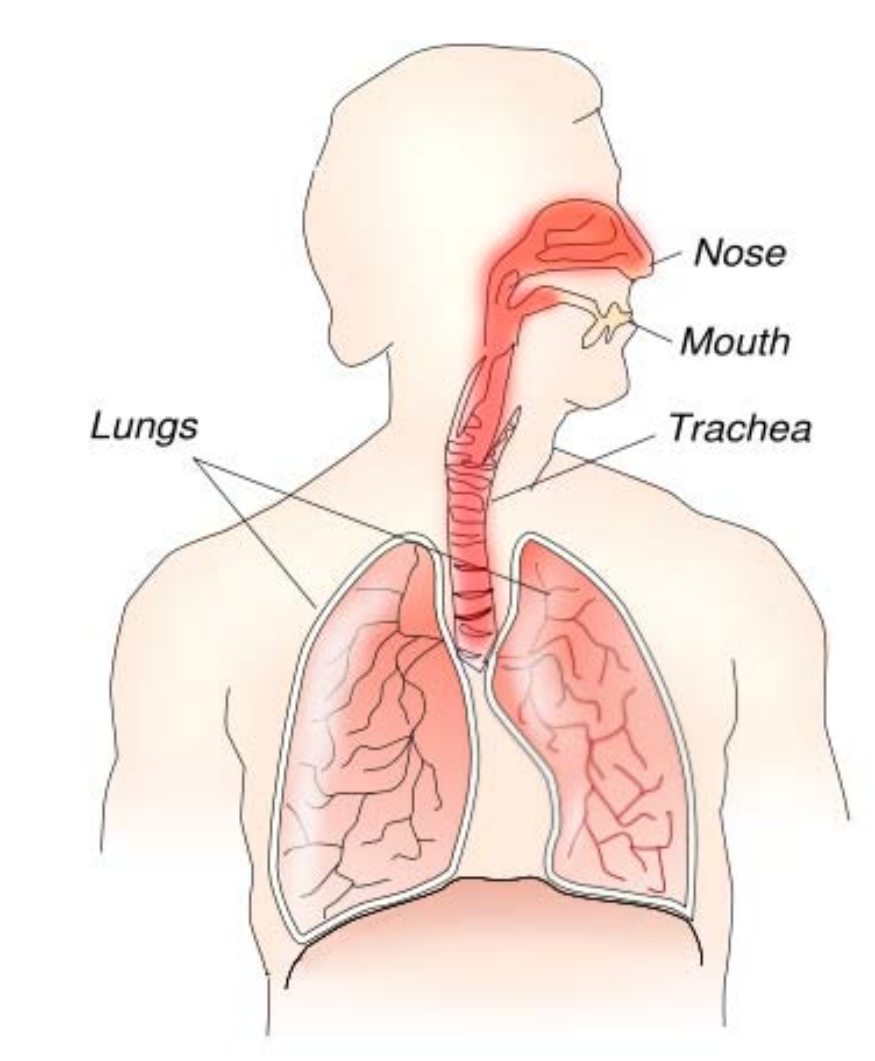
Courtesy Frank van der Panne

Virus antigen expression in duck intestine

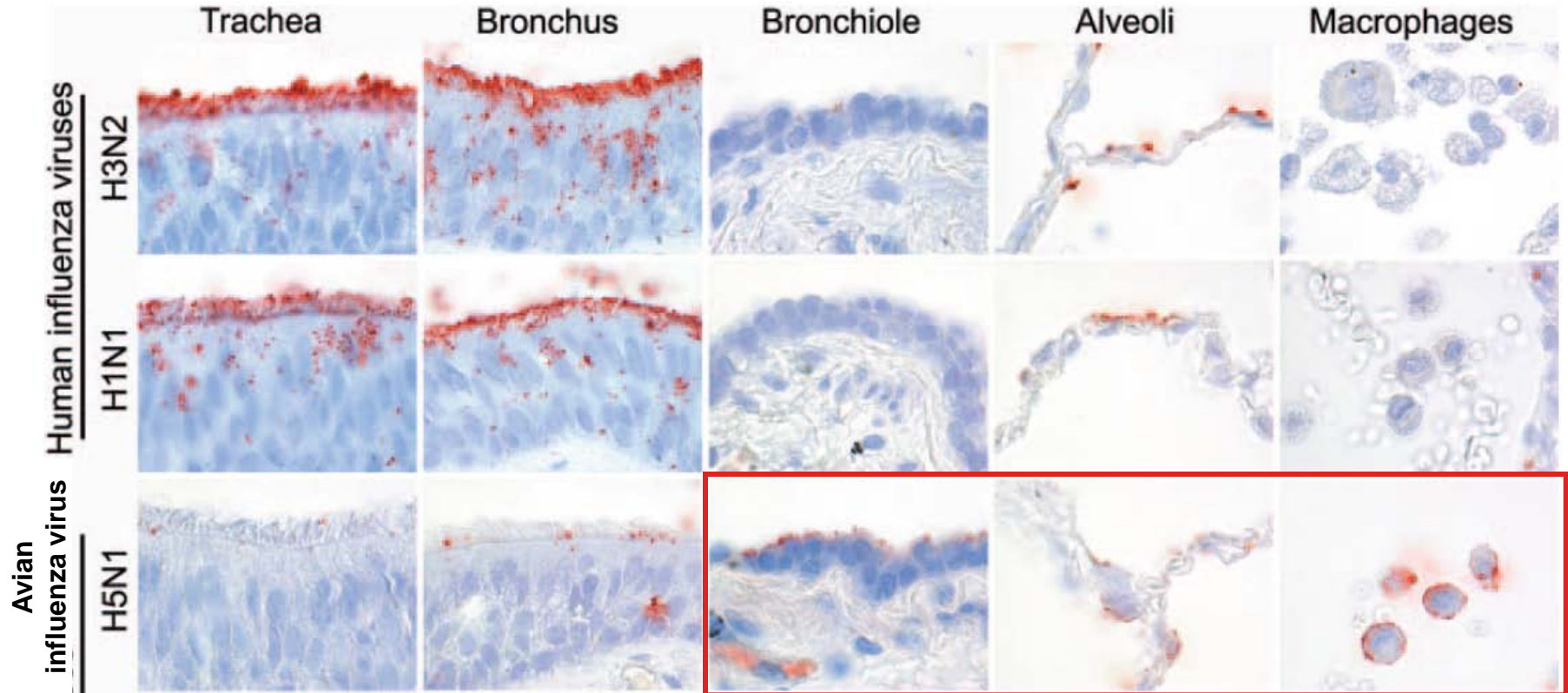
(Daoust et al. 2012, Vet Pathol)



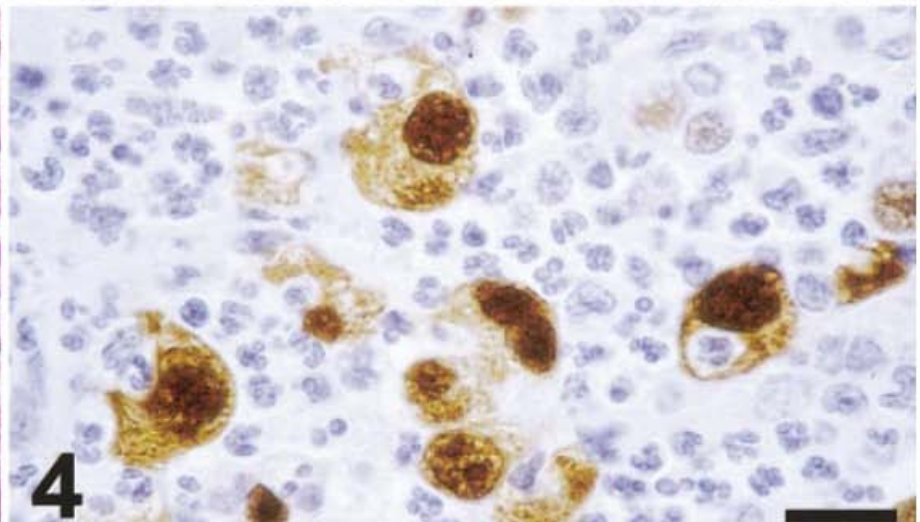
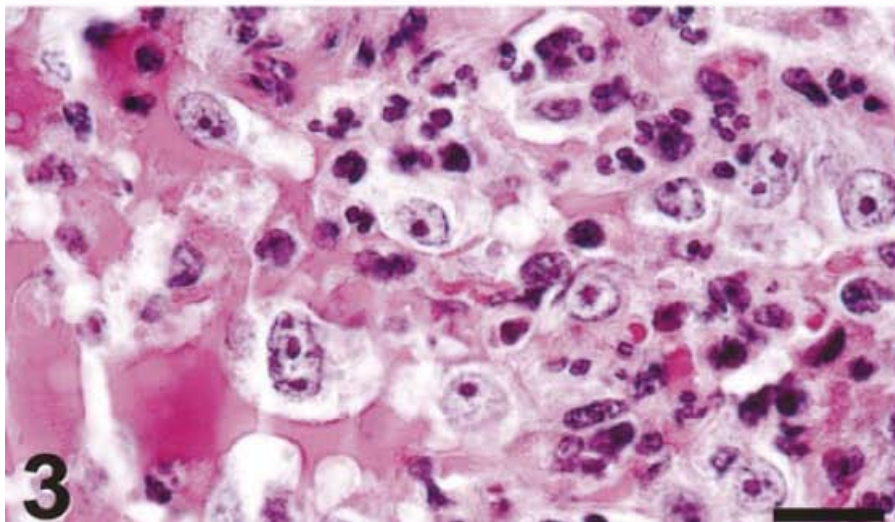
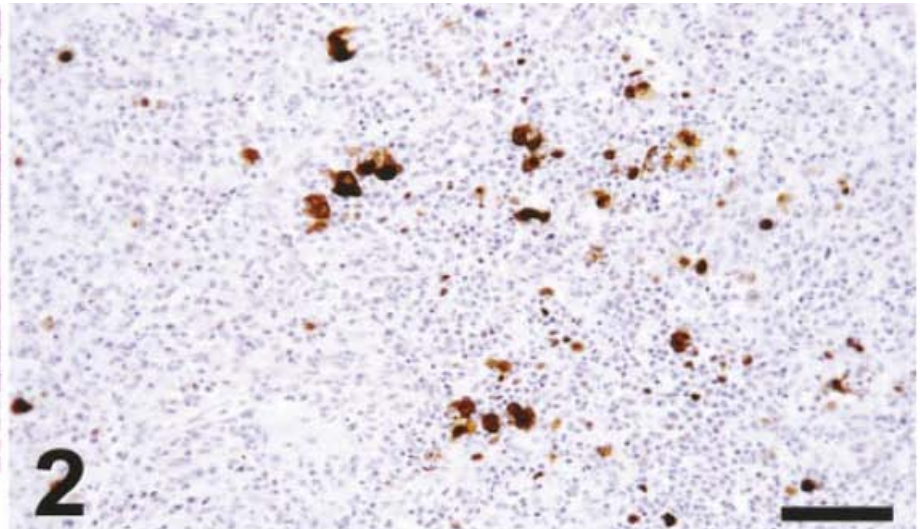
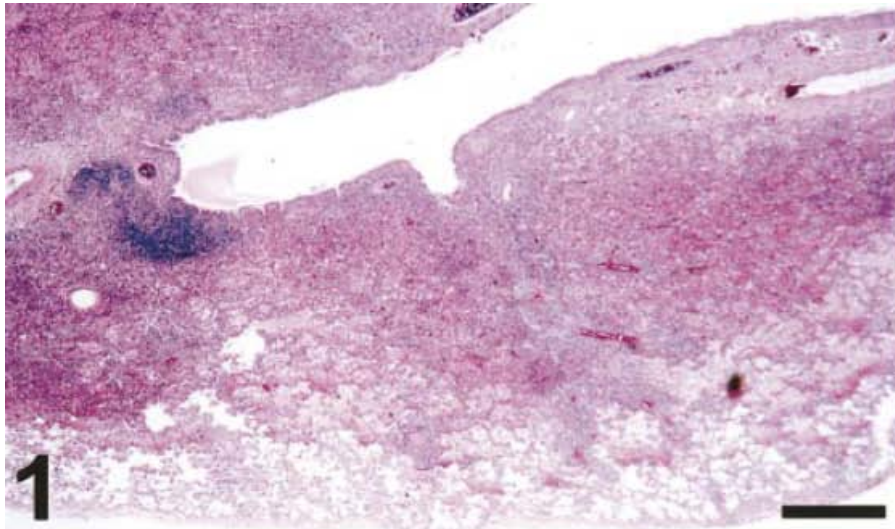
Influenza virus in human beings: respiratory infection



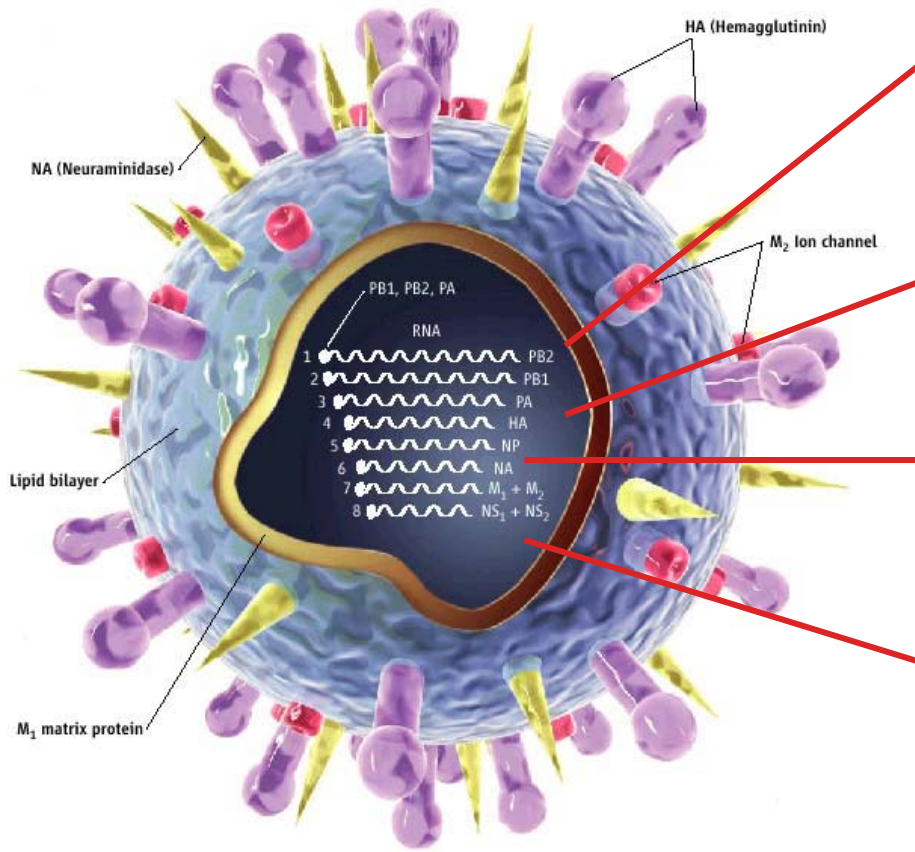
Avian influenza virus can attach to human respiratory epithelium *(van Riel et al. 2007, Am J Pathol)*



Avian influenza (H5N1) virus in the lung of a non-human primate *(Kuiken et al. 2004 Vet Pathol)*

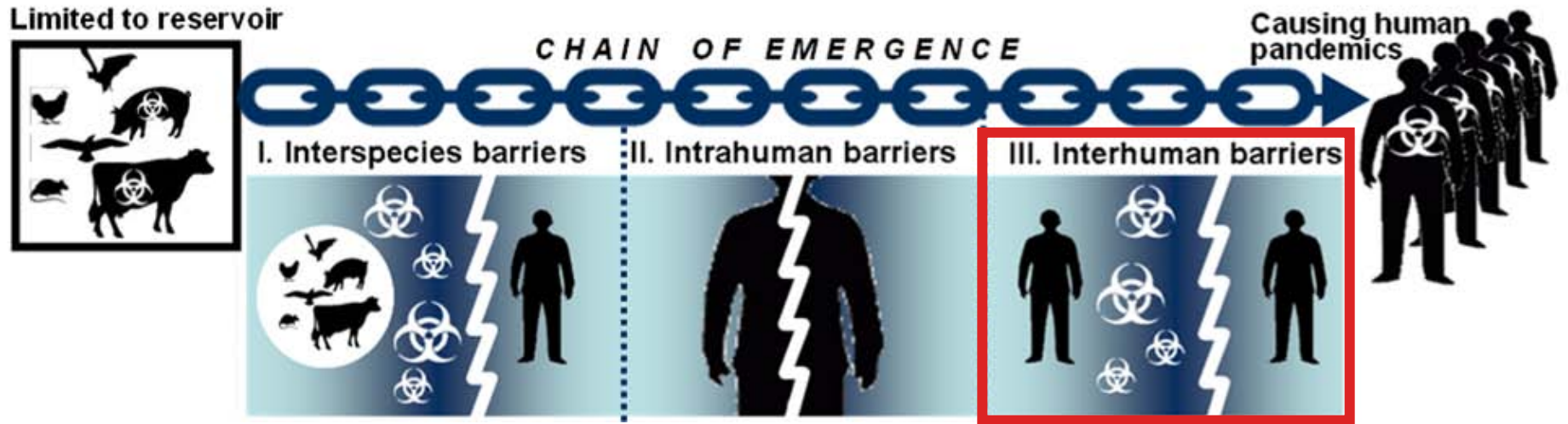


Overcoming the intrahuman barrier: genetic adaptation of avian influenza virus to replication in humans *(de Wit & Fouchier 2008 J Clin Virol)*



- PB2: efficient replication in mammals
- HA: receptor specificity
- NA: ability to replicate in absence of trypsin
- NS1: antagonism of innate immune response

3. Interhuman barrier



The interhuman barriers are the final ones that a zoonotic pathogen must overcome in order to transmit efficiently among humans and cause human epidemics or pandemics.

Airborne transmission required for influenza virus to spread efficiently among humans

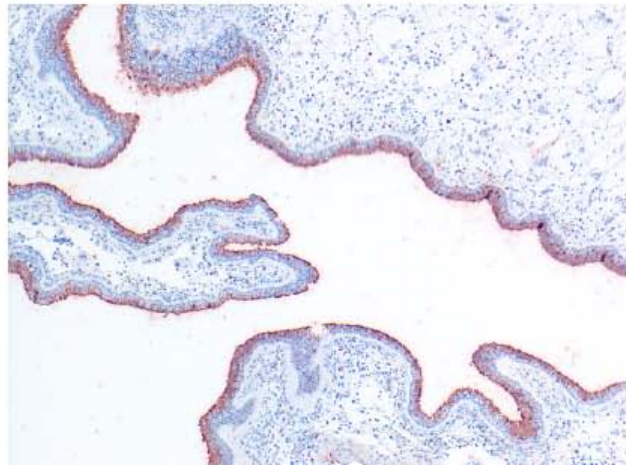


Virus attachment in human URT

(van Riel et al. 2010 Am J Pathol)

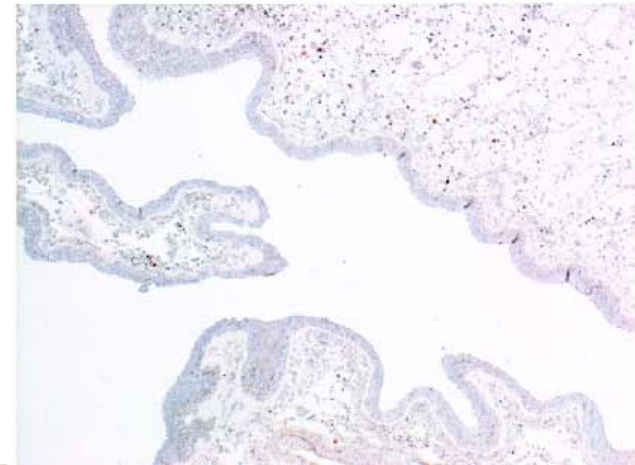
Human

Seasonal H3N2



Avian

HPAIV H5N1



Virus attachment in human URT

(van Riel et al. 2010 Am J Pathol)

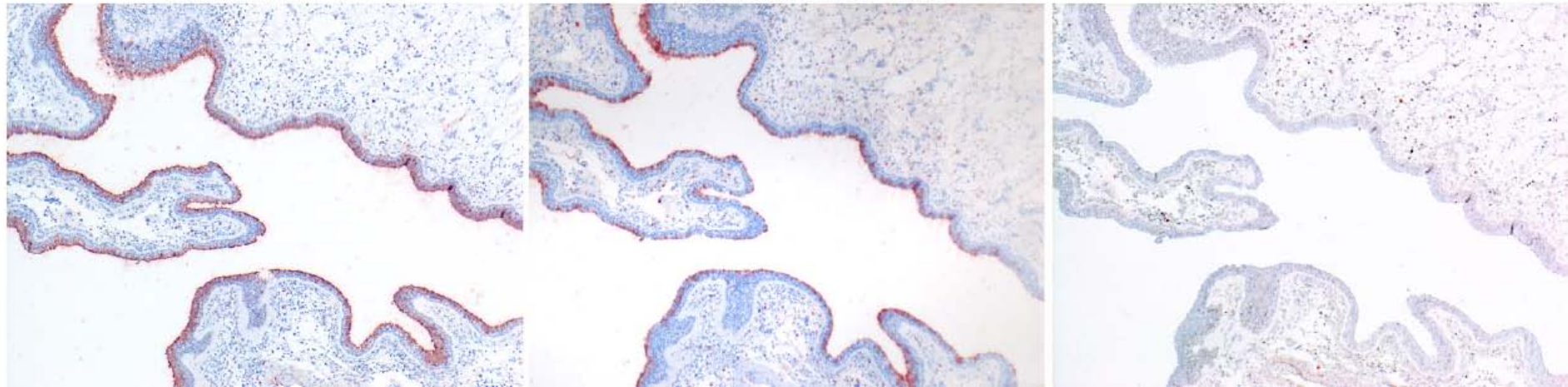
Human

Seasonal H3N2

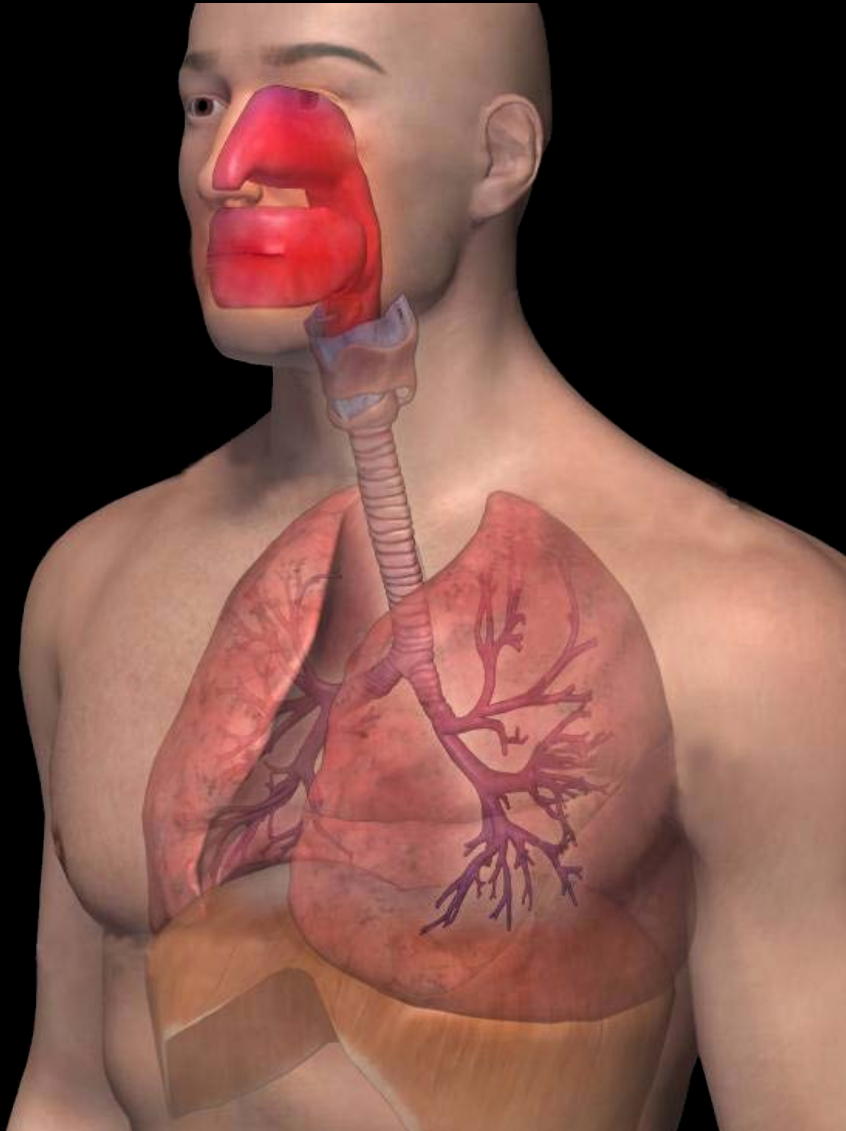
Pandemic H1N1

Avian

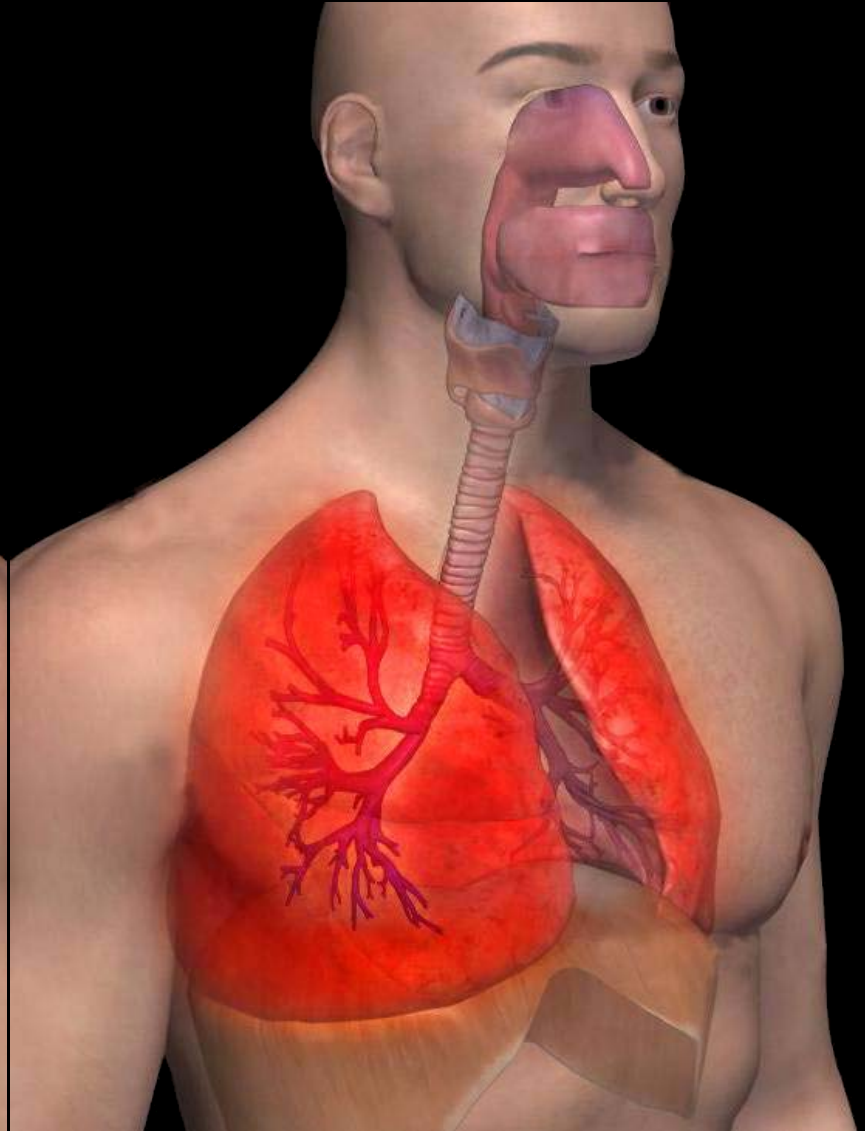
HPAIV H5N1



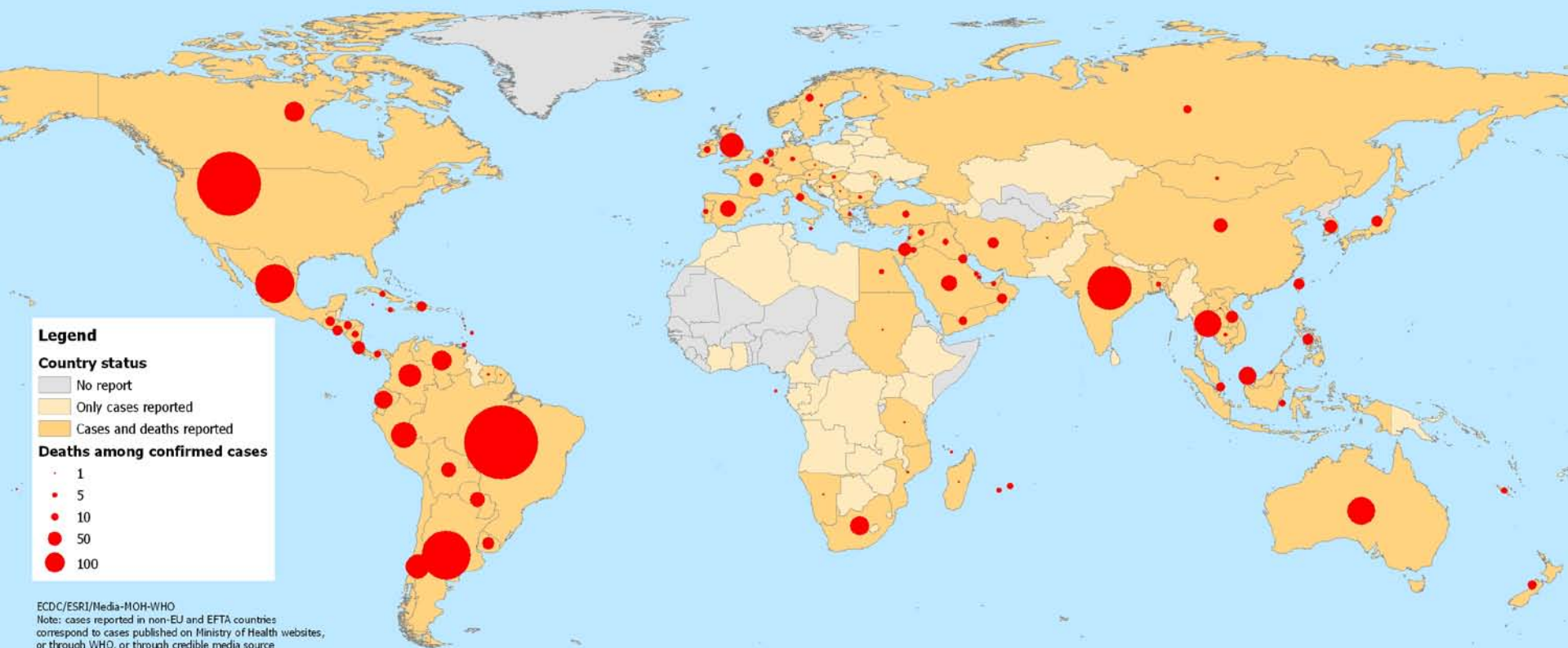
**Pandemic H1N1:
Efficient transmission**



**H5N1 HPAIV:
Inefficient transmission**



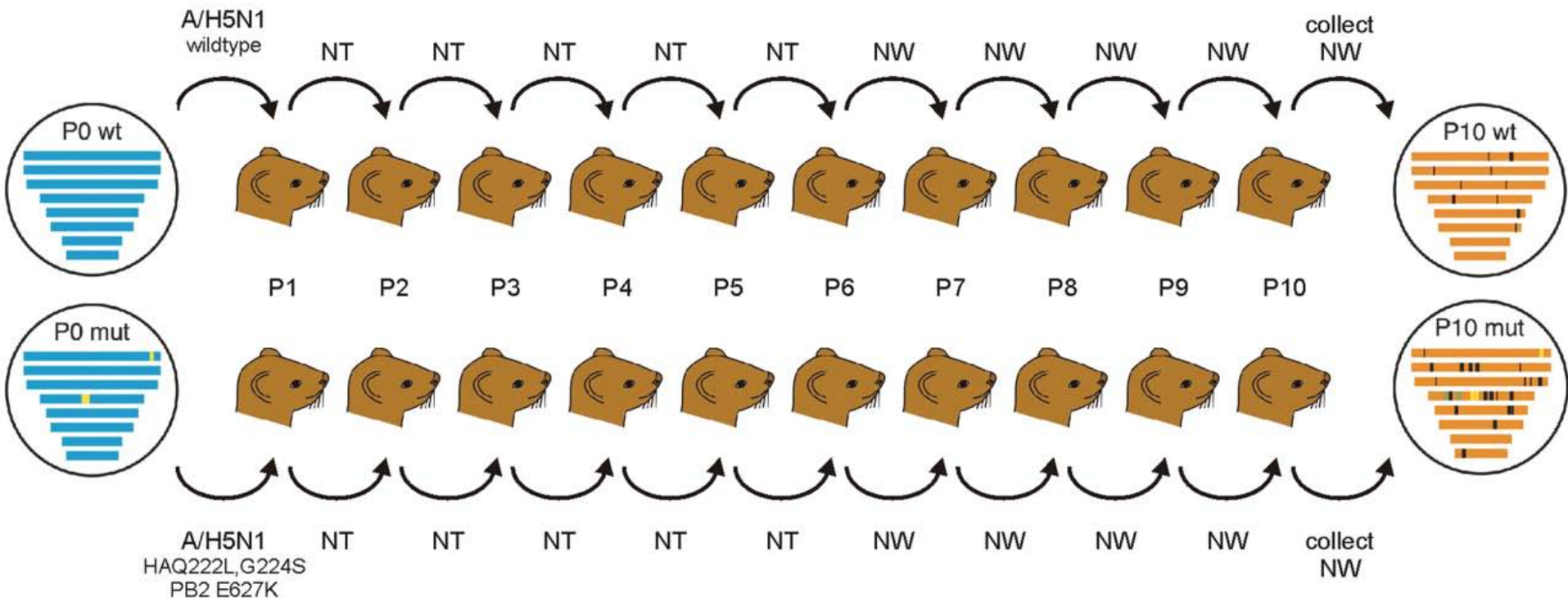
Reported cumulative number of confirmed fatal cases of influenza A(H1N1)v and country reporting status by country, as of 03 November 2009, 16:00 hours CEST



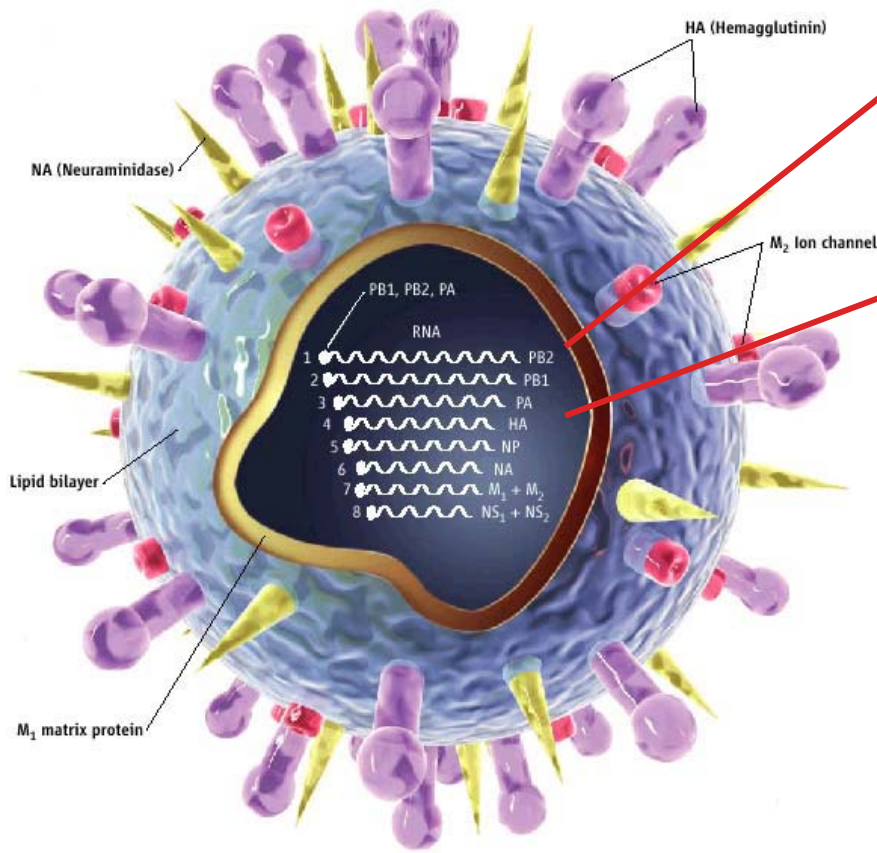
ECDC/ESRI/Media-MOH-WHO
Note: cases reported in non-EU and EFTA countries correspond to cases published on Ministry of Health websites, or through WHO, or through credible media source quoting national authorities. Therefore, some of these cases may be taken out at a later stage if not validated.

Airborne transmission of influenza A/H5N1 virus between ferrets

(Herfst et al. 2012, Science)



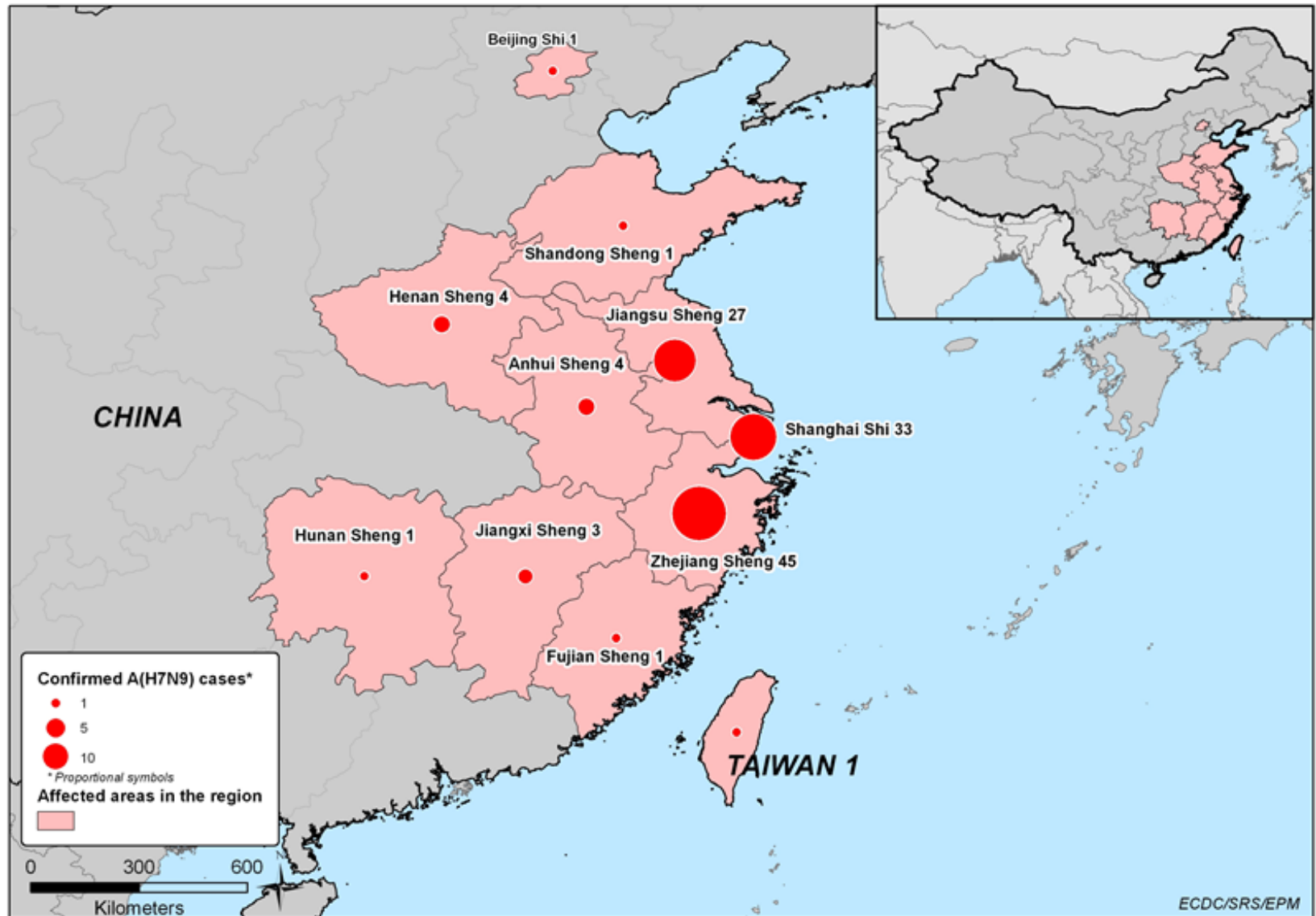
Overcoming the interhuman barrier: genetic adaptation of avian influenza virus to airborne transmission in ferrets *(Herfst et al. 2012 Science, Imai et al. 2012 Nature)*



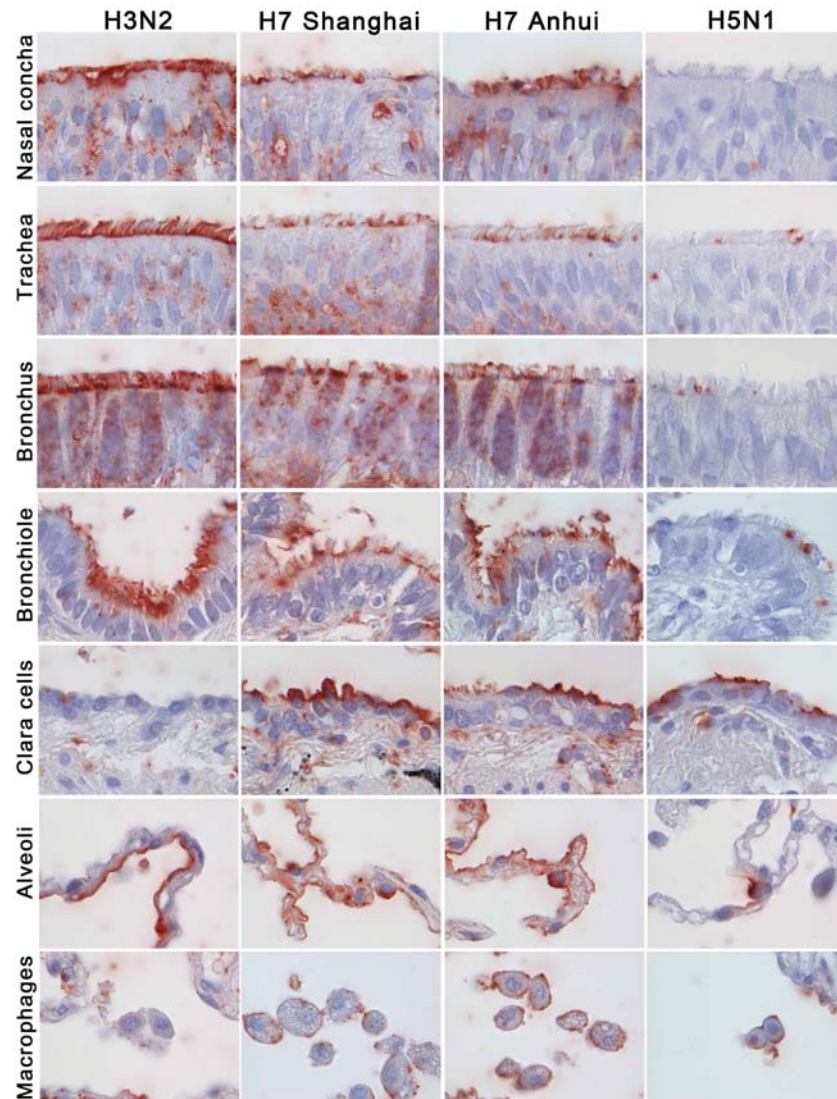
- PB2: efficient replication in mammals
- HA: receptor specificity from alpha-2,3-linked sialic acids to alpha-2,6-linked sialic acids

H7N9 cases in China, 19 Feb – 29 April 2013

(ecdc.europa.eu)



Avian-origin H7N9 virus attaches well to both upper and lower respiratory tract *(van Riel et al. submitted)*



Single-discipline approach to pathogens crossing species barrier

- Disciplines involved
 - Human medicine
 - Veterinary medicine
 - Ecology
 - Economy
 - Sociology
 - Anthropology
 - Etc.
- Diseases cross species barriers more easily than people cross disciplines

Manhattan principles on One Health, 2004

(<http://www.oneworldonehealth.org/>)

“Only by breaking down the barriers among agencies, individuals, specialties and sectors can we unleash the innovation and expertise needed to meet the many serious challenges to the health of people, domestic animals, and wildlife and to the integrity of ecosystems.”

R.A. Cook, W.B. Karesh, and S.A. Osofsky

Wildlife Conservation Society, New York, USA



Strategies for collaboration in the interdisciplinary field of emerging zoonotic diseases

(Anholt et al. 2012 Zoonoses Public Health)

1. Encouragement of professional social networks across disciplines
2. Cultivation of passionate interdisciplinary leaders
3. Focus on building a culture of trust and respect among disciplines
4. Interdisciplinary teams need shared vision for tasks at hand
5. Establishment of processes to allow for collaborative work

“Education and experiential learning opportunities remain our best tools to develop the interdisciplinarian at this time.”

How do people react to message that human health and wildlife health are linked? *(Decker et al. 2010 ILAR J)*

- Including wildlife under the umbrella of One Health helps emphasize that a healthy wildlife population contributes to human health—and at the same time implicitly suggests that unhealthy wildlife may pose threats to human health.
- Some people may regard wildlife as simply a means to improved human health, thereby ignoring the One Health Initiative's mission to improve the well-being of *all* species.
- Of particular concern is the possibility that some members of the public may perceive wildlife as a threat to humans and domestic animals.

Summary

- Species barrier
 - Interspecies
 - Intrahuman
 - Interhuman
- One health approach
 - break down barriers among disciplines
 - improve health of humans, domestic animals and livestock
 - improve integrity of ecosystems

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Landbouw en Innovatie



Netherlands Genomics Initiative

