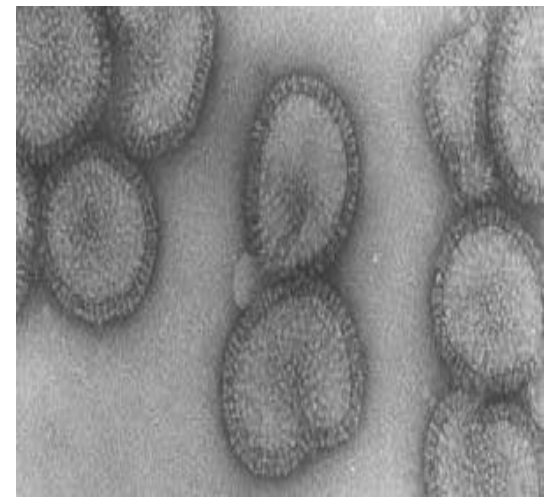


Apport de la PCR dans le diagnostic des infections virales respiratoires

Pr H Fleury MD, PhD

Laboratoire de Virologie et CNRS UMR 5234 Université de Bordeaux



Plan de la présentation

Les virus respiratoires émergents : définitions et actualités

Les virus respiratoires circulant en zones tempérées

Les outils du diagnostic virologique

L'apport de la Biologie Moléculaire au diagnostic virologique et au suivi de patients infectés par des virus respiratoires

LES VIRUS RESPIRATOIRES ÉMERGENTS ; DÉFINITION ET ACTUALITÉS

- ***Fièvre hémorragique avec syndrome rénal (FHSR) (Hantavirus)***
- Fièvre hémorragique de Corée (2500 cas dans le corps expéditionnaire US entre 1950 et 1953)
- Pathologie similaire décrite en Chine (10eme siècle) et à Vladivostok en 1913
- Néphropathie épidémique en Scandinavie

- Bunyavirus Hantaan isolé du mulot strié (*Apodemus agrarius*) en Corée ; libéré dans les urines du rongeur et contamine l'homme par aérosol . Souches Seoul et Dobrava-Belgrade
- Puumala isolé d'un rongeur en Scandinavie
- Cas humains décrits en Asie, en Europe de l'Est, en Scandinavie, en Grèce et en France (Champagne Ardennes) .
- Sujets ayant surtout une activité agricole et forestière .

Multiplex PCR–Based Next-Generation Sequencing and Global Diversity of Seoul Virus in Humans and Rats

Won-Keun Kim¹, Jin Sun No¹, Seung-Ho Lee, Dong Hyun Song, Daesang Lee, Jeong-Ah Kim, Se Hun Gu, Sunhye Park, Seong Tae Jeong, Heung-Chul Kim, Terry A. Klein, Michael R. Wiley, Gustavo Palacios, and Jin-Won Song✉

Author affiliations: Korea University, Seoul, South Korea (W.-K. Kim, J.S. No, S.-H. Lee, J.-A. Kim, J.-W. Song); Agency for Defense Development, Daejeon, South Korea (D.H. Song, D. Lee, S.H. Gu, S. Park, S.T. Jeong); 65th Medical Brigade/Medical Department Activity–Korea, Seoul (H.-C. Kim, T.A. Klein); US Army Medical Research Institute of Infectious Disease, Fort Detrick, Maryland, USA (M.R. Wiley, G. Palacios)

[Main Article](#)

Figure 4

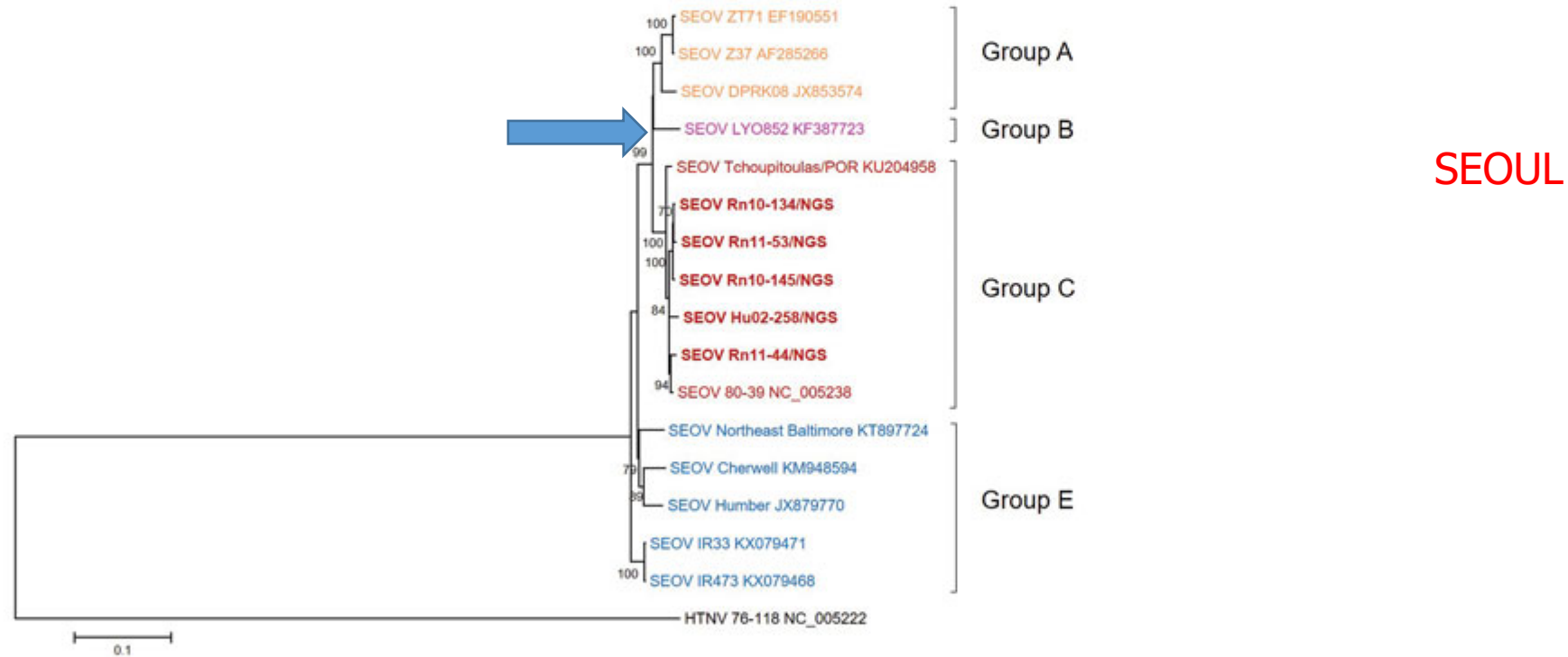
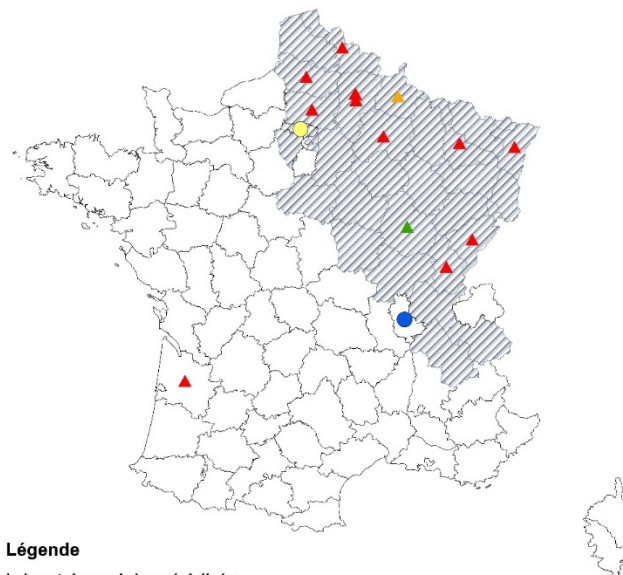


Figure 4. Phylogenetic analysis of SEOV large RNA segments, South Korea, 2000–2016, and reference strains. A phylogenetic tree was generated by using the maximum-likelihood method with the TN93 + gamma + invariant model of evolution and alignment of large segment sequences (nt 1–6510) of SEOV strains. Colored groups indicate the areas where SEOV strains were identified: group A, southeastern China and North Korea; group B, Europe (France); group C, South Korea and the United States; group E, United Kingdom and the United States. Bold red indicates SEOV strains sequenced in this study. Topologies were evaluated by bootstrap analyses of 1,000 iterations. Numbers along branches are bootstrap values. GenBank accession number are provided. Scale bar indicates nucleotide substitutions per site. SEOV, Seoul virus.





Légende

Laboratoires privés spécialisés

- Euroimmun Pool Eurasia IgG et IgM
- Focus Hanta IgG et IgM

Laboratoires hospitaliers publics

- ▲ Reagent POC Puumala IgM
- ▲ Reagent POC Puumala et Focus Hanta IgG et IgM
- ▲ Reagent POC Puumala et Dobrava-Hantaan

▨ Zone d'endémicité du virus Puumala

- Clinique : céphalées, nausées, vomissements, protéinurie, hématurie et insuffisance rénale ; forme Scandinave et Française moins sévère . Incubation peut atteindre 50 jours
- **USA, 1993** : syndrome pulmonaire humain (Human Pulmonary Syndrome, HPS) observé dans 4 états du Sud (Arizona, Nouveau Mexique, Colorado, Utah) ; virus isolé : Hantavirus (FCV, Sin Nombre Virus : SNV) ; réservoir : rongeur Pathologie rencontrée du Canada à la Patagonie.



Deer mouse




Cotton rat



Rice rat


Principaux rongeurs infectés par des Hantavirus aux USA

responsible for thousands of Eurasian cases annually. Serologic evidence for infection with Seoul-like hantaviruses has been found in rodents in major cities of the United States, and this virus was recently implicated in human cases of HFRS in Baltimore. One report has also associated Seoul virus with chronic renal disease. A mild form of HFRS, caused by Puumala virus, is responsible for nephropathia epidemica in Scandinavia, with an estimated mortality rate of 1% to 3%.

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Characteristics of Some Known Hantaviruses

Hantaviruses	Geographic Region	Reservoir	Pathology	Mortality
Hantaan	Asia	Field mouse	Renal	5-15%
Seoul	Worldwide	Domestic rat	Renal	1%
Puumala	Northern Europe	Bank vole	Renal	1%
Prospect Hill	United States	Meadow vole	No known human disease	N/A
Sin Nombre	North America	Deer mouse	Pulmonary	50%

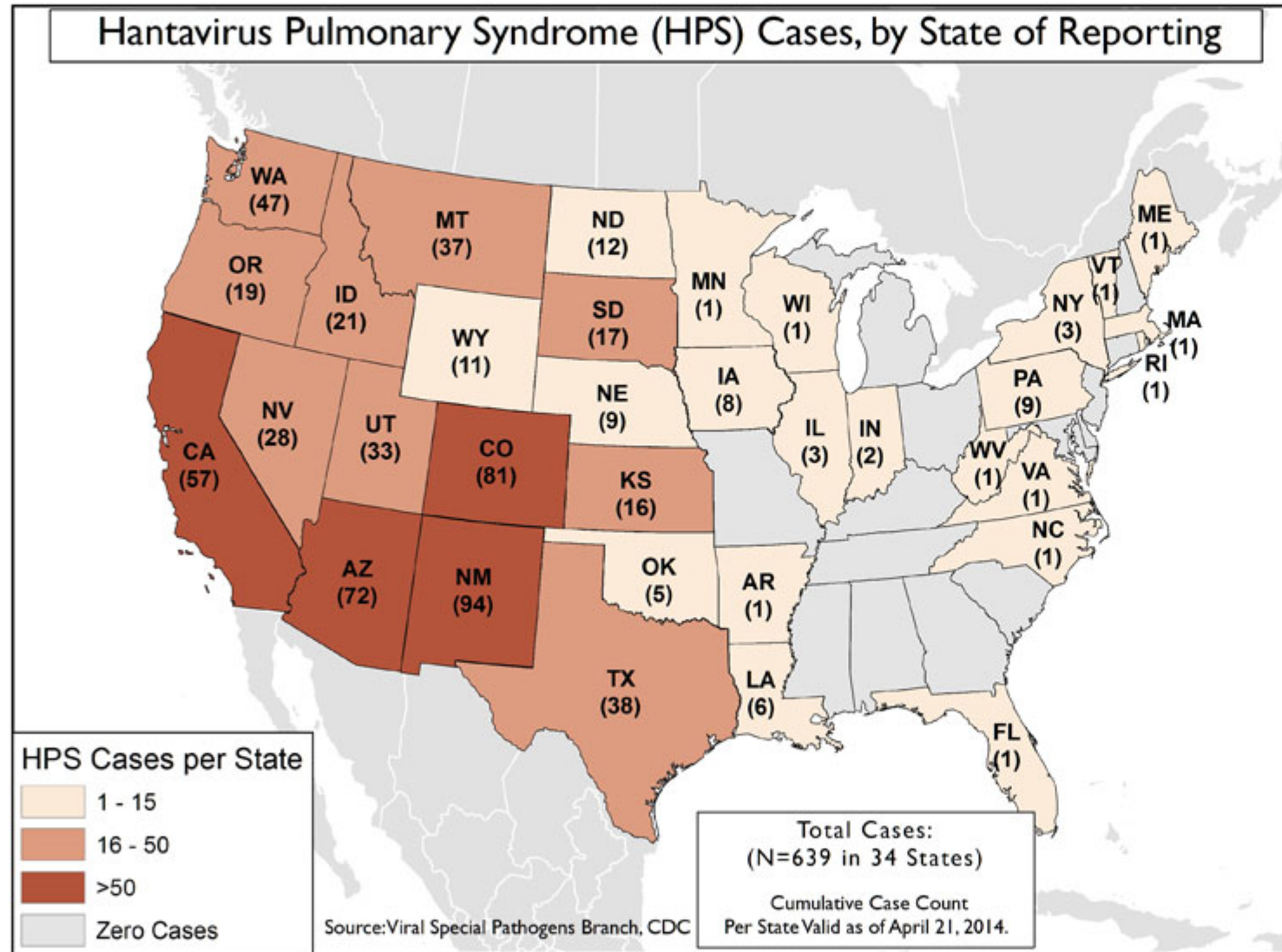
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Comparison of HFRS and HPS

Feature	HFRS	HPS
Major target organ	Kidney	Lung
First phase	Febrile	Febrile "prodrome"
Second phase	Shock	Shock, pulmonary edema
Evolution	Oliguria, diureses, convalescence	Diureses, convalescence
Mortality	1-15%	50%

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U.S. HPS Cases, by Reporting State



Total Cases: 639 (Cumulative case count per state valid as of April 21, 2014)*



Tracking a Mystery Disease: The Detailed Story of Hantavirus Pulmonary Syndrome (HPS)

The "First" Outbreak

In May 1993, an outbreak of an unexplained pulmonary illness occurred in the southwestern United States, in an area shared by Arizona, New Mexico, Colorado and Utah known as "The Four Corners". A young, physically fit Navajo man suffering from shortness of breath was rushed to a hospital in New Mexico and died very rapidly.

While reviewing the results of the case, medical personnel discovered that the young man's fiancée had died a few days before after showing similar symptoms, a piece of information that proved key to discovering the disease. As Dr. James Cheek of the Indian Health Service (IHS) noted, "I think if it hadn't been for that initial pair of people that became sick within a week of each other, we never would have discovered the illness at all".



An investigation combing the entire Four Corners region was launched by the New Mexico Office of Medical Investigations (OMI) to find any other people who had a similar case history. Within a few hours, Dr. Bruce Tempest of IHS, working with OMI, had located five young, healthy people who had all died after acute respiratory failure.

A series of laboratory tests had failed to identify any of the deaths as caused by a known disease, such as bubonic plague. At this point, the CDC Special Pathogens Branch was notified. CDC, the state health departments of New Mexico, Colorado and Utah, the Indian Health Service, the Navajo Nation, and the University of New Mexico all joined together to confront the outbreak.



During the next few weeks, as additional cases of the disease were reported in the Four Corners area, physicians and other scientific experts worked intensively to narrow down the list of possible causes. The particular mixture of symptoms and clinical findings pointed researchers away from possible causes, such as exposure to a herbicide or a new type of influenza, and toward some type of virus. Samples of tissue from patients who had gotten the disease were sent to CDC for

On this Page

- [The "First" Outbreak](#)
- [Researchers Launch Investigations to Pin Down the Carrier of the New Virus](#)
- [HPS Not Really a New Disease](#)
- [Why Did the Outbreak Occur in the Four Corners Area?](#)
- [Person-to-Person Spread of HPS Decided Unlikely](#)
- [HPS Since the First Outbreak](#)
- [References](#)





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Contact Us:

 Centers for Disease Control and Prevention
Viral Special Pathogens Branch
1600 Clifton Rd
Atlanta, GA 30333

 Hantavirus Hotline
(877) 232-3322
(404) 639-1510

 800-CDC-INFO
(800-232-4636)
TTY: (888) 232-6348

[Contact CDC-INFO](#)

 [About VSPB \(Viral Special Pathogens Branch\)](#)



Sin Nombre
New York
Bayou
Black creek

Choclo

Andes
Laguna Negra
Araraquara

BRAZIL

NORTH PACIFIC OCEAN

NORTH ATLANTIC OCEAN

UNITED STATES

MEXICO

THE BAHAMAS

CUBA

JAMAICA

HAITI

DOMINICAN REPUBLIC

GUATEMALA

HONDURAS

EL SALVADOR

NICARAGUA

COSTA RICA

PANAMA

VENEZUELA

GUYANA

SURINAME

COLOMBIA

ECUADOR

PERU

BOLIVIA

PARAGUAY

(23°27')

Tropic of Capricorn (23°27')

Gulf of Mexico

Caribbean Sea

AZORES (PORT.)

CAPE VERDE
Praia

PENEDES DE SÃO PEDRO E SÃO PAULO (BRAZIL)

ARQUIPÉLAGO DE FERNANDO DE NORONHA (BRAZIL)

Martin Vaz (BRAZIL)

Adamstown Pitcairn Islands (U.K.)

Easter Island (CHILE)

Isla Sala y Gómez (CHILE)

Isla San Félix (CHILE)

Isla San Ambrosio (CHILE)

Anofagasta

San Miguel de Tucumán

Asunción

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Jornillo

Florianópolis

Santos

Rio de Janeiro

São Paulo

Campinas

Viçosa

Belo Horizonte

Uberlândia

Gotúnia

Brasília

Salvador

Maceió

Recife

Natal

Fortaleza

Belém

São Luís

Manaus

Pórtio Velho

La Paz

Sucre

Cochabamba

Santa Cruz

La Paz

Asunción

Curitiba

Jornillo

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Santos

Rio de Janeiro

São Paulo

Campinas

Viçosa

Belo Horizonte

Uberlândia

Gotúnia

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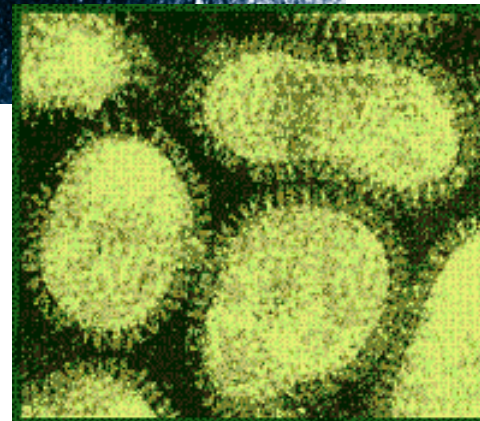
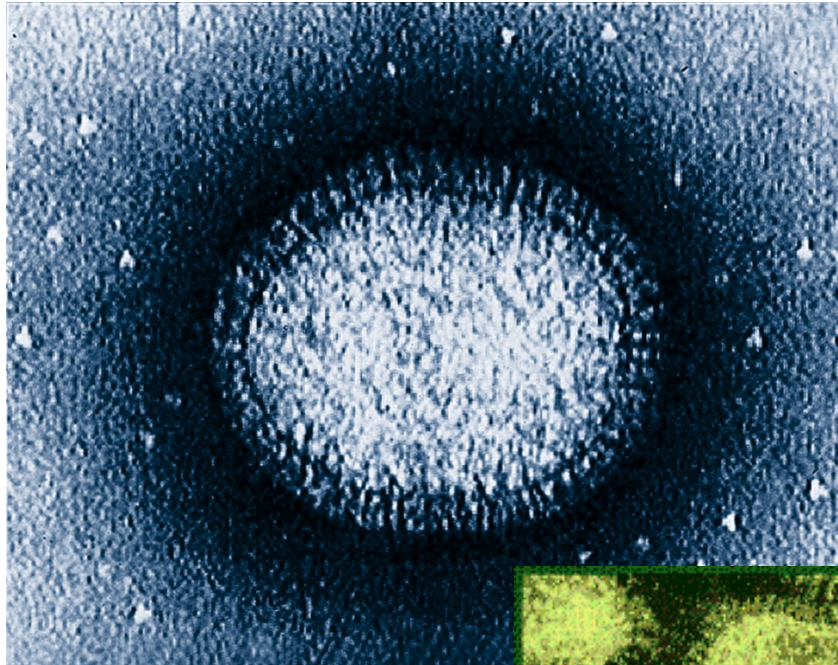
La Paz

Asunción

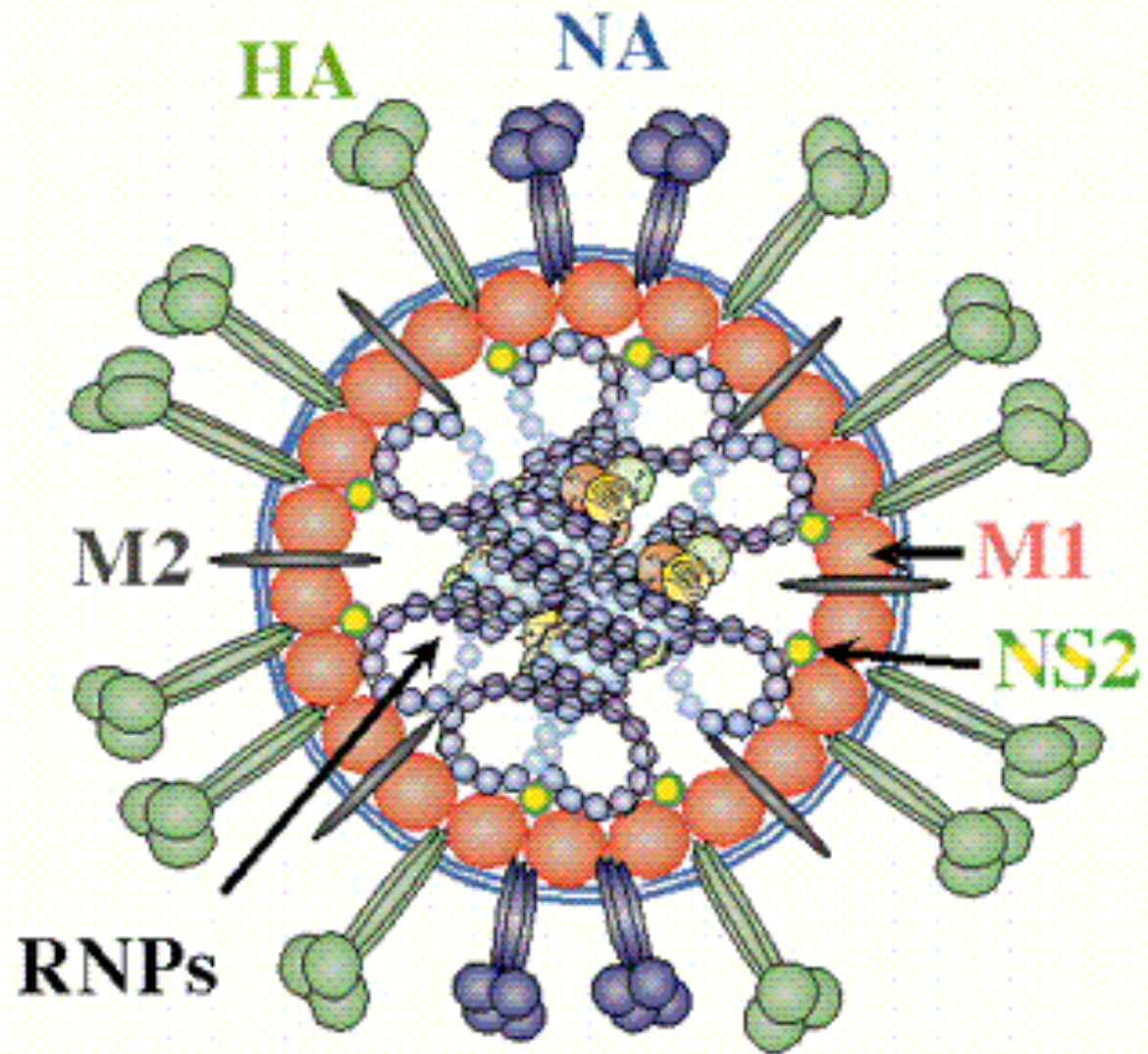
Curitiba

Jornillo

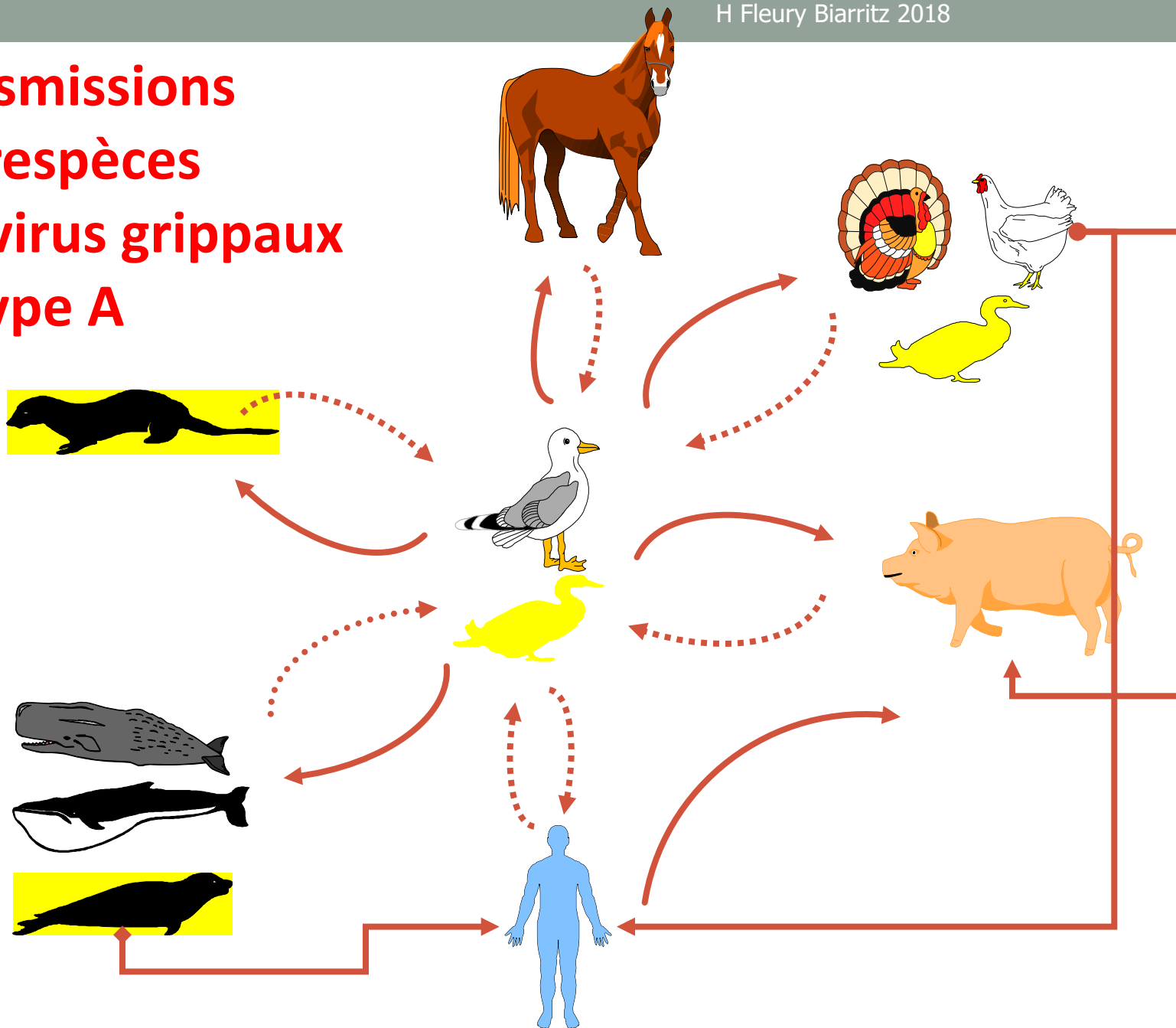
Le virus grippal



- 80 à 120 nm de diamètre
- Une nucléoprotéine virale à **ARN**
- Une enveloppe lipidique à la surface de laquelle sont ancrées **l'hémagglutinine et la neuraminidase.**



Transmissions interespèces des virus grippaux de type A



Virus grippaux A chez l'homme depuis 1918

- 1918 H1N1 (pandémique)
- 1957 Singapour H2N2 (pandémique)
- 1968 Hong Kong H3N2 (pandémique)
- 1997 H5N1 (non pandémique)
- 2009 H1N1pdm (pandémique)
- 2013 H7N9 (non pandémique)



Infectious virus in exhaled breath of symptomatic seasonal influenza cases from a college community

Jing Yan^{a,b}, Michael Grantham^{a,1}, Jovan Pantelic^{a,2}, P. Jacob Bueno de Mesquita^a, Barbara Albert^a, Fengjie Liu^{a,3}, Sheryl Ehrman^{b,4}, Donald K. Milton^{a,5}, and EMIT Consortium⁶

^aMaryland Institute for Applied Environmental Health, School of Public Health, University of Maryland, College Park, MD 20742; and ^bDepartment of Chemical and Biomolecular Engineering, Clark School of Engineering, University of Maryland, College Park, MD 20742

Edited by Peter Palese, Icahn School of Medicine at Mount Sinai, New York, NY, and approved December 15, 2017 (received for review September 19, 2017)

Little is known about the amount and infectiousness of influenza virus shed into exhaled breath. This contributes to uncertainty about the importance of airborne influenza transmission. We screened 355 symptomatic volunteers with acute respiratory illness and report 142 cases with confirmed influenza infection who provided 218 paired nasopharyngeal (NP) and 30-minute breath samples (coarse $>5\text{-}\mu\text{m}$ and fine $\leq 5\text{-}\mu\text{m}$ fractions) on days 1–3 after symptom onset. We assessed viral RNA copy number for all samples and cultured NP swabs and fine aerosols. We recovered infectious virus from 52 (39%) of the fine aerosols and 150 (89%) of the NP swabs with valid cultures. The geometric mean RNA copy numbers were $3.8 \times 10^4/30\text{-minutes}$ fine-, $1.2 \times 10^4/30\text{-minutes}$ coarse-aerosol sample, and 8.2×10^8 per NP swab. Fine- and coarse-aerosol viral RNA were positively associated with body mass index and number of coughs and negatively associated with increasing days since symptom onset in adjusted models. Fine-aerosol viral RNA was also positively associated with having influenza vaccination for both the current and prior season. NP swab viral RNA was positively associated with upper respiratory symptoms and negatively associated with age but was not significantly associated with fine- or coarse-aerosol viral RNA or their predictors. Sneezing was rare, and sneezing and coughing were not necessary for infectious aerosol generation. Our observations suggest that influenza infection in the upper and lower airways are compartmentalized and independent.

influenza virus | aerosol | airborne infection | vaccination effects | viral shedding

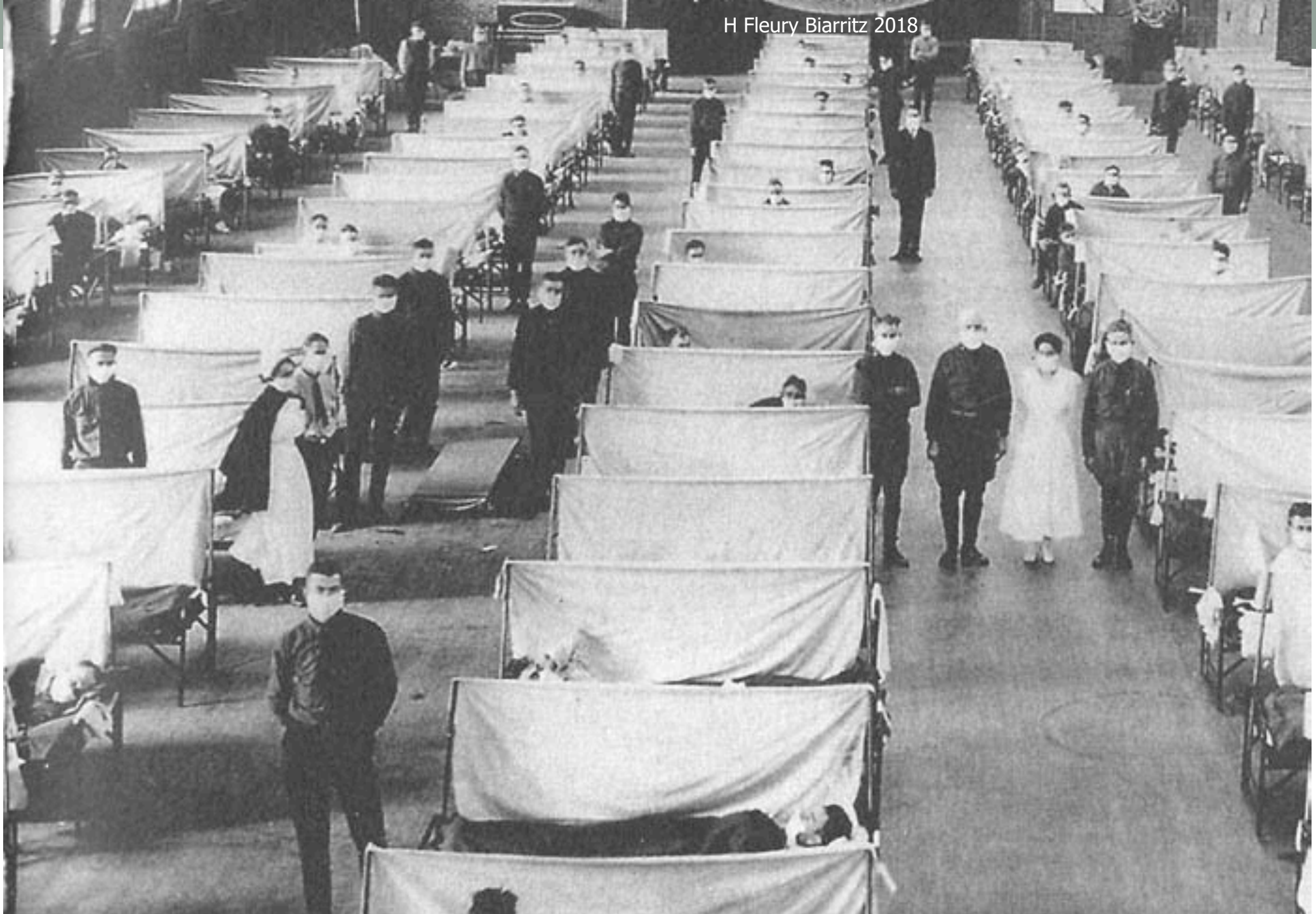
gaps by characterizing influenza virus in exhaled breath from community-acquired influenza cases during natural breathing, prompted speech, coughing, and sneezing, and assess the infectivity of naturally occurring influenza aerosols.

Results

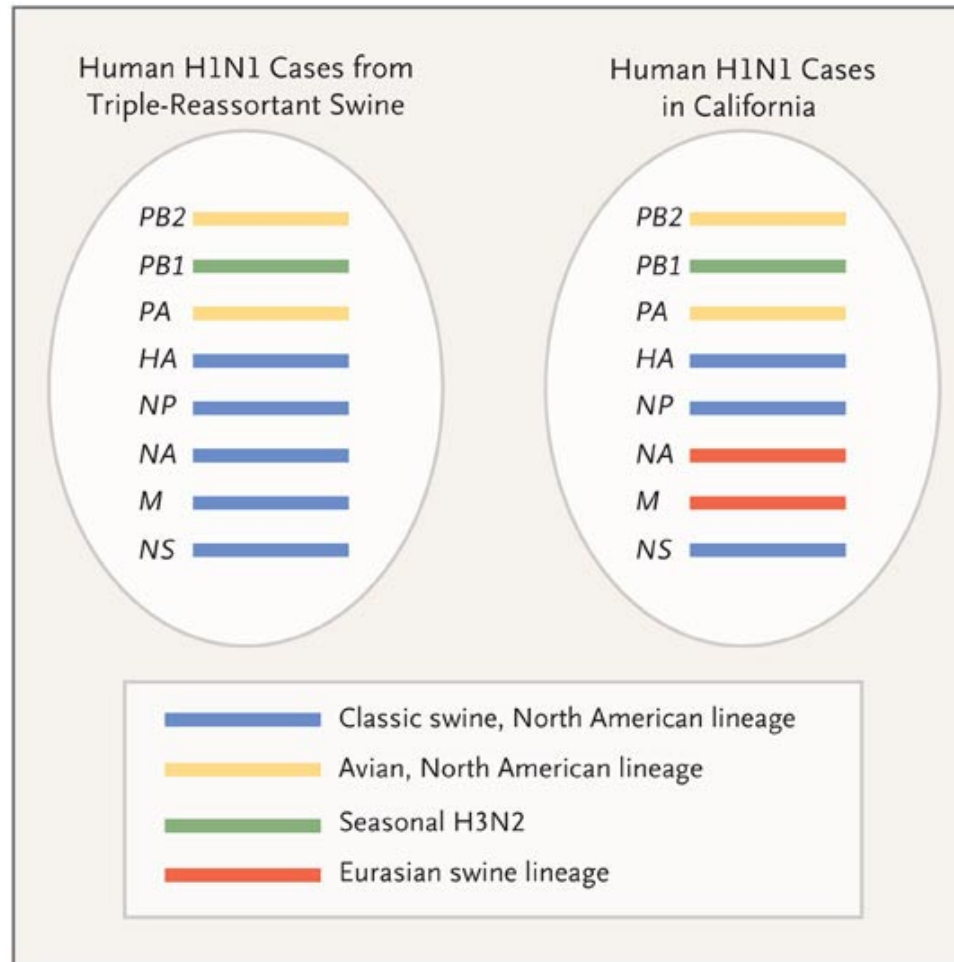
We screened 355 volunteers with acute respiratory illness; the 178 volunteers who met enrollment criteria provided 278 visits for sample collection. We confirmed influenza infection in 156 (88%) of the enrolled participants using qRT-PCR; 152 had at least one positive nasopharyngeal (NP) swab and 4 (3%) were confirmed based on positive aerosol samples alone. NP swab analysis was positive for 8 (33%) of 24 randomly selected volunteers from among the 177 screened who did not meet enrollment criteria; thus, sensitivity and specificity of our enrollment criteria, during the 2012–2013 season, were $\sim 73\%$ [95% confidence interval (CI) 62–84%] and 84% (95% CI 80–88%), respectively. In the reported analyses, we excluded 8 visits made on the day of symptom onset, 10 made >3 d after onset, 7 with missing data for cough, and 3 with

Significance

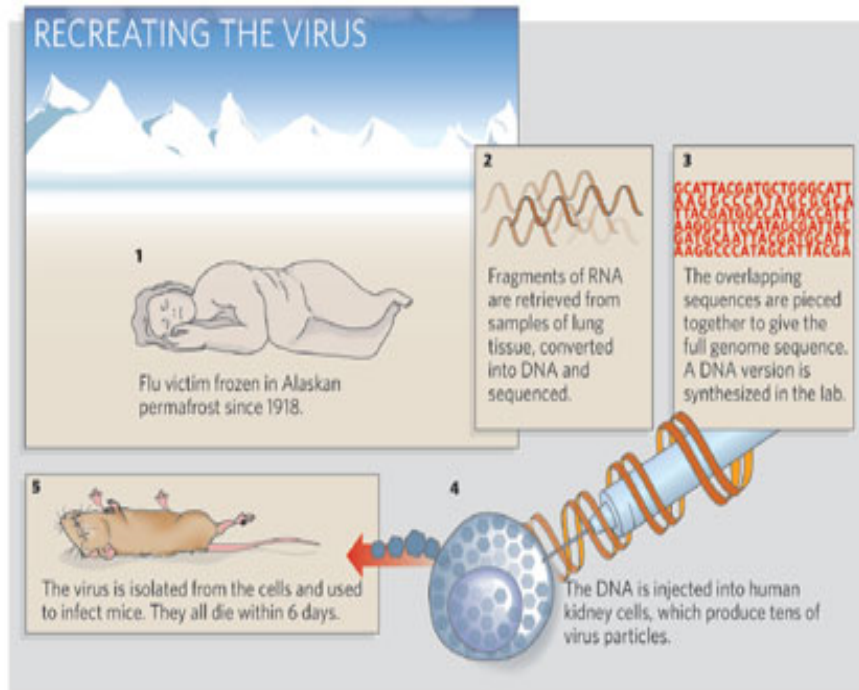
Lack of human data on influenza virus aerosol shedding fuels debate over the importance of airborne transmission. We provide overwhelming evidence that humans generate infectious aerosols and quantitative data to improve mathematical models of transmission and public health interventions. We show that sneezing is rare and not important for—and that coughing is not required for—influenza virus aerosolization.







- **Infections humaines à virus grippaux aviaires**
- **H5N1** (1^{er} cas de transmission à l'homme en 1997 à Hong Kong) (*oiseaux domestiques malades*)
- H7N7 en Hollande (2004 ; pathologie limitée à conjonctivite)
- **H7N9** (*oiseaux domestiques non malades*)
- Grippe 1918 et faisan de Washington DC ?



Jeffery Taubenberger of the Armed Forces Institute of Pathology in Rockville, Maryland, is the lead author of the sequencing study.

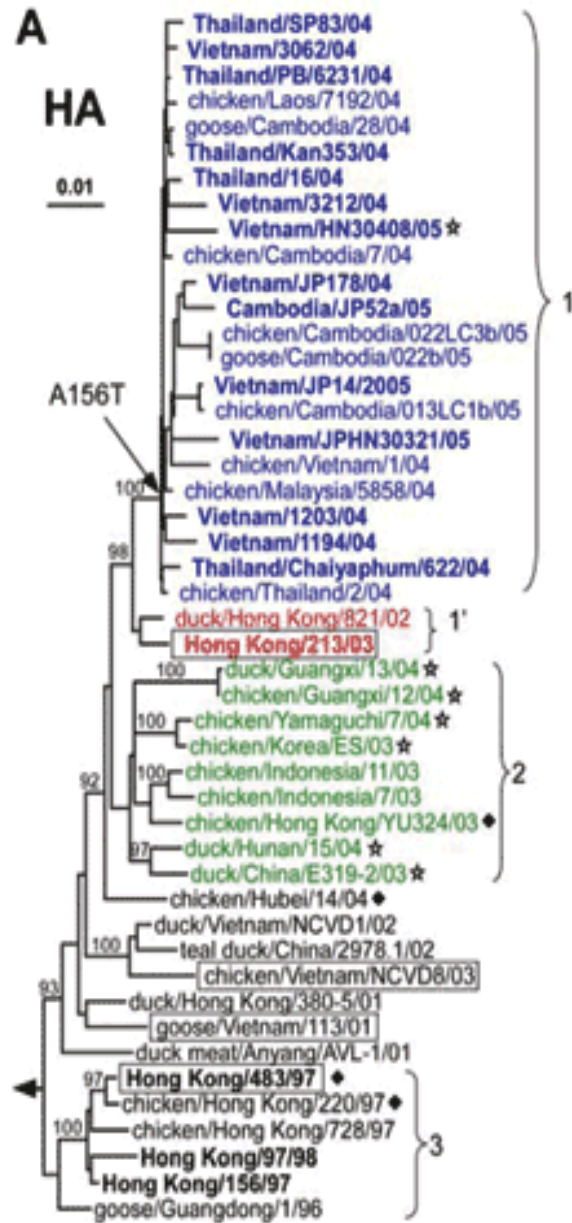
The full sequence is strong evidence that the 1918 flu virus is derived wholly from an ancestor that originally infected birds

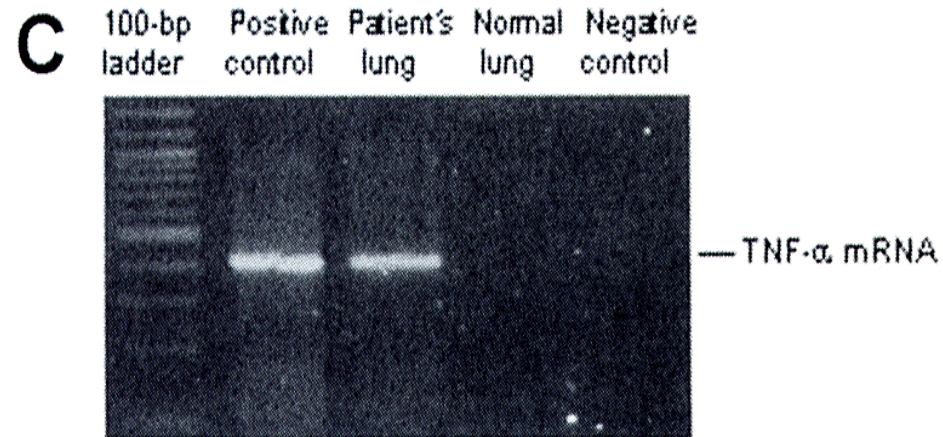
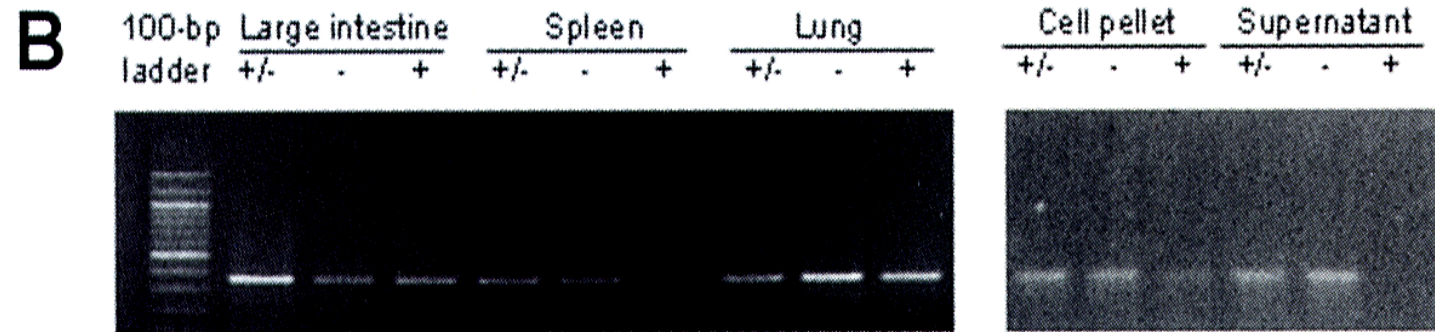
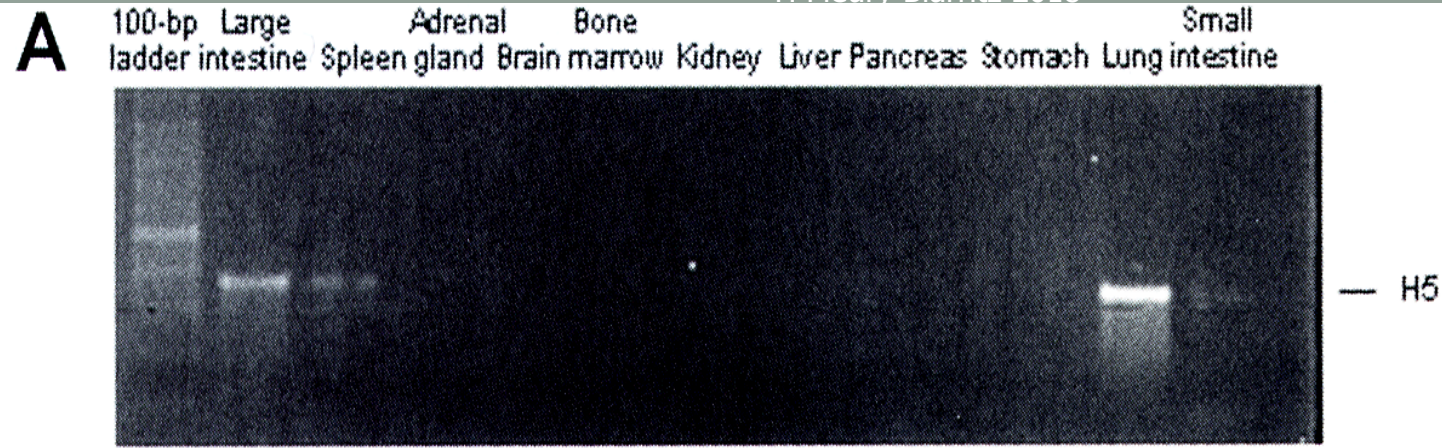
- Grippe aviaire H5N1 sévit en Asie du Sud Est depuis 2003/2004 ; épizootie : Cambodge, Chine, Corée du sud, Indonésie, Japon, Laos, Malaisie, Thaïlande, Vietnam
- Russie (Sibérie) touchée dans la deuxième partie de 2005
- Oiseaux infectés : domestiques (poulets...) et sauvages (canards, oies...)

- Transmission possible de l'oiseau infecté à l'homme
- Transmission inter-humaine démontrée en 2004 en Thaïlande mais peu efficace
- Clinique : à noter une incubation plus longue que celle de la grippe saisonnière ; 2 à 5 jours pour H5N1 avec un maximum à 17 jours; 1 à 10 jours pour H7N9 avec une moyenne à 5 jours

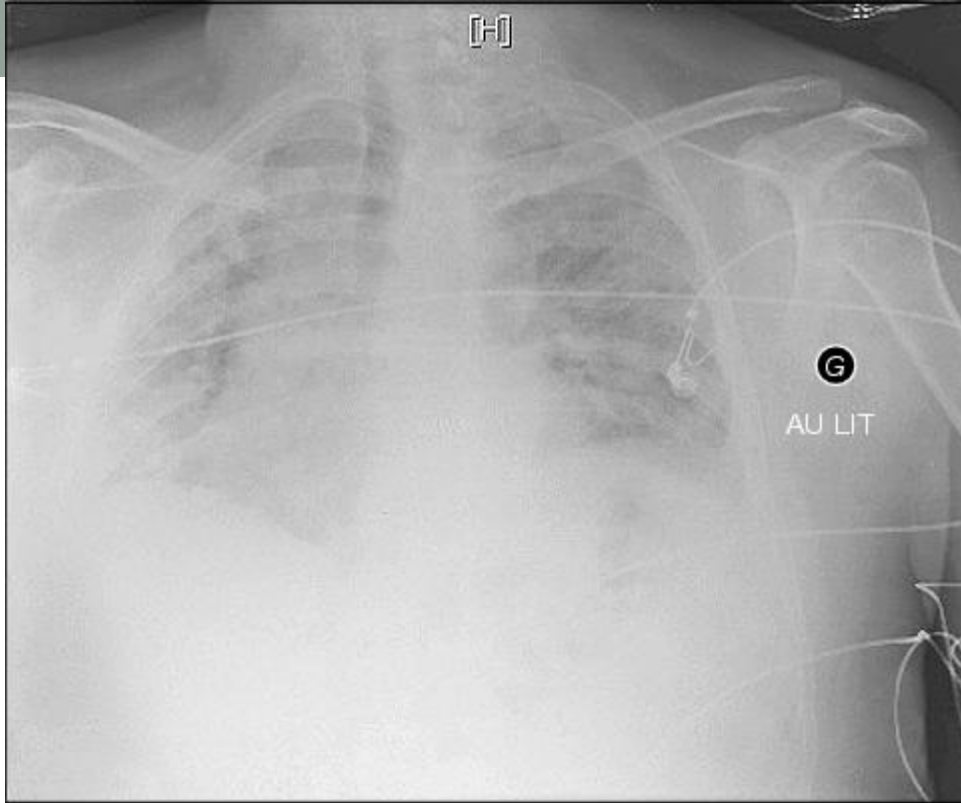
- Réplication chez l'homme : poumon et intestin
- Virus transmissible expérimentalement à la souris et aux félins (chats)
- Evènement à craindre : recombinaison entre H5N1 et un virus humain A chez un humain co-infecté ou un porc hôte intermédiaire infecté par virus A humain + virus A aviaire
- Conduite à tenir chez l'animal : abattage des animaux infectés ou vaccination



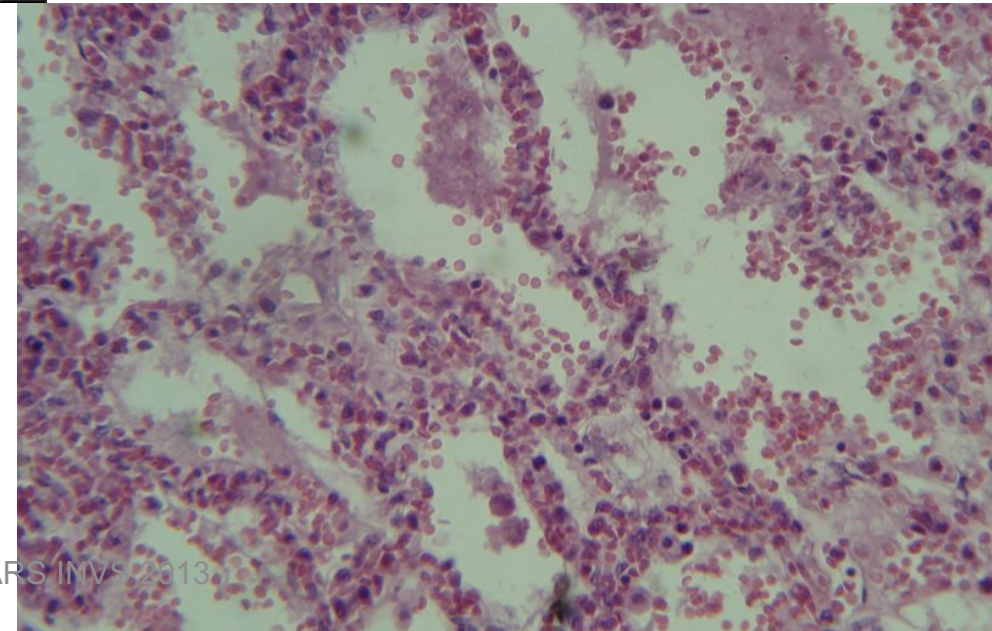




H5N1



ARDS



Les inhibiteurs de neuraminidase

Oseltamivir (Tamiflu ®)

- **Forme orale**
- **Gélules et suspension**
- **Diffusion systémique**

- **Traitement curatif adulte**
- **Traitement curatif enfant >1**
- **Traitement prophylactique adultes**
- **Tolérance : troubles digestifs modérés et transitoires**

Zanamivir(Relenza ®)

- **Poudre pour inhalation**
- **Diskalher**
- **Déposition principalement au niveau de l'oropharynx**
- **Traitement curatif adulte**
- **Pas d'indication**

- **Pas d'indication**
- **Tolérance : rares bronchospasmes**

Action sur H5N1

Virus	Oseltamivir IC ₅₀ *
H1N1 (H274)†	0.69
H1N1 (Y274)†	85.92
H3N2 (R292)‡	1.99
H3N2 (K292)‡	1,600.00
Hong Kong/483/97	4.86
Hong Kong/213/03	5.07
Vietnam /1194/04	2.49
Vietnam/1203/04	7.68
Chicken/VN/NCVD1/04	5.87
Chicken/VN/NCVD8/03	9.90

Cumulative number of confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2018

Country	2003-2009*		2010-2014**		2015		2016		2017		2018		Total	
	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths
Azerbaijan	8	5	0	0	0	0	0	0	0	0	0	0	8	5
Bangladesh	1	0	6	1	1	0	0	0	0	0	0	0	8	1
Cambodia	9	7	47	30	0	0	0	0	0	0	0	0	56	37
Canada	0	0	1	1	0	0	0	0	0	0	0	0	1	1
China	38	25	9	5	6	1	0	0	0	0	0	0	53	31
Djibouti	1	0	0	0	0	0	0	0	0	0	0	0	1	0
Egypt	90	27	120	50	136	39	10	3	3	1	0	0	359	120
Indonesia	162	134	35	31	2	2	0	0	1	1	0	0	200	168
Iraq	3	2	0	0	0	0	0	0	0	0	0	0	3	2
Lao People's Democratic Republic	2	2	0	0	0	0	0	0	0	0	0	0	2	2
Myanmar	1	0	0	0	0	0	0	0	0	0	0	0	1	0
Nigeria	1	1	0	0	0	0	0	0	0	0	0	0	1	1
Pakistan	3	1	0	0	0	0	0	0	0	0	0	0	3	1
Thailand	25	17	0	0	0	0	0	0	0	0	0	0	25	17
Turkey	12	4	0	0	0	0	0	0	0	0	0	0	12	4
Viet Nam	112	57	15	7	0	0	0	0	0	0	0	0	127	64
Total	468	282	233	125	145	42	10	3	4	2	0	0	860	454

* 2003-2009 total figures. Breakdowns by year available on subsequent tables.

** 2010-2014 total figures. Breakdowns by year available on subsequent tables.

Total number of cases includes number of deaths.
WHO reports only laboratory cases.
All dates refer to onset of illness.

Source: WHO/CID, data in HQ as of 25 January 2018

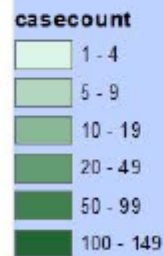


A(H7N9)

Areas reporting confirmed human cases for influenza A(H7N9) to WHO from 2013-06-01 *



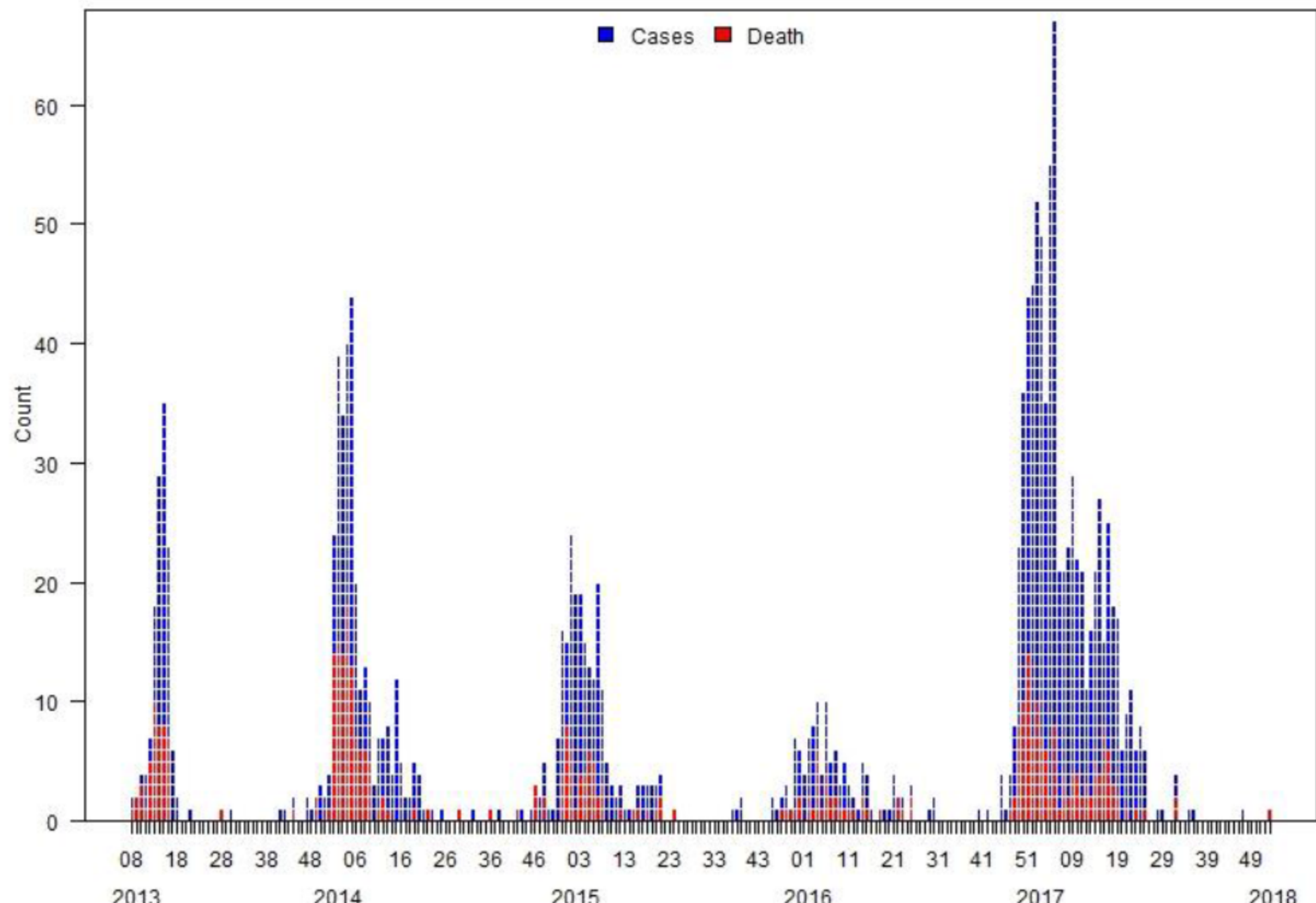
Number of cases by reporting area



*All dates refer to onset of illness
Data as of 14/07/2014
Source: WHO

The designations employed and the presentation of the material in this publication do not imply the endorsement of any view on the part of the World Health Organization concerning the legal status of any country, territory, city or area, with authorities, or concerning the delimitation of its frontiers or boundaries. Noted and dashed lines on maps represent approximate boundaries for which there may not yet be full agreement.
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- Highly Pathogenic Avian Influenza A(H7N9) Virus, Tennessee, USA, March 2017**
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Volume 23, Number 11—November 2017

Dispatch

Highly Pathogenic Avian Influenza A(H7N9) Virus, Tennessee, USA, March 2017

Dong-Hun Lee, Mia K. Torchetti, Mary Lea Killian, Yohannes Berhane, and David E. Swayne✉

Author affiliations: US Department of Agriculture, Athens, Georgia, USA (D.-H. Lee, D.E. Swayne); US Department of Agriculture, Ames, Iowa, USA (M.K. Torchetti, M.L. Killian); National Centre for Foreign Animal Disease, Winnipeg, Manitoba, Canada (Y. Berhane)

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Abstract

In March 2017, highly pathogenic avian influenza A(H7N9) was detected at 2 poultry farms in Tennessee, USA. Surveillance data and genetic analyses indicated multiple introductions of low pathogenicity avian influenza virus before mutation to high pathogenicity and interfarm transmission. Poultry surveillance should continue because low pathogenicity viruses circulate and spill over into commercial poultry.


In early March 2017, concurrent outbreaks of highly pathogenic avian influenza (HPAI) and low pathogenicity avian influenza (LPAI) A(H7N9) were occurring at poultry farms in Tennessee, USA. The first report of high loss due to death was received from a commercial broiler breeder facility in Lincoln County, Tennessee. The facility contained 74,000 chickens in 6 houses, but only 1 house was affected. Signs of disease included respiratory distress and increased death. Two days after disease onset, the number of dead birds increased from 50 to 500 within 24 hours, and oropharyngeal swab samples tested positive by real-time reverse transcription PCR (rRT-PCR) for the matrix and H7 genes at the C. E. Kord Animal Health Diagnostic Laboratory (Nashville, Tennessee). Samples were forwarded to the National Veterinary Services Laboratories of the US Department of Agriculture

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- Tables**
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- [Technical Appendix 1](#)

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H7N9 AVIAN FLU

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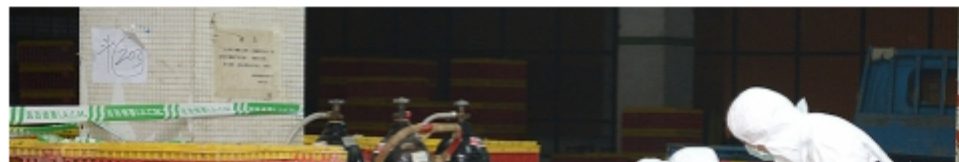
Sichuan man dies in first human case of H5N6 bird flu

Death of 49-year-old after contact with infected dead poultry an isolated incident, say experts

[Zhuang Pinghui and Lo Wei](#)

PUBLISHED : Tuesday, 06 May, 2014, 10:02pm

UPDATED : Wednesday, 07 May, 2014, 8:27am



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Recombinant Work with Human H2N2, 1918 H1N1 and Highly Pathogenic Avian H5N1 Influenza Viruses



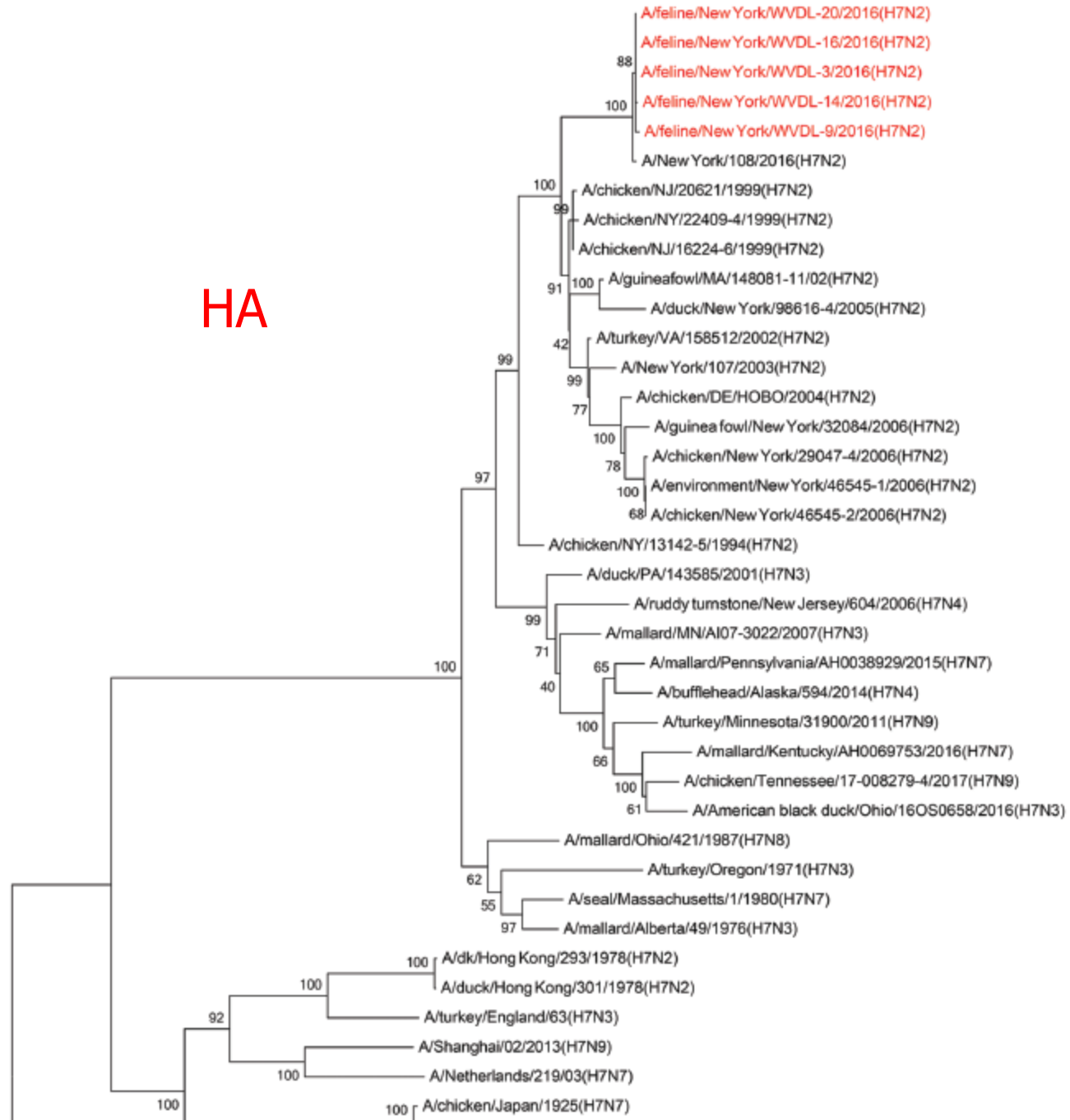
December 3, 2008



Characterization of a Feline Influenza A(H7N2) Virus

Masato Hatta,¹Gongxun Zhong,¹Yuwei Gao,¹Noriko Nakajima,¹Shufang Fan,¹Shiho Chiba, Kathleen M. Deering, Mutsumi Ito, Masaki Imai, Maki Kiso, Sumiho Nakatsu, Tiago J. Lopes, Andrew J. Thompson, Ryan McBride, David L. Suarez, Catherine A. Macken, Shigeo Sugita, Gabriele Neumann, Hideki Hasegawa, James C. Paulson, Kathy L. Toohy-Kurth, Yoshihiro Kawaoka

HA



American
avian

Eurasian
avian

Co-circulation of Influenza A H5, H7, and H9 Viruses and Co-infected Poultry in Live Bird Markets, Cambodia

Paul F. Horwood, Srey Viseth Horm,
Annika Suttie, Sopheak Thet, Phalla Y,
Sareth Rith, San Sorn, Davun Holl, Sothyra Tum,
Sowath Ly, Erik A. Karlsson, Arnaud Tarantola,
Philippe Dussart

Longitudinal surveillance of 2 live bird markets in Cambodia revealed year-round, high co-circulation of H5, H7, and H9 influenza viruses. We detected influenza A viruses in 51.3% of ducks and 39.6% of chickens, and co-infections, mainly by H5 and H9 viruses, in 0.8% of ducks and 4.5% of chickens.

A large variety of avian influenza viruses (AIVs) circulate in live bird markets (LBMs) in countries where highly pathogenic influenza A(H5N1) viruses are endemic (1). The low pathogenicity AIVs A(H7N9) and A(H9N2) are also potential threats for global public health, related to the ability of these viruses to cause human infections in people in close contact with infected poultry (2). The segmented genomes of influenza A viruses indicate that co-infections can result in progeny with mixed genomes. Therefore, co-circulation of a large diversity of AIVs is a risk for emergence of novel reassortant viruses affecting

LBMs have been established as critical for persistence, amplification, and dissemination of AIVs (6).

Surveillance studies in LBMs in Cambodia have revealed some of the highest AIV detection rates in poultry globally (1,7). As of November 2017, a total of 56 human cases (including 37 deaths) and 49 poultry outbreaks of influenza A(H5N1) have been recorded in Cambodia (8–10). However, little is known about other AIV subtypes at risk for pandemic emergence, mainly H7 and H9. We investigated the circulation of potentially highly pathogenic AIV subtypes (H5, H7, and H9), that have known public health risks in Cambodia LBMs during 2015.

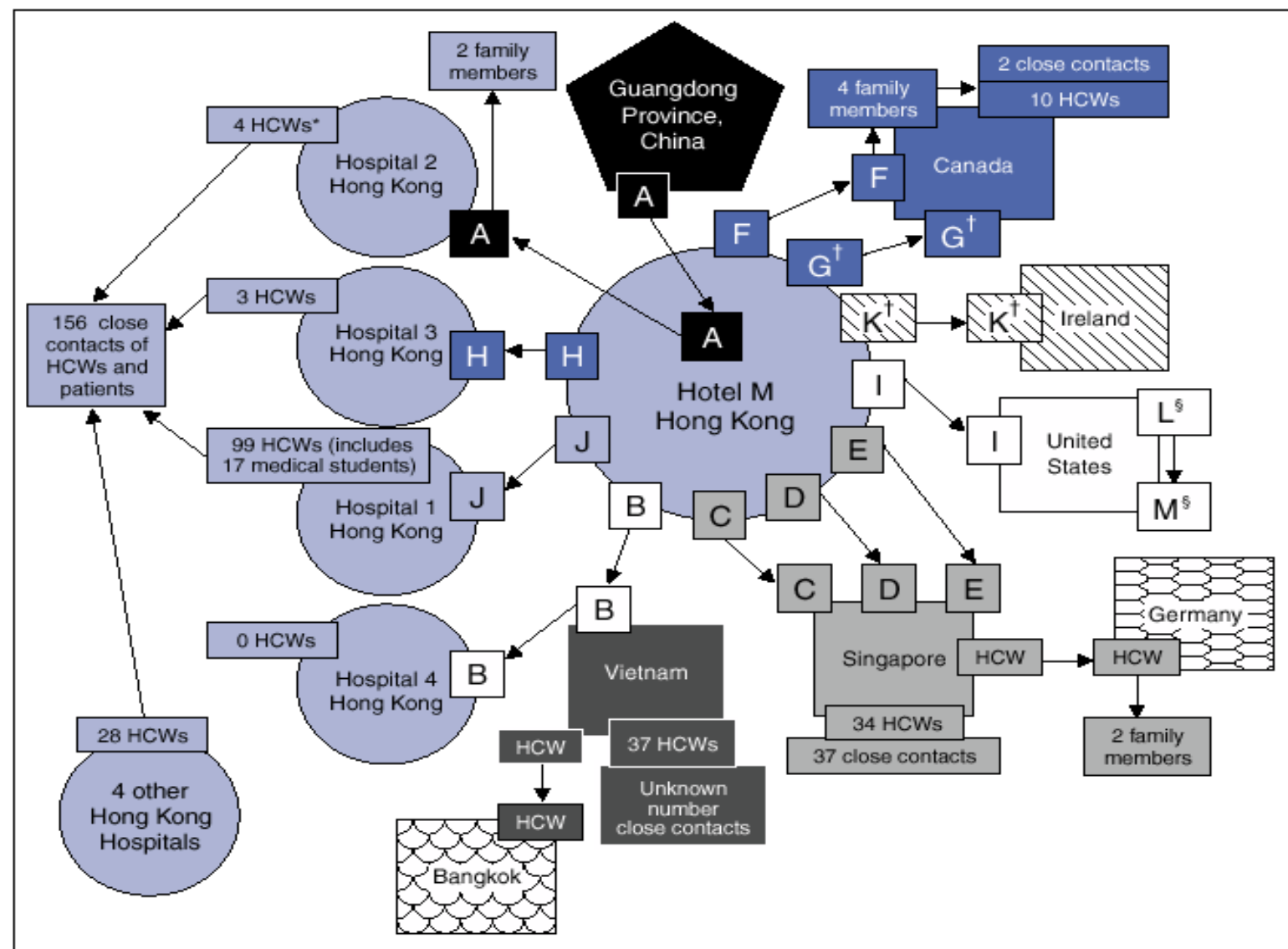
The Study

We administered a longitudinal survey in 2 LBMs in the highly populated southeast region of Cambodia during February–December (weeks 7–53), 2015. Market 1 is a large LBM in central Phnom Penh that serves as a hub for poultry commerce in the southeast region. Market 2 is a smaller provincial market in Takeo Province. Weekly, we collected pooled oropharyngeal and cloacal swabs from 4 chickens and 4 ducks, randomly selected, in each LBM. We also collected 50-mL samples of carcass wash water (CWW; large buckets of water that are used to wash freshly

- **SARS**
- Epidémie de pneumonie atypique signalée en Chine, dans le province de Guangdong (Canton) en novembre 2002 (« Pneumonia causes panic in Guangdong province » BMJ, février 2003) . Grippe aviaire évoquée .
- Rapidement, il devient évident qu'il s'agit d'une nouvelle maladie : syndrome respiratoire aigu sévère (SRAS) , severe acute respiratory syndrome (SARS) .

- La maladie touche au début principalement des soignants (HCWs) et des sujets contacts proches (parents).
- Les deux sites d'alerte sont Hanoi (Vietnam)(1er cas le 26 février à l'hôpital Français) et Hong Kong qui sont d'ailleurs reliés par un patient commun (ce patient quitte Hanoi et décède à HK le 12 mars) ; HK a d'ailleurs le premier cas de SARS rétrospectif = médecin venant de Canton , ayant séjourné à l'hôtel Metropole et hospitalisé à HK le 22 février .

FIGURE 1. Chain of transmission among guests at Hotel M — Hong Kong, 2003



* Health-care workers.

† All guests except G and K stayed on the 9th floor of the hotel. Guest G stayed on the 14th floor, and Guest K stayed on the 11th floor.

§ Guests L and M (spouses) were not at Hotel M during the same time as index Guest A but were at the hotel during the same times as Guests G, H, and I, who were ill during this period.

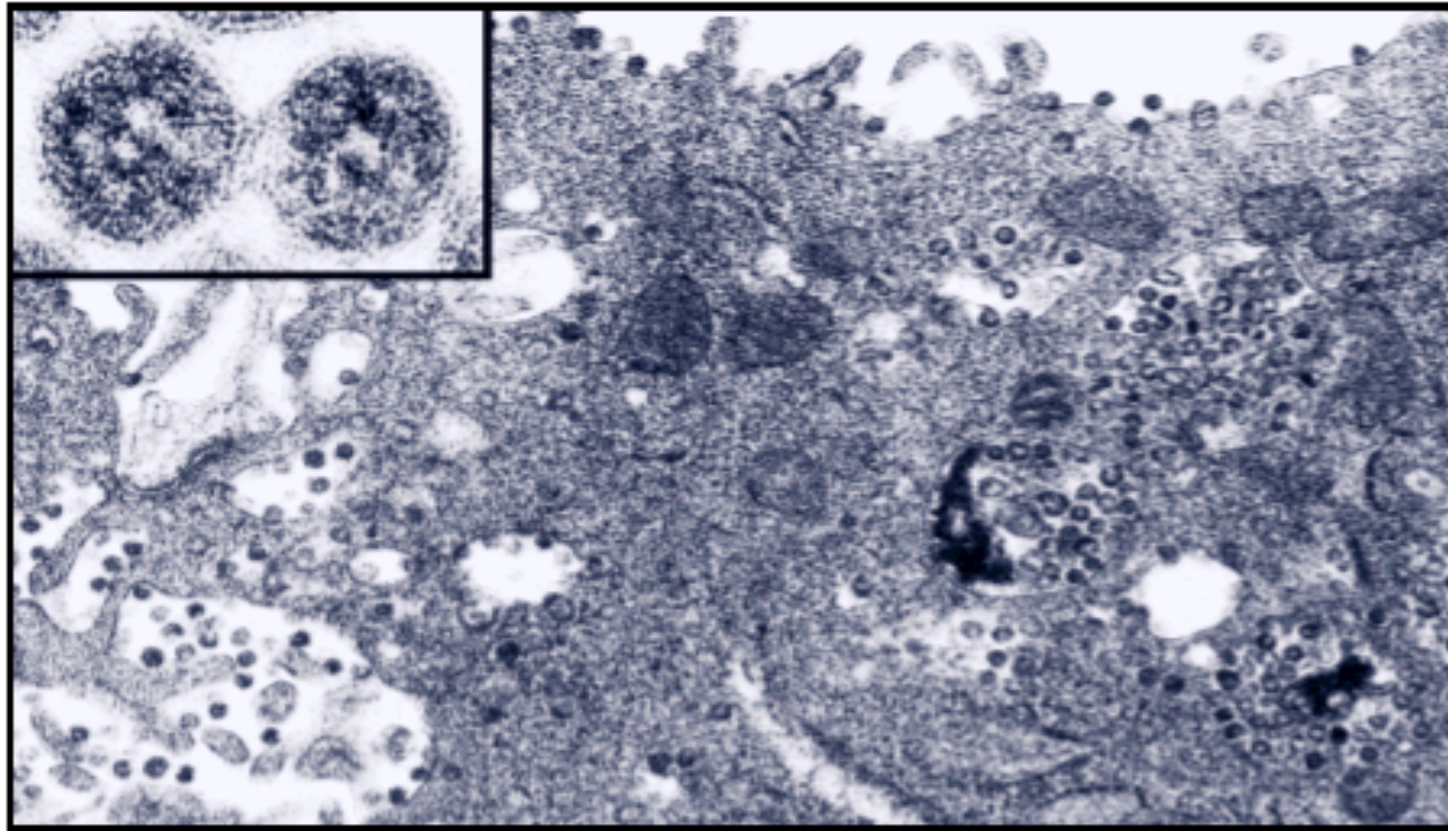
- Deux épicentres à HK : Prince of Wales Hospital (PWH) et groupe d'immeubles « Amoy gardens »
- Très rapidement, le SARS est confirmé et/ou détecté en Chine continentale (Canton, Shanxi, Pékin), au Vietnam, au Canada (Toronto), à Singapour, en Thaïlande, à Taiwan

- Clinique : incubation de 3 à 10j, fièvre, frissons, toux non productive, myalgies, céphalées, dyspnée, signes radiologiques de pneumonie
- Biologie : hypoxie, anémie, lymphopénie, thrombocytopénie , augmentation LDH
- Cas suspect (définition internationale) : fièvre au dessus de 38°C + un ou plusieurs signes respiratoires (toux, dyspnée, radiologie) + voyage dans les 10 jours dans une zone géographique de SARS ou contact avec personne atteinte de SARS ou revenant d'une zone de SARS

- Evolution et traitement
- 30% des patients reçoivent de l'oxygène
- 10% ne développent pas d'infiltrat pulmonaire
- Traitement associe antibiotique+Ribavirine+corticostéroïde
- La plupart des patients quittent l'hôpital à J14
- 20% ont une hospitalisation plus longue dont certains reçoivent une ventilation assistée
- Mortalité ayant évolué de 5 à 11% (nulle chez les moins de 8 ans et 50% chez les plus de 60 ans)

- Recherche étiologique : Influenza A et B, Parainfluenza 1, 2, et 3, Adenovirus, VRS et Metapneumovirus
- Mise en évidence de l'ARN d'un Coronavirus dans les sécrétions bronchiques et les prélèvements de poumon ; présence simultanée chez quelques patients d'un Metapneumovirus mais serait liée à un portage sans association étiologique

FIGURE 3. Thin section electron micrograph of infected Vero E6 cell, showing coronavirus particles within cytoplasmic membrane-bound vacuoles and the cisternae of the rough endoplasmic reticulum. Extracellular particles accumulate in large clusters, and are frequently seen lining the surface of the plasma membrane. Inset, higher magnification of coronavirus particles.

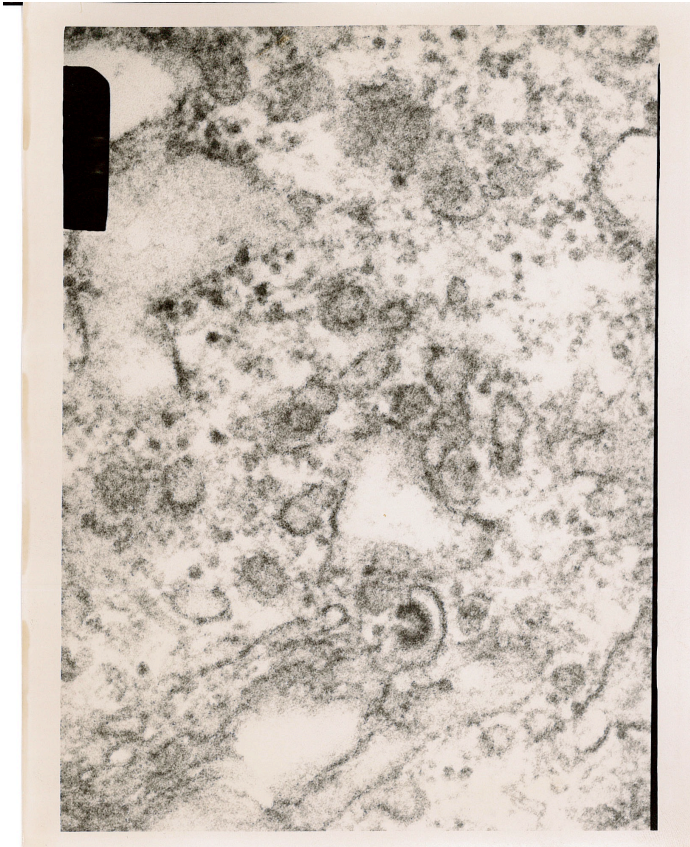
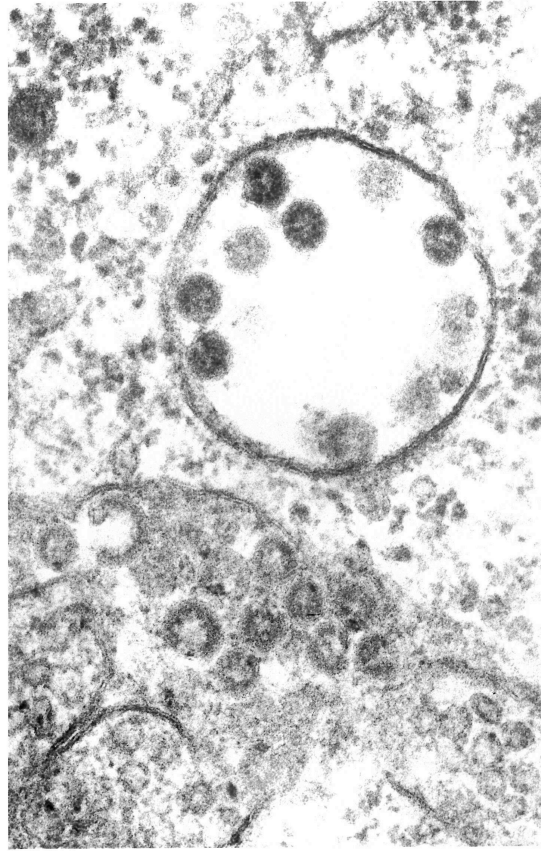


Photo/CDC.

[Neuropathol Appl Neurobiol.](#) 1980 May-Jun;6(3):165-79.

Further ultrastructural observations of virus morphogenesis and myelin pathology in JHM virus encephalomyelitis.

[Fleury HJ](#), [Sheppard RD](#), [Bomstein MB](#), [Raine CS](#)



- Coronavirus SARS (SARS-CoV)
- ARN de 30000 bases
- Présent dans sécrétions respiratoires, poumons, sang, selles
- Virus enveloppé de 80-90 nm de diamètre
- Différent des Coronavirus connus chez l'homme (dont HCoV-229E)
- 2 sous-types très proches (dont souche Urbani)

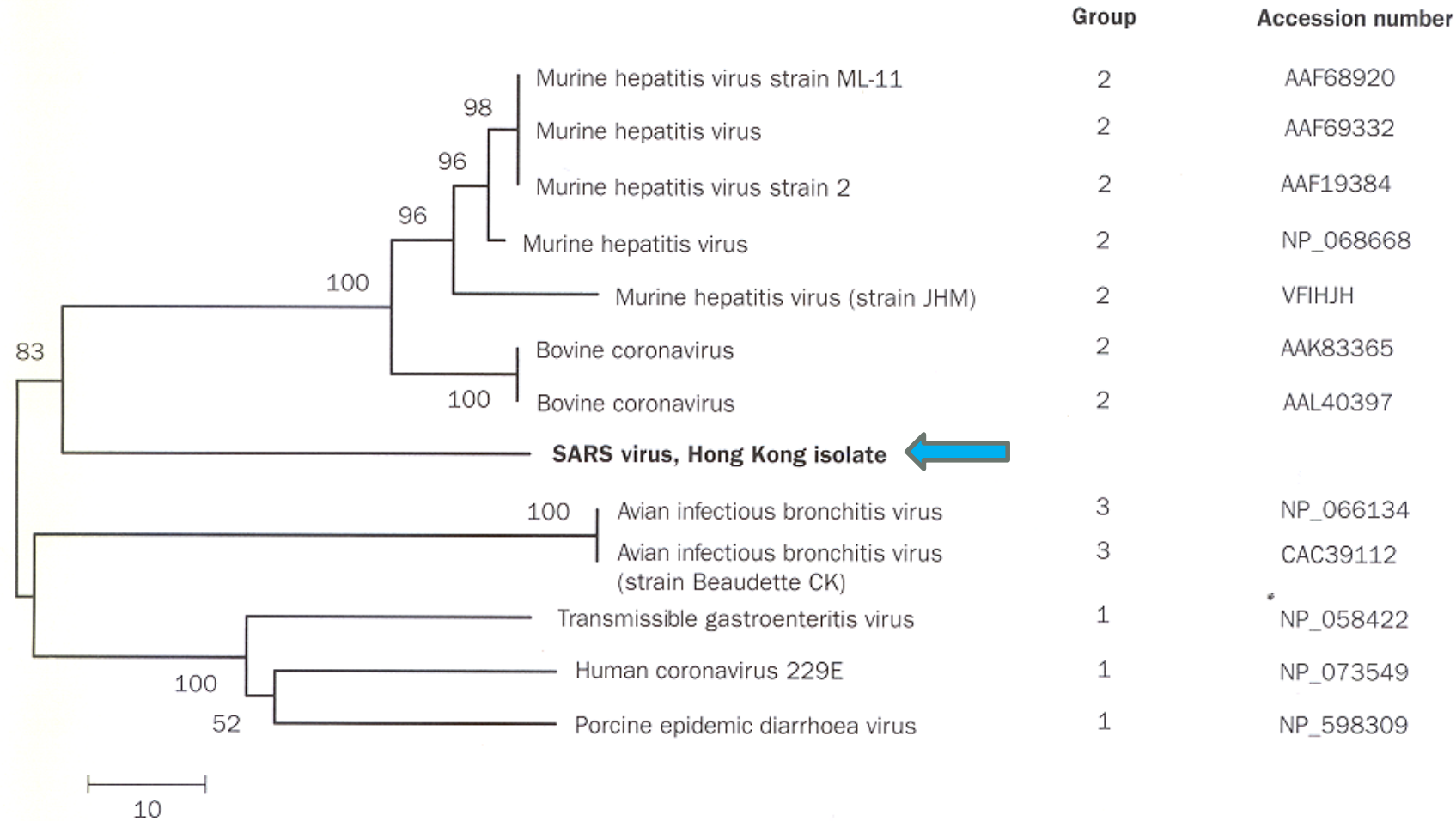


Figure 3: **Phylogenetic analysis of the partial protein sequence (215 aminoacids) of the coronavirus (SARS)**

GenBank accession number AY268070. Tree is constructed by neighbour-joining method. Horizontal-line distance represents number of sites at which the two sequences compared are different. Bootstrap values deduced from 500 replicates.

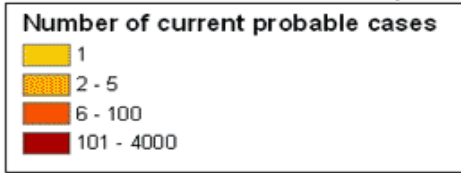
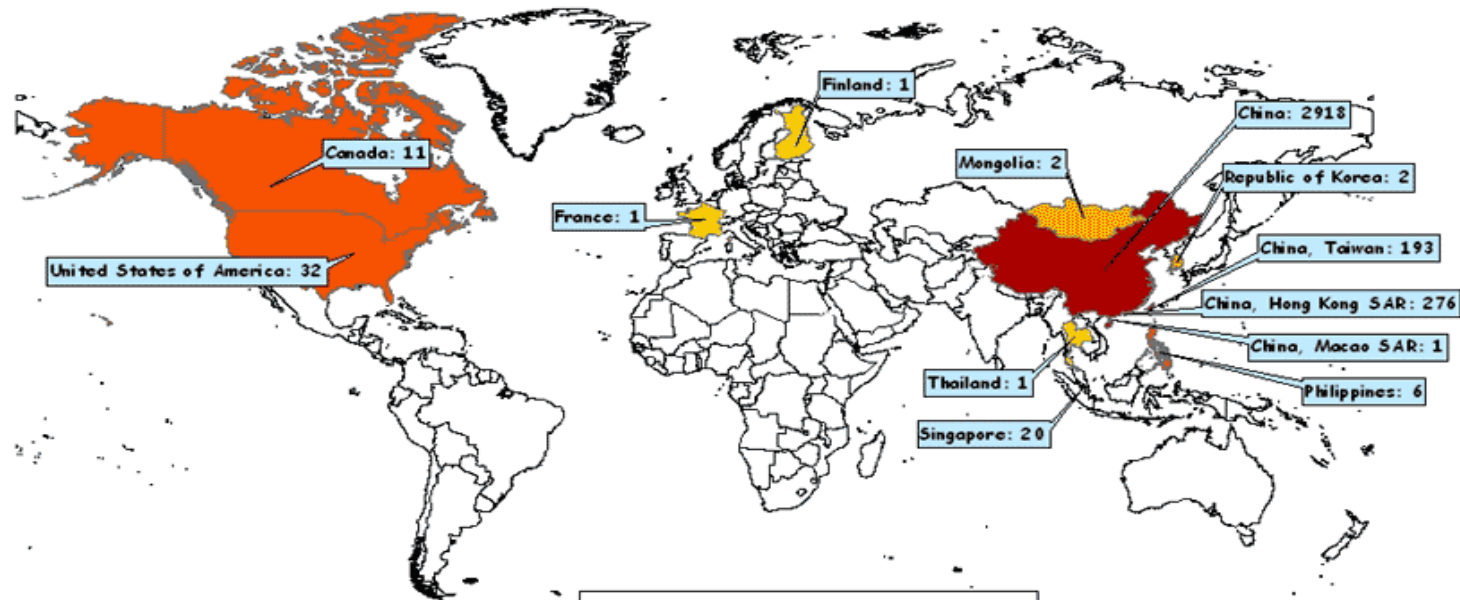
- Pousse en culture cellulaire (Vero) avec ECP en 2-4 jours
- Quantification dans les sécrétions bronchiques par PCR temps réel : 100 millions de copies d'ARN viral/ml ; en faveur de transmission aérienne (par gouttelettes) ; les masques protègent le personnel de l'infection dans les hopitaux (The Lancet , mai 2003).
- Transmission aérienne (directe interhumaine ; climatisation ?) mais aussi possible par les mains sales . Poignées de porte ? Boutons d'ascenseur ?



Block E of the Amoy Gardens residential complex is the focus of a major Hong Kong investigation.

- Poignées de porte testées par PCR à HK dans la résidence Amoy Gardens donnent un signal positif
- Virus résistant en milieu extérieur (pouvoir infectieux conservé pendant 24 heures sur surface inerte)
- Affiner les données sur la transmission et l'éventuel portage sain pour savoir si quarantaine+protection par masque+lavage des mains seront des mesures suffisantes pour réduire l'épidémie

SARS : Number of Current Probable Cases as of 17 May 2003, 14:00 GMT+2



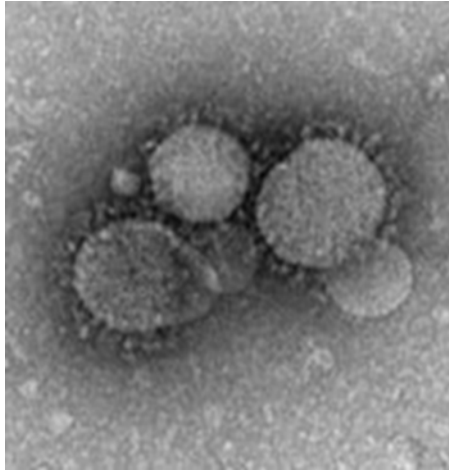
The presentation of material on the maps contained herein does not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or areas or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Data Source: World Health Organization
 Map Production: Public Health Mapping Team
 Communicable Diseases (CDS)
 © World Health Organization, May 2003



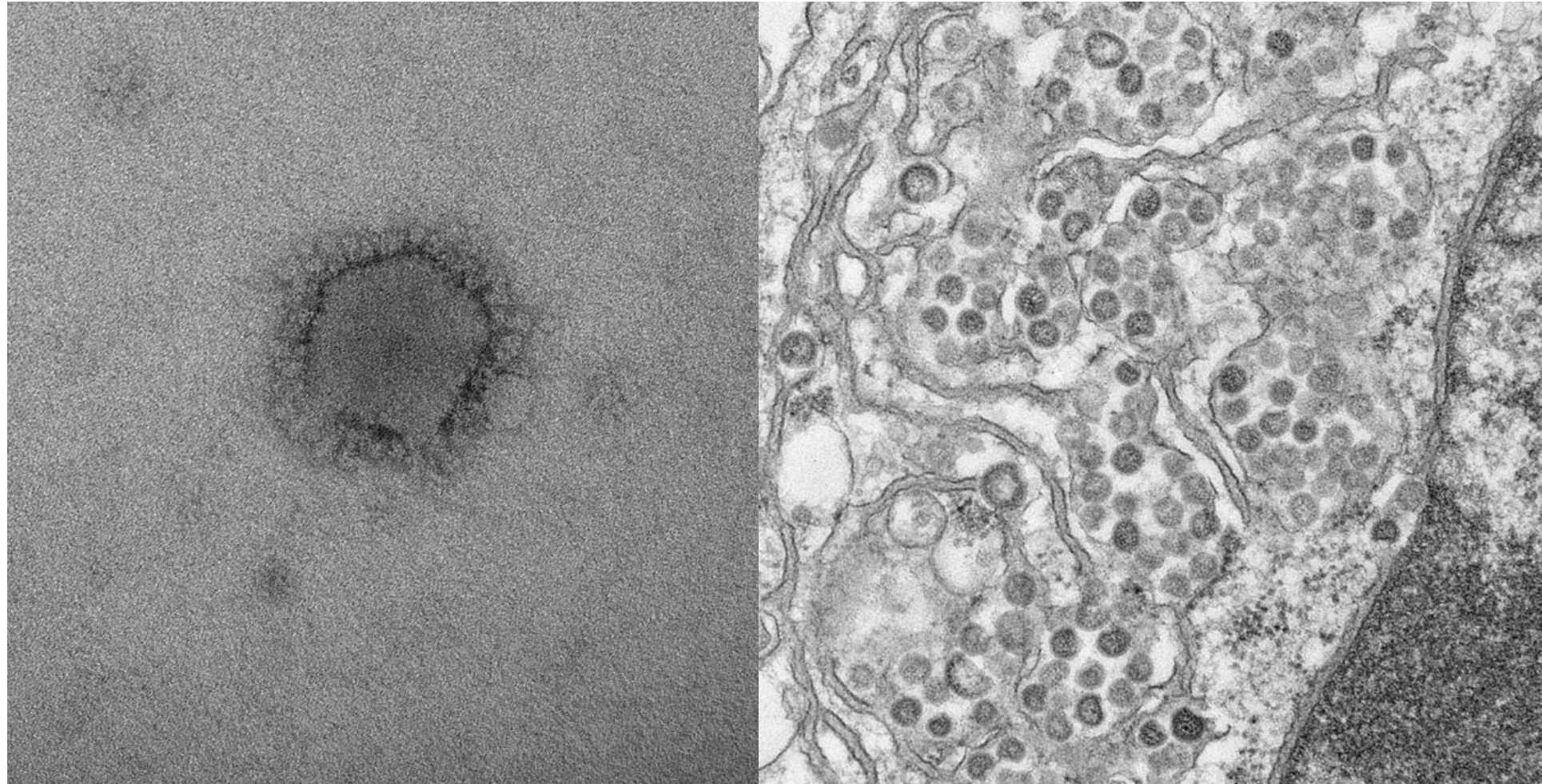
SARS 2003
8000 cas
Environ 800 décès





- **Nouveau Coronavirus**
- **nCoV . MERS CoV**
 - Différent du SARS Coronavirus de 2003
 - Zone d'émergence : péninsule Arabique: Arabie Saoudite, Qatar, Emirats Arabes Unis, Jordanie (1^{er} cas en avril 2012)
 - Réservoir : chauves souris; réservoir intermédiaire inconnu (chameau?)

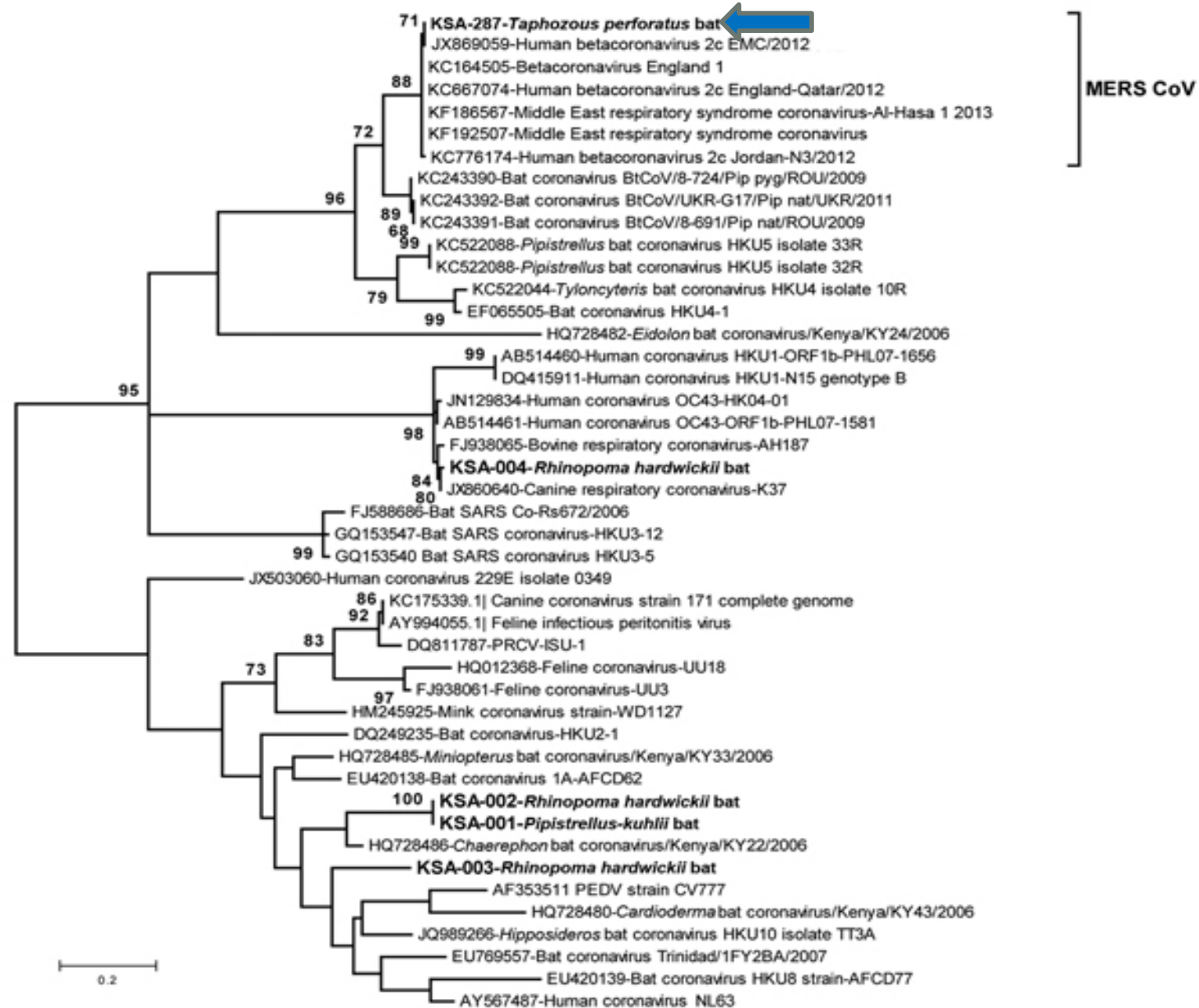




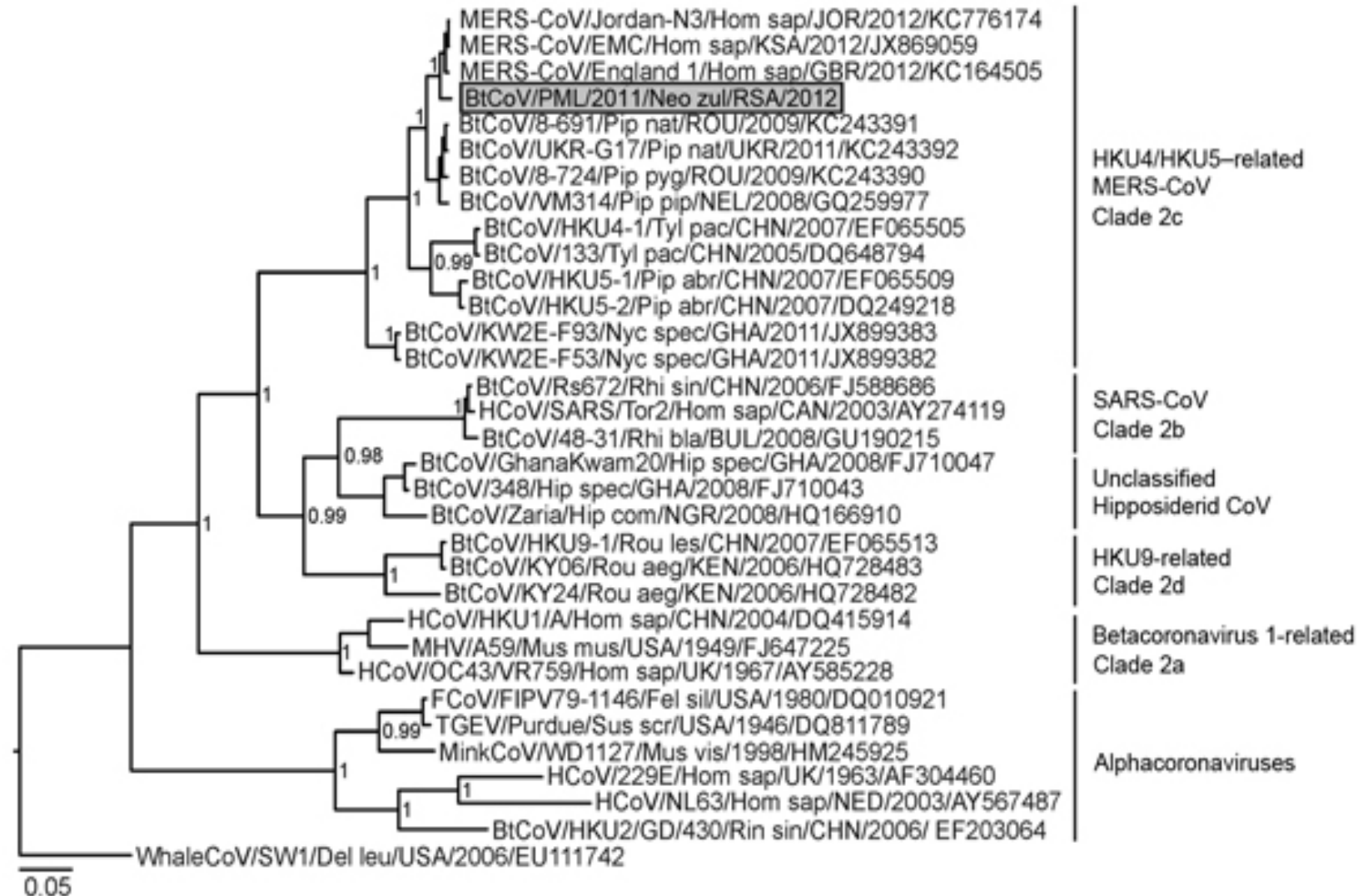
13-036 nCoV Neg Stain - 2.tif
Neg Stain EM13-036
nCoV - MM box 130116 (T7)
Print Mag: 330000x @ 135 mm
15:54 03/21/13

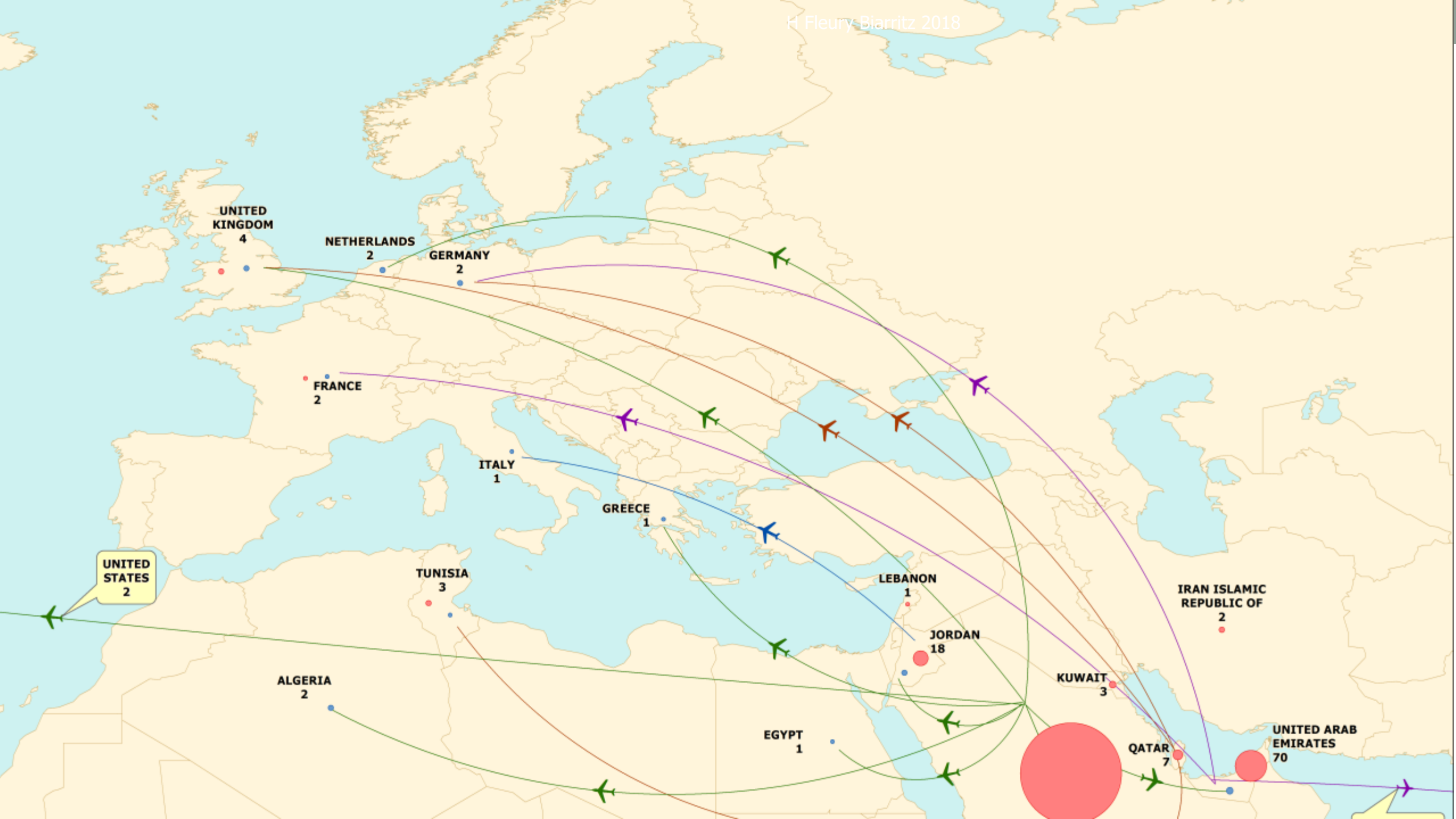
20 nm
HV=80.0kV
Direct Mag: 110000x
CDC Pathology - FEI Spirit

Middle East Respiratory Syndrome Coronavirus in Bats, Saudi Arabia



Close Relative of Human Middle East Respiratory Syndrome Coronavirus in Bat, South Africa



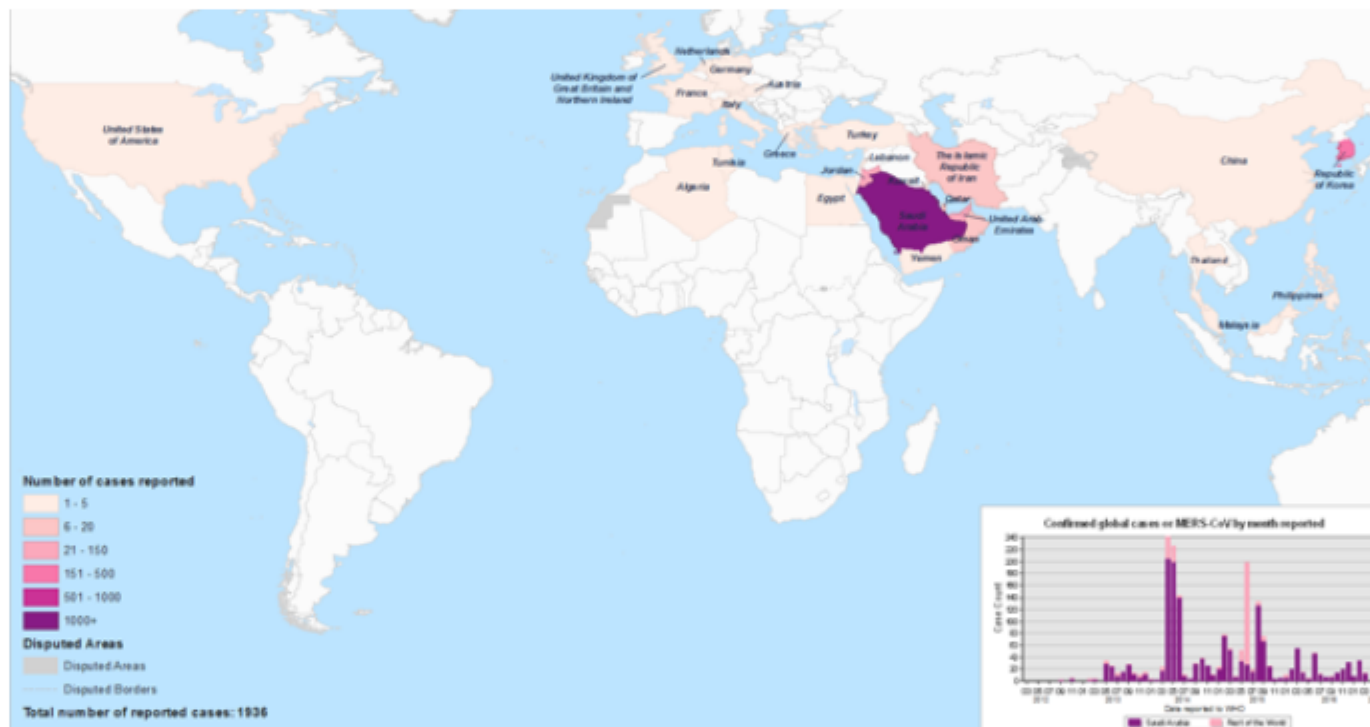


Middle East respiratory syndrome coronavirus (MERS-CoV)

Infection prevention and control measures are critical

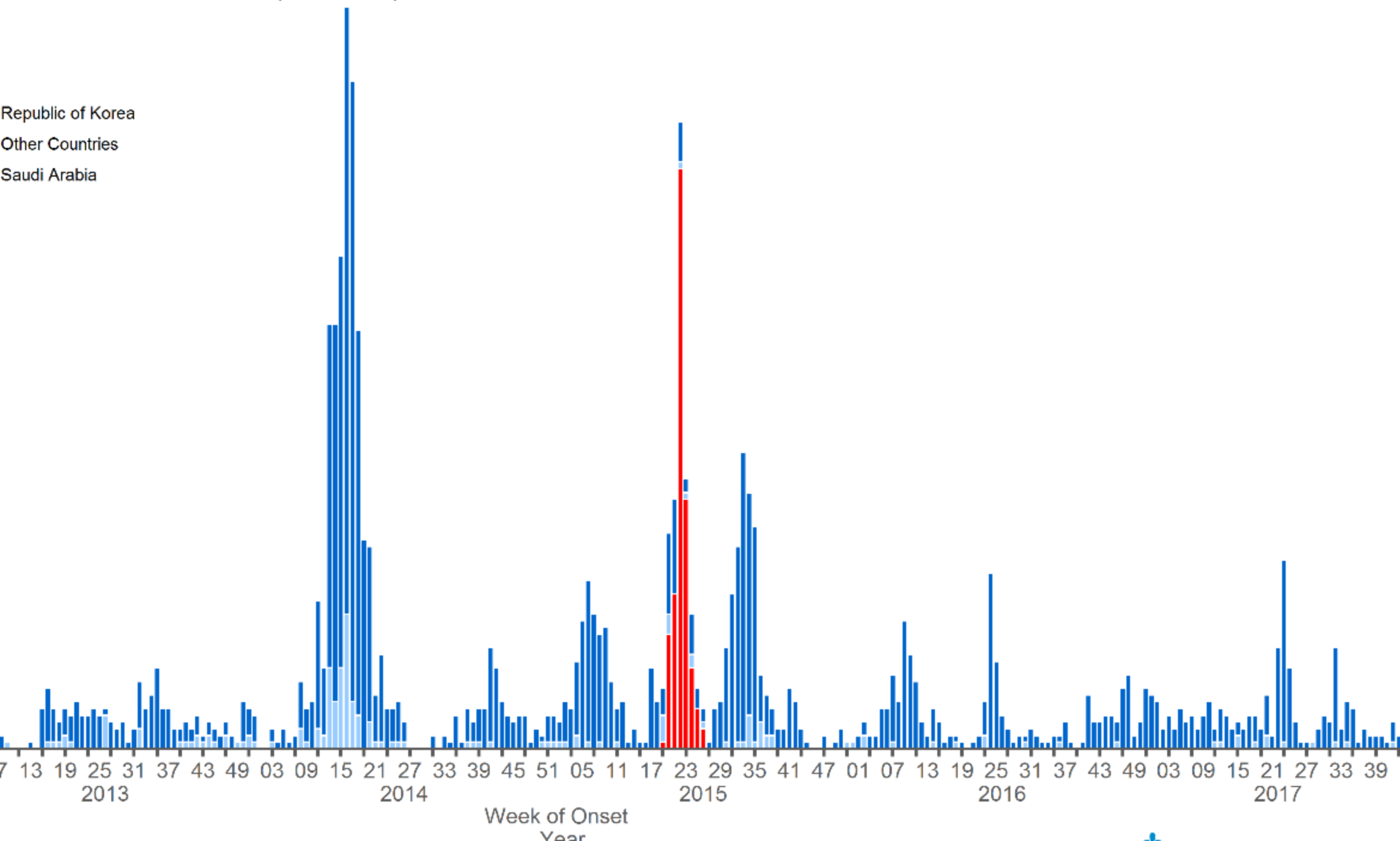
April 2017 -- Based on the current situation and available information, WHO encourages all Member States to continue their surveillance for acute respiratory infections and to carefully review any unusual patterns. Infection prevention and control measures are critical to prevent the possible spread of MERS-CoV in health care facilities.

[Q&As on MERS-CoV](#)



as of 17 Nov 2017 (n=2103)

Republic of Korea
Other Countries
Saudi Arabia



Middle East Respiratory Syndrome (MERS)

MERS

FAQs

Healthcare Providers

Interim Guidance for Health Professionals

► Case Definitions

Preparedness

Infection Prevention and Control

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Case Definitions

Patient Under Investigation (PUI)

A patient under investigation (PUI) is a person with the following characteristics:

- fever ($\geq 38^{\circ}\text{C}$, 100.4°F) and pneumonia or acute respiratory distress syndrome (based on clinical or radiological evidence);

AND EITHER

- history of travel from countries in or near the Arabian Peninsula¹ within 14 days before symptom onset;

OR

- close contact² with a symptomatic traveler who developed fever and acute respiratory illness (not necessarily pneumonia) within 14 days after traveling from countries in or near the Arabian Peninsula;¹

OR

- is a member of a cluster of patients with severe acute respiratory illness (e.g. fever and pneumonia requiring hospitalization) of unknown etiology in which MERS-CoV is being evaluated, in consultation with state and local health departments.

Contact Us:

Centers for Disease Control and Prevention
1600 Clifton Rd
Atlanta, GA 30333

800-CDC-INFO (800-232-4636)
TTY: (888) 232-6348
[Contact CDC-INFO](#)

Learn more about MERS and the virus that causes it.



Disponible en español

Confirmed Case

A confirmed case is a person with laboratory confirmation³ of MERS-CoV infection.



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Treatment with interferon- α 2b and ribavirin improves outcome in MERS-CoV-infected rhesus macaques

Darryl Falzarano, Emmie de Wit, Angela L Rasmussen, Friederike Feldmann, Atsushi Okumura, Dana P Scott, Doug Brining, Trenton Bushmaker, Cynthia Martellaro, Laura Baseler, Arndt G Benecke, Michael G Katze, Vincent J Munster & Heinz Feldmann

[Affiliations](#) | [Contributions](#) | [Corresponding author](#)

Nature Medicine **19**, 1313–1317 (2013) | doi:10.1038/nm.3362
Received 24 May 2013 | Accepted 27 August 2013 | Published online 08 September 2013

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Abstract

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The emergence of Middle East respiratory syndrome coronavirus (MERS-CoV) is of global concern:

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- ***Cas de suspicion Bx***
- Patiente arrivant de La Mecque avec syndrome grippal
- Réanimation Pellegrin
- Prélèvements vers P3
- PCR nCoV négative (4 heures)
- J+1 PCR multiplex positive pour grippe A
- J+2 Identification de H3
- Conclusion : grippe A H3N2

New case of MERS-CoV identified in the United Kingdom

news

24 Aug 2018



A new case of Middle East respiratory syndrome coronavirus (MERS-CoV) has been confirmed by Public Health England (PHE) on the 23 August. Health authorities are identifying close contacts of the patient as a precautionary measure. This is the fifth case of MERS-CoV diagnosed in England, where there have been no cases since 2013.

The patient is a resident of the Middle East, where they are believed to have been infected before travelling to the UK. The case was initially admitted to a hospital in Leeds and subsequently transferred to the Royal Liverpool Hospital, an expert respiratory infectious disease centre. The patient is currently stable and receiving treatment.

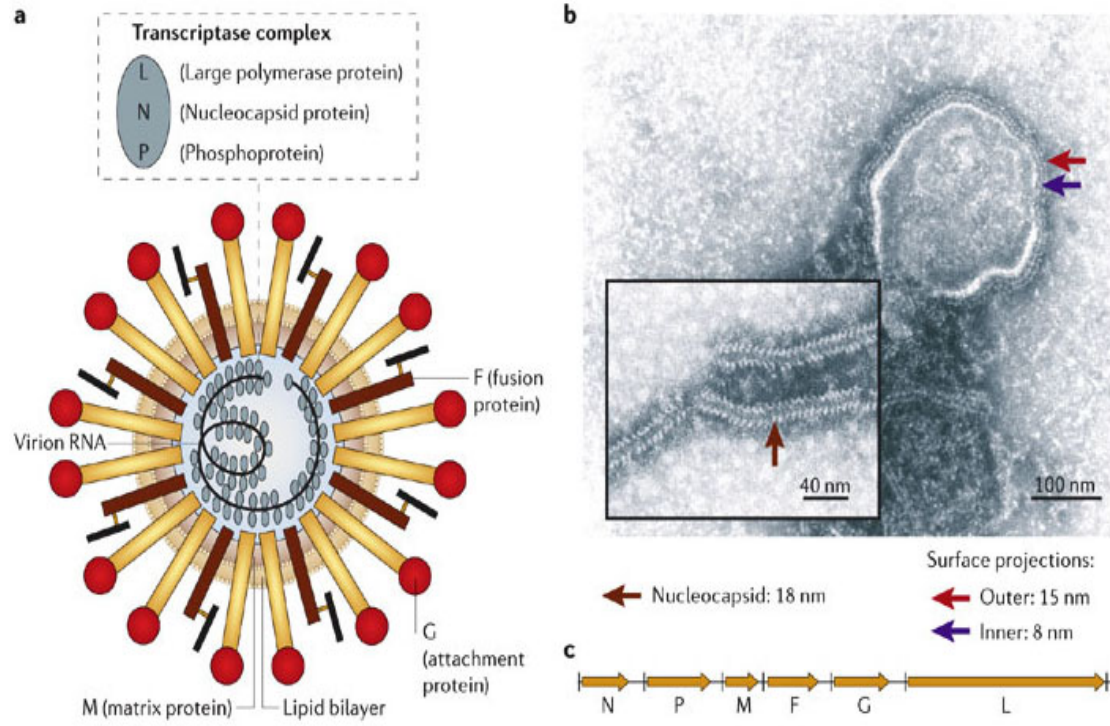
The national authorities are currently identifying close contacts with the individual to monitor their symptoms and provide health advice. This includes a small number of passengers who travelled in close proximity to the patient on flight Saudi Arabian Airlines SV123 to the UK on 16 August. In its risk assessment, ECDC recommends that close contacts of confirmed cases must be monitored for symptoms for 14 days after the last exposure.

Imported cases of MERS-CoV are not unexpected and have been observed in Europe before. According to Public Health England (PHE), the risk of transmission to the general population from this case is very low. The rapid

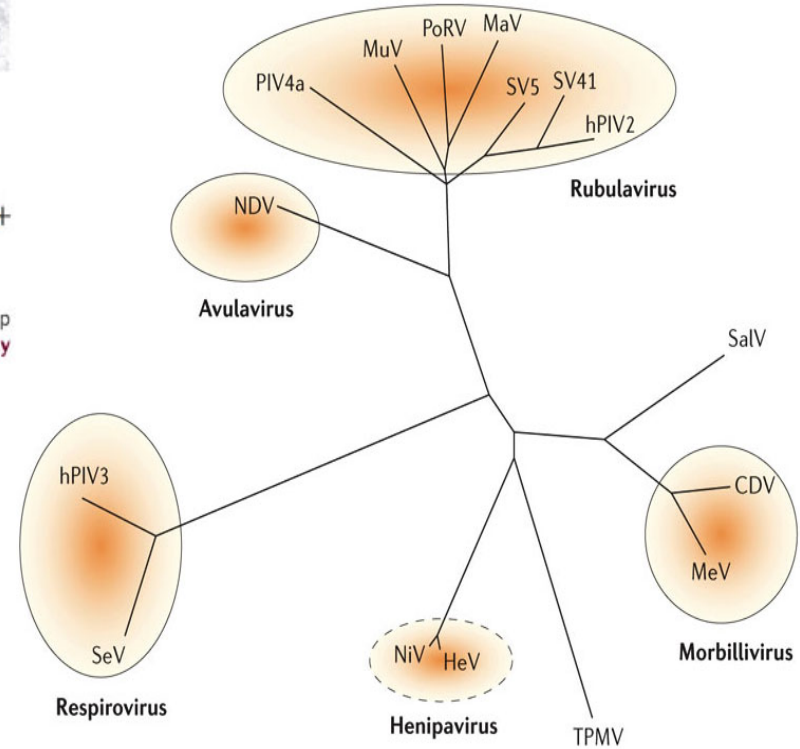
Hendra et Nipah

- Hendra a été découvert en Australie (Brisbane) en 1994 lors d'une épidémie respiratoire et neurologique chez des chevaux et des humains ; virus d'abord appelé « Equine morbillivirus »
- Nipah est proche de Hendra et appartient aux Paramyxoviridae ; initialement observé lors d'une épidémie humaine (respiratoire et neurologique) en Malaisie et Singapour en 1999

- **Hendra**
- Réservoir : chauves souris (genre Pteropus)
- Chevaux touchés et humains contaminés à partir des sécrétions de chevaux infectés
- **Nipah**
- Réservoir : chauves souris (Pteropus)
- Porcs touchés et source de contamination pour humains, chiens et chats

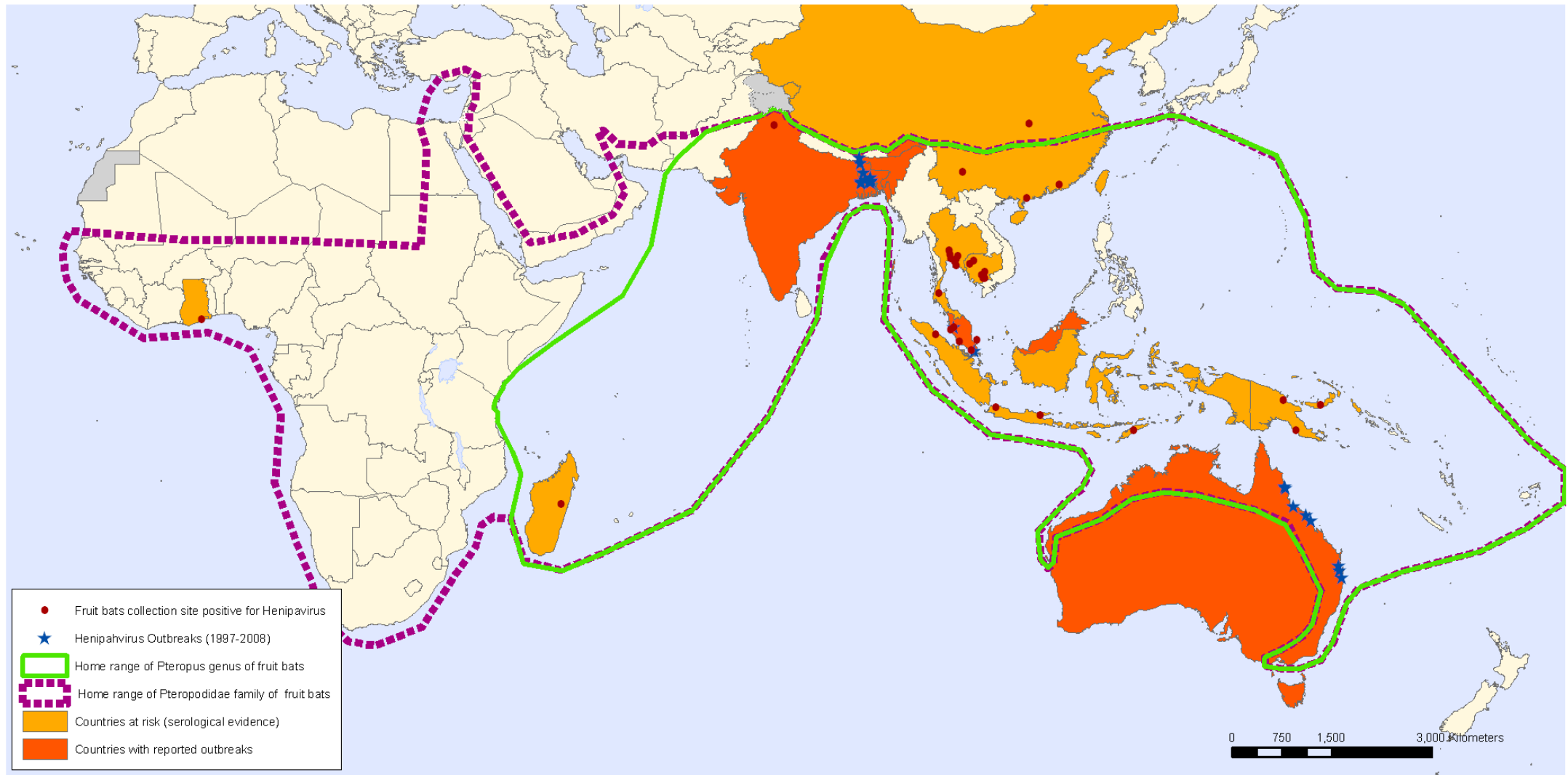


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Geographic distribution of Henipavirus outbreaks and fruit bats of Pteropodidae Family



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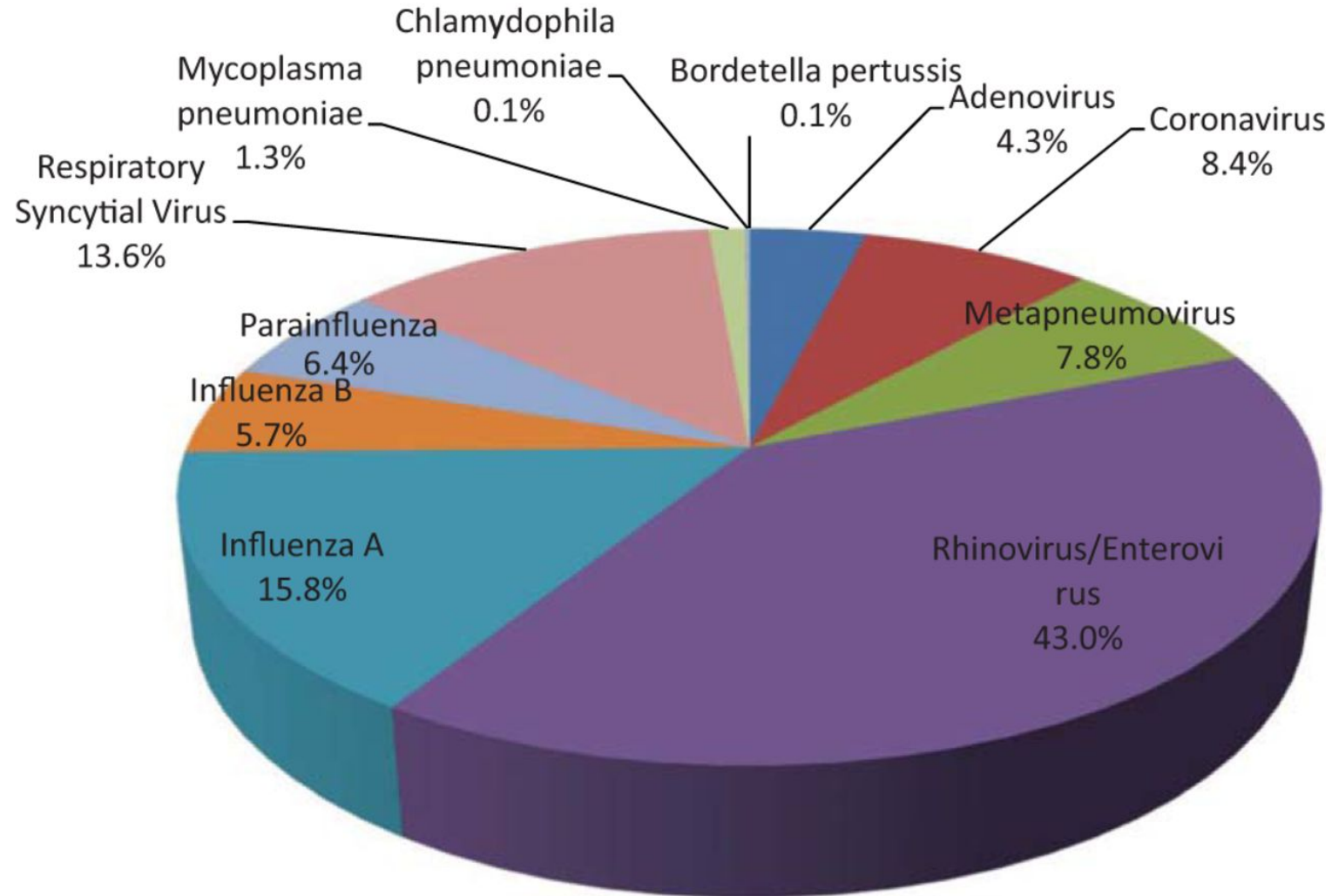
Data Source: Global Alert and Response Department
World Health Organization
Map Production: Public Health Information
and Geographic Information Systems (GIS)
World Health Organization



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Les virus respiratoires circulant en zones tempérées

Incidence of viruses present in respiratory specimens at Loyola University Medical Center, 1 October 2013 to 27 September 2014.



Paul C. Schreckenberger, and Alexander J. McAdam J. Clin. Microbiol. 2015;53:3110-3115

Journal of Clinical Microbiology

- **Métapneumovirus (HMPV)**

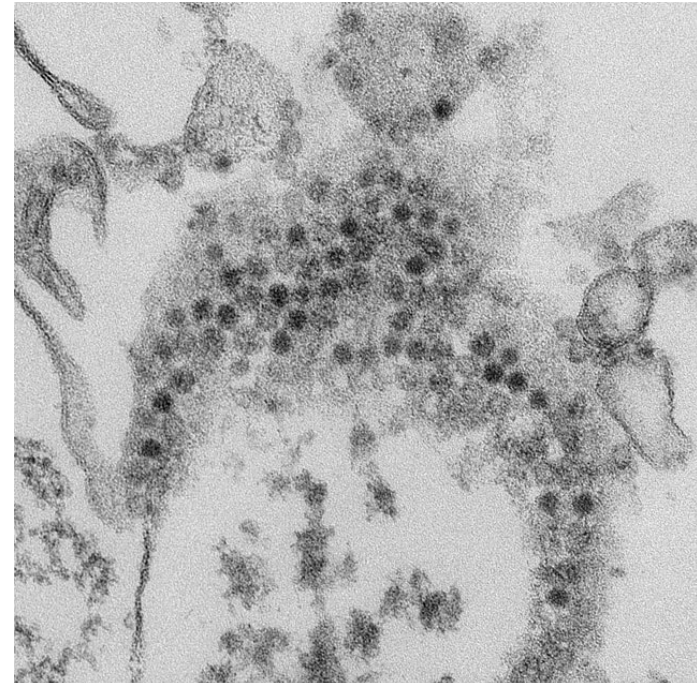
- Identifié en 2001 par une équipe hollandaise
- Proche d'un pneumovirus aviaire (virus de la trachéite du dindon), membre du genre Metapneumovirus)
- HMPV est proche du virus respiratoire syncytial (VRS); deux sous types A et B
- La prévalence du HMPV dans les infections du tractus respiratoire est de 5 à 15 %

- **Bocavirus humain (HBoV)**

- Appartenant à la famille des Parvoviridae a été identifié en Suède en 2005
- Quatre types de HBoV, le type 1 est retrouvé au niveau respiratoire; autres types ds les selles
- Au niveau respiratoire, le HBoV a été détecté dans des proportions allant de 1 à 20% chez des patients présentant une infection respiratoire; des taux de co-infection parfois supérieurs à 50 % ont été rapportés dans les différentes études

- **Coronavirus**
- Coronavirus « Historiques » HCoV-OC43 et HCoV-229E
- NL63 (prévalence 2 à 10%) et HKU1 (prévalence 4%)
- Infections respiratoires hautes telles que les rhinites ou les sinusites.
- Portage prolongé après infection aigüe

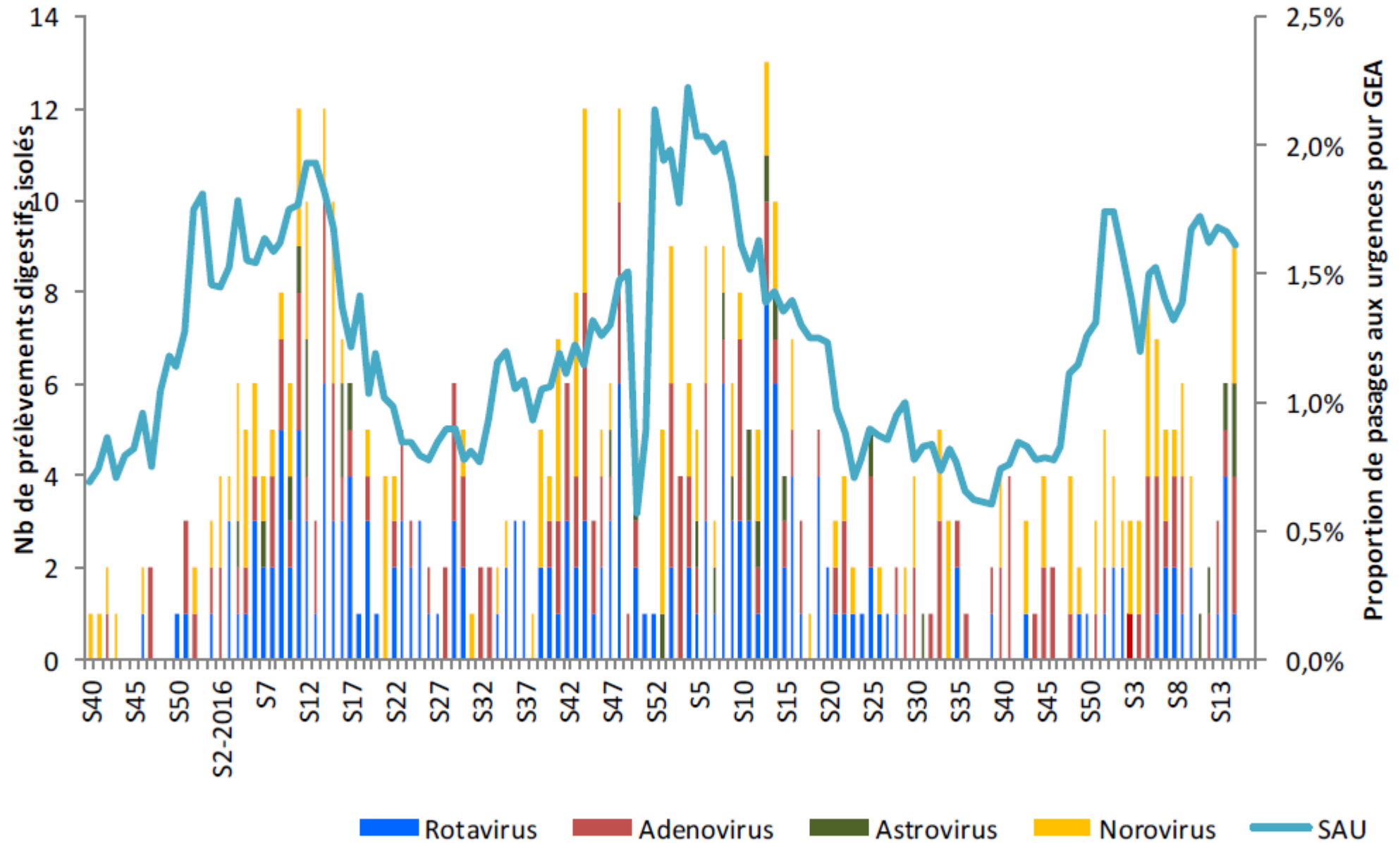
Enterovirus EV-D68



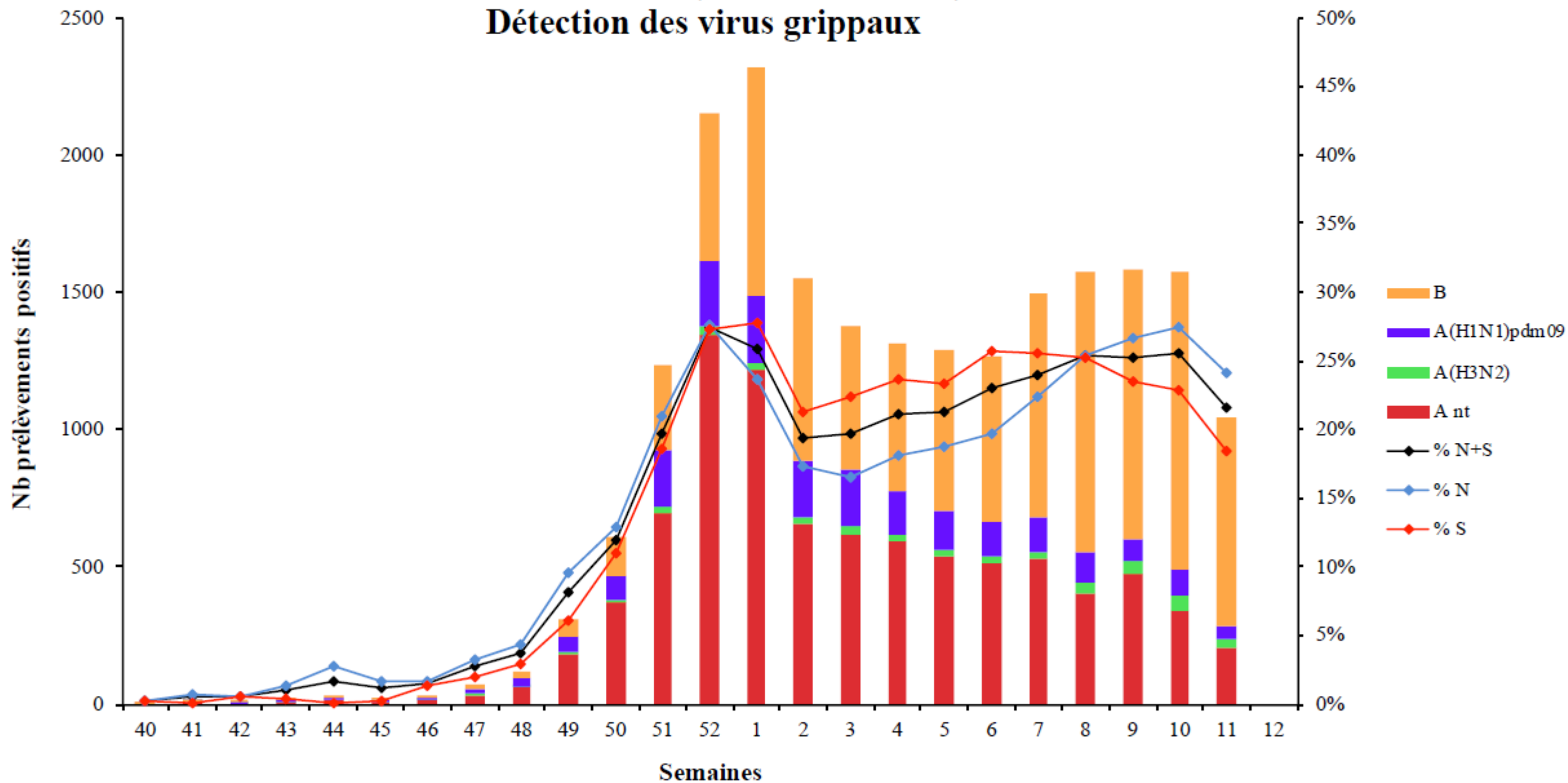
Virus	Eté	Automne	Hiver	Printemps
Influenza			■	■
Parainfluenza			■	
VRS		■	■	
MPV			■	
Rougeole	■	■	■	■
ADV	■	■	■	■
BoV			■	■
Coronavirus			■	
Entérovirus	■	■		
Rhinovirus		■	■	■

Prévalence élevée : ■ Prévalence modérée : ■

Figure 1 : Répartition saisonnière des virus respiratoires dans les régions tempérées.

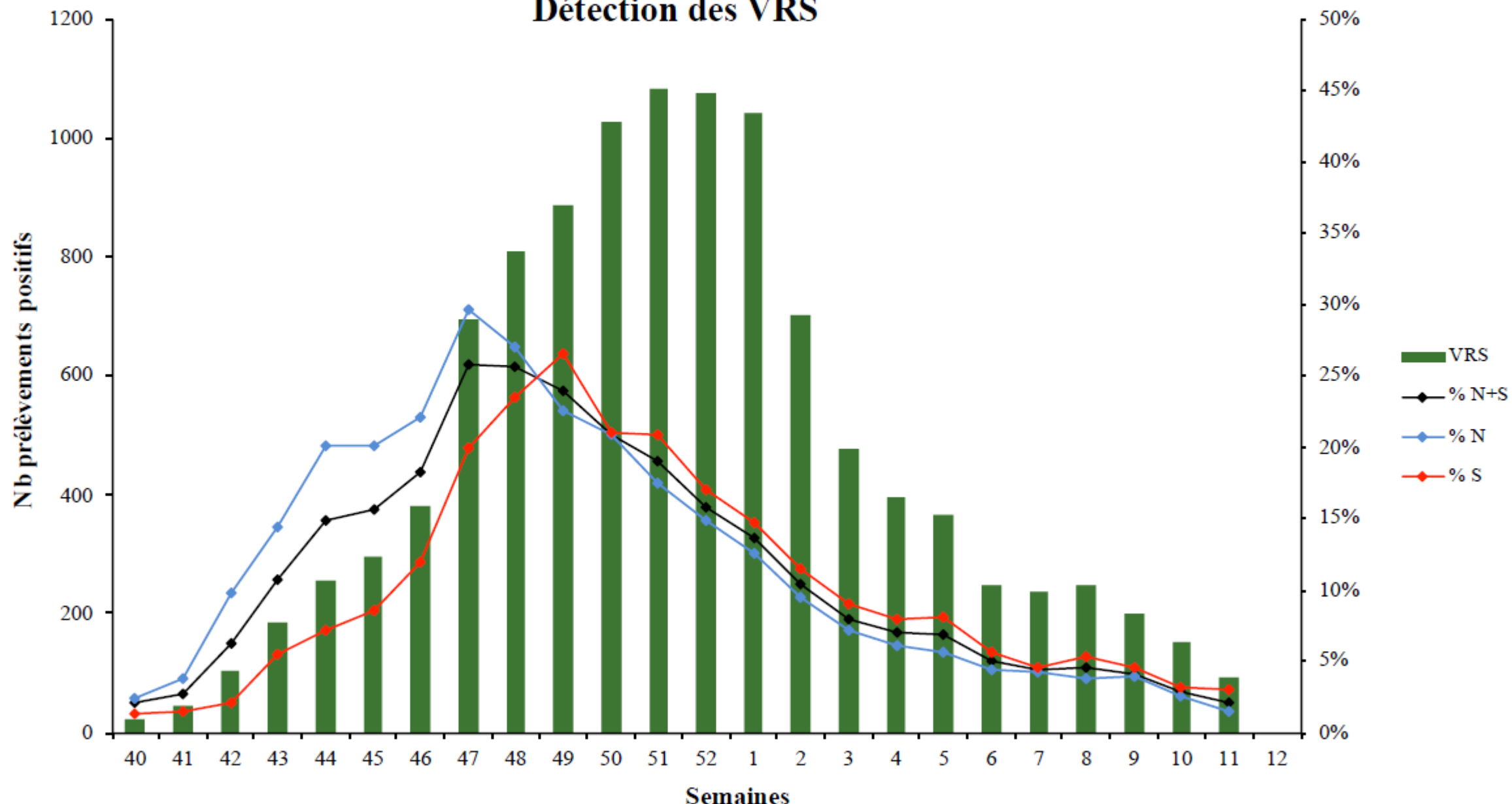


Réseau RENAL (saison 2017/2018) Détection des virus grippaux



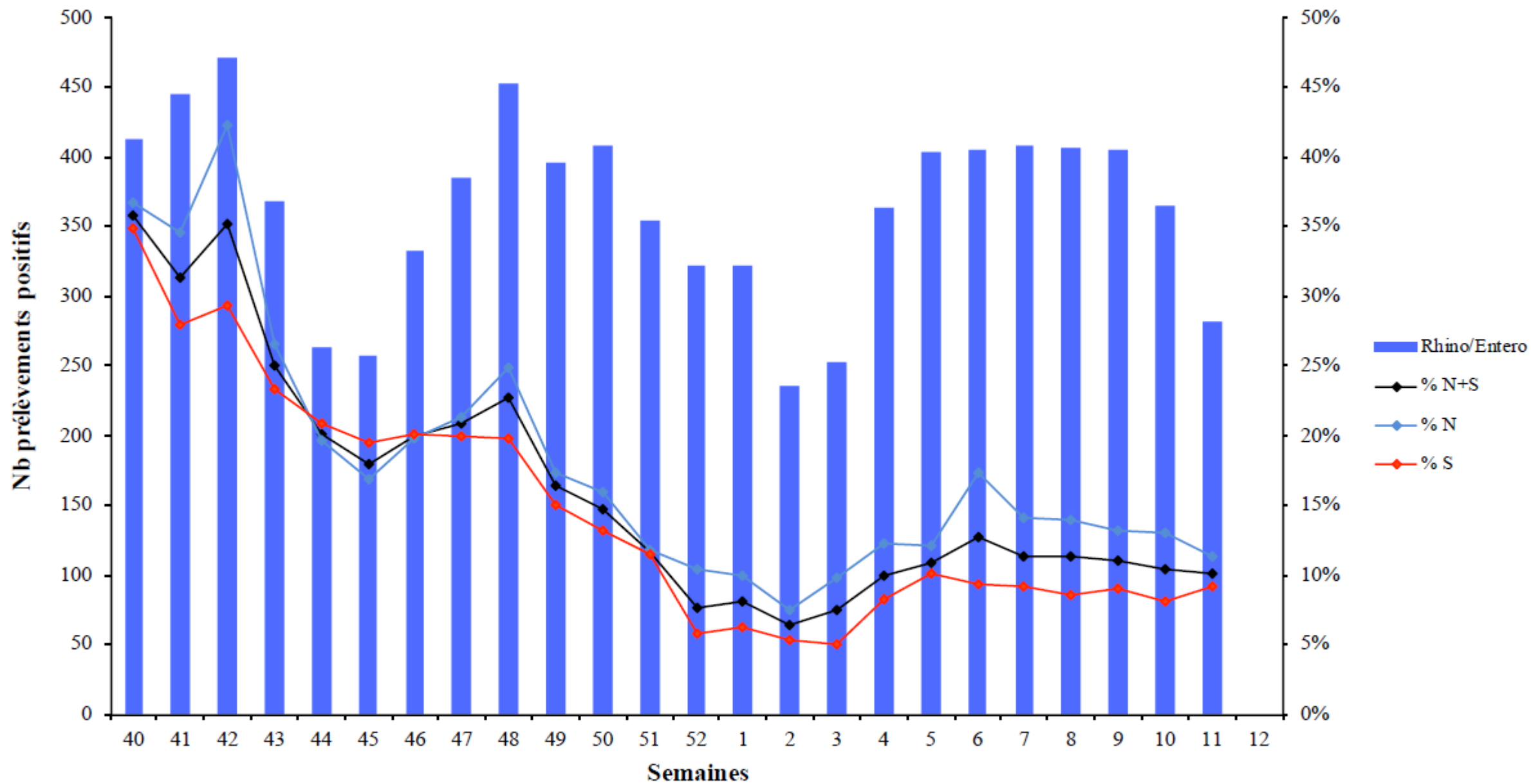
Réseau RENAL (saison 2017/2018)

Détection des VRS

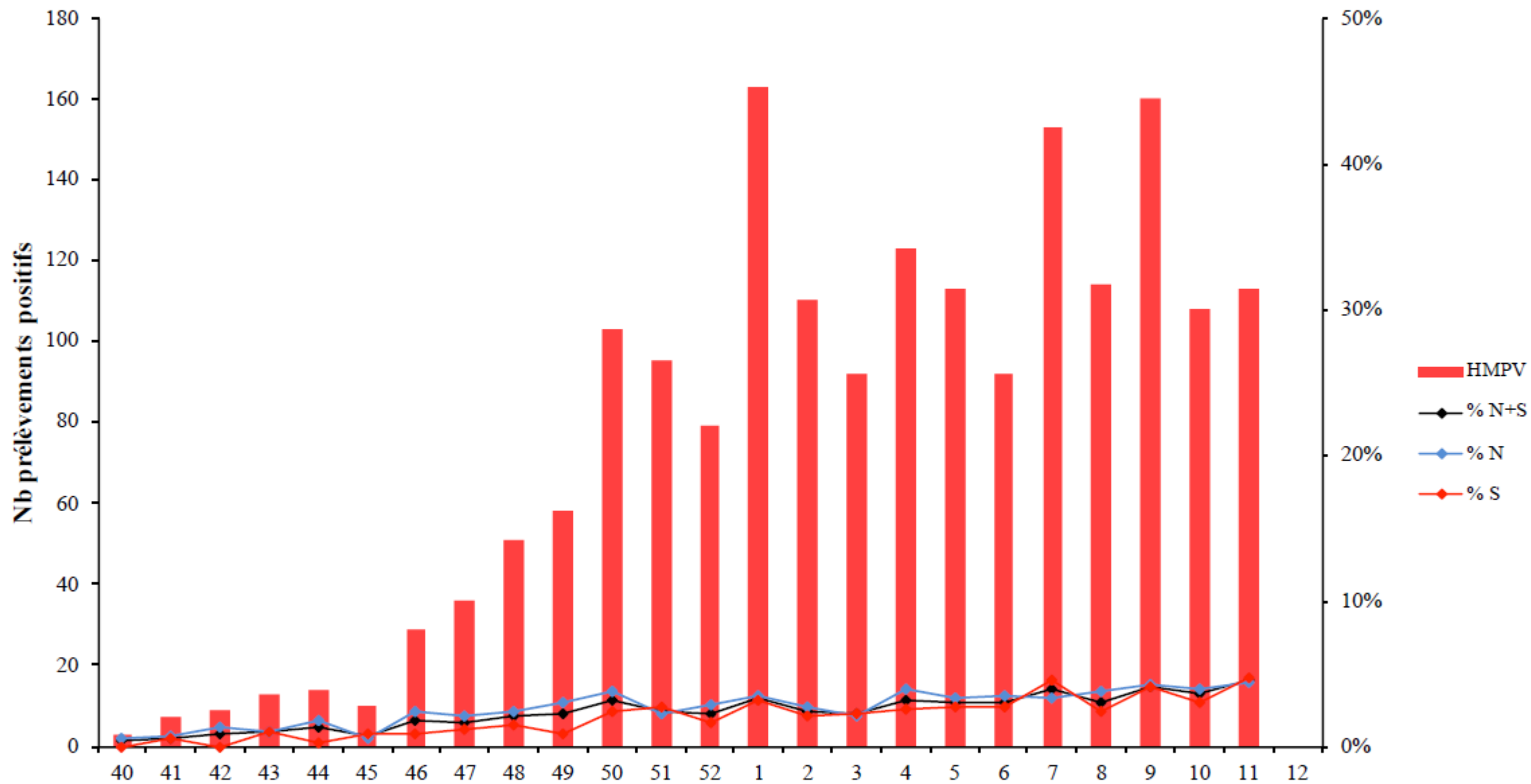


Réseau RENAL (saison 2017/2018)

Détection des rhino/entérovirus



Réseau RENAL (saison 2017/2018) Détection des métapneumovirus humains



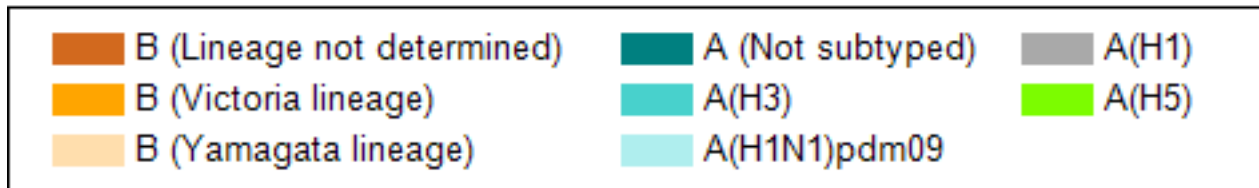
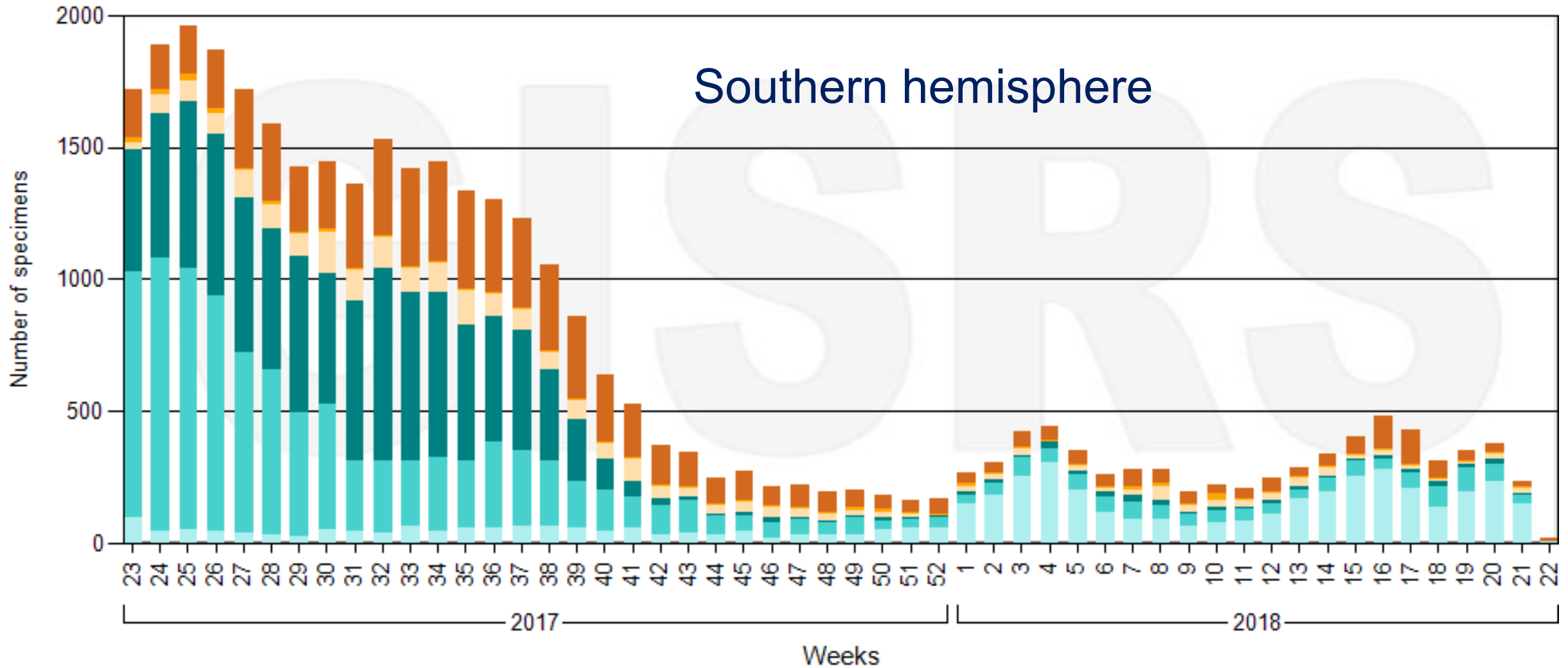


Table 3

Influenza viruses characterised by clade and study site, Europe, influenza season 2017/18 (n = 886)

	Clade	ES ^a		UK		EU-PC ^b		DK ^c	
		n	%	n	%	n	%	n	%
Total influenza A(H1N1)		n = 142		n = 20		n = 469		n = 113	
Sequenced		28	100	10	100	25	100	23	100
A/Michigan/45/2015	6B.1	28	100	10	100	25	100	23	100
Total influenza A(H3N2)		n = 233		n = 174		n = 229		n = 144	
Sequenced		51	100	59	100	43	100	51	100
A/HongKong/4801/2014	3C.2a	20	39	46	78	27	63	36	71
A/Singapore/INFIMH-16-0019/2016	3C.2a1	31	61	10	17	16	37	15	29
A/Switzerland/9715293/2013	3C.3a	0	0	3	5	0	0	0	0
Total influenza B		n = 1,022		n = 209		n = 1,469		n = 625	
Sequenced		164	100	116	100	207	100	109	100
B/Yamagata		136	83	116	100	198	96	109	100
B/Phuket/3073/2013	3	136	100	0	0	198	100	109	100
B/Victoria		28	17	0	0	9	4	0	0
B/Norway/2409/2017	1A Δ(K162, N163)	20	71	0	0	5	56	0	0
B/Brisbane/60/2008	1A	8	29	0	0	4	44	0	0

^a 50 specimens from ES are also included in EU-PC data.^b The specimens sequenced from Spain are originating from the entire National Influenza Surveillance System between weeks 44/2017 and 03/2018.^c Sequence information is based on a sub-sample of influenza positive samples received for surveillance at the National Influenza Center Denmark from week 40/2017 to 4/2018.

USA CDC 2017/2018

How effective was the 2017-2018 flu vaccine?

The overall vaccine effectiveness (VE) of the 2017-2018 flu vaccine against both influenza A and B viruses is estimated to be 40%. This means the flu vaccine reduced a person's overall risk of having to seek medical care at a doctor's office for flu illness by 40%. Protection by virus type and subtype was: **25% against A(H3N2)**, 65% against A(H1N1) and 49% against influenza B viruses. These VE estimates were presented to the [Advisory Committee on Immunization Practices on June 20, 2018](https://www.cdc.gov/vaccines/acip/meetings/meetings-info.html)(<https://www.cdc.gov/vaccines/acip/meetings/meetings-info.html>).

How many antiviral resistant viruses were detected during the 2017-2018 season?

Antiviral

[resistance\(https://www.cdc.gov/flu/about/qa/antiviralresistance.htm\)](https://www.cdc.gov/flu/about/qa/antiviralresistance.htm) means that a virus has changed in such a way that antiviral drugs are less effective or not effective at all in treating or preventing illnesses with that virus. Since October 1, 2017, CDC tested 1,147 influenza A(H1N1)pdm09, 2,354 influenza A(H3N2), and 1,118 influenza B viruses for resistance to antiviral medications (i.e., oseltamivir, zanamivir, or peramivir). While the majority of the tested viruses showed susceptibility to the antiviral drugs, 11 (1.0%) H1N1pdm09 viruses were resistant to both oseltamivir and peramivir, but were sensitive to zanamivir. ***These results indicate that these antiviral drugs continue to be recommended treatment options for illness caused by currently circulating influenza viruses.***



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Contemporary H3N2 influenza viruses have a glycosylation site that alters binding of antibodies elicited by egg-adapted vaccine strains

Seth J. Zost, Kaela Parkhouse, Megan E. Gumina, Kangchon Kim, Sebastian Diaz Perez, Patrick C. Wilson, John J. Treanor, Andrea J. Sant, Sarah Cobey, and Scott E. Hensley

PNAS November 21, 2017 114 (47) 12578-12583; published ahead of print November 6, 2017

<https://doi.org/10.1073/pnas.1712377114>

Edited by Peter Palese, Icahn School of Medicine at Mount Sinai, New York, NY, and approved October 12, 2017 (received for review July 11, 2017)

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Significance

The majority of influenza vaccine antigens are prepared in chicken eggs. Human vaccine



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Vaccin pour hiver 2018/2019

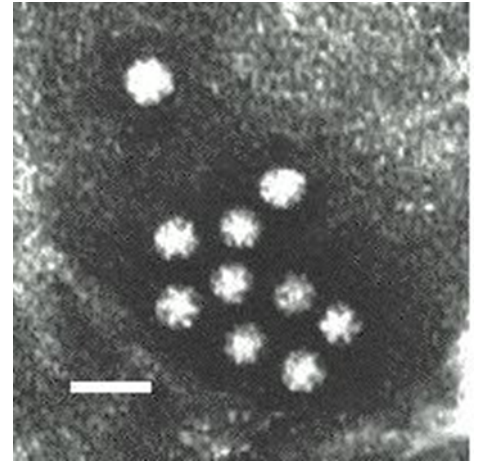
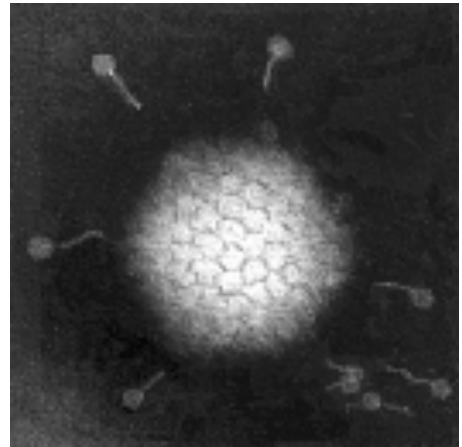
- **Souche A/Michigan/45/2015 (H1N1)pdm09** : sans changement ;
- **Souche A/Singapore/INFIMH-16-0019/2016 (H3N2)** : nouvelle souche ;
- **Souche B/Colorado/06/2017 (lignée B/Victoria/2/87)** : nouvelle souche ;
- Souche B/Phuket/3073/2013 (lignée Yamagata/16/88) pour les vaccins tétravalents : sans changement

Les outils du diagnostic virologique



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Electron microscopy



1908



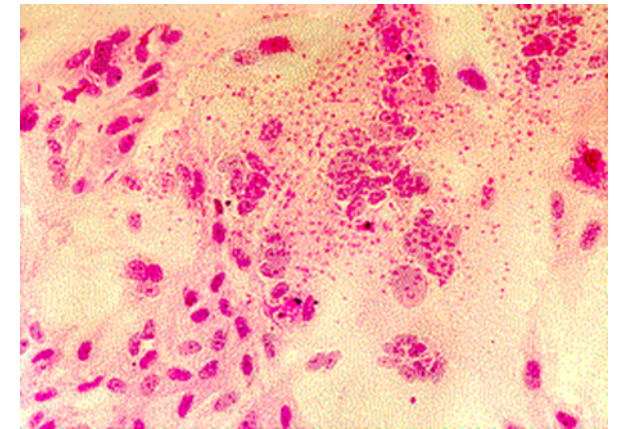
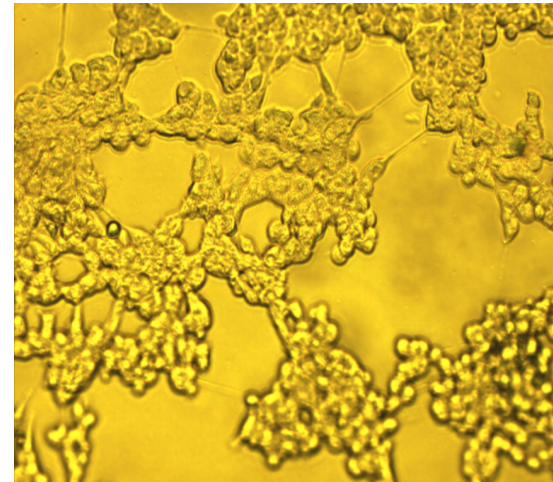
Inoculation to animals and eggs





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Cell cultures





Direct detection of virus antigens

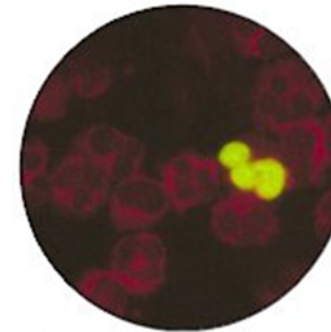


Figure 4 CMV pp65 antigens detected in nuclei of peripheral blood neutrophils

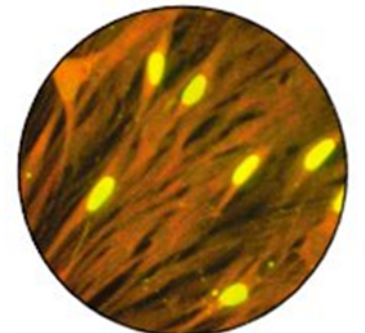
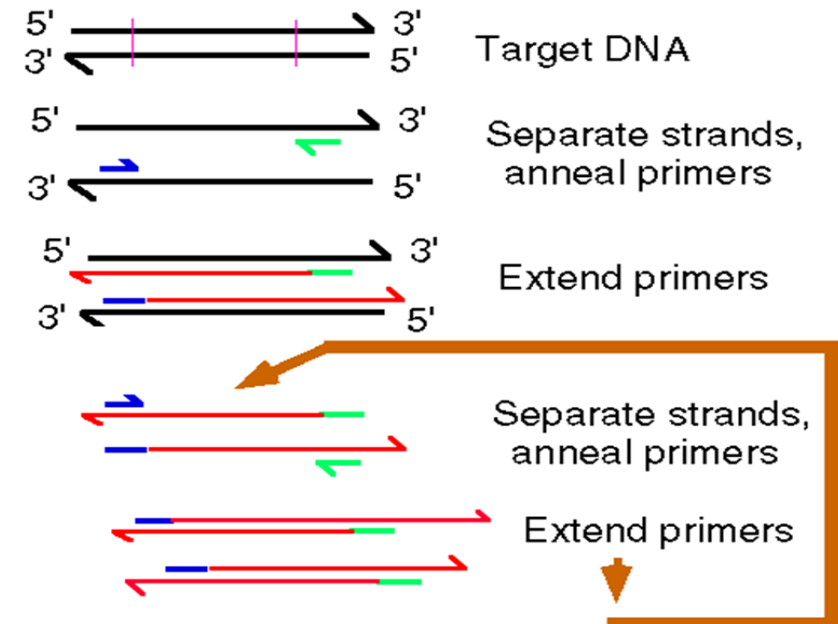


Fig. 2, CMV centrifugation culture fixed and stained 16 hrs after inoculation showing viral proteins in nuclei of infected human fibroblast cells



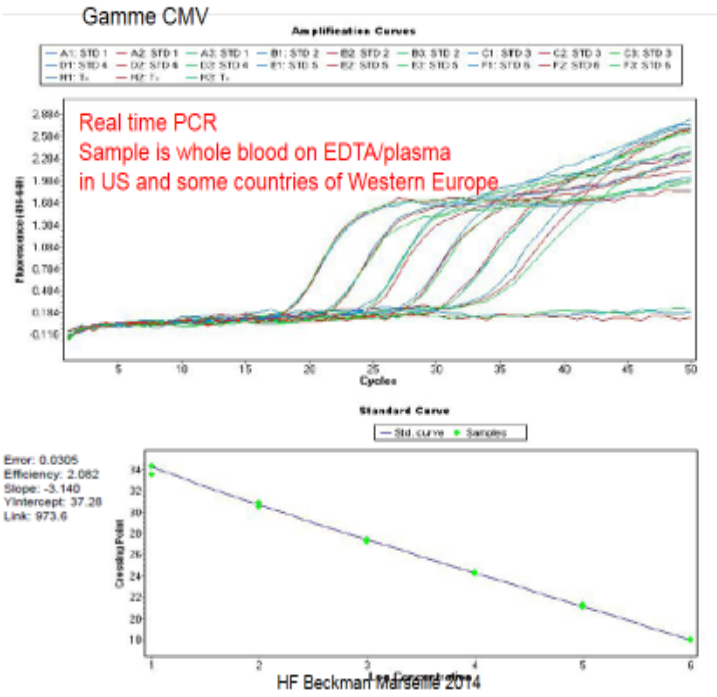
PCR amplification of nucleic acids



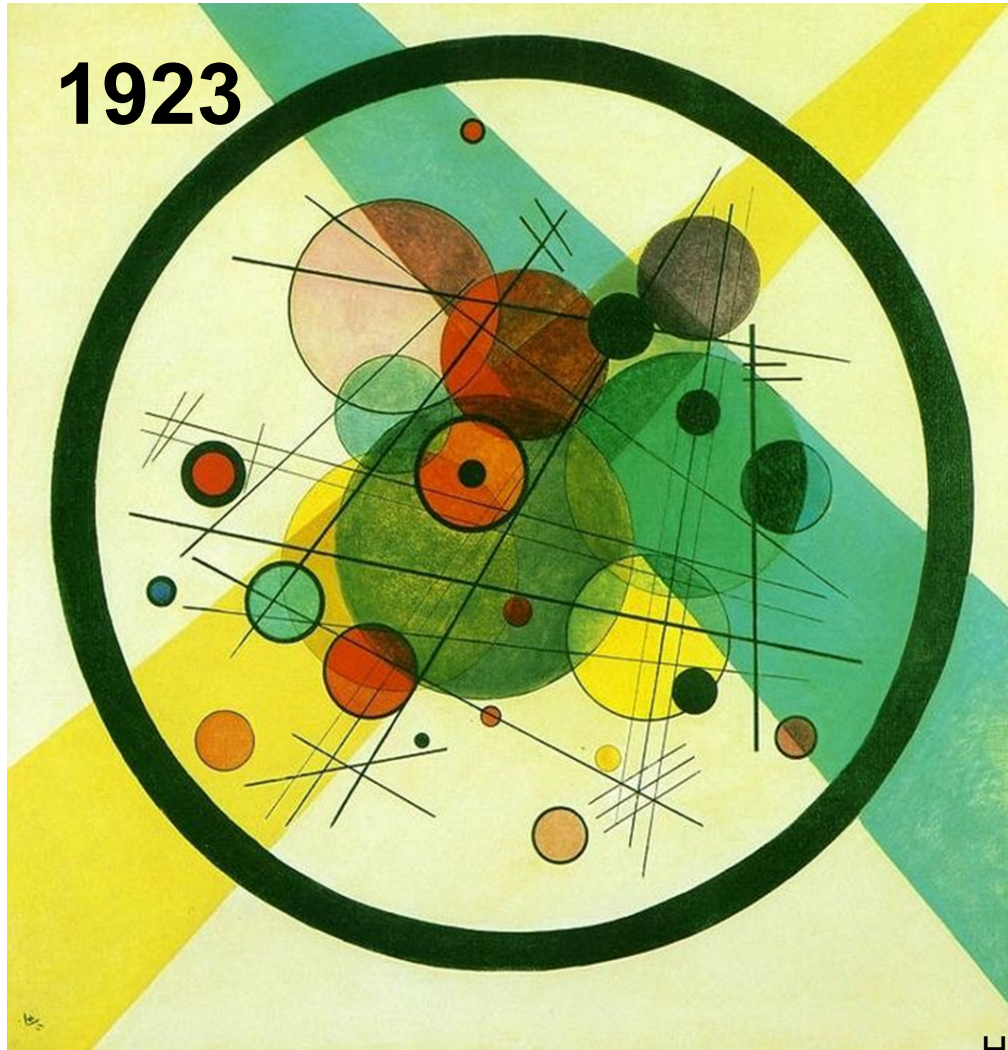


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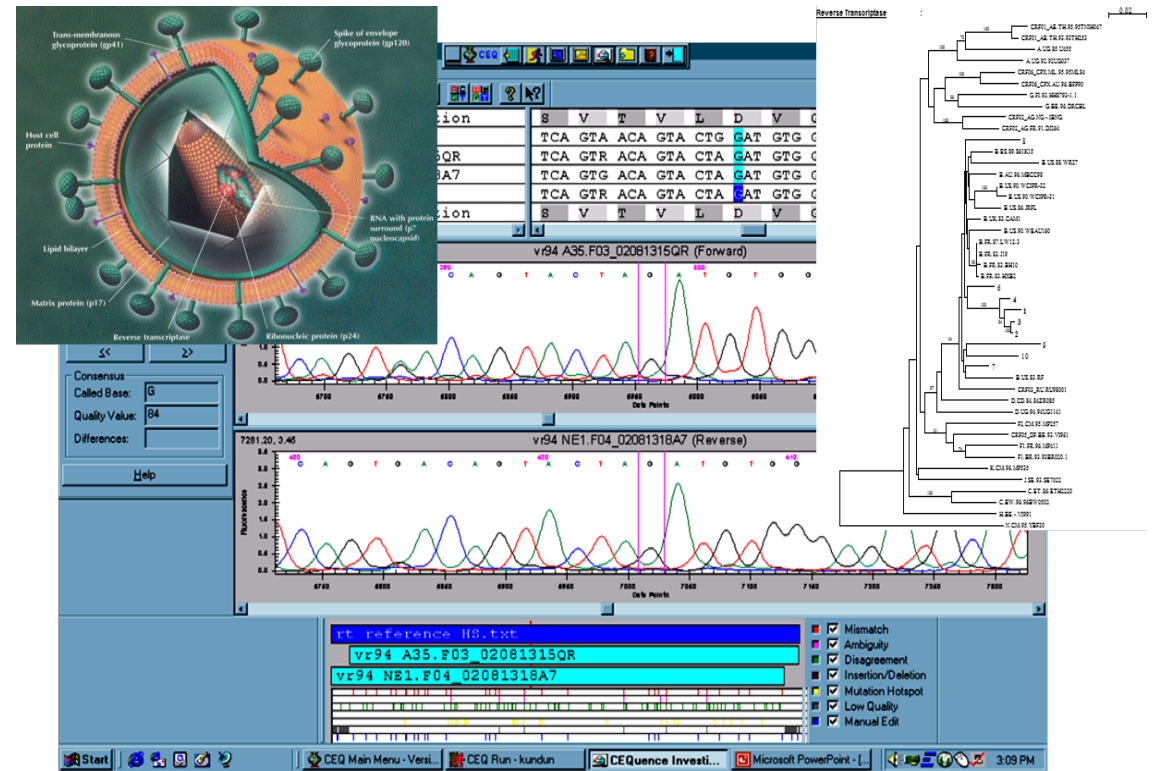
Real time PCR



1923



Sequencing techniques from Sanger to NGS



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L'apport de la Biologie Moléculaire au diagnostic virologique et au suivi de patients infectés par des virus respiratoires

K Mullis

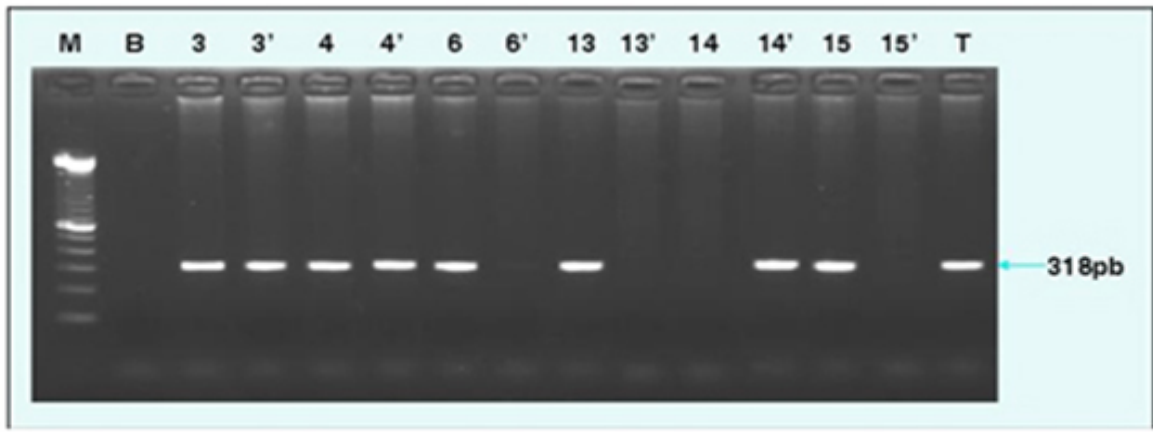
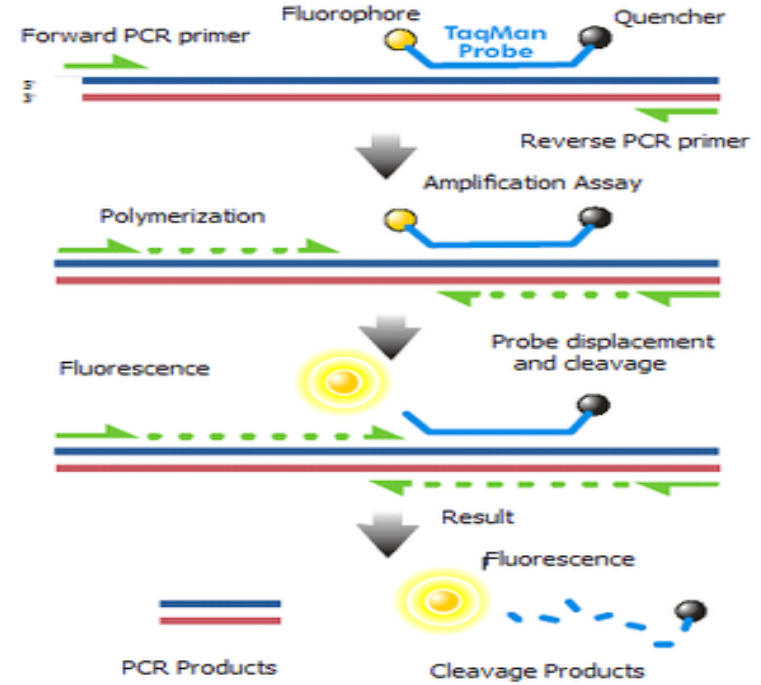
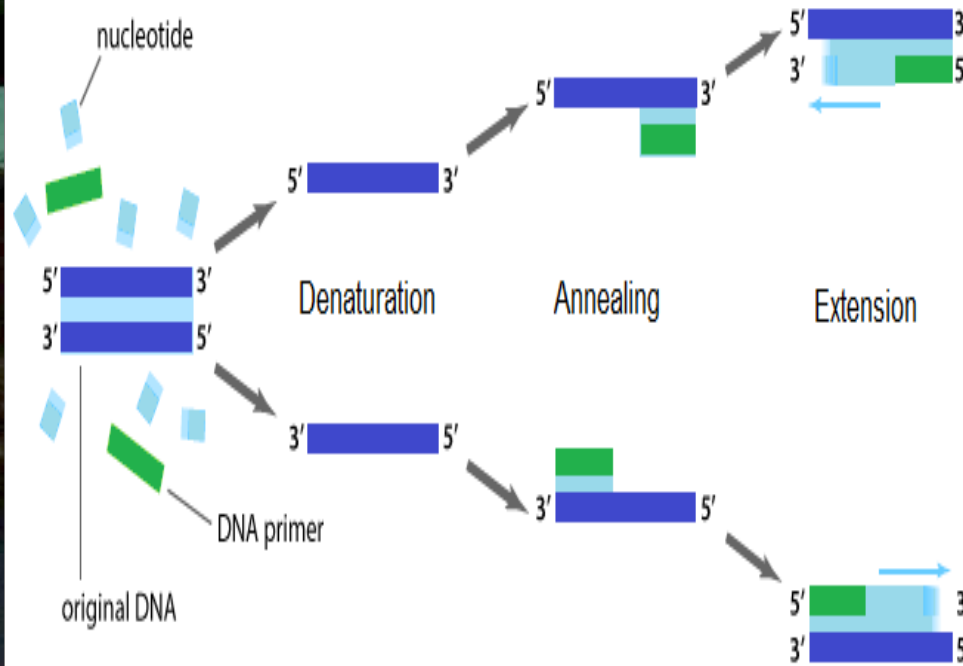
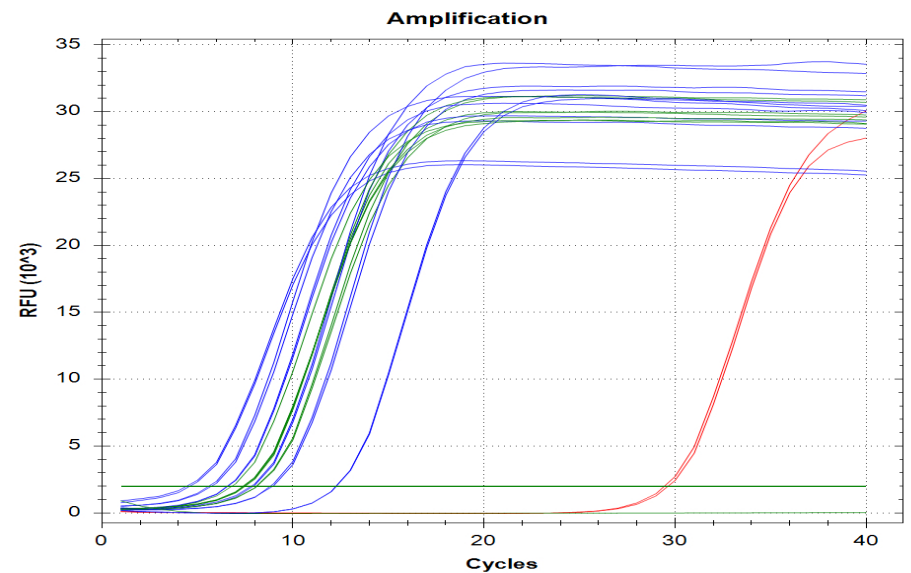
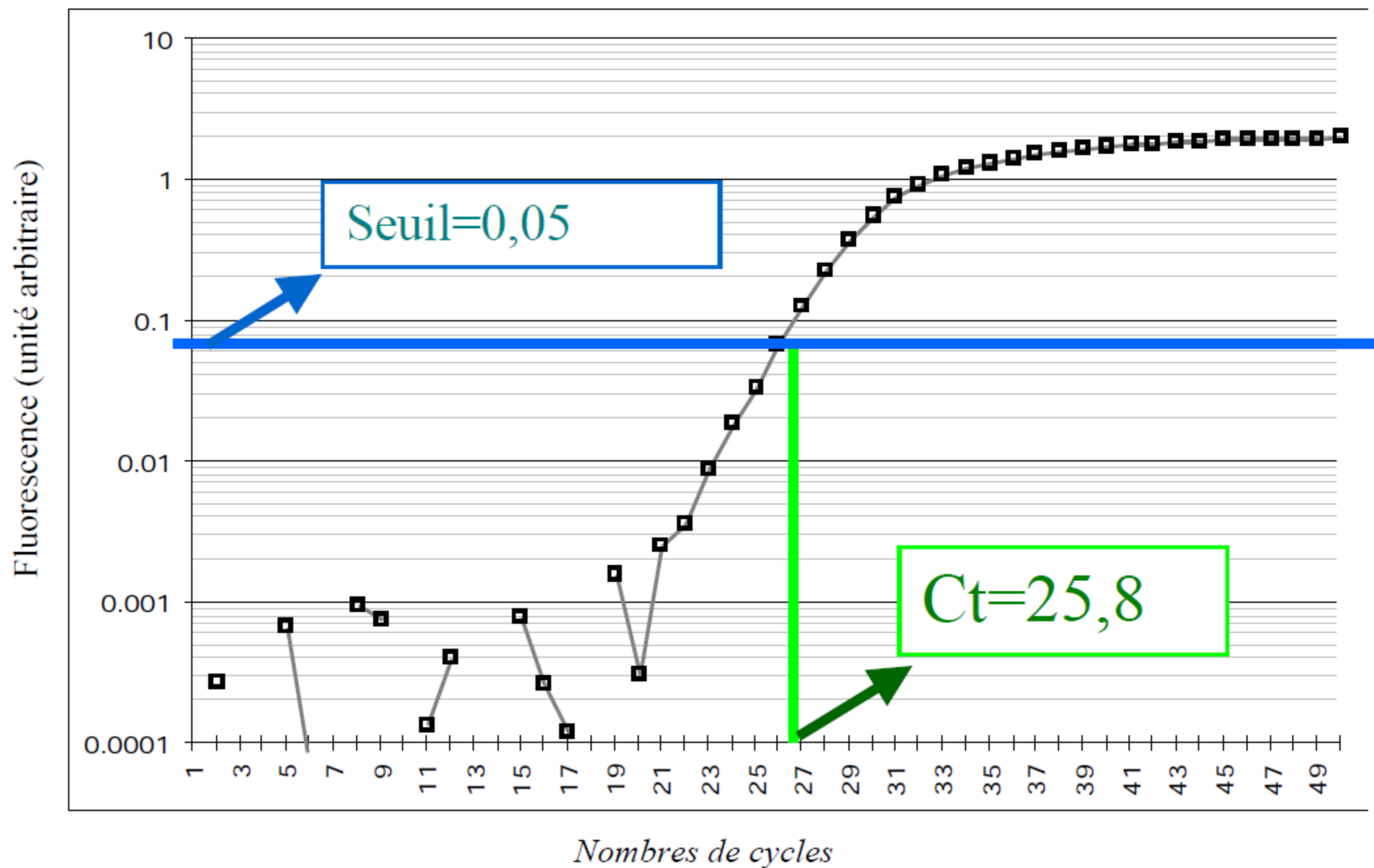
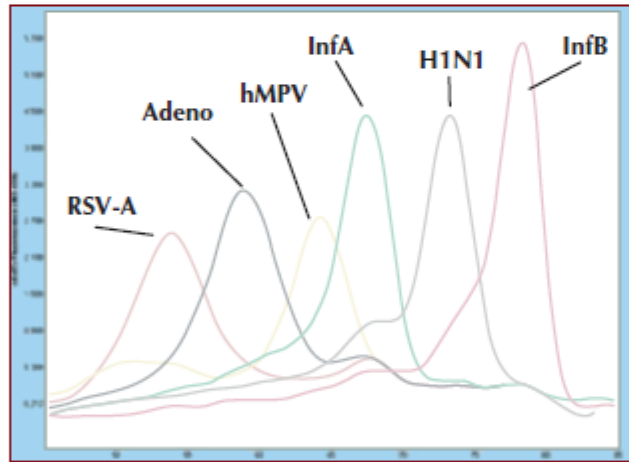


Figure 2 : Visualisation de bandes d'ADN sur gel d'agarose

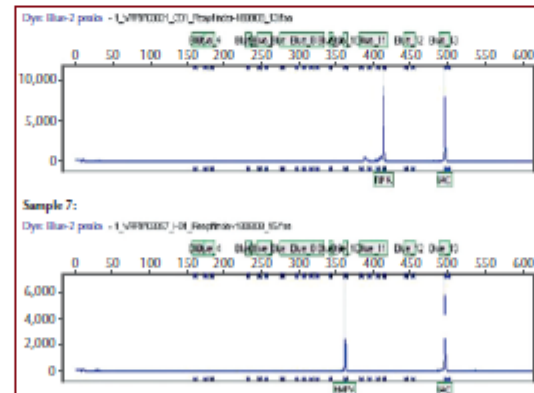
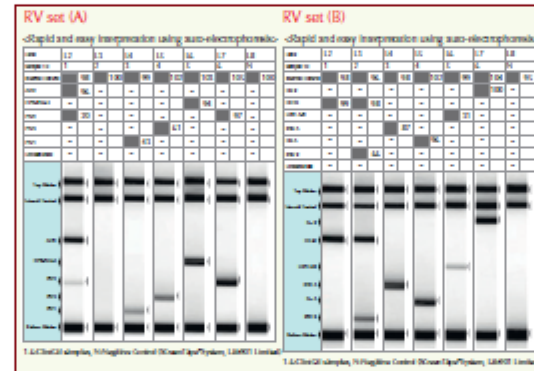




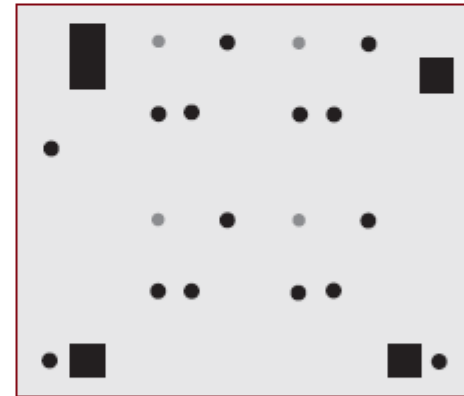
Amplification "multiplex"



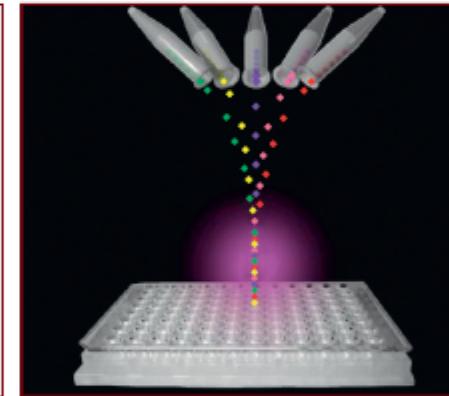
PCR temps réel



Analyse de fragments



Biopuces

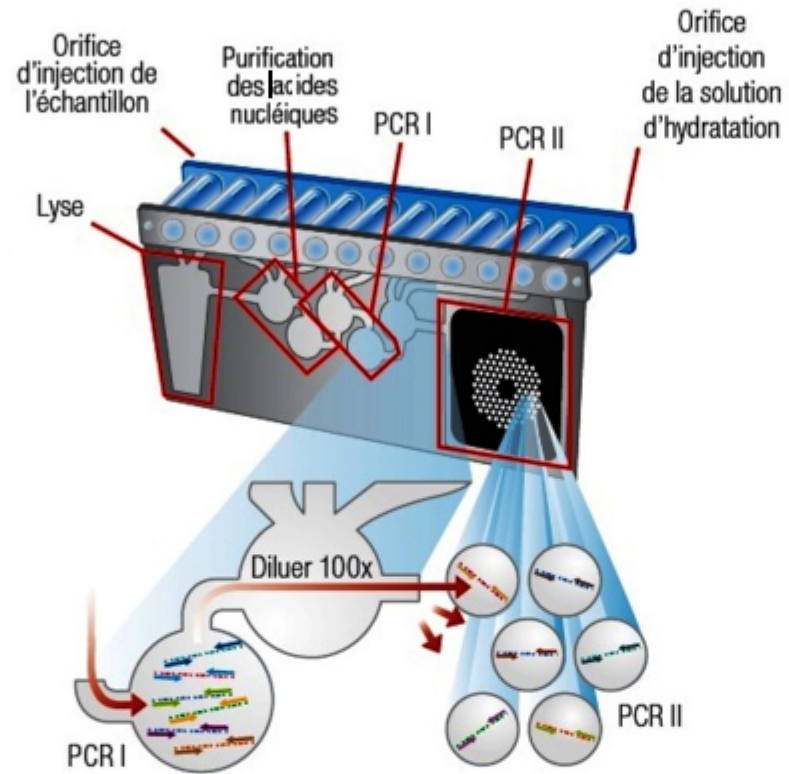


Luminex



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La cassette FilmArray®



**1 test. 20 pathogènes respiratoires.
Résultats en 1 heure environ**

HAUT ↕

Virus	Bactéries
<ul style="list-style-type: none">● Adénovirus● Coronavirus HKU1● Coronavirus NL63● Coronavirus 229E	<ul style="list-style-type: none">● <i>Bordetella pertussis</i>● <i>Chlamydomphila pneumoniae</i>● <i>Mycoplasma pneumoniae</i>



up to synchronize this system. Miniature heaters developed through thermal analysis allow for localized PCR on the cartridge, and magnetic actuators allow the manipulation of beads for biologic capture. And yet from the outside, the user simply loads a cartridge and touches the screen.

Development proceeded in accordance with IEC 61010 for hardware and IEC 62304 for embedded firmware, culminating in full-scale device verification and transfer of design for manufacturing. Key to the success of the ePlex development was tight-knit collaboration between Key Tech and GenMark teams. Dozens of prototypes were hand built for day zero panel testing. The electromechanical design iterated in lock-step with the panel design. Embedded software features were updated and new versions were distributed over Ethernet with short turnaround. Each design choice and feature was examined and



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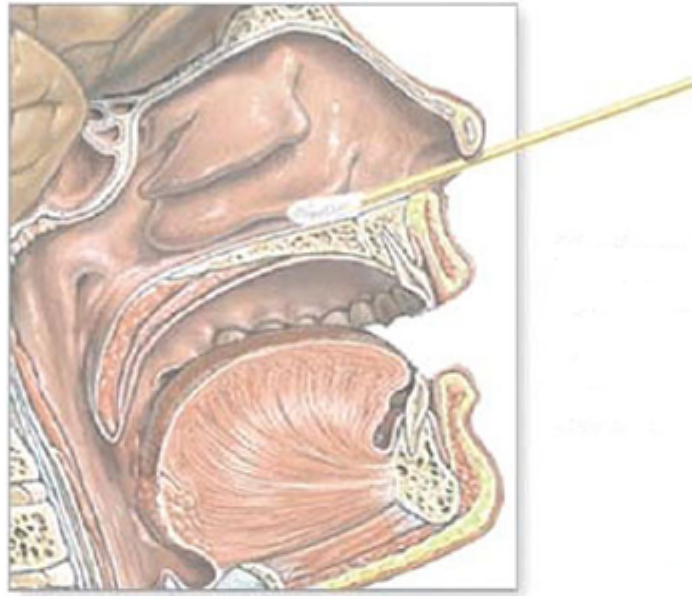


Figure 4 : Écouvillonnage endonasal

Et dans le liquide broncho- alvéolaire ?

Chez les patients immunodéprimés, il faut savoir qu'après quelques jours d'évolution, le ou les virus associé(s) à la pneumopathie peuvent être détectés par PCR dans le LBA cependant qu'ils ne sont plus détectables(s) dans l'arbre respiratoire supérieur et en particulier dans les fosses nasales. Dans ces cas précis, il faut alors favoriser une aspiration de liquide bronchoalvéolaire (LBA), compte tenu de sa richesse en cellules respiratoires.

1 test. 20 pathogènes respiratoires. Résultats en 1 heure environ

HAUT 

Virus	Bactéries
<ul style="list-style-type: none">● Adénovirus● Coronavirus HKU1● Coronavirus NL63● Coronavirus 229E● Coronavirus OC43● Métapneumovirus humain● Rhinovirus humain/Entérovirus● Virus de la grippe A● Virus de la grippe A/H1● Virus de la grippe A/H1-2009● Virus de la grippe A/H3● Virus de la grippe B● Virus parainfluenza 1● Virus parainfluenza 2● Virus parainfluenza 3● Virus parainfluenza 4● Virus respiratoire syncytial	<ul style="list-style-type: none">● <i>Bordetella pertussis</i>● <i>Chlamydomphila pneumoniae</i>● <i>Mycoplasma pneumoniae</i>

Fabricant : BioFire Diagnostics, LLC - 390 Wakara Way, Salt Lake City - UT 84108, USA.

BioFire est une filiale détenue à 100% par bioMérieux.

Ces produits sont destinés aux professionnels de santé (Pour usage diagnostique *in-vitro* FDA Cleared | Certifié CE-IVD)

Rapid communications

Prolonged shedding of influenza A(H1N1)v virus: two case reports from France 2009

H Fleury¹, S Burrel¹, C Balick Weber², R Hadrien³, P Blanco⁴, C Cazanave⁵, M Dupon⁵

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We observed a prolonged shedding of virus 14 and 28 days after symptom onset in two patients with pandemic H1N1 influenza, who did not have immunodepression and were treated with neuraminidase inhibitor. This prolonged shedding was not associated with the emergence of resistance mutation H275Y in the viral neuraminidase gene.

From 1 May until the beginning of October 2009, the virology laboratory in Bordeaux received more than 1,200 nasopharyngeal samples from the southwest of France for diagnosis of influenza A(H1N1)v virus by realtime RT-PCR, 186 of which were found positive. For five pandemic H1N1 influenza cases, we had the opportunity to monitor the duration of viral shedding and present here two cases of prolonged shedding.

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Research articles

Pandemic influenza A(H1N1)2009: molecular characterisation and duration of viral shedding in intensive care patients in Bordeaux, south-west France, May 2009 to January 2010

L Malato^{1,2}, V Llavador^{1,2}, E Marmier¹, J Youssef³, C Balick Weber³, H Rozé³, E Bessede⁴, H J Fleury¹

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From May 2009 to January 2010, the Virology Laboratory at the University Hospital of Bordeaux received more than 4,000 nasopharyngeal samples from the Aquitaine region (south-west France) for the diagnosis of pandemic influenza A(H1N1)2009. Eighty-three infected patients deteriorated and were admitted to intensive care units. Our study focused on 24 of these patients. Positivity for influenza A(H1N1)2009 was monitored by realtime PCR and duration of viral shedding was determined. The first available sample of each patient was analysed for bacterial, fungal and viral co-infection. We observed six bacterial (or bacterial/fungal) co-infections and one viral co-infection

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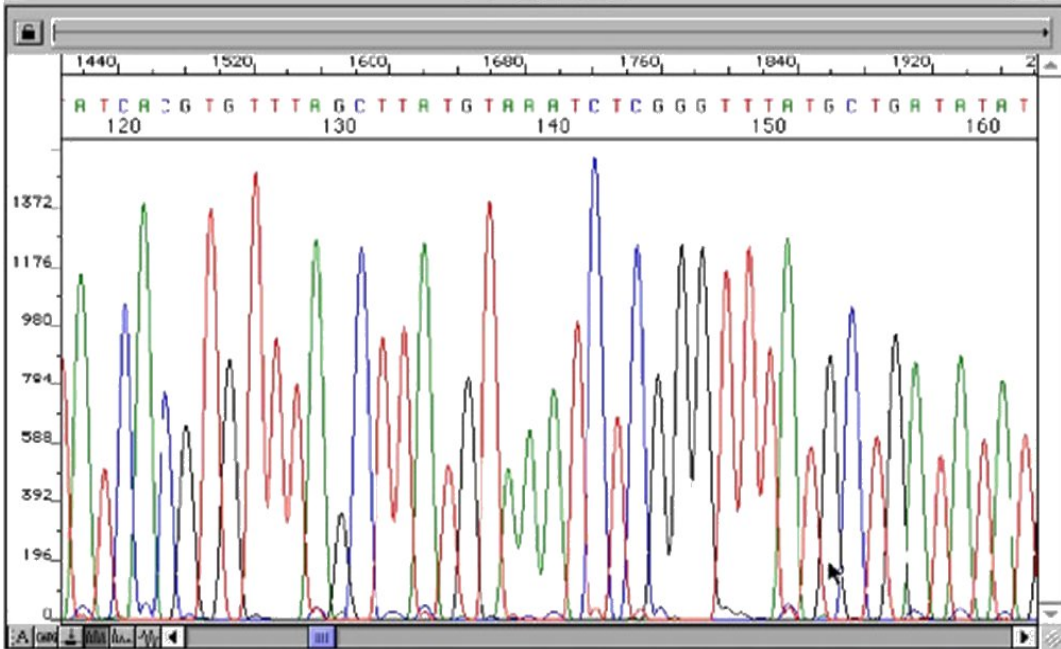
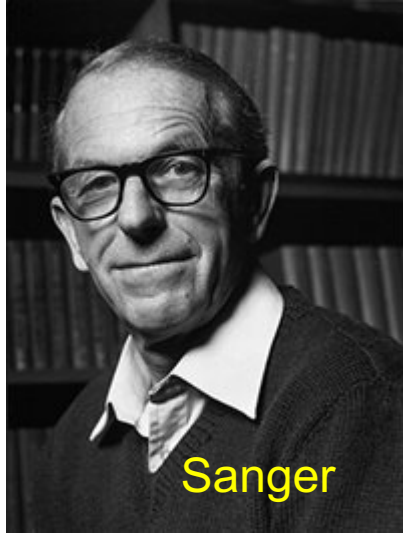
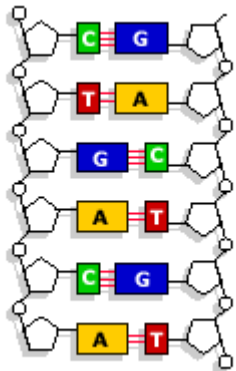
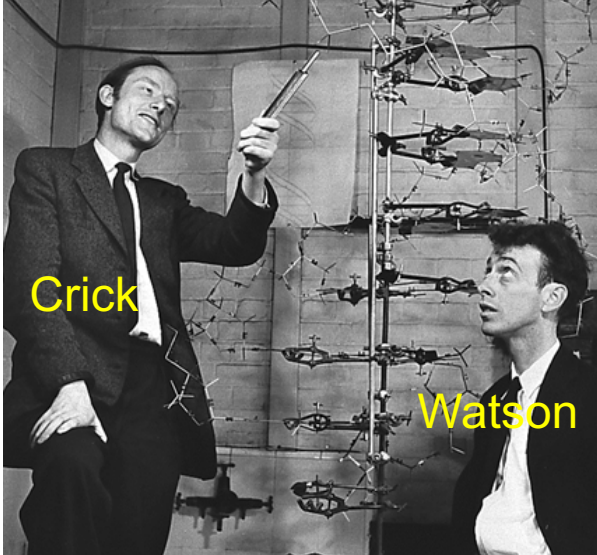
Viral shedding in intensive care patients determined by detection of A(H1N1)2009 RNA by realtime PCR, Bordeaux, May 2009–January 2010 (n=18)

Patient	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Day 15	Day 16	Day 17	Day 18	Day 19	Day 20	Day 21	Day 22	Day 23	Day 24	Day 25	Day 26	Day 27	Day 28
1								+		+	+	+	+	+					+						+	+	+	+	
2					+	+		+					+			+								+		+	+	+	
3	+			+		+				+					+			+	+										
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Day0: Day of onset of symptoms (or first positive PCR when onset of symptoms could not be determined).

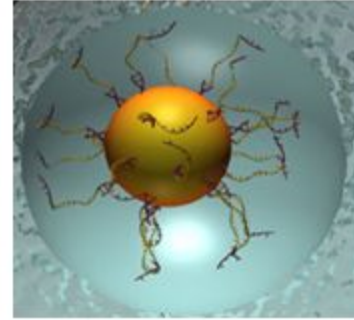
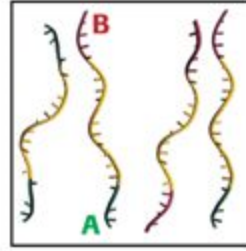
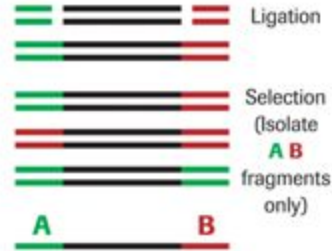
The H275Y mutation was not detected in any of our patients, nor was any other mutation at position 275 of the neuraminidase gene

ADN et séquençage



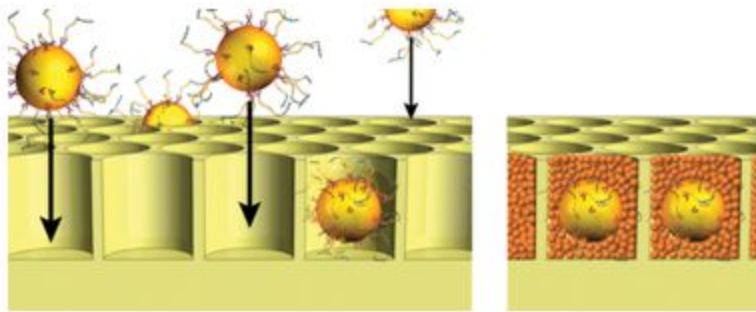
NGS

Overview of The 454 Sequencing System

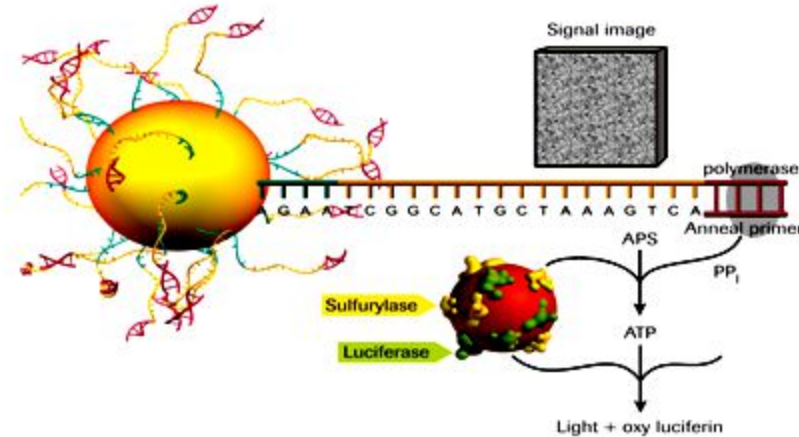


1) Prepare Adapter Ligated ssDNA Library (A-[insert]-B)

2) EmPCR: Clonal Amplification on 28 μ beads followed by enrichment



3) Load beads and enzymes in PicoTiterPlate™



4) Perform sequencing-by-synthesis on the 454 Sequencer

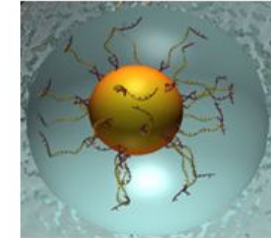
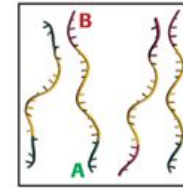
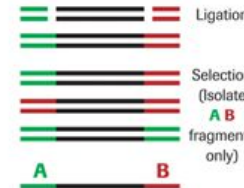
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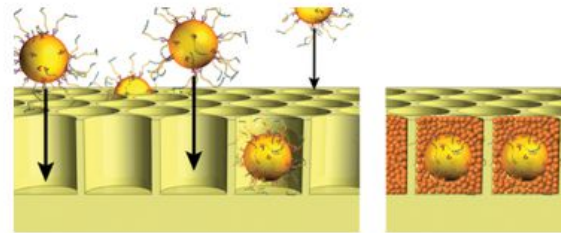
Illumina

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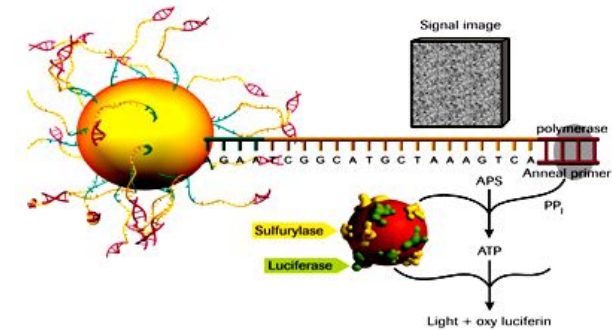


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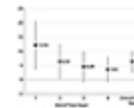
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Oseltamivir Resistance during Treatment of Influenza A (H5N1) Infection

Menno D. de Jong, M.D., Ph.D., Tran Tan Thanh, M.Sc., Truong Huu Khanh, M.D., Vo Minh Hien, M.D., Gavin J.D. Smith, Ph.D., Nguyen Vinh Chau, M.D., Bach Van Cam, M.D., Phan Tu Qui, M.D., Do Quang Ha, M.D., Ph.D., Yi Guan, M.D., Ph.D., J.S. Malik Peiris, D.Phil., M.D., Tran Tinh Hien, M.D., Ph.D., [et al.](#)

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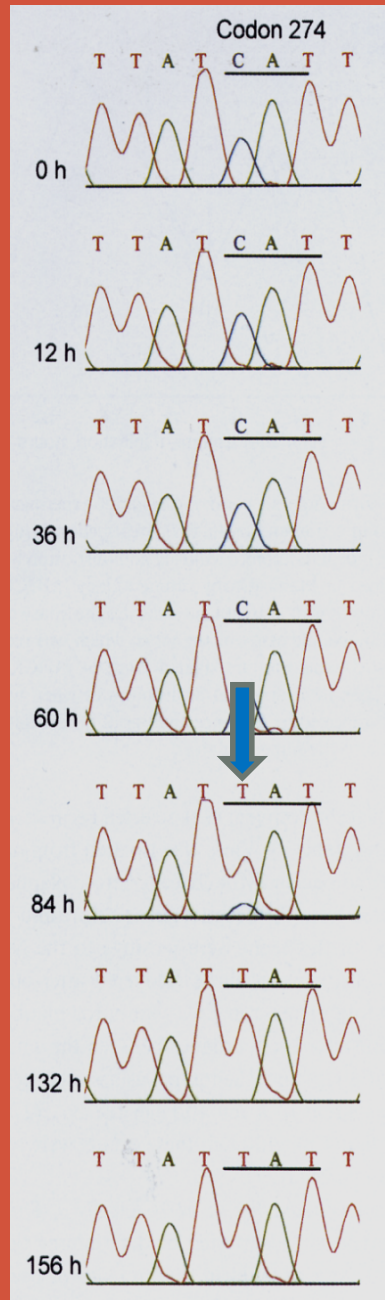
N Engl J Med 2005; 353:2667-2672

DOI: 10.1056/NEJMoa054512

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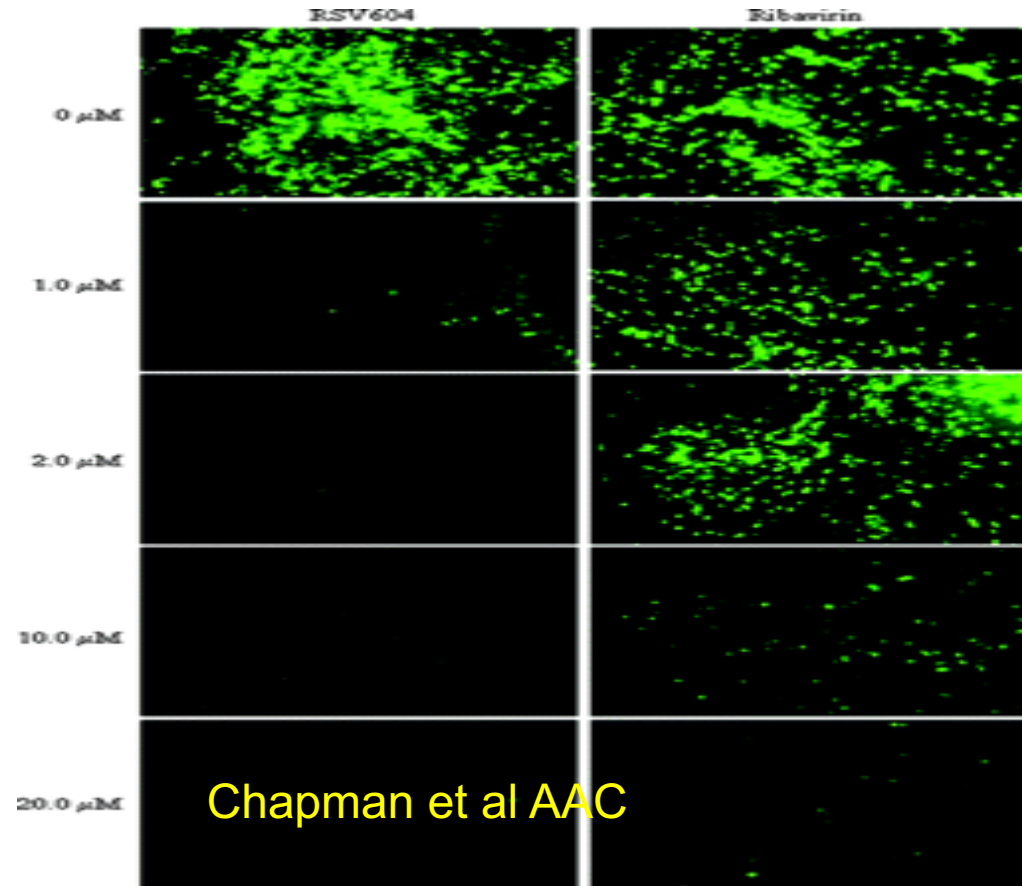
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CAT: histidine
TAT: tyrosine

Antiviraux

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- **VRS**: Ribavirin, Palivizumab, RSV-604, Favipravir
- **HPIV** : Ribavirin
- **HMPV**: Ribavirin



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2. European Program for Intervention Epidemiology Training
3. Direction Départementale de l'Action Sanitaire et Sociale, Pyrénées Atlantiques, France
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