



# Emergences virales et risques épidémiques : du MERS CoV, a Influenza pour finir par Ebola.

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# Etat des lieux depuis 1970 (liste non exhaustive)

1973	Rotavirus	1995	Virus de l' Hépatite G
1977	Ebola virus		HHV8
	Hantaan virus	1996	ESB (?)
	Influenza A H1N1		Australian bat lyssavirus
1980	HTLV-1	1997	Influenza A H5N1 (1er)
1982	HTLV-2		Virus Menangle
1983	HIV-1	1999	Virus Nipah
1986	HIV-2		Influenza A H9N2
1988	Virus de l' Hépatite E		Virus West Nile (Amériques)
	HHV6		Metapneumovirus humain
	2000	2003	Influenza A H5N1 (2e)
1990	Virus Guanarito		Sars-Co
1993	Virus Sin Nombre		Influenza A H7N7
1994	Virus Sabia	2004	Influenza A H5N1 (suite)
	Virus Hendra		other Influenza A viruses
			NL coronavirus
		2009	Influenza A H1N1pdm
		2011	Influenza A H3N2v
		2012	Mers CoV...
		2013	Influenza A H10N7
			Influenza A H6N1

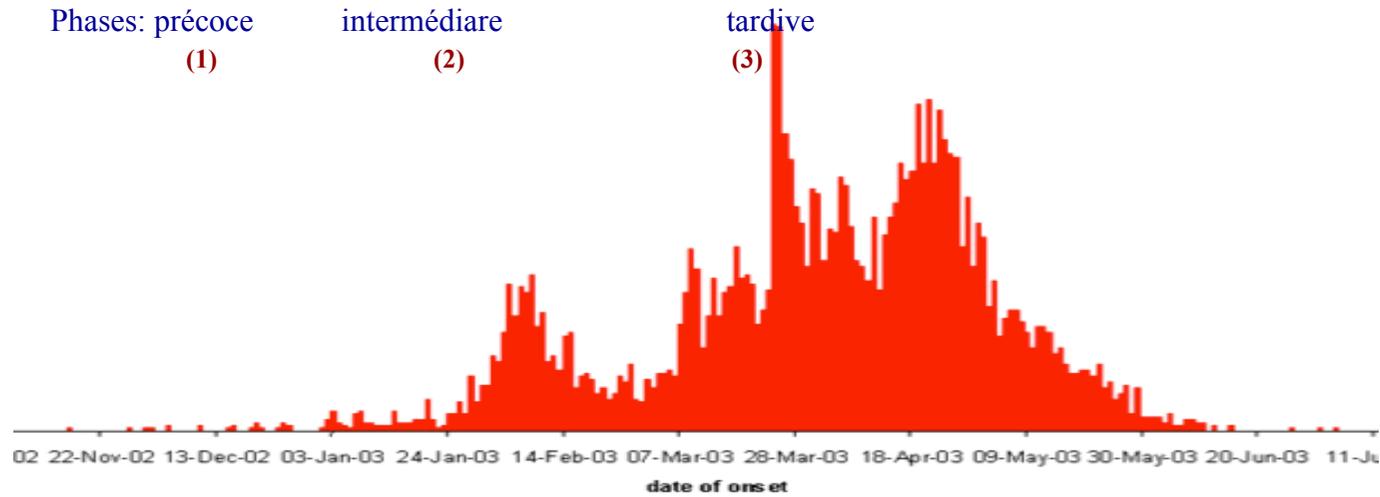
# Introductions depuis un réservoir animal (exemples)

- Rongeurs
  - Hantaan virus (inclus Dobrava et Puumala)
- Volailles, Oiseaux
  - Influenza A,
  - Virus West Nile
- Cochons
  - Influenza A,
  - Virus Nipah
- Chauve-souris
  - Australian bat lyssavirus,
  - Virus Hendra,
  - Virus Menangle,
  - Ebola virus,
  - Sars-Co
  - MersCoV
- Singes
  - HIV-1

# Epidémiologie des virus émergents

- Afrique
  - Ebola, West Nile, etc..
- Amériques
  - Guanarito, Sin Nombre, Sabia, West Nile, etc...
- Asie & Océanie
  - Influenza, SARS-Co, Encéphalite Japonaise, Hendra, Nipah, Menangle, Hantaan virus, etc
- Moyen Orient
  - NCoV
- Europe
  - Influenza, Encephalite à tique, Pumalaa, Dobrava, etc

**Novembre 2002-Janvier 2003** : dans la province de Guangdong quelques cas de pneumonies atypiques progressant vers une détresse respiratoire

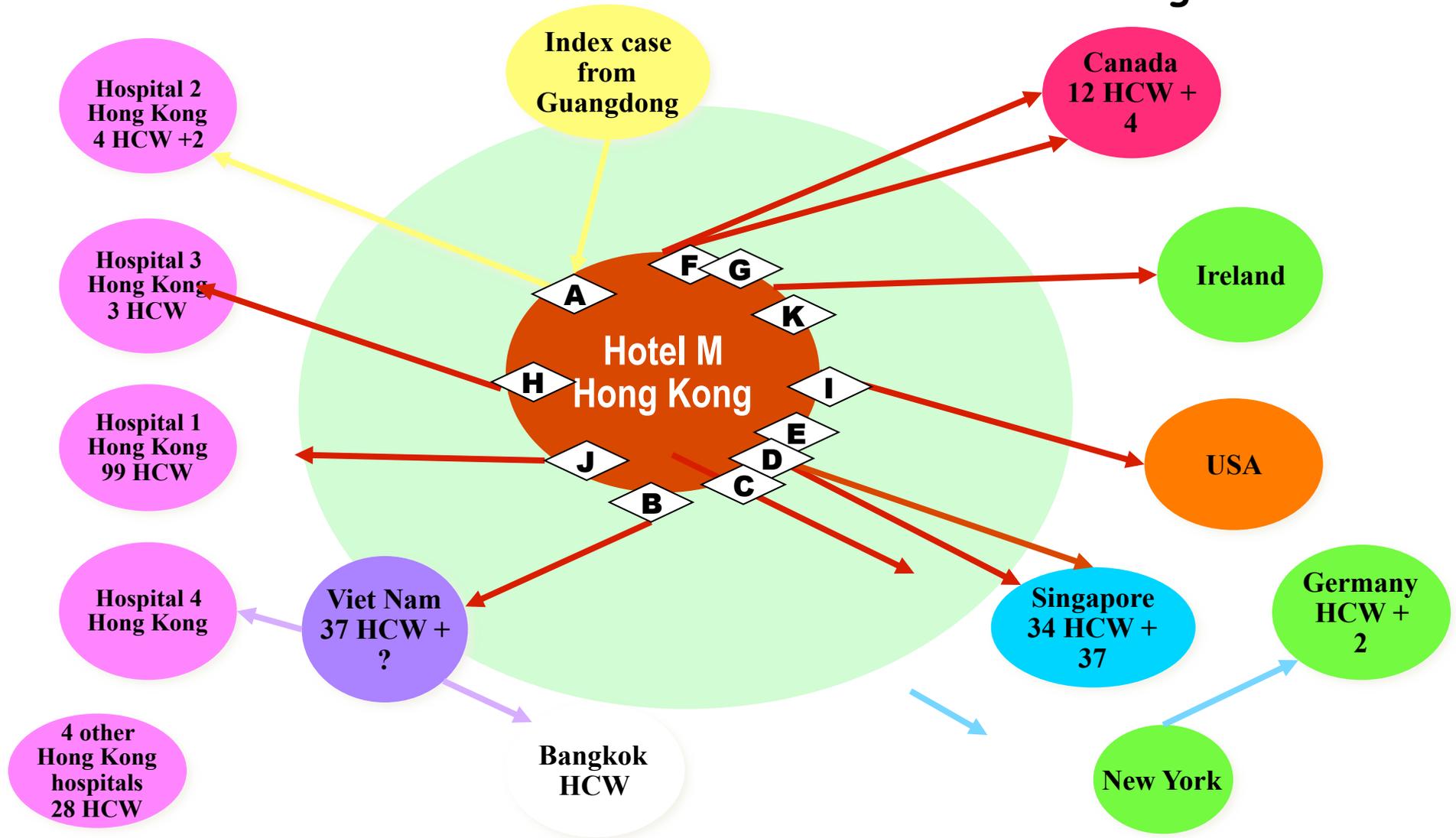


- **Janvier-Février 2003**: épidémies nosocomiales (2)
- **Février 2003**: épisode de l'hôtel M. à Hong Kong (3)
  - diffusion mondiale en China (5327), à Hong Kong (1755), Taiwan (686), Singapoure (206), au Vietnam (63), au Canada (250) et en Europe (37) ....
- **Mars 2003** :
  - mise en place des stratégies pour contenir l'épidémie
  - identification du SARS-CoV
- **Juillet 2003** : Notification par l'OMS de la fin de l'épidémie :

**8460 cas probables et 808 décès**

# Hôtel M. à Hong Kong , février 2003

219 soignants  
30 non-soignants



Il existe des « super transmetteurs » dans le SARS (> 8 cas secondaires)

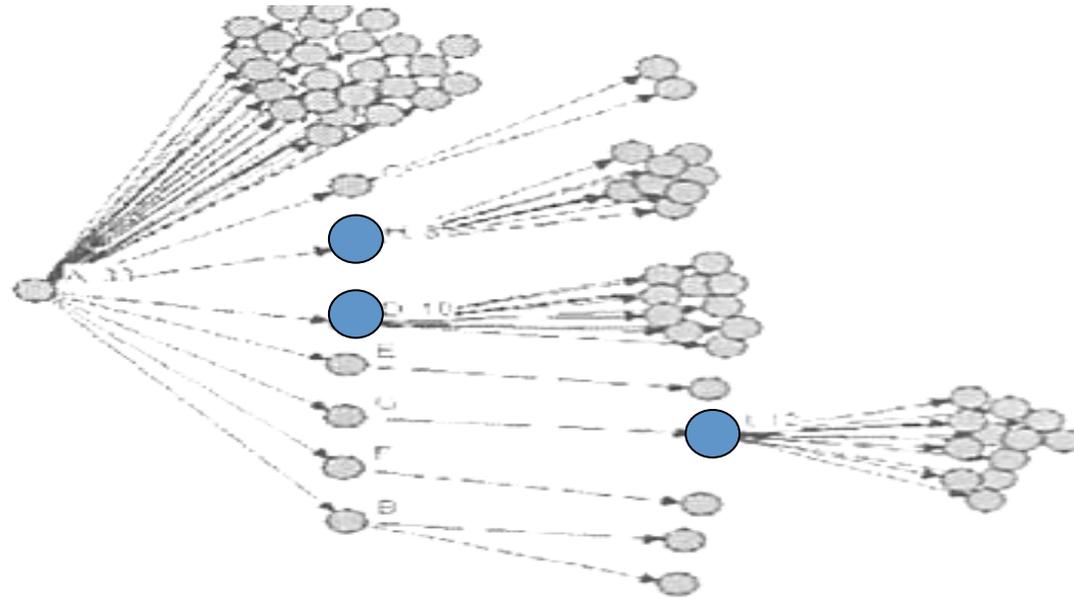


Figure 2. Probable cases of severe acute respiratory syndrome by source of transmission in chain of 77 cases in Beijing, 2003.

**Avènement non rare: # 5%**

**Relation avec:**

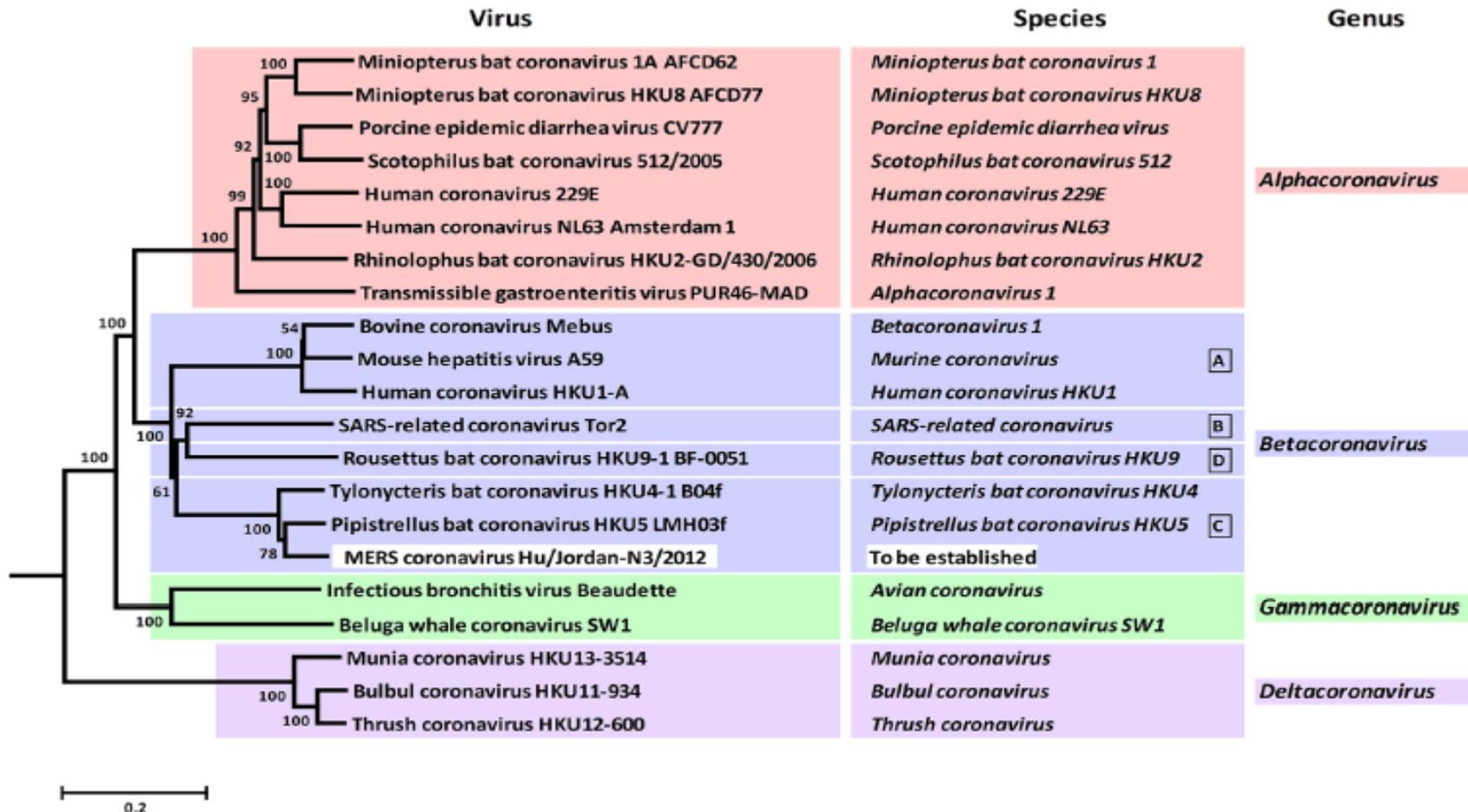
- facteurs environnementaux: hôpital.....
- patients âgés ou atteints gravement.....
- propriétés génétiques des souches ?

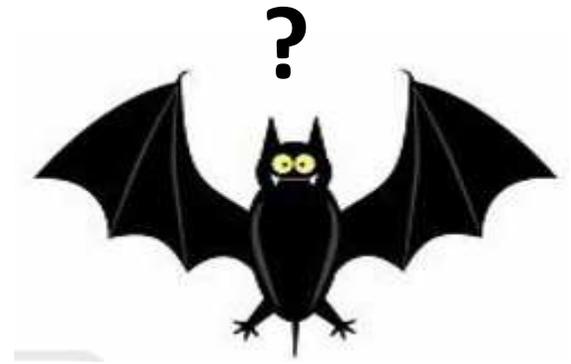
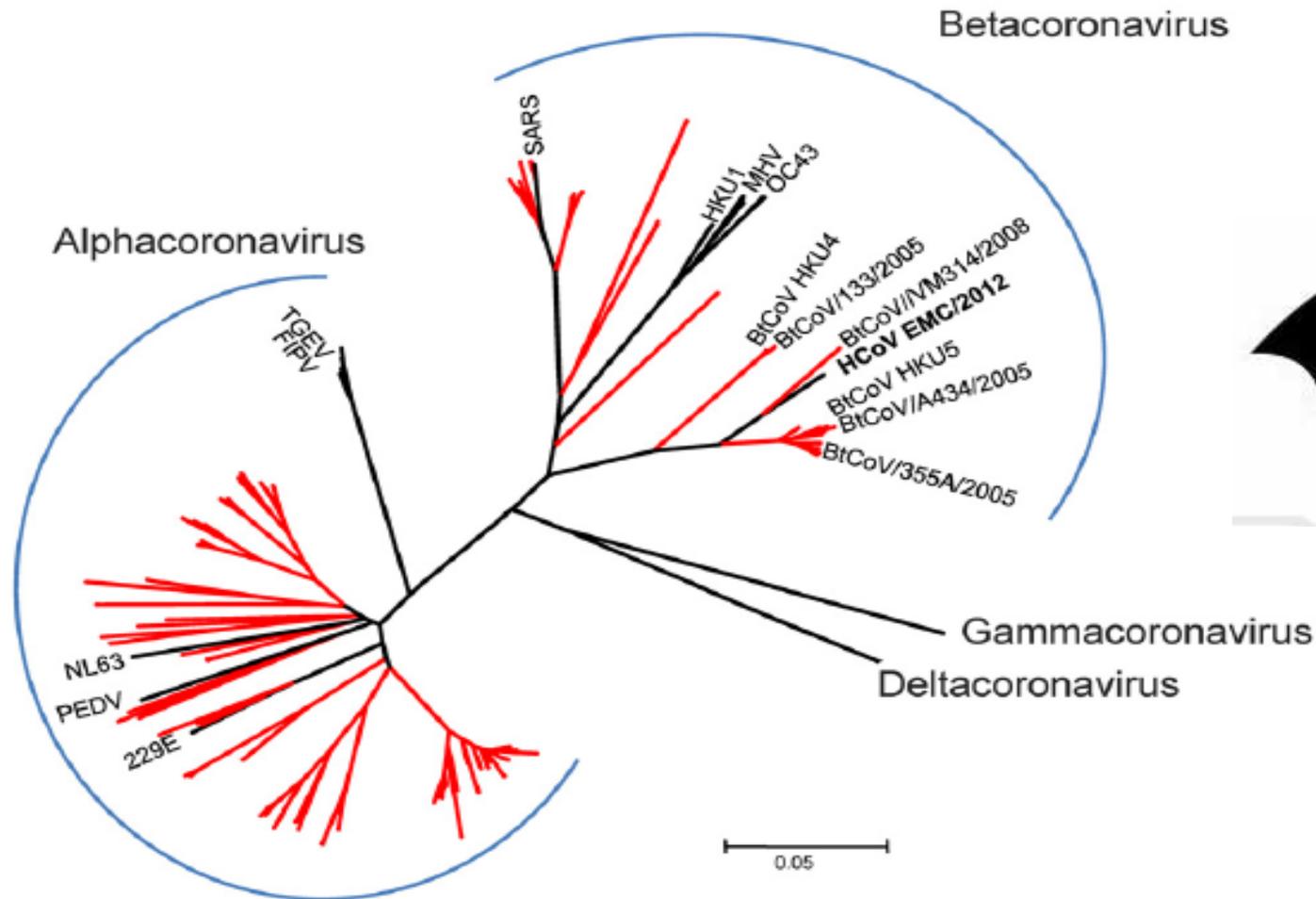
# Le Mers CoV

## Jordanian initial cluster (1)

- Premiers cas en Jordanie en Avril 2012, identifiés 7 mois plus tard après l'identification de cas au Qatar et en Arabie Saoudite.
- Parmi ces 13 cas confirmés ou probables, 10 étaient des soignants et 2 des contacts familiaux . Ces cas secondaires sont survenus en 2 vagues.
- Le cas index avait 25 ans, et a développé les symptômes le 21 mars. Il fut hospitalisé le 4 avril. Les premiers cas secondaires ont été des infirmières. Elles sont décédées toutes les deux.
- Un rapport sur l'épidémie disait : “afin d'éviter la stigmatisation des patients, le personnel soignant avait décidé de ne pas porter d'équipement de protection individuel (excepté des gants) lors de la prise en charge des cas...

# Identification du MERS-CoV (2012) et hypothèses sur le réservoir

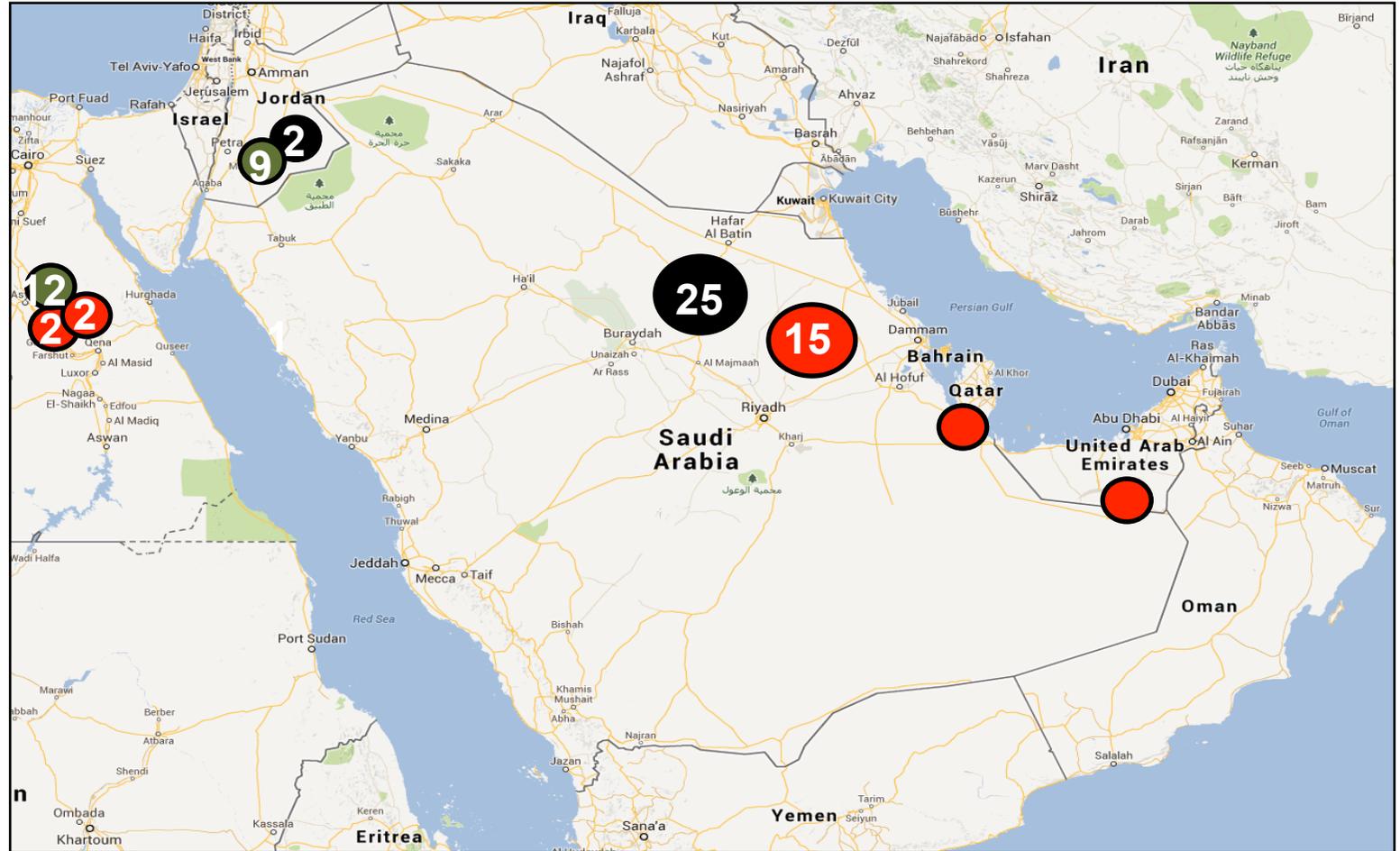




Bat coronavirus	Host	Location	Accession number
BtCoV/VM314/2008	<i>Pipistrellus</i> bat	Netherlands	GQ259977
BtCoV/133/2005	<i>Tylonycteris</i> bat	China	DQ648794.1
BtCoV/ 355A/2005	<i>Pipistrellus</i> bat	China	DQ648809.1
BtCoV/A434/2005	<i>Pipistrellus</i> bat	China	DQ648819.1
HKU4	<i>Pipistrellus</i> bat	China (HK)	DQ249214.1
HKU5	<i>Tylonycteris</i> bat	China (HK)	DQ249217.1

# Emergence du MERS-CoV (2012)

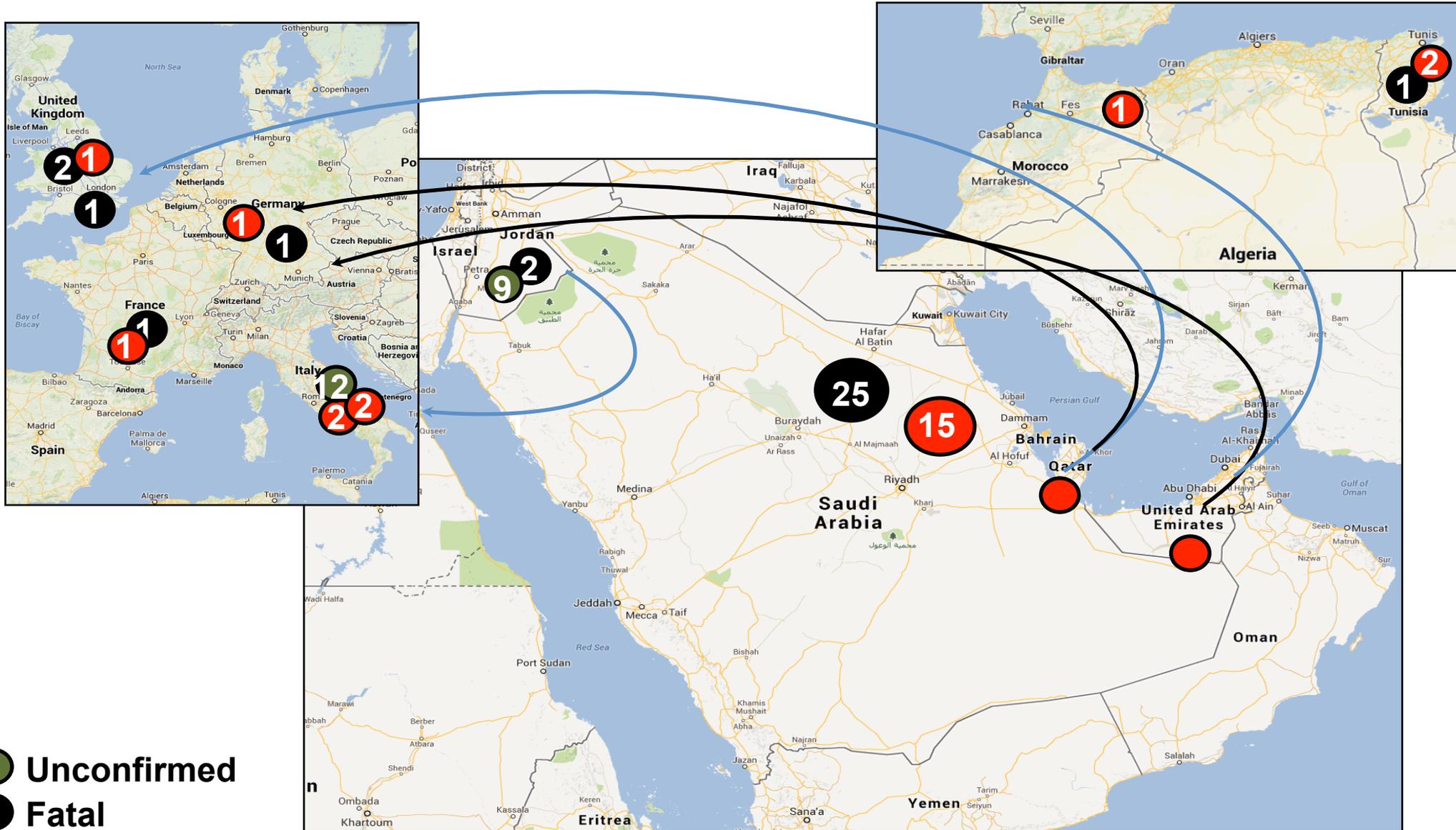
- 55 confirmed cases, 31 deceased, 56% CFR -



-  Unconfirmed
-  Fatal
-  Under care/recovered

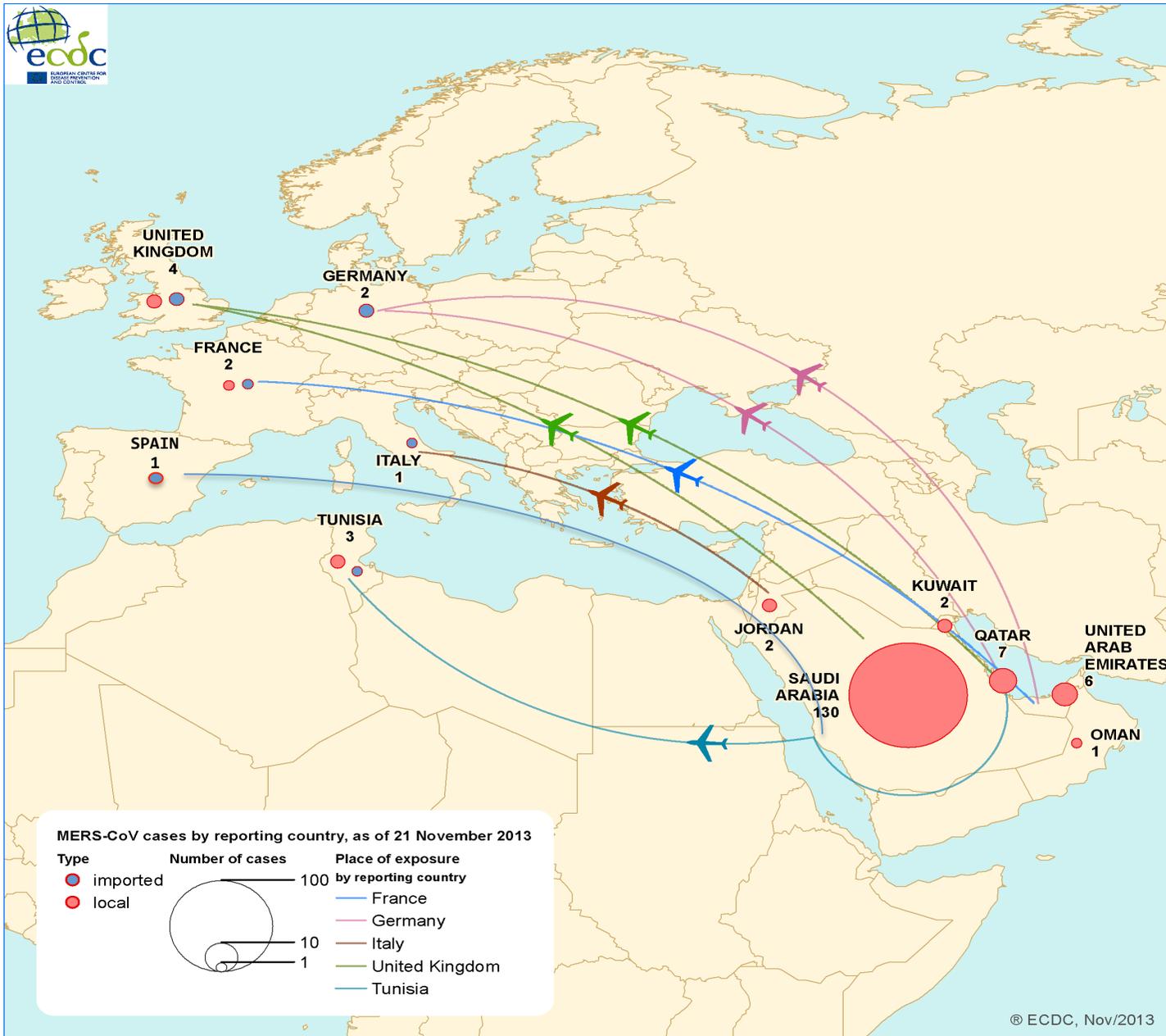
# Emergence of MERS-CoV et des cas exportés

- 55 confirmed cases, 31 deceased, 56% CFR -

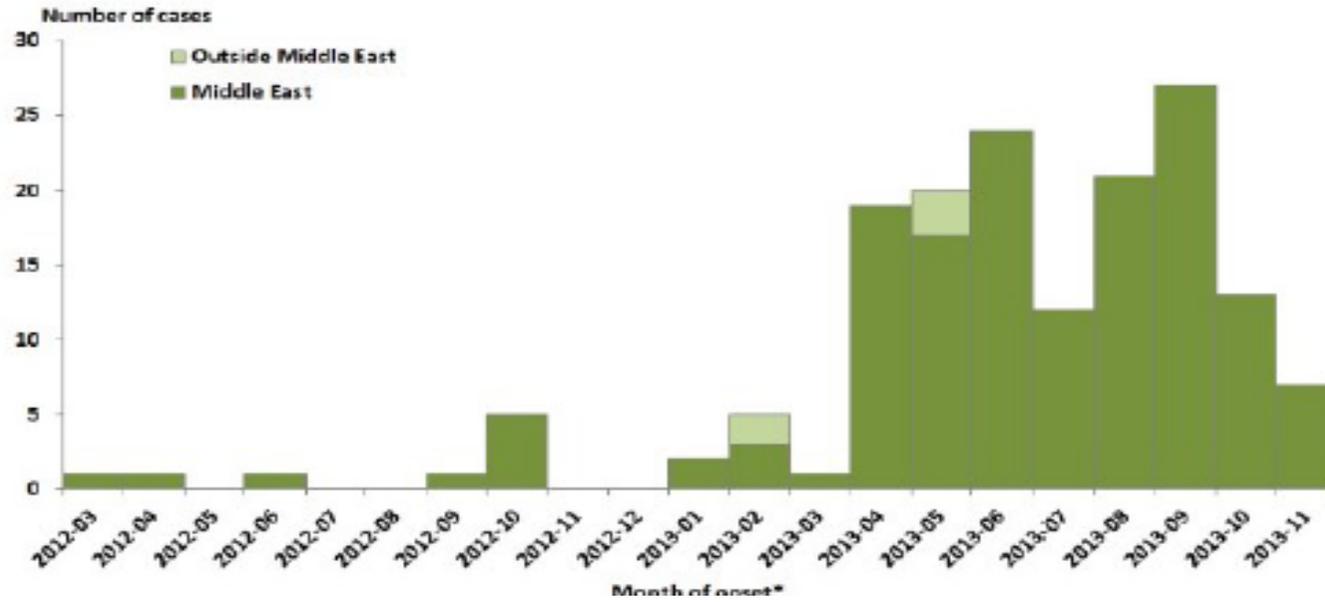


- Unconfirmed
- Fatal
- Under care/recovered

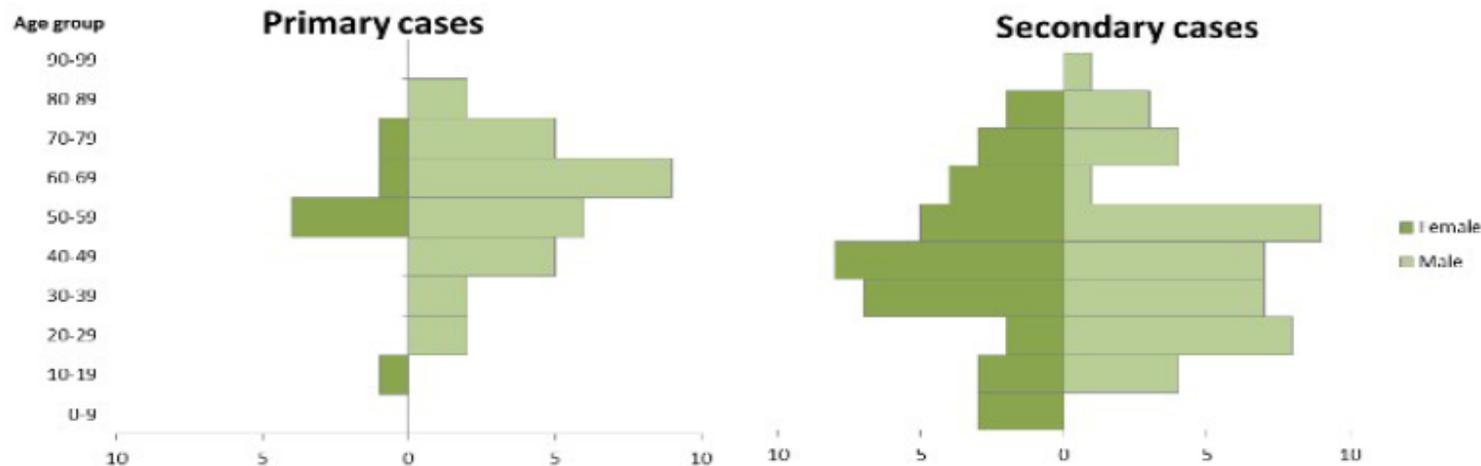
# Etat des lieux au 22 Novembre 2013



**Figure 1. Distribution of confirmed cases\* of MERS-CoV by month of onset and probable place of infection, March 2012 – 22 November 2013 (n=160\*\*)**



**Figure 3. Distribution of confirmed cases of MERS-CoV by primary (N=39) and secondary cases (N=83) by gender and age group, March 2012 - 22 November 2013**



# Courbe épidémique des 669 cas confirmés de MERS-CoV (2012-2014) avant le pèlerinage de 2014

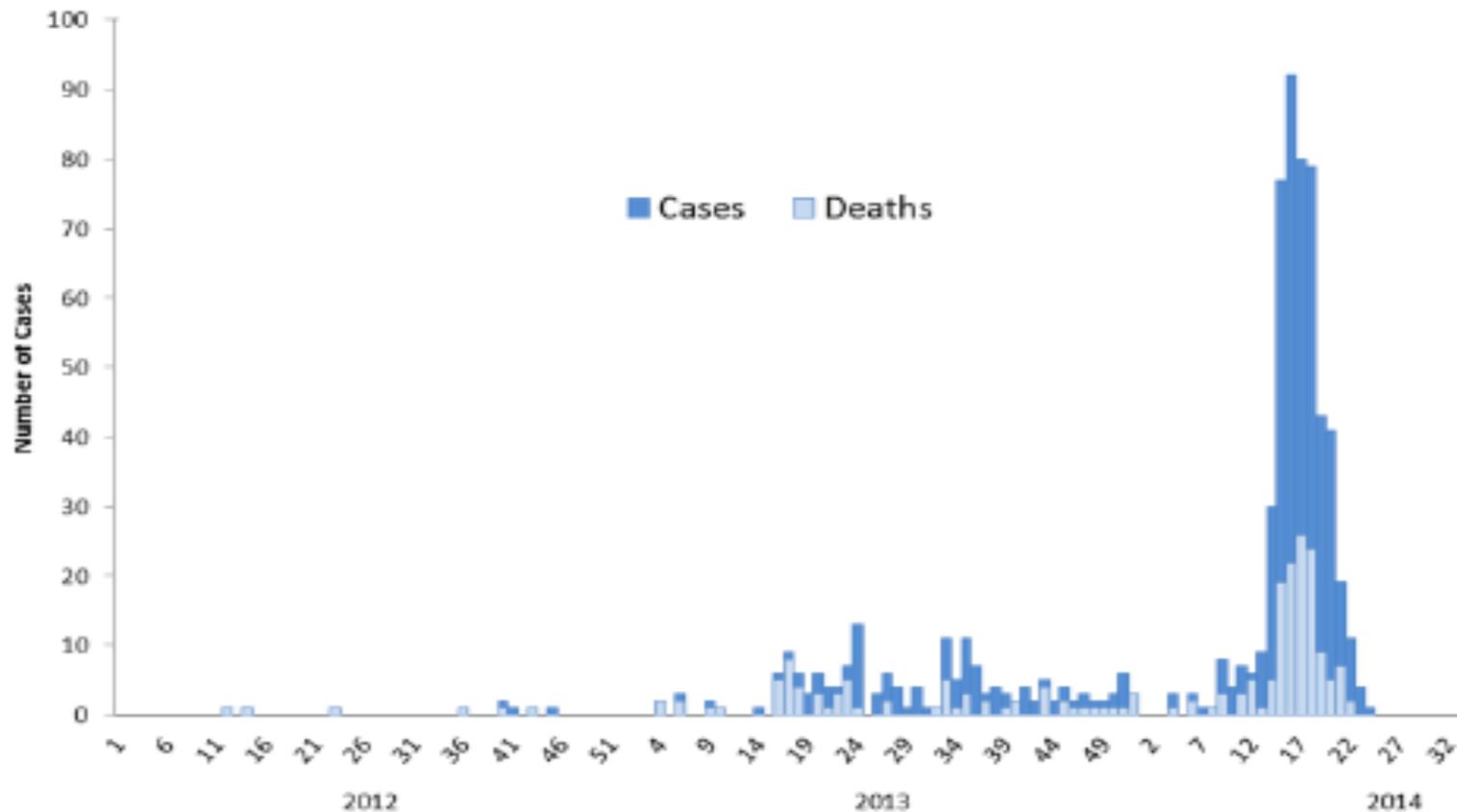
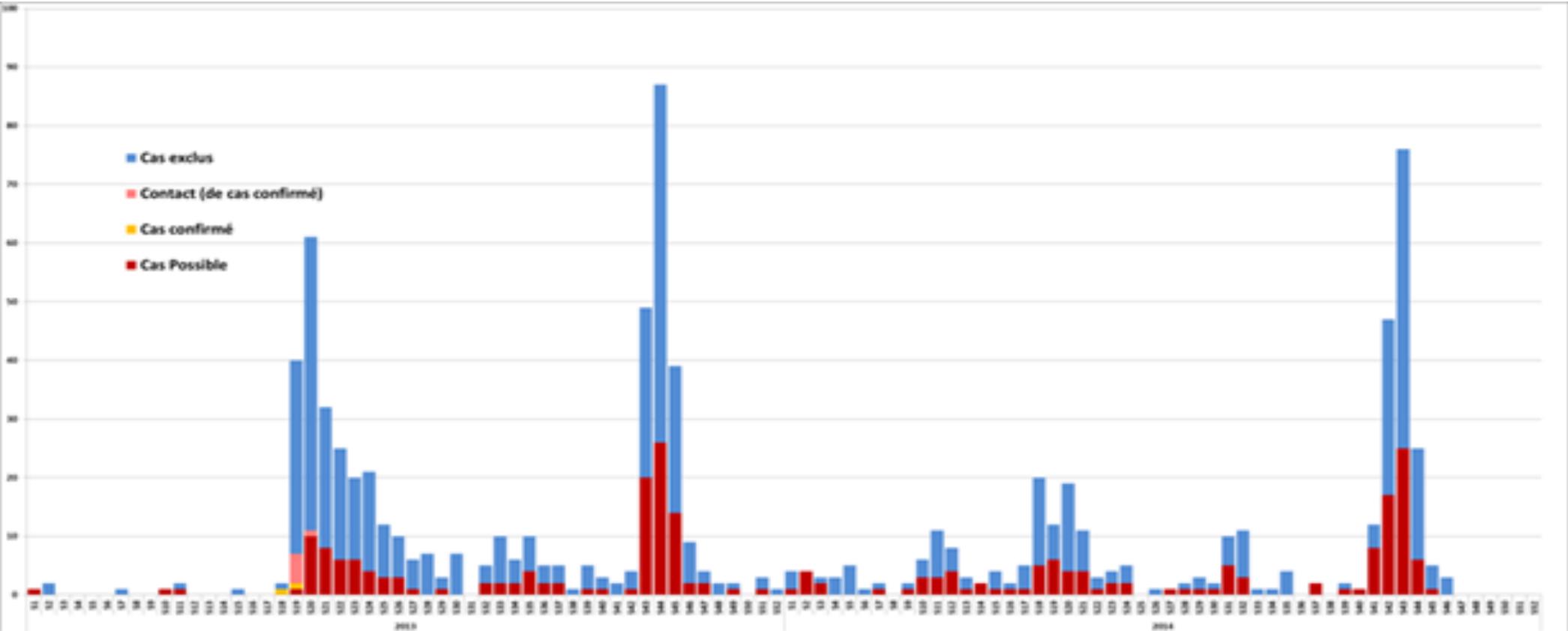


Figure 1. Epidemic Curve of MERS-CoV Cases as of 9 June 2014 (n=699)\*

\*Does not include 113 cases announced on MOH website on 3 June as these cases are currently undergoing verification

# Cas investigués en France au 20 nov 2014 (source INVS)



## tests virologiques

N° InVS	DATE RÉCEPTION	ORIGINE PRÉLÈVEMENT	NATURE PLT	MERS-CoV	1er Rés
?	10/05/2013	CHU Grenoble	Nasopharyngé	Négatif	Négatif
S55	13/05/2013	CHU Bordeaux	indéterminé	Négatif	Grippe A H3N2
S83	17/05/2013	CH Chambéry	Nasopharyngé	Négatif	Picornavirus
S118	24/05/2013	Hôpital Desgenettes	Nasopharyngé	Négatif	Négatif
S120	26/05/2013	CH Saint-Etienne	Nasopharyngé	Négatif	Picornavirus
MP002	20/05/2013	CH Toulouse	Nasopharyngé	Négatif	ParaInfluenza
S143	30/05/2013	CHU Lyon - HEH	LBA	Négatif	Négatif
S165	07/06/2013	CHU Lyon - CHLS	Nasopharyngé	Négatif	Picornavirus
S172 (sud011)	11/06/2013	Hôpital Nord - Marseille	Crachat	Négatif	Grippe A H3N2
S203	23/06/2013	Centre Hospitalier - Cannes	Nasopharyngé	Négatif	Grippe A H3N2
CAQ009	27/08/2013	CH - Bordeaux	Nasopharyngé	Négatif	Grippe A H3N2
S274	24/09/2013	CH St Jospheh-St Luc	Crachat	Négatif	Coronavirus
SUD021	25/10/2013	CH Avignon	Nasopharyngé	Négatif	Picornavirus
CRA019	25/10/2013	CH Valence	Nasopharyngé	Négatif	Coronavirus
Cas 30-20	25/10/2013	CHU Nimes	Nasopharyngé	Négatif	Grippe A H3N2
CRA020	26/10/2013	CHU Lyon - X Rousse / Chalier	Aspiration	Négatif	Négatif
976-01	28/10/2013	Mayotte / La Réunion	Aspiration	Négatif	Picornavirus
S304	28/10/2013	CHU Lyon - X Rousse / Mallet	Aspiration	Négatif	Grippe A H3N2 + corona
Cas 30-20	29/10/2013	CHU Nimes	Crachat	Négatif	Grippe A H3N2
CRA021	30/10/2013	CH Lyon - HEH / Surv Cont N1	Nasopharyngé	Négatif	Grippe A H3N2 & H1N1pdm
CRA022	30/10/2013	CH Lyon - HEH / UHCD N	Nasopharyngé	Négatif	Coronavirus + picorna
CRA023	31/10/2013	CH du pays de Gier - St Chamond	Crachat	Négatif	Grippe A
CLR30-02	31/10/2013	CHU Nimes	Nasopharyngé	Négatif	Picornavirus
976-01	31/10/2013	Mayotte / La Réunion	Aspiration	Négatif	Picornavirus + Para
976-02	31/10/2013	Mayotte / La Réunion	Aspiration	Négatif	Pico+Corona OC43
AM06	01/11/2013	CHRA Annecy	ANP	Négatif	Picornavirus
JD002	02/11/2013	HIA Desgenettes	Nasopharyngé	Négatif	Grippe A H3N2
Cluster#1	02/11/2013	CHU Toulouse	Nasopharyngé	Négatif	Grippe A (H1N1)pdm09
Cluster #2	02/11/2013	CHU Toulouse	Nasopharyngé	Négatif	Grippe A (H1N1)pdm09
AM13	02/11/2013	CHU Clermont-Ferrand / Aurillac	Nasopharyngé	Négatif	Grippe A H3N2
CRA024	04/11/2013	CH Lucien Hussen - Vienne	Nasopharyngé	Négatif	Négatif
CRA027-DC	06/11/2013	HIA Desgenettes	Nasopharyngé	Négatif	Picornavirus + adv
CRA026	06/11/2013	CHU St Etienne	Crachat	Négatif	Picornavirus
Auv_10	12/11/2013	CHU Clermont-Ferrand	Nasopharyngé	Négatif	Grippe A
Cas Contact Auv_10	12/11/2013	CHU Clermont-Ferrand	Nasopharyngé	Négatif	Grippe A
CE181113	19/11/2013	CH Macon	Crachat	Négatif	ADV

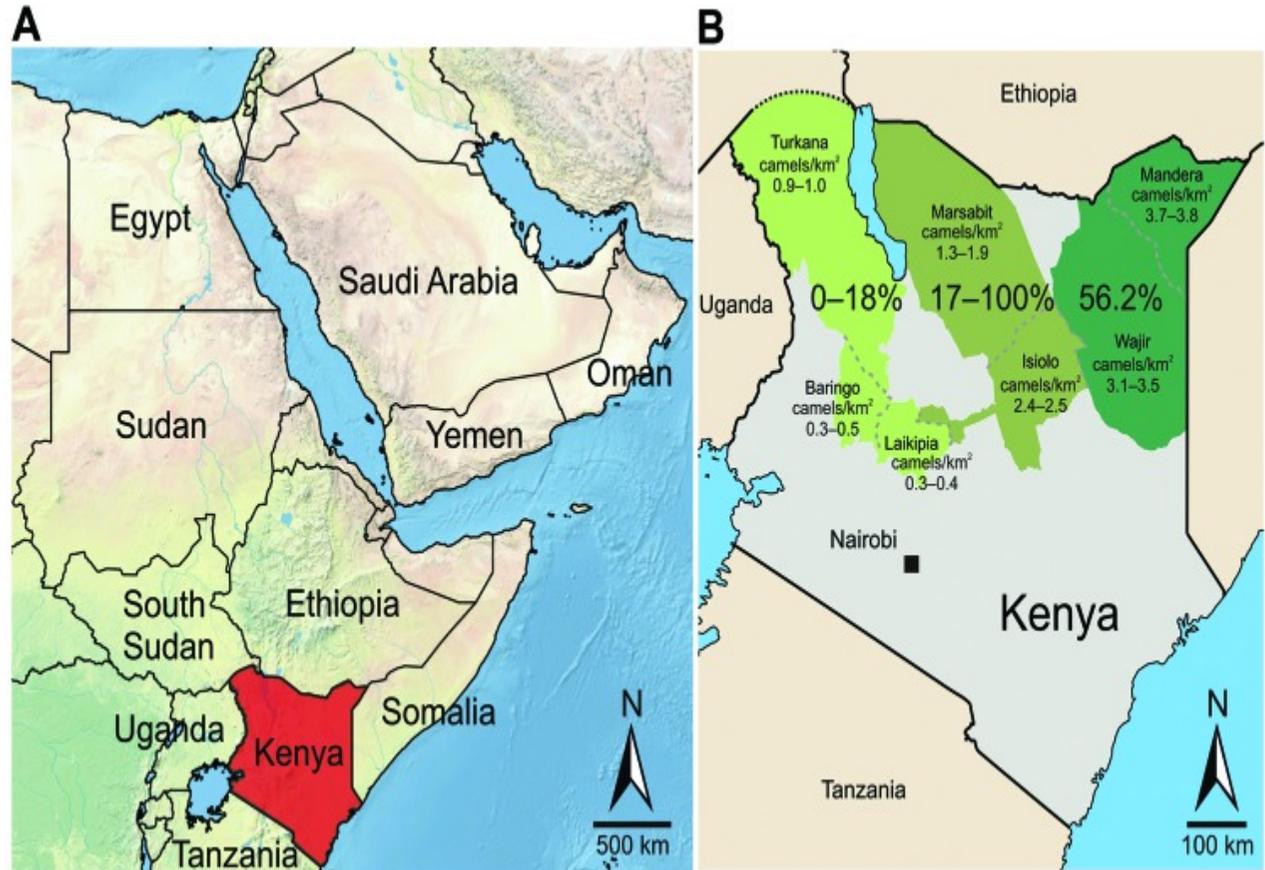
# Origine du Virus? Etude N°1

## Dromadaires



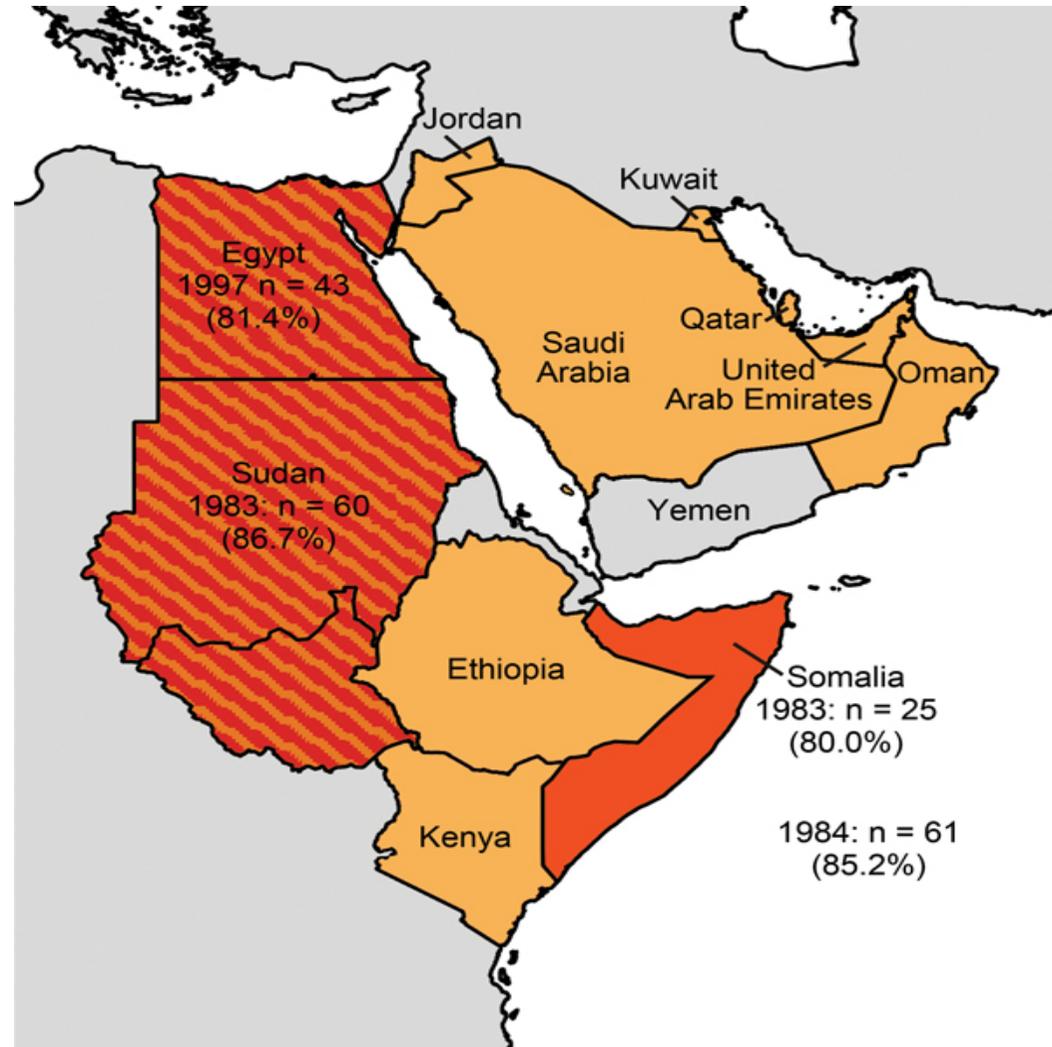
sérologie positive dromadaires (14-100%)

Détection virale par RT-PCR (4-35%)

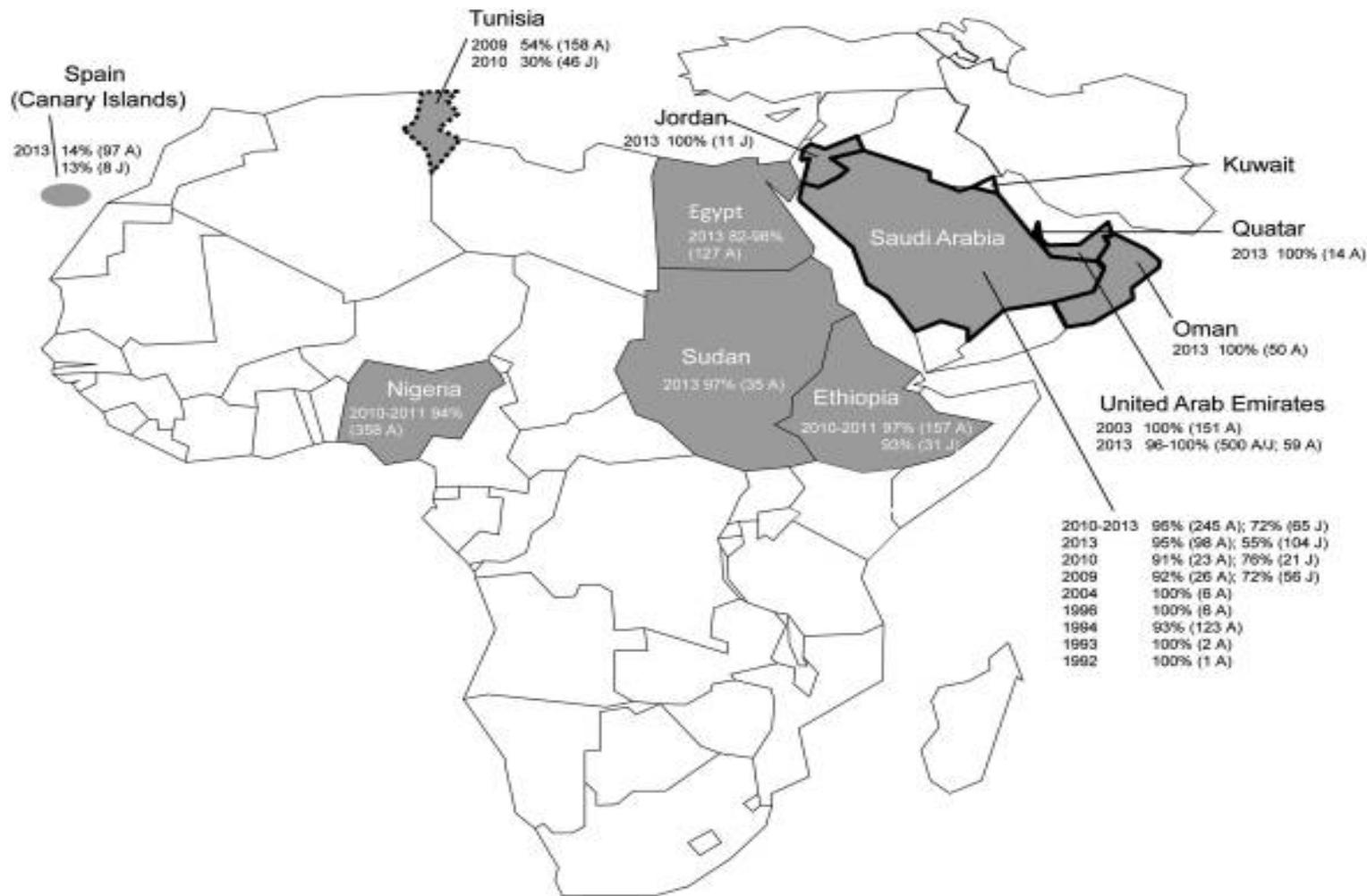


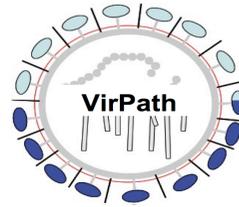
## Origine du Virus? Etude N°2 dans les pays fournisseurs

*Figure. Arabian Peninsula and neighboring countries of the Greater Horn of Africa in 2014. The study sites Egypt, Sudan (separated into Sudan and South Sudan), and Somalia are in dark orange and labeled with the year the camels were sampled, the number of samples, and the percentage of samples that were reactive in the MERS-CoV ELISA. Countries with previously reported MERS-CoV seropositive dromedaries are in light orange (overlap shown in stripes).*



# Etude N°3 : Prévalence des Anticorps contre le virus du MERS-CoV chez les camélidés en Afrique et en péninsule Arabique





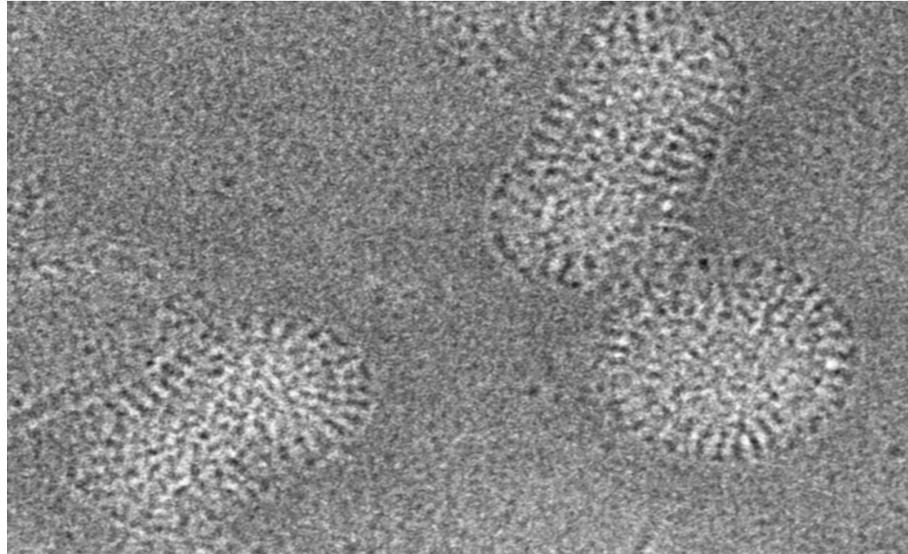
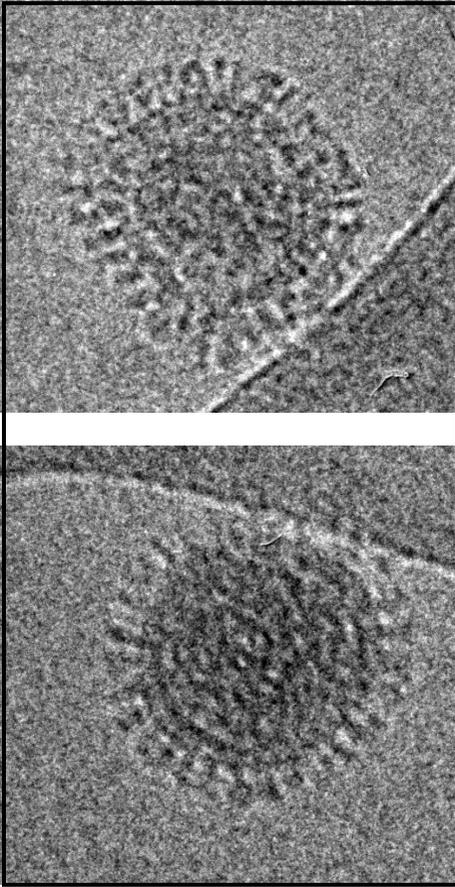
# influenzavirus emergents

**Bruno Lina**

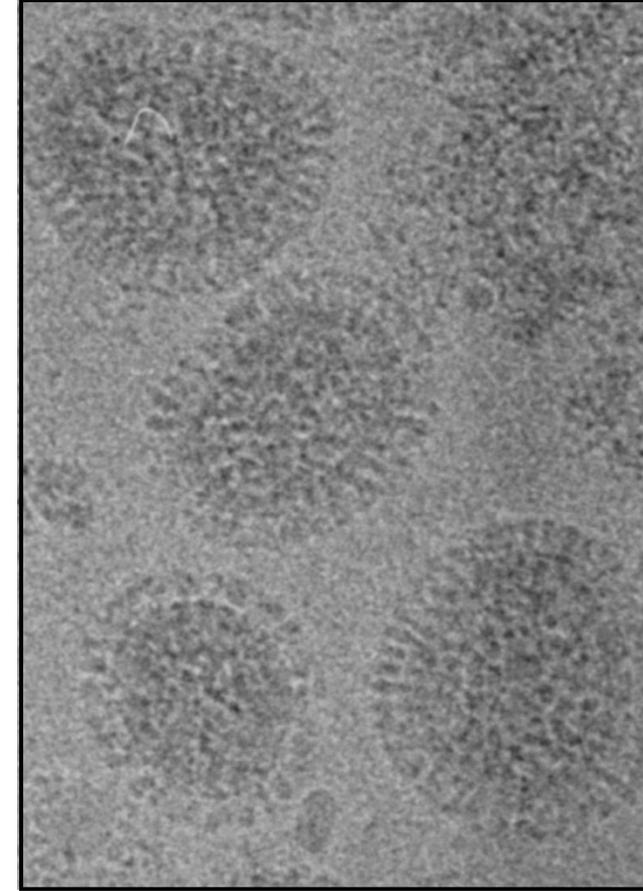
Hospices Civils de Lyon, CNR des virus influenza (Sud), F69677, Bron  
VirPath, EMR 4610, Université de Lyon, F69372, Lyon

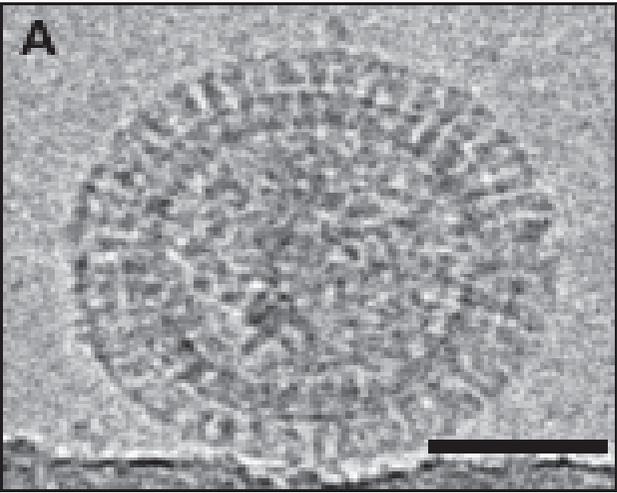
# *Acteur #1 : le virus*

*H1N1 A/NewCaledonia/20/99*

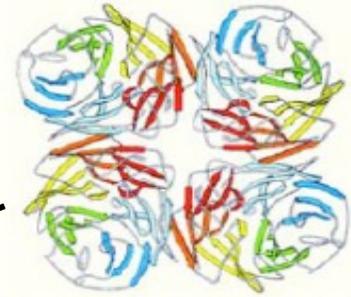


*H3N2 A/California/07/04*

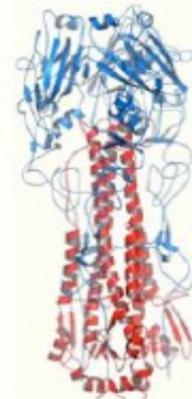
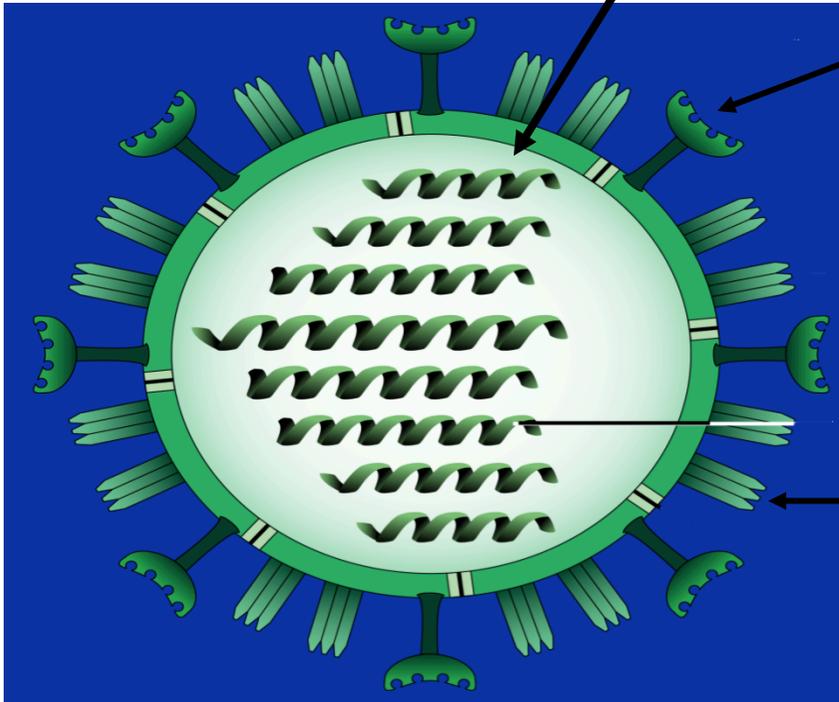




*Genome segmenté*



Neuraminidase (N)

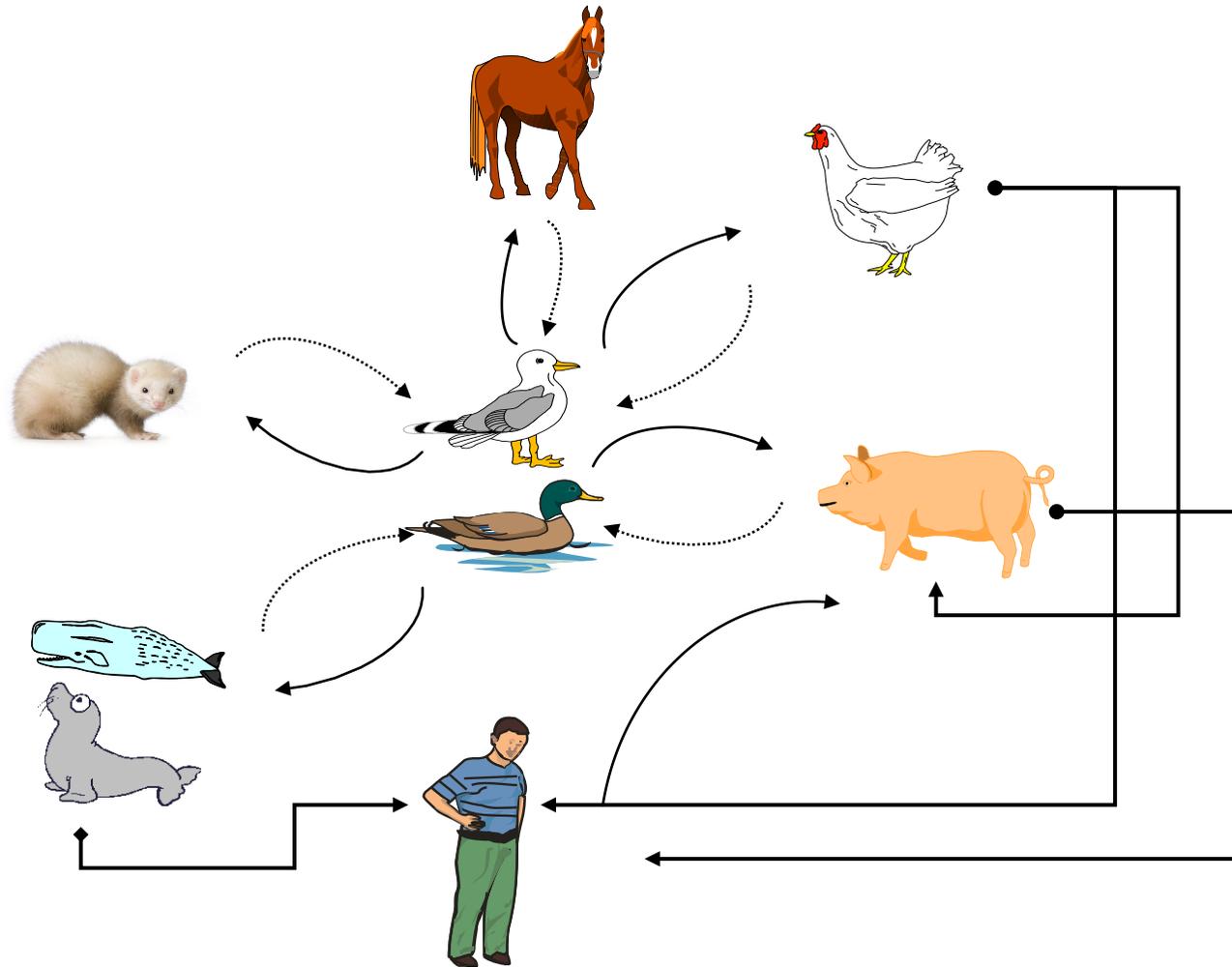


Haemagglutinin (H)

# *Acteur #2 : le vecteur*

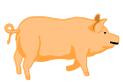
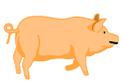


# Acteurs #3 : les vecteurs animaux\*



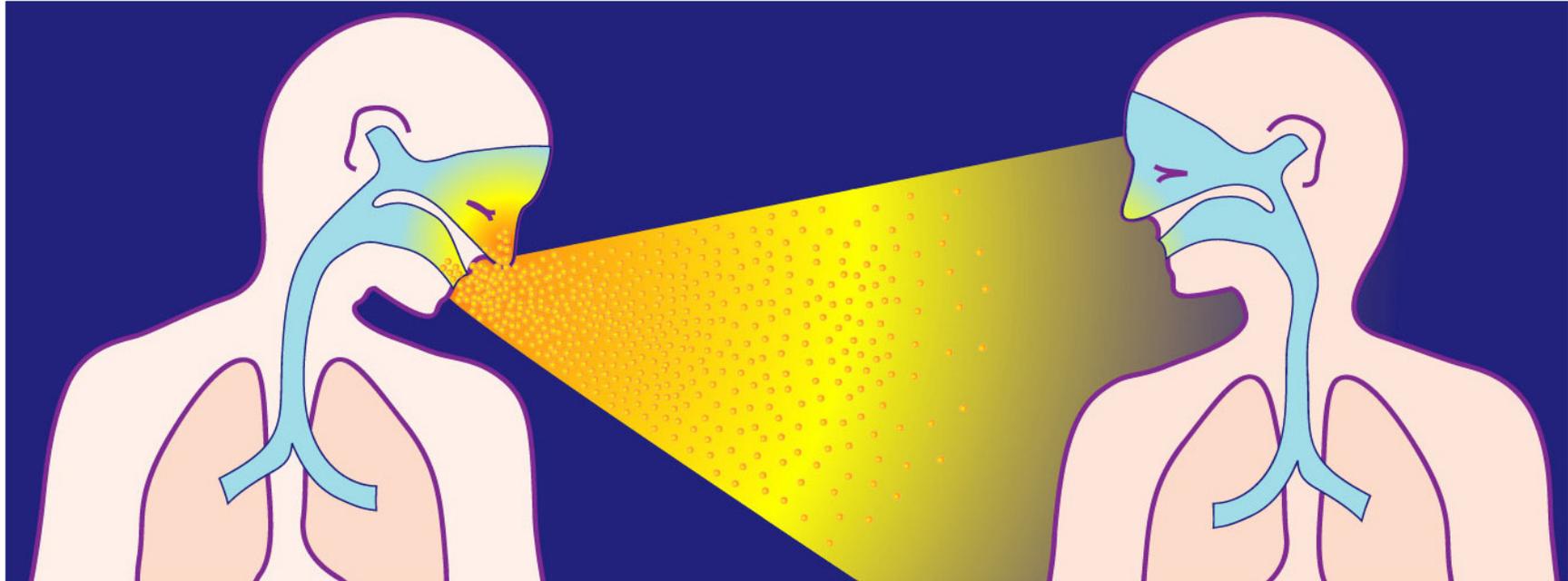
\* Uniquement pour les pandémies

H1				
H2				
H3				
H4				
H5				
H6				
H7				
H8				
H9				
H10				
H11				
H12				
H13				
H14				
H15				
H16				

N1				
N2				
N3				
N4				
N5				
N6				
N7				
N8				
N9				

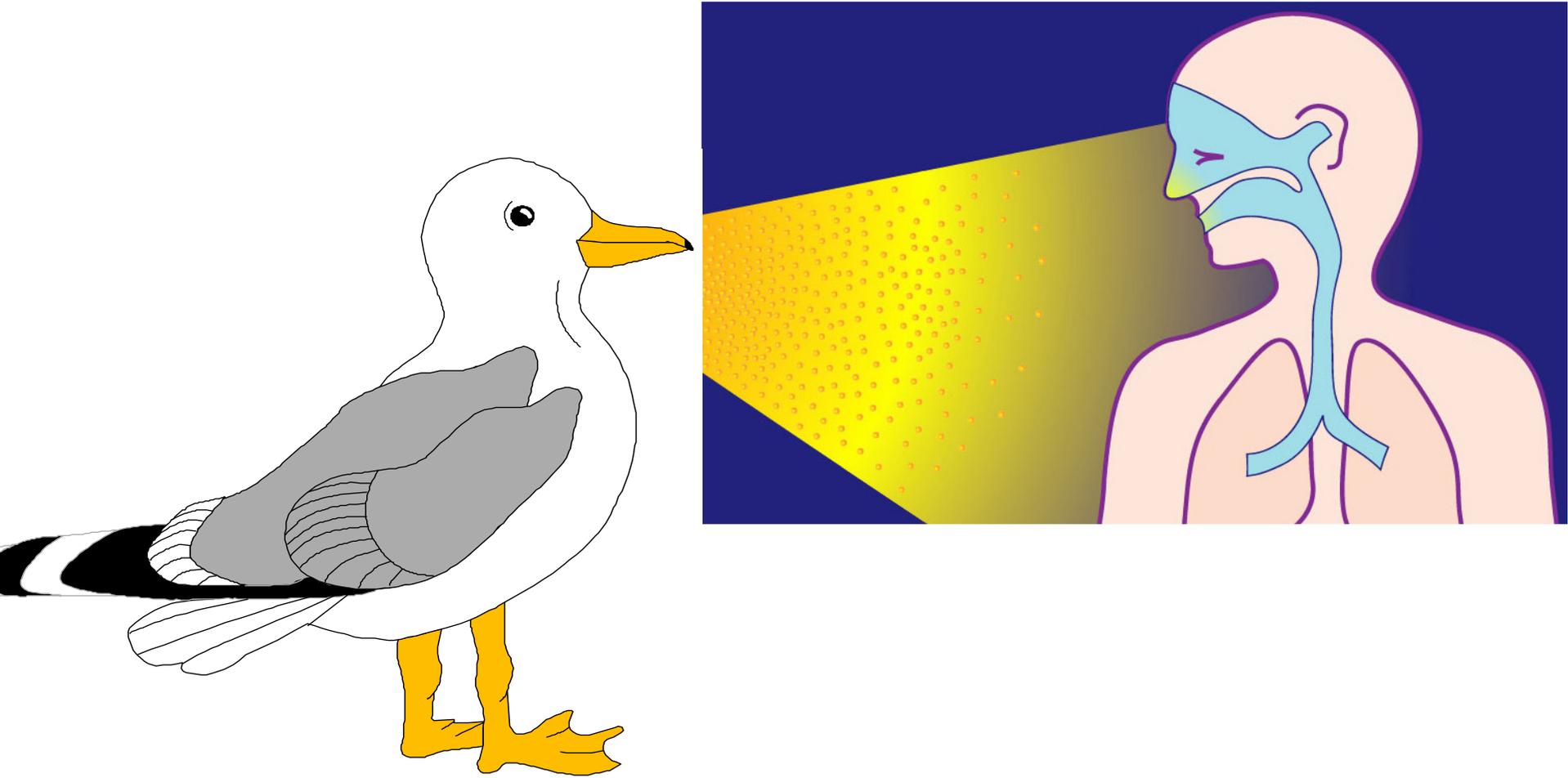
*Les hôtes des différents sous-types de virus influenza A*

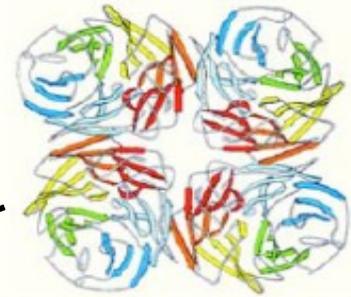
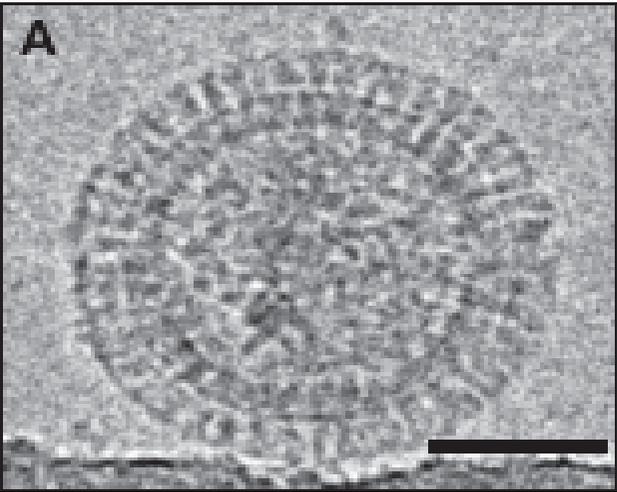
# La grippe: une infection virale à transmission aérienne



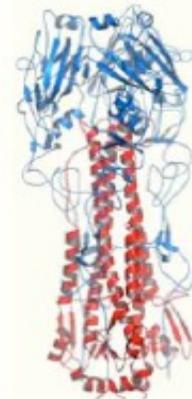
Le virus se propage par le biais des gouttelettes de salive et des petites particules en suspension dans l'air projetées par la toux ou les éternuements. Le virus pénètre dans l'organisme via le nez, la bouche et les yeux

# La grippe aviaire: une infection impossible

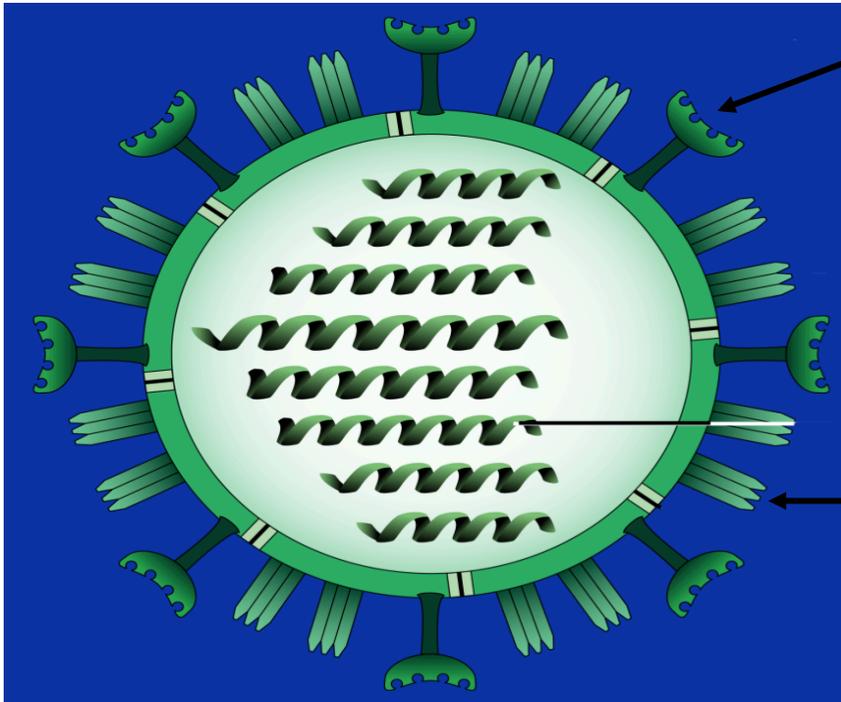




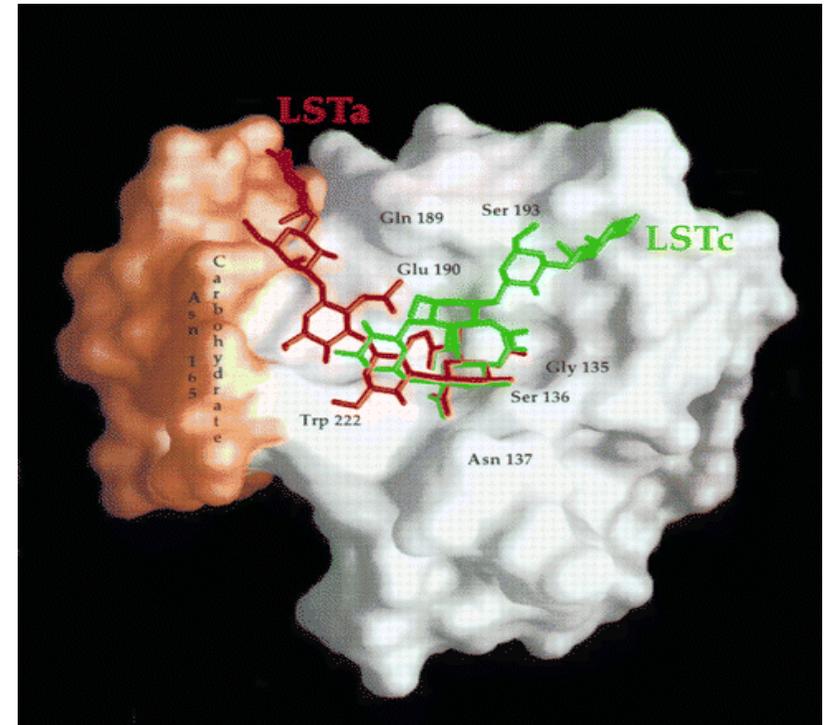
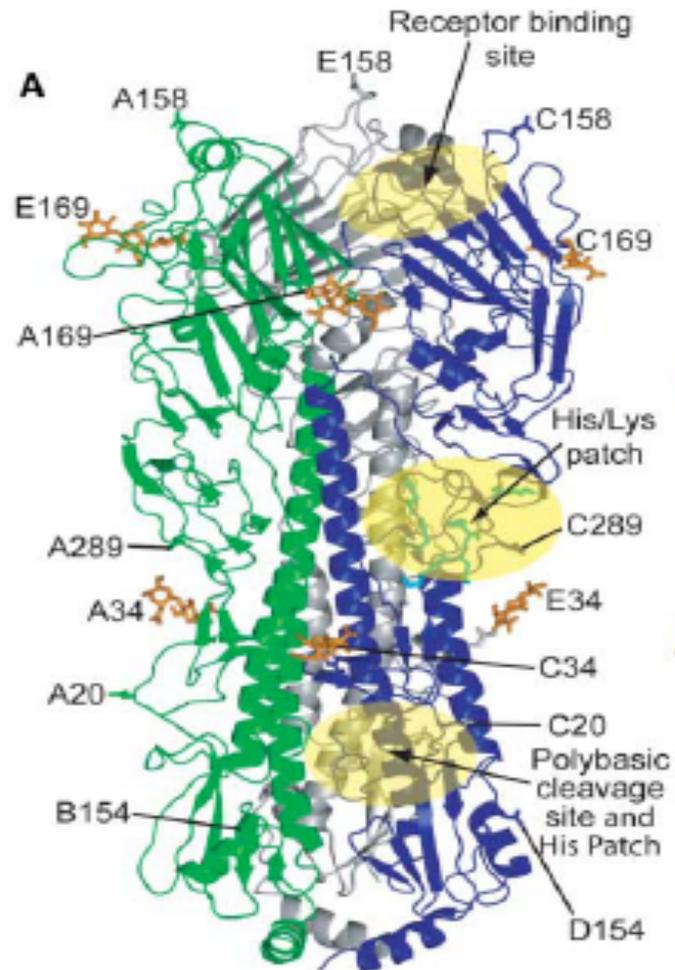
Neuraminidase (N)



Haemagglutinin (H)

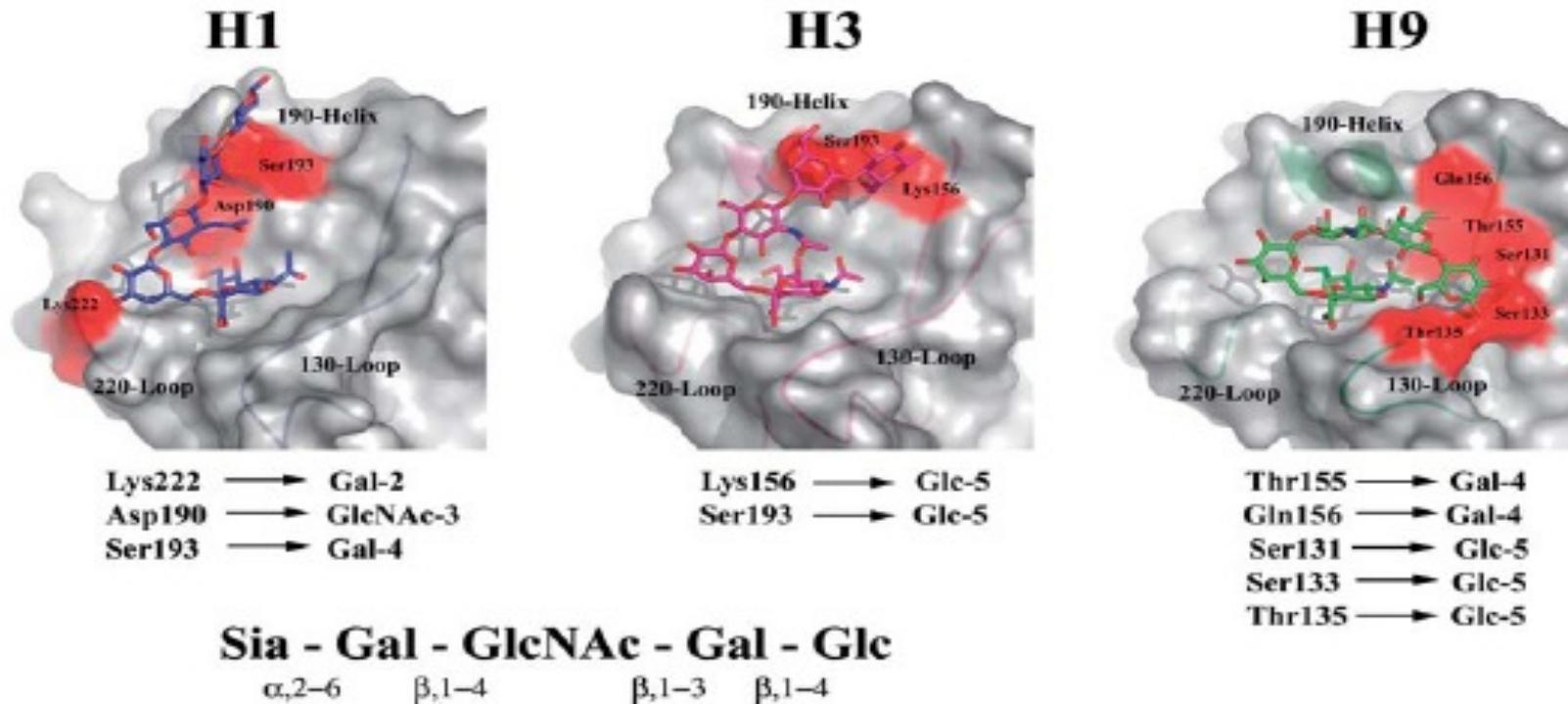


# Variations sur le RBS : $\alpha 2,3$ et $\alpha 2,6$



*D'après Skehel & Wiley, 2000*

# Zone d'interaction entre acide sialique de type $\alpha 2,6$ et le RBS



**Table 2**

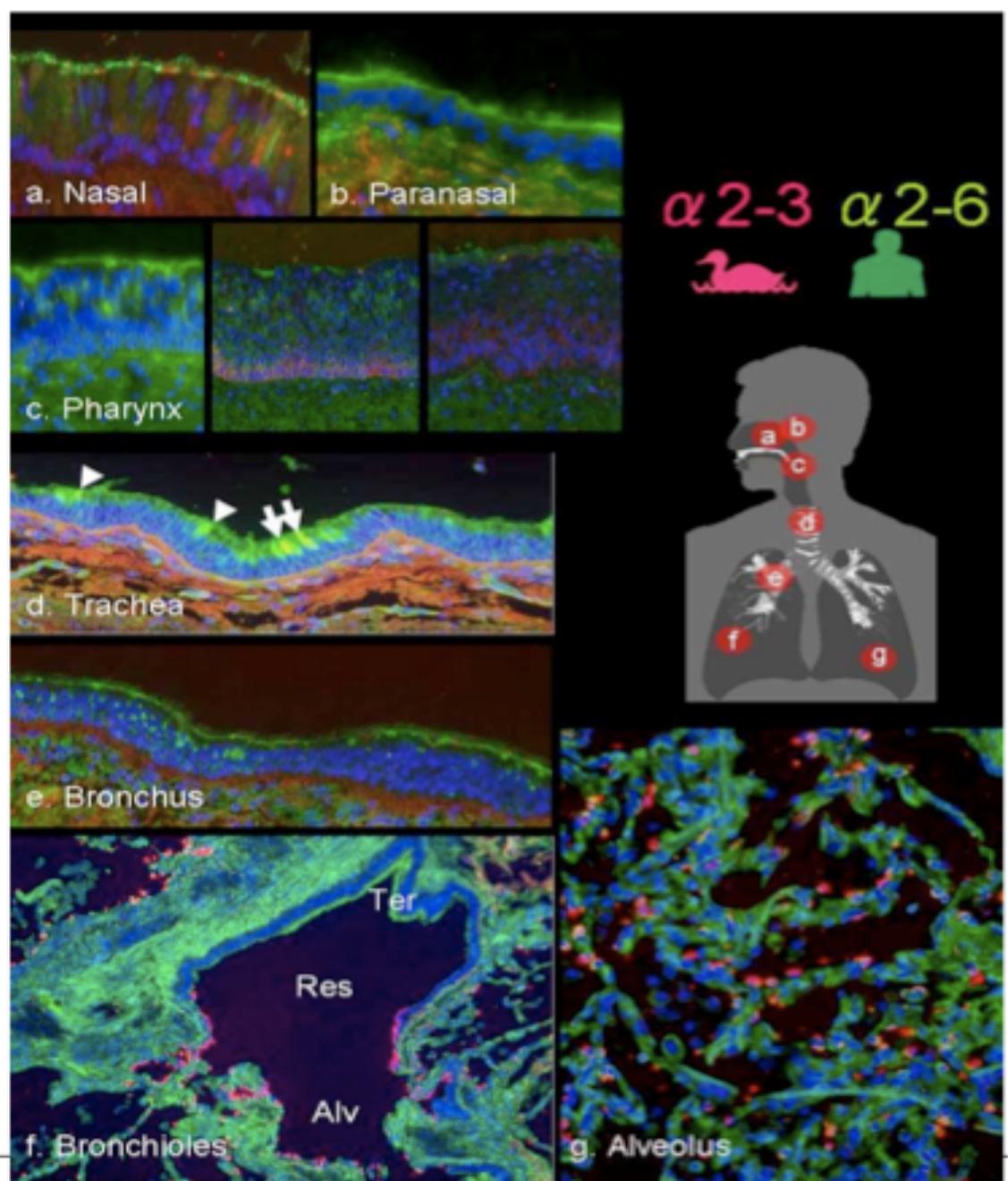
Known mutations and associated mechanisms of adaptation of zoonotic influenza viruses to human hosts via the crossing of virus–cell interaction barriers.

Virus–cell interaction barrier	Protein	Mutation	Adaptive mechanism	Ref.
Virus attachment	HA	N154S	Increases $\alpha$ 2,6 binding in H5 subtype	[194]
		N182K	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194,195]
		E190D	Increases $\alpha$ 2,6 binding in H1 subtype	[86,196]
		Q192R	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[195]
		D222G	Increases $\alpha$ 2,3 binding in H1 subtype	[75,197]
		Q222L	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194]
		S223N	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194]
		G224S	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194]
		G225D	Decreases $\alpha$ 2,3 binding in H1 and H9 subtypes	[81,86,196]
		Q226L	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H2, H3, H4, H5 and H9 subtypes	[81,86,198,199]
		S227N	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[200,201]
		G228S	Decreases $\alpha$ 2,3 binding in H3 subtype	[86,198,201]
		L129V + A134V	Increases $\alpha$ 2,6 binding in H2 and H5 subtypes	[202]
		G139R + N182K	Increases $\alpha$ 2,6 binding possibly in H5 subtype	[194]
		Q192R + S223N	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194]
		Q222L + G224S	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194]
		S227N + NST158 – 150NNA	Increases $\alpha$ 2,6 binding in H5 subtype	[203]
		N158S + Q226L + N248D	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194,204]
		N182K + Q222L + G224S	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194]
		Q192R + Q222L + G224S	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194]
		Q222L + S223N + G224S	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194]
		NST158–150NNA + K193R + Q226L + G228S	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[205]
		N182K + Q222L + S223N + G224S	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194]
Q192R + Q222L + S223N + G224S	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194]		
N182K + Q192R + Q222L + S223N + G224S	Increases $\alpha$ 2,6 binding in H5 subtype	[194]		
Virus–cell fusion	HA	Single R cleaved site	Allows cleavage by extracellular host proteases restricted to respiratory tract in humans	[92]
		Multi-basic cleaved site	Allows cleavage by ubiquitous intracellular host proteases present in various tissues in humans	[92]
Viral replication	PB1 + PB2	Unknown	Increases polymerase activity of HPAIV H5N1 in human cells (unknown mechanism)	[126]
		PB2	Increases polymerase activity of HPAIV H5N1 in human cells (unknown mechanism)	[121]
	PB2	T271A	Increases polymerase activity of LPAIV H3N2 in human cells (unknown mechanism)	[124]
		Q591 K	Increases polymerase of HPAIV H5N1 activity in human cells (unknown mechanism)	[120]
		E627 K	Increases polymerase activity by increasing PB2 and NP binding in human cells	[118]
		D253N + Q291 K	Increases polymerase activity of LPAIV H9N2 in human cells (unknown mechanism)	[122]
		G590S + Q591R	Increases polymerase activity of 2009 pandemic H1N1 virus in human cells (unknown mechanism)	[123]
		PA	Increases polymerase activity of avian influenza viruses in mammalian cells and increases pathogenicity in mice (unknown mechanism)	[125]
	NP + PB2	N319K + D701 N	Increases polymerase activity by increasing binding of vRNP to importin- $\alpha$ 1, and shifting nuclear import dependency from importin- $\alpha$ 3 to importin- $\alpha$ 7 in human and other mammalian cells	[112]
	Virus release	NA	I275V	Increases $\alpha$ 2,6 substrate specificity in N2 subtype
HA		Antigenic shift	D92E	Escapes pre-existing humoral immunity
	P42S		Confers HPAIV H5N1 resistance to IFN- $\alpha$ , IFN- $\gamma$ and TNF- $\alpha$ (unknown mechanism)	[139]
	L103F + I106M	P42S	Prevents double-stranded RNA-mediated activation of NF- $\kappa$ B and IRF-3 pathways during HPAIV H5N1 infection	[140]
		L103F + I106M	Allows binding of HPAIV H5N1 NS1 protein and CPSF30 resulting in decreased INF- $\beta$ mRNA production	[141]
	Viral escape from host immune responses	NS1	PDZ domain ligand in C-terminus	Disruption of protein–protein interactions, including impairment of IFN-stimulated signaling, disruption of tight junctions, and reduction of apoptosis
PB1–F2				N66S

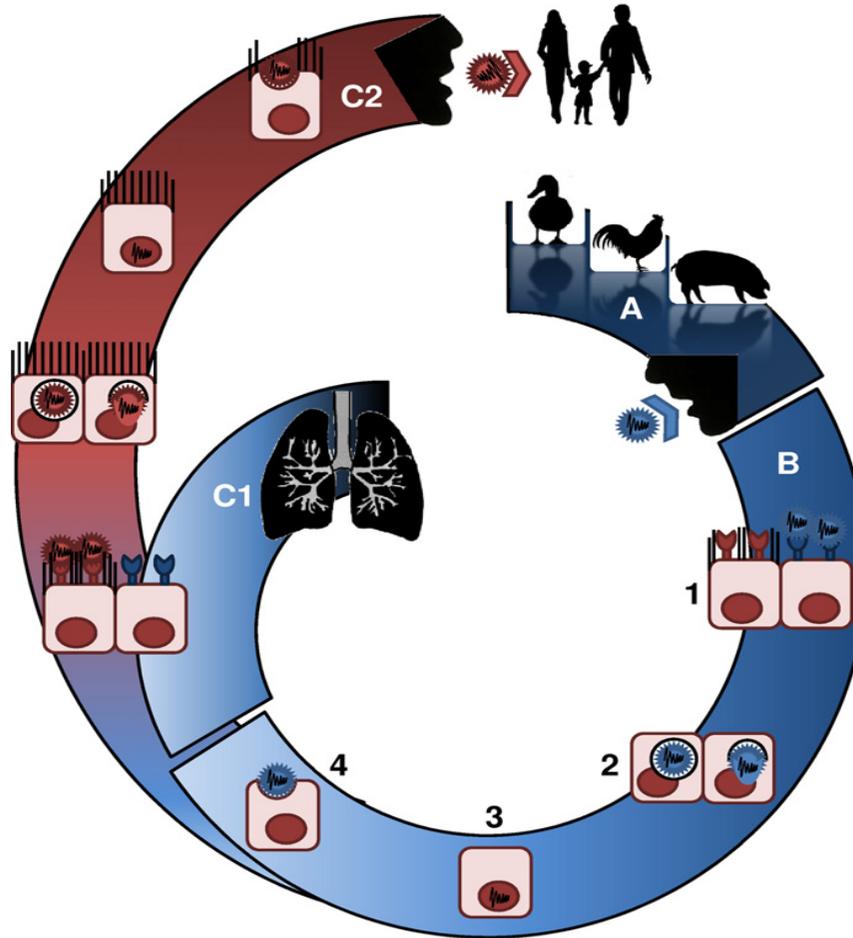
*Les (nombreux) facteurs limitants*

**MAIS...**

# Distribution des récepteurs $\alpha 2-6$ et $\alpha 2-3$ dans l'arbre respiratoire humain



# Les étapes du franchissement



# Influenza pandemics in the XXth century



**1918: “Spanish Flu”**

**40-50  
million**  
H1N1



**1957: “Asian Flu”**

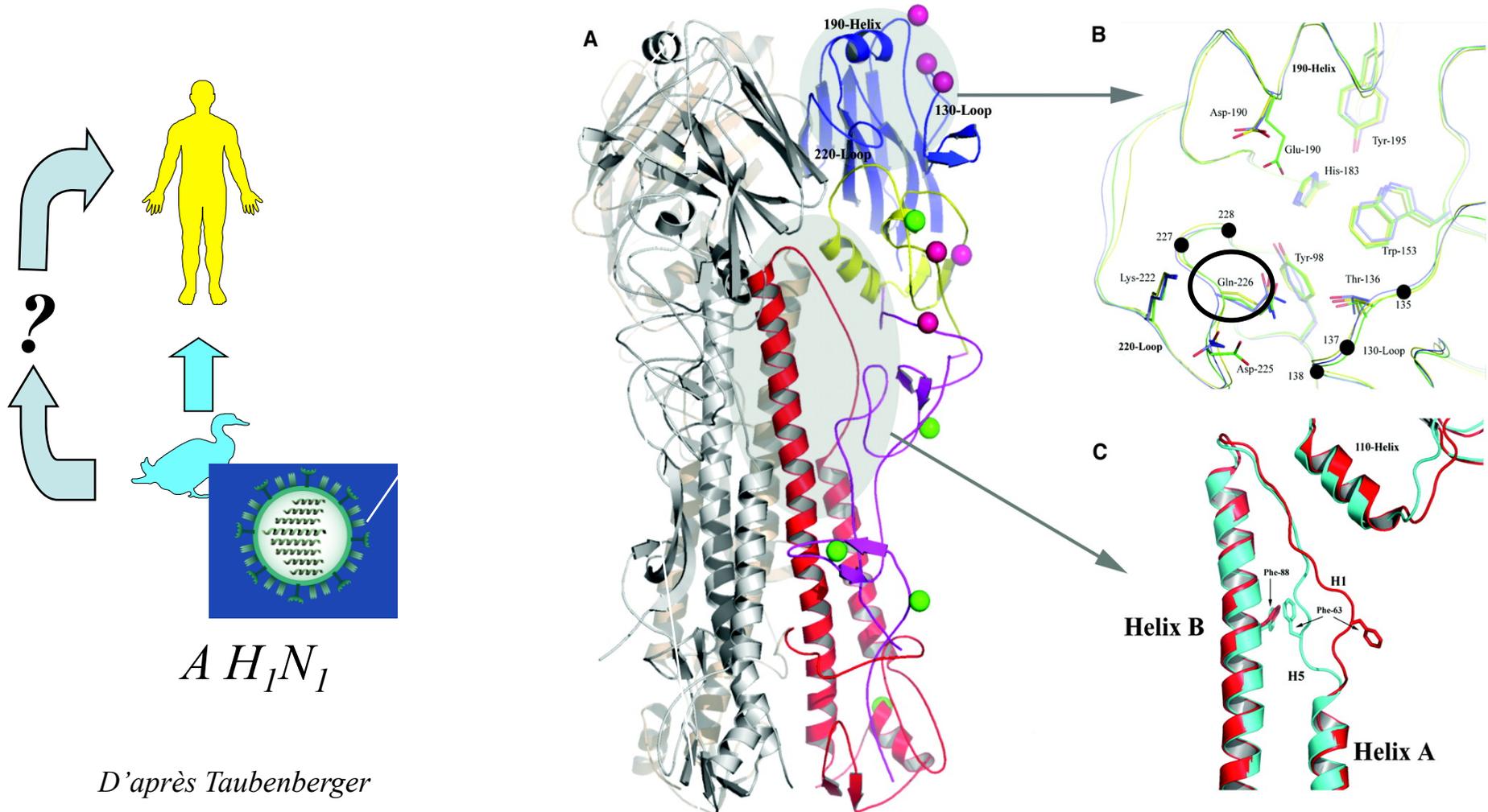
**1-4  
million**  
H2N2



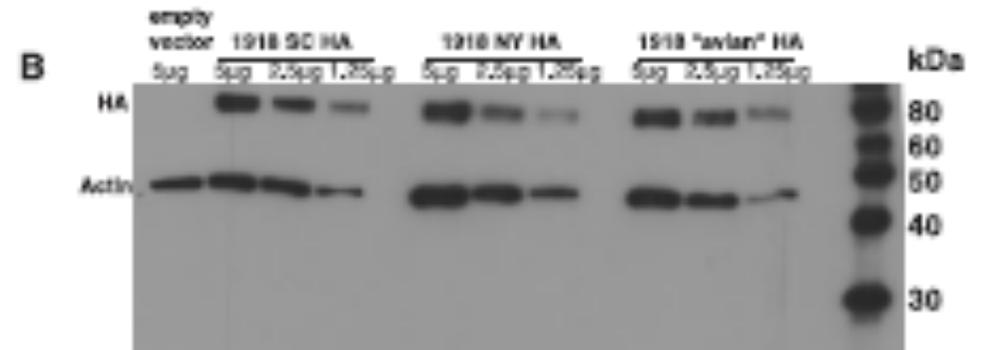
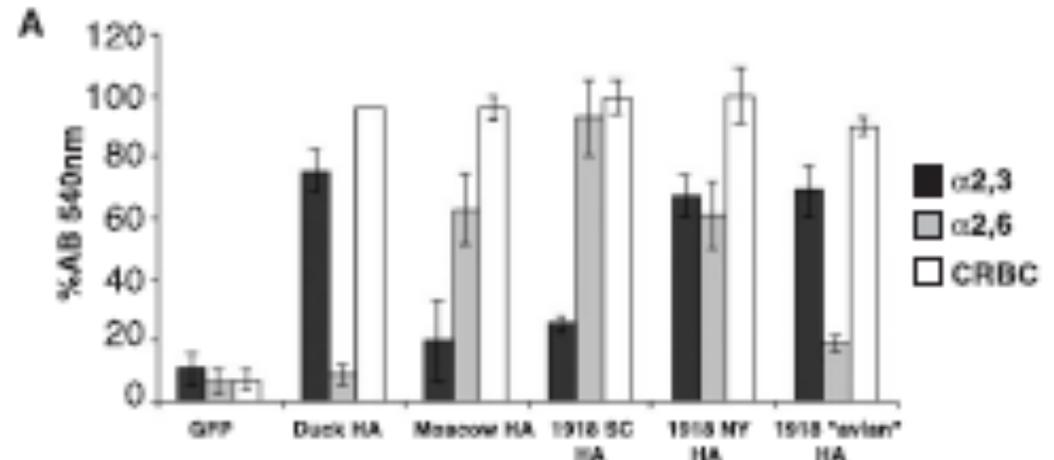
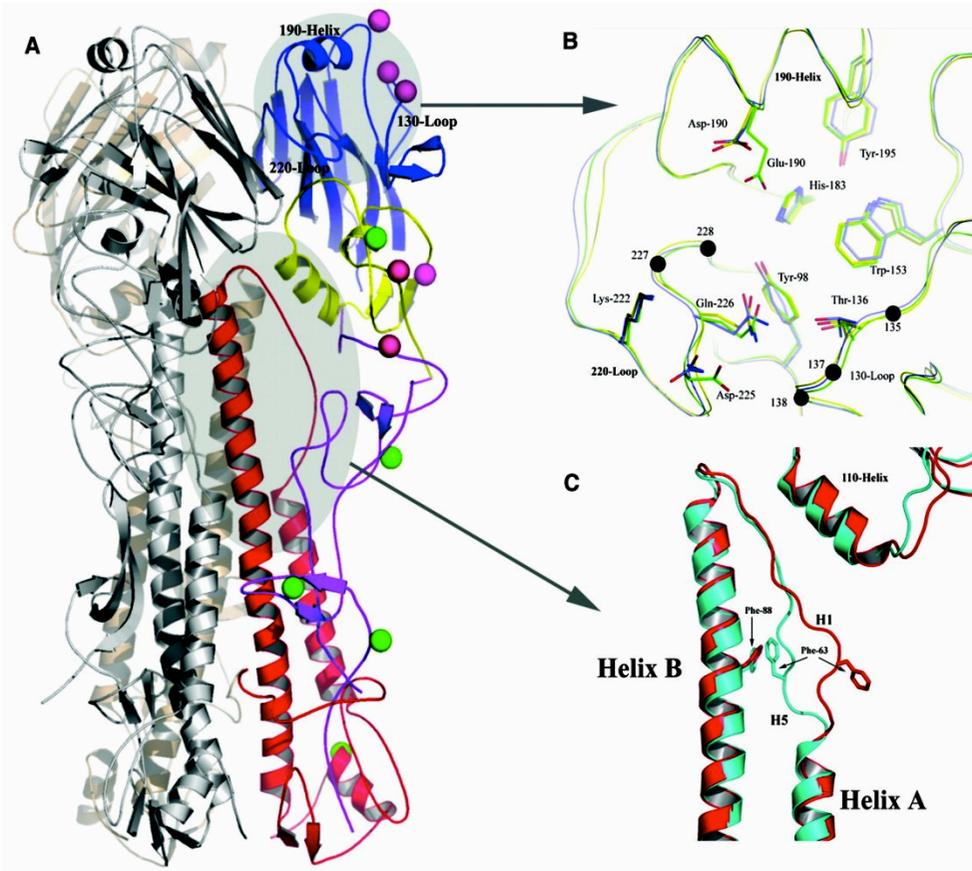
**1968: “Hong Kong Flu”**

**1  
million**  
H3N2

# Mécanisme théorique de l'émergence du virus A H1N1 : mutation du RBS



# Bascule de l'attachement de H1N1 en 1918

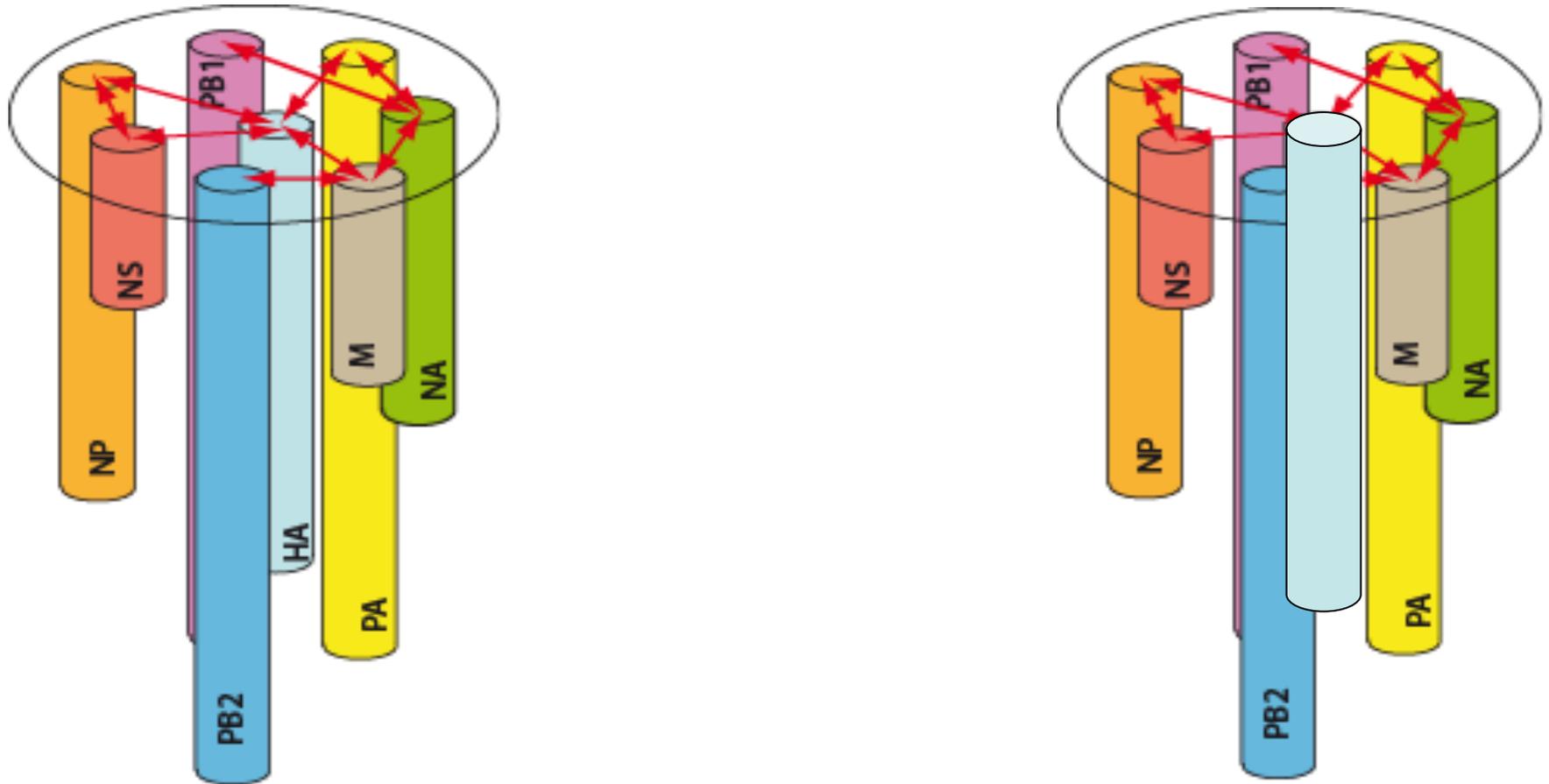


D'après Taubenberger

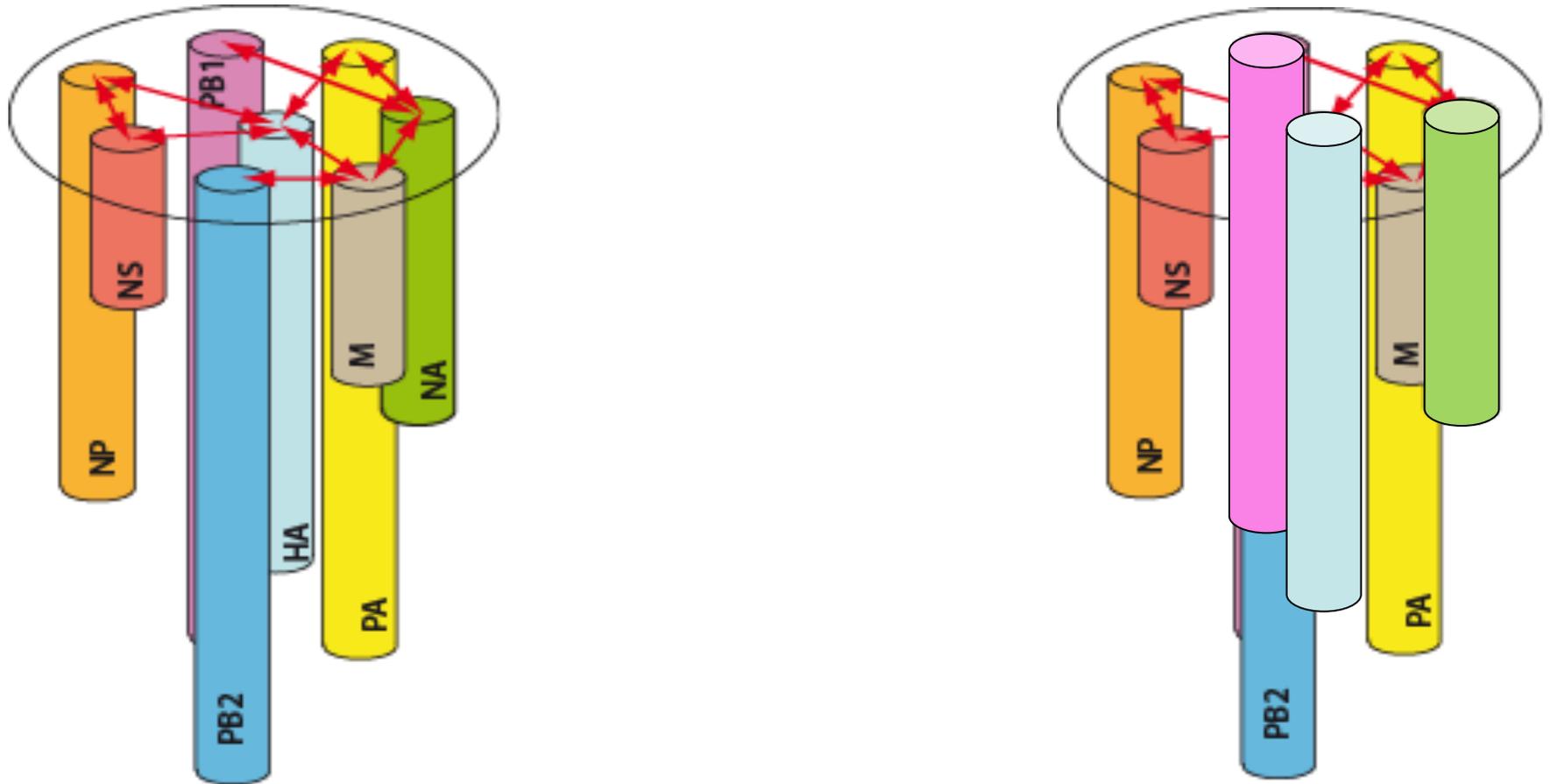
Les deux modes d'adaptation des  
virus influenza :  
réassortiments et mutations



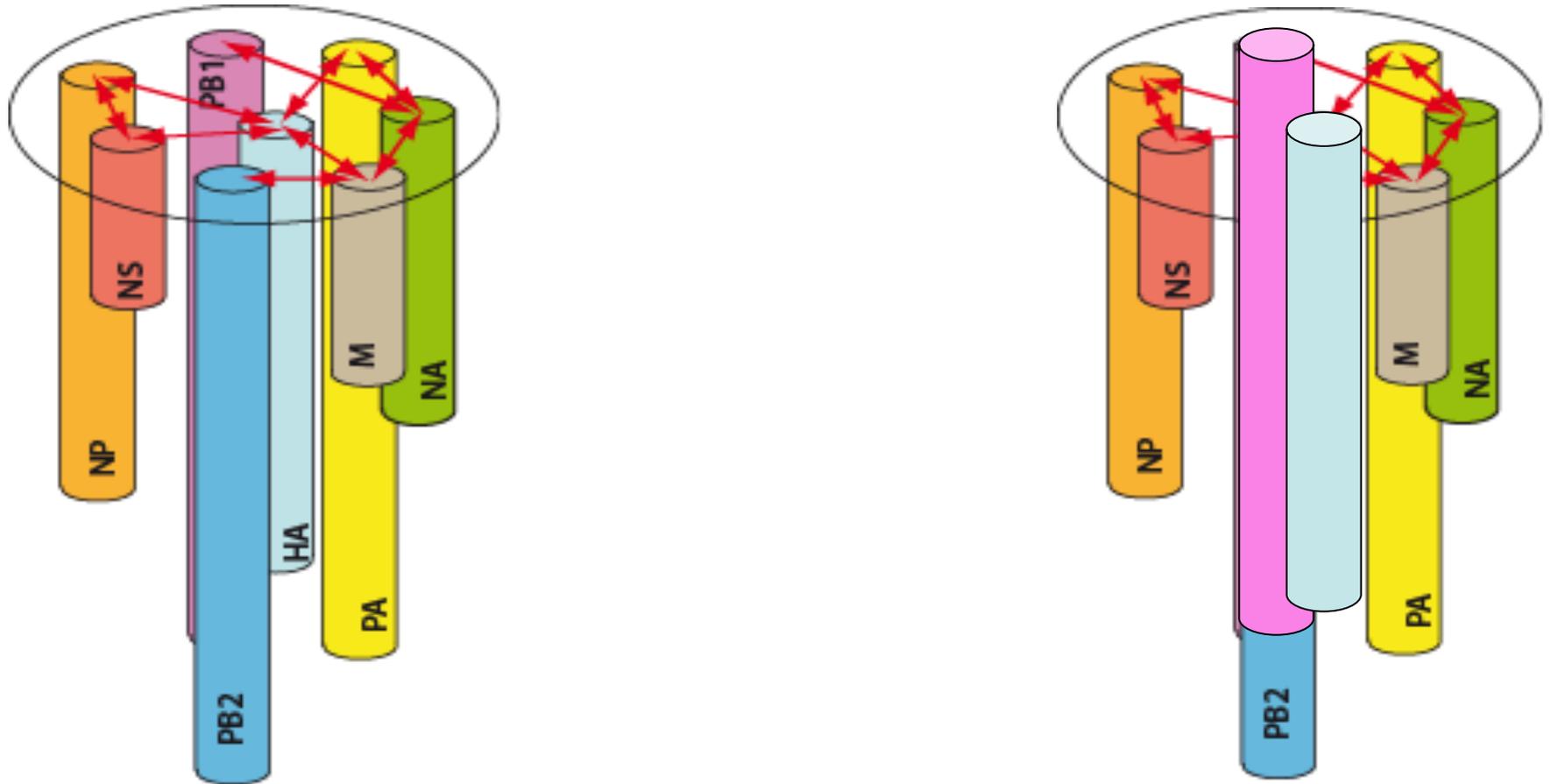
# Réassortiment génétique : échanges de gènes entre virus



# Réassortiment génétique en 1957 : introduction des gènes Ha/PB1/Na



# Réassortiment génétique en 1968 : introduction des gènes Ha/PB1



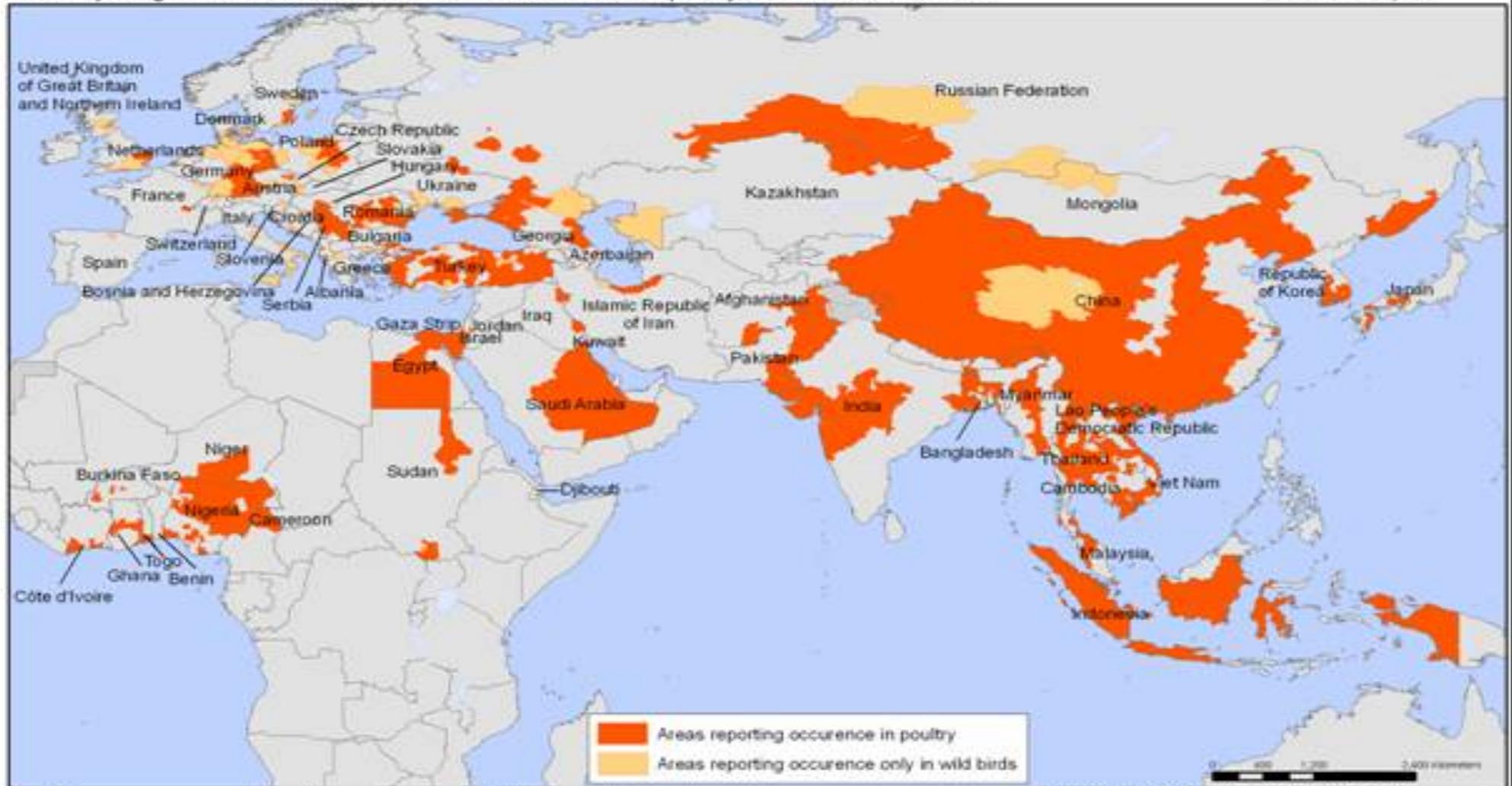
Les deux modes d'adaptation des  
virus influenza :  
réassortiments et mutations

**Alerte N°1 : H5N1**

# H5N1 (grippe aviaire)

Areas reporting confirmed occurrence of H5N1 avian influenza in poultry and wild birds since 2003

Status as of 14 April 2008  
Latest available update

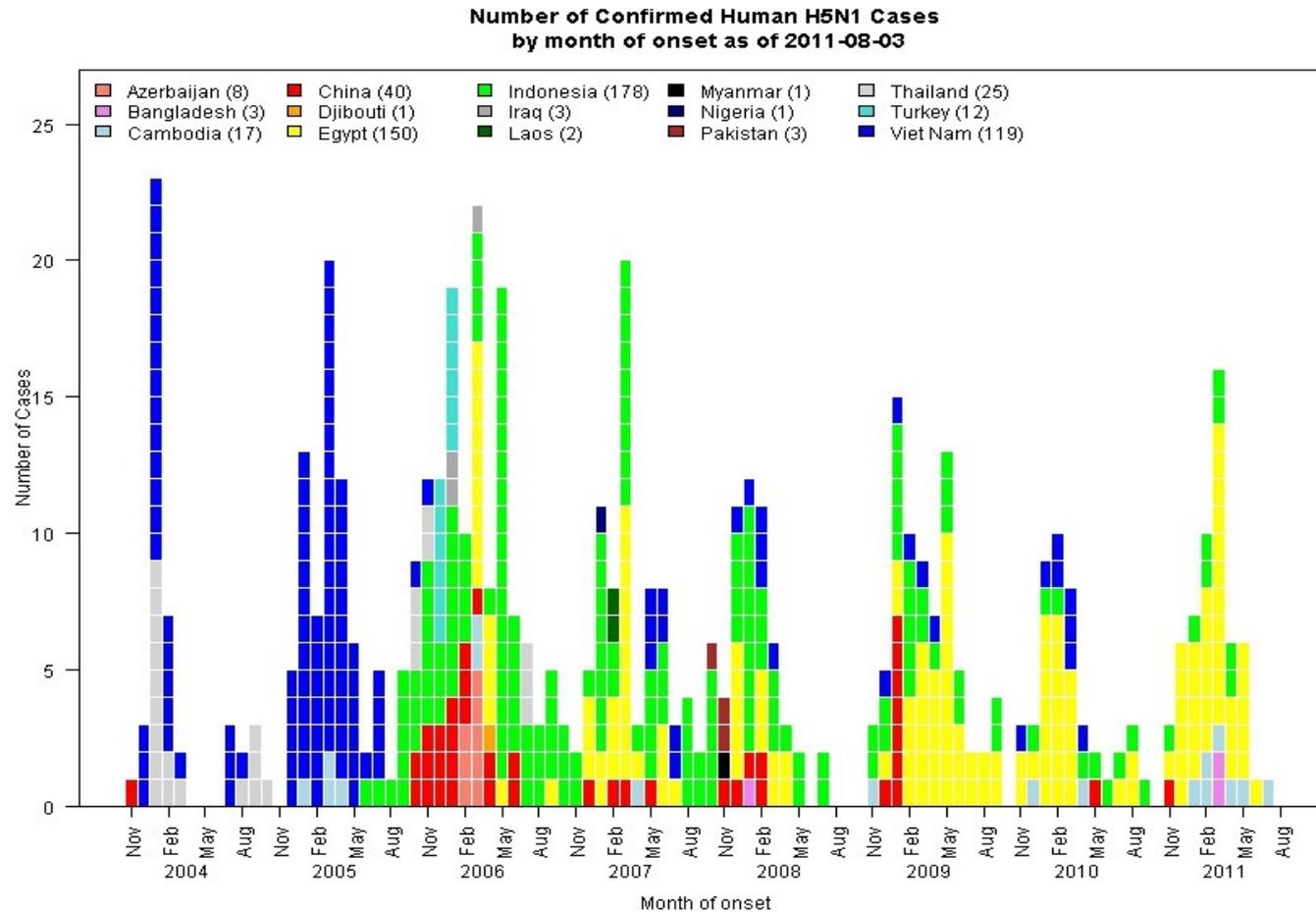


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Data Source: World Organisation for Animal Health (OIE) and national governments  
Map Production: Public Health Mapping and GIS  
World Health Organization

# Distribution of the death recorded



# H5N1

*Virus attachement*  
**NON**

*Virus fusion* **NON**

*Virus répllication* **OK**

**Table 2**

Known mutations and associated mechanisms of adaptation of zoonotic influenza viruses to human hosts via the crossing of virus–cell interaction barriers.

Virus–cell interaction barrier	Protein	Mutation	Adaptive mechanism	Ref.
Virus attachment	HA	N154S	Increases $\alpha$ 2,6 binding in H5 subtype	[194]
		N182K	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194,195]
		E190D	Increases $\alpha$ 2,6 binding in H1 subtype	[86,196]
		Q192R	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[195]
		D222G	Increases $\alpha$ 2,3 binding in H1 subtype	[75,197]
		Q222L	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194]
		S223N	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194]
		G224S	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194]
		G225D	Decreases $\alpha$ 2,3 binding in H1 and H9 subtypes	[81,86,196]
		Q226L	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H2, H3, H4, H5 and H9 subtypes	[81,86,198,199]
		S227N	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[200,201]
		G228S	Decreases $\alpha$ 2,3 binding in H3 subtype	[86,198,201]
		L129V + A134V	Increases $\alpha$ 2,6 binding in H2 and H5 subtypes	[202]
		G139R + N182K	Increases $\alpha$ 2,6 binding possibly in H5 subtype	[194]
		Q192R + S223N	Increases $\alpha$ 2,6 binding in H5 subtype	[194]
		Q222L + G224S	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194]
		S227N + NST158 – 150NNA	Increases $\alpha$ 2,6 binding in H5 subtype	[203]
		N158S + Q226L + N248D	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194,204]
		N182K + Q222L + G224S	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194]
		Q192R + Q222L + G224S	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194]
		Q222L + S223N + G224S	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194]
		NST158–150NNA + K193R + Q226L + G228S	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[205]
		N182K + Q222L + S223N + G224S	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194]
Q192R + Q222L + S223N + G224S	Increases $\alpha$ 2,6 binding and decreases $\alpha$ 2,3 binding in H5 subtype	[194]		
N182K + Q192R + Q222L + S223N + G224S	Increases $\alpha$ 2,6 binding in H5 subtype	[194]		
Virus–cell fusion	HA	Single R cleaved site	Allows cleavage by extracellular host proteases restricted to respiratory tract in humans	[92]
		Multi-basic cleaved site	Allows cleavage by ubiquitous intracellular host proteases present in various tissues in humans	[92]
Viral replication	PB1 + PB2	Unknown	Increases polymerase activity of HPAIV H5N1 in human cells (unknown mechanism)	[126]
		PB2	Increases polymerase activity of HPAIV H5N1 in human cells (unknown mechanism)	[121]
	PB2	T271A	Increases polymerase activity of LPAIV H3N2 in human cells (unknown mechanism)	[124]
		Q591 K	Increases polymerase of HPAIV H5N1 activity in human cells (unknown mechanism)	[120]
		E627 K	Increases polymerase activity by increasing PB2 and NP binding in human cells	[118]
		D253N + Q291 K	Increases polymerase activity of LPAIV H9N2 in human cells (unknown mechanism)	[122]
		G590S + Q591R	Increases polymerase activity of 2009 pandemic H1N1 virus in human cells (unknown mechanism)	[123]
		PA	Increases polymerase activity of avian influenza viruses in mammalian cells and increases pathogenicity in mice (unknown mechanism)	[125]
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	Viral escape from host immune responses	NS1	D92E	Confers HPAIV H5N1 resistance to IFN- $\alpha$ , IFN- $\gamma$ and TNF- $\alpha$ (unknown mechanism)
P42S			Prevents double-stranded RNA-mediated activation of NF- $\kappa$ B and IRF-3 pathways during HPAIV H5N1 infection	[140]
L103F + I106M		Allows binding of HPAIV H5N1 NS1 protein and CPSF30 resulting in decreased INF- $\beta$ mRNA production	[141]	
PDZ domain ligand in C-terminus		Disruption of protein–protein interactions, including impairment of IFN-stimulated signaling, disruption of tight junctions, and reduction of apoptosis	[142–145]	
PB1–F2		N66S	Unknown mechanism associated with apoptosis pathway regulation	[150]

**Alerte N°3 : H5N8**

**Alerte N°3 : H7N9**

**Alerte N°3 : H10N7**

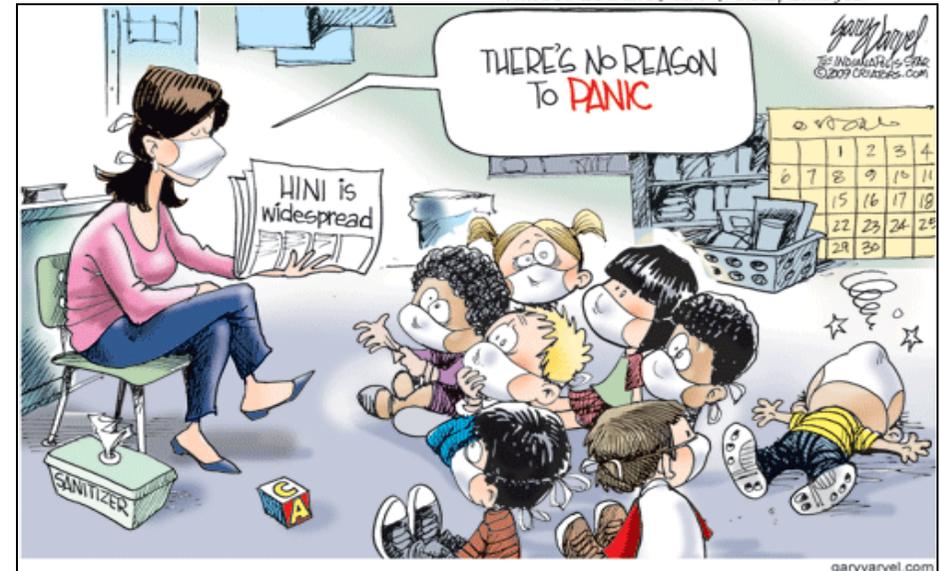
# Gestion de la situation des virus influenza zoonotiques

C'est un défi :

- Expliquer l'incertitude
- Expliquer que c'est évolutif
- Expliquer qu'on peut changer de braquet
- Expliquer qu'il faut envisager le pire en espérant le meilleur



Alfredo Estrella / AFP / Getty Images





# Caractéristiques des épidémies à virus Ebola

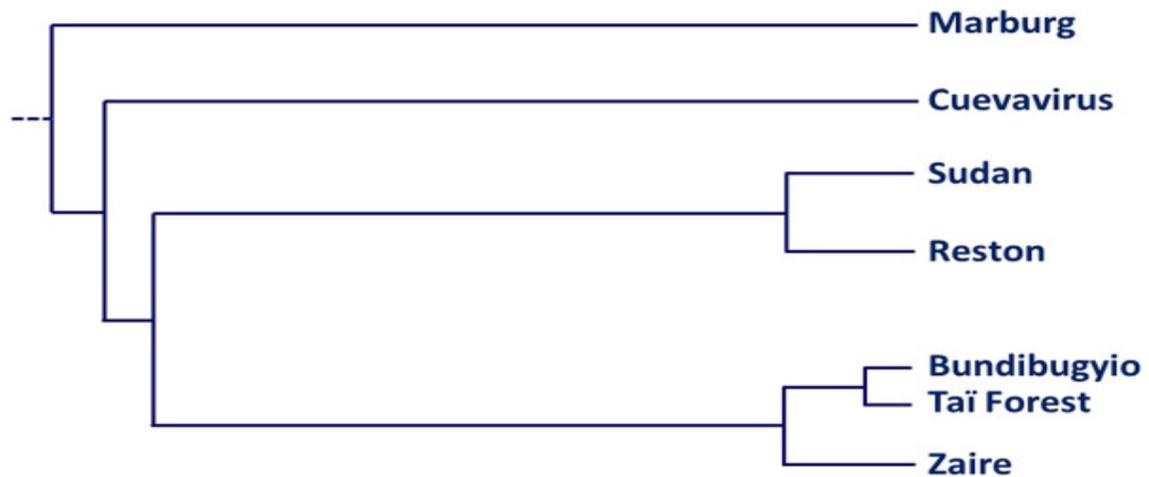
Bruno LINA

*Laboratoire de Virologie Est, HCL, CNR des virus influenzae*

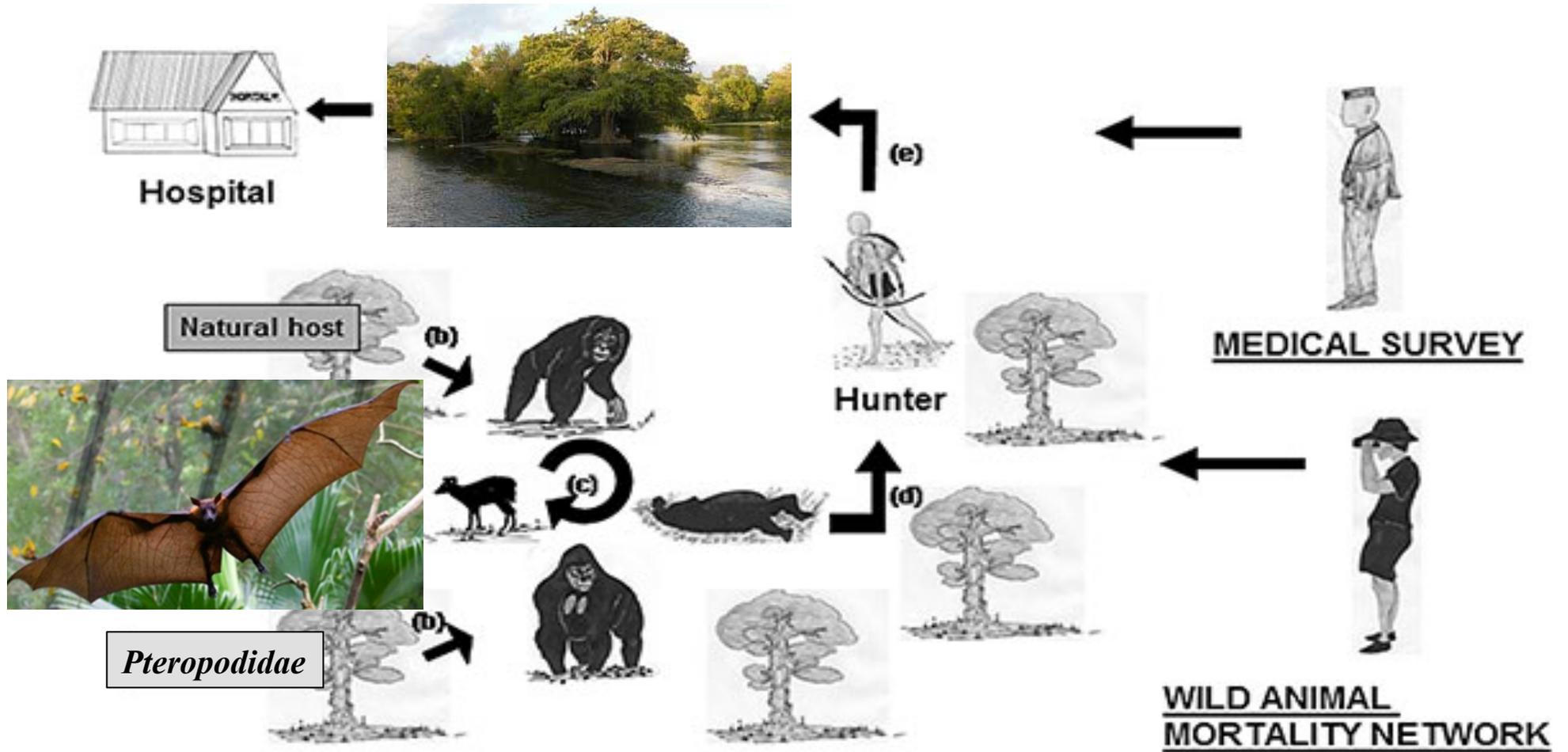
*VIRPATH - EMR 4610, Université Claude Bernard Lyon 1*

*LYON, France*

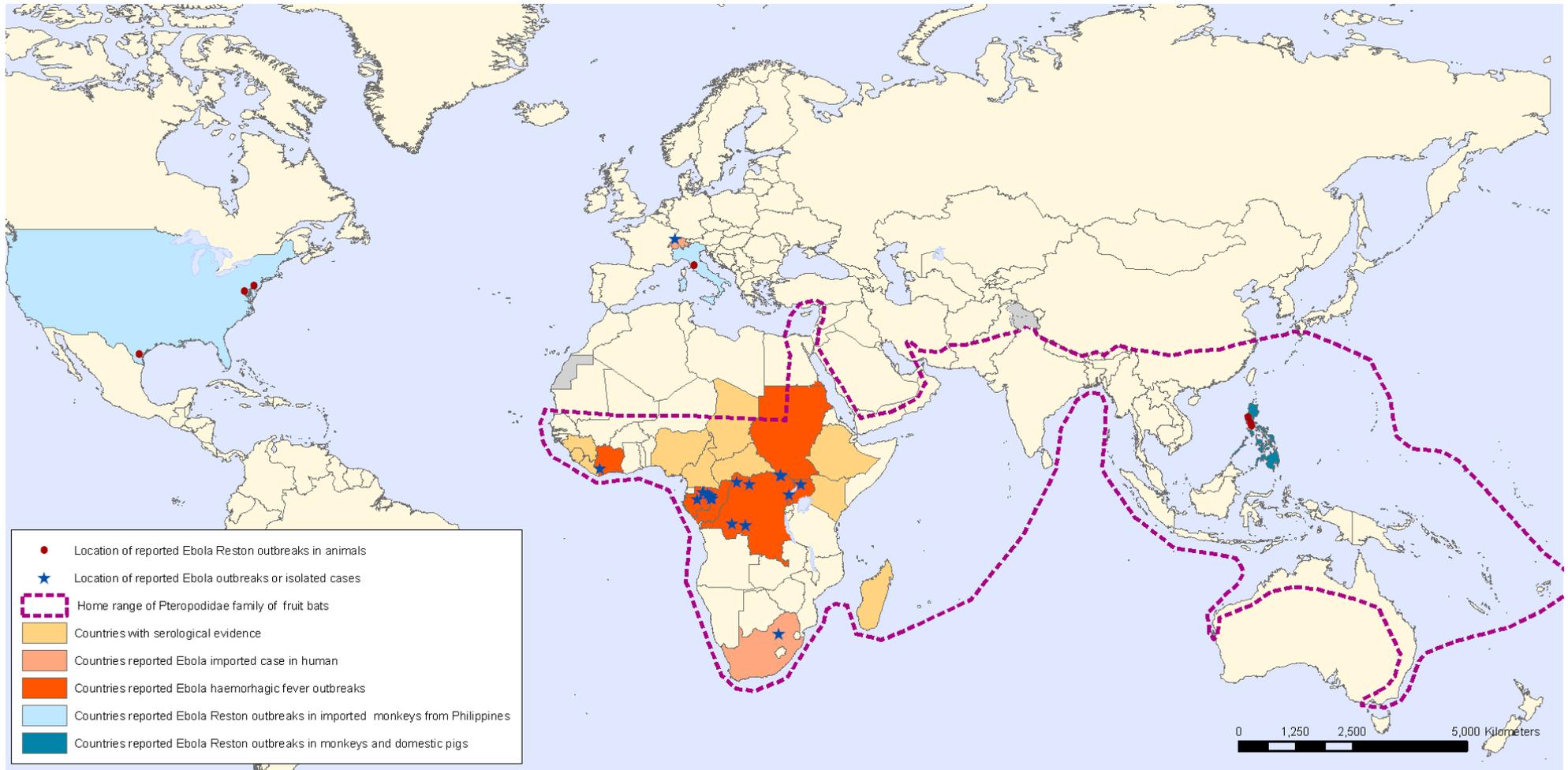
# Les Ebolavirus



# Ebola : comment ça marche?



# Epidémiologie du vecteur et des virus



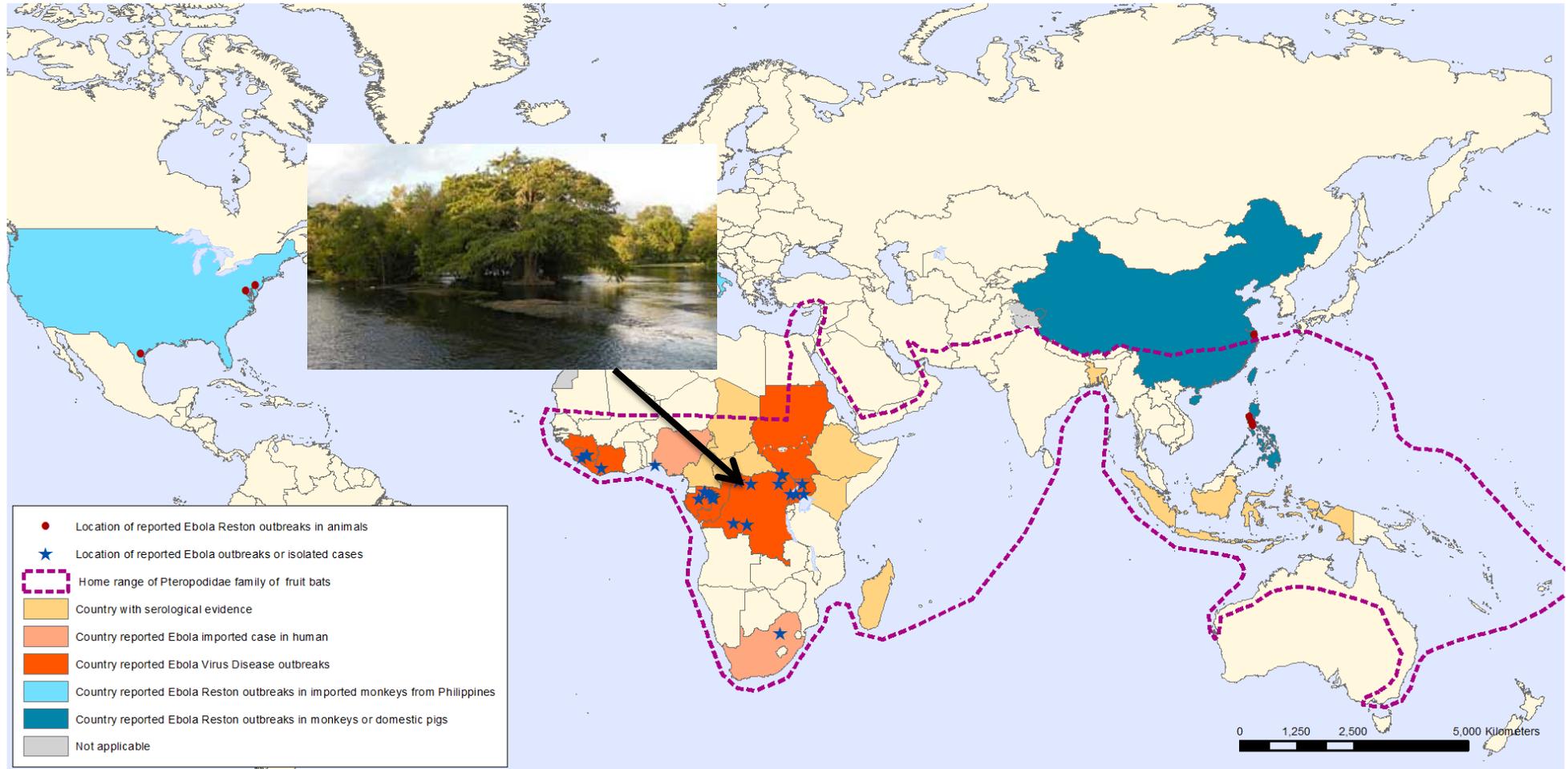
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Data Source: Global Alert and Response Department  
World Health Organization  
Map Production: Public Health Information  
and Geographic Information Systems (GIS)  
World Health Organization



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# Distribution géographique des virus Ebola et des cas/épidémies chez l'homme ou l'animal



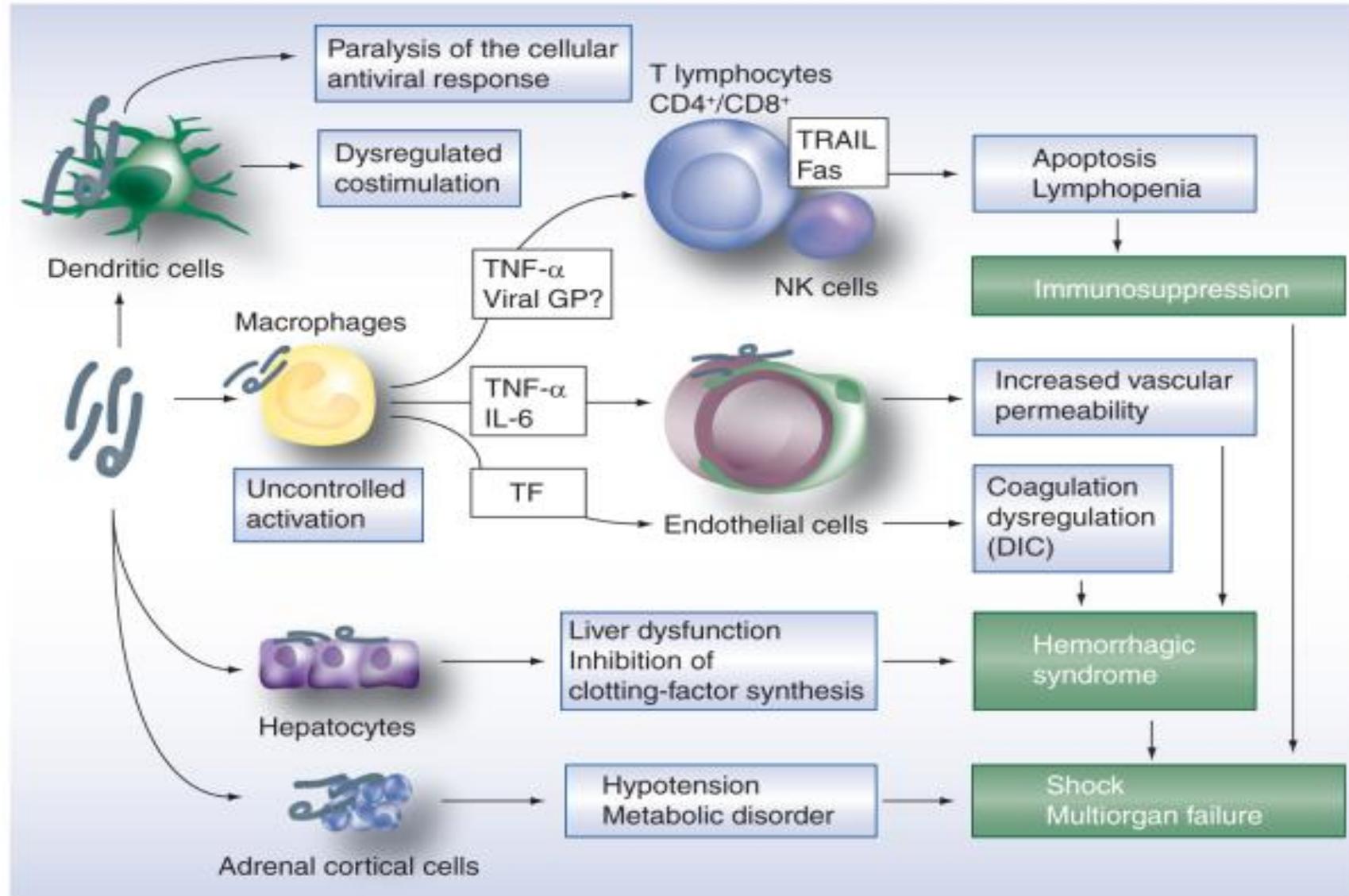
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization  
Map Production: Health Statistics and  
Information Systems (HSI)  
World Health Organization

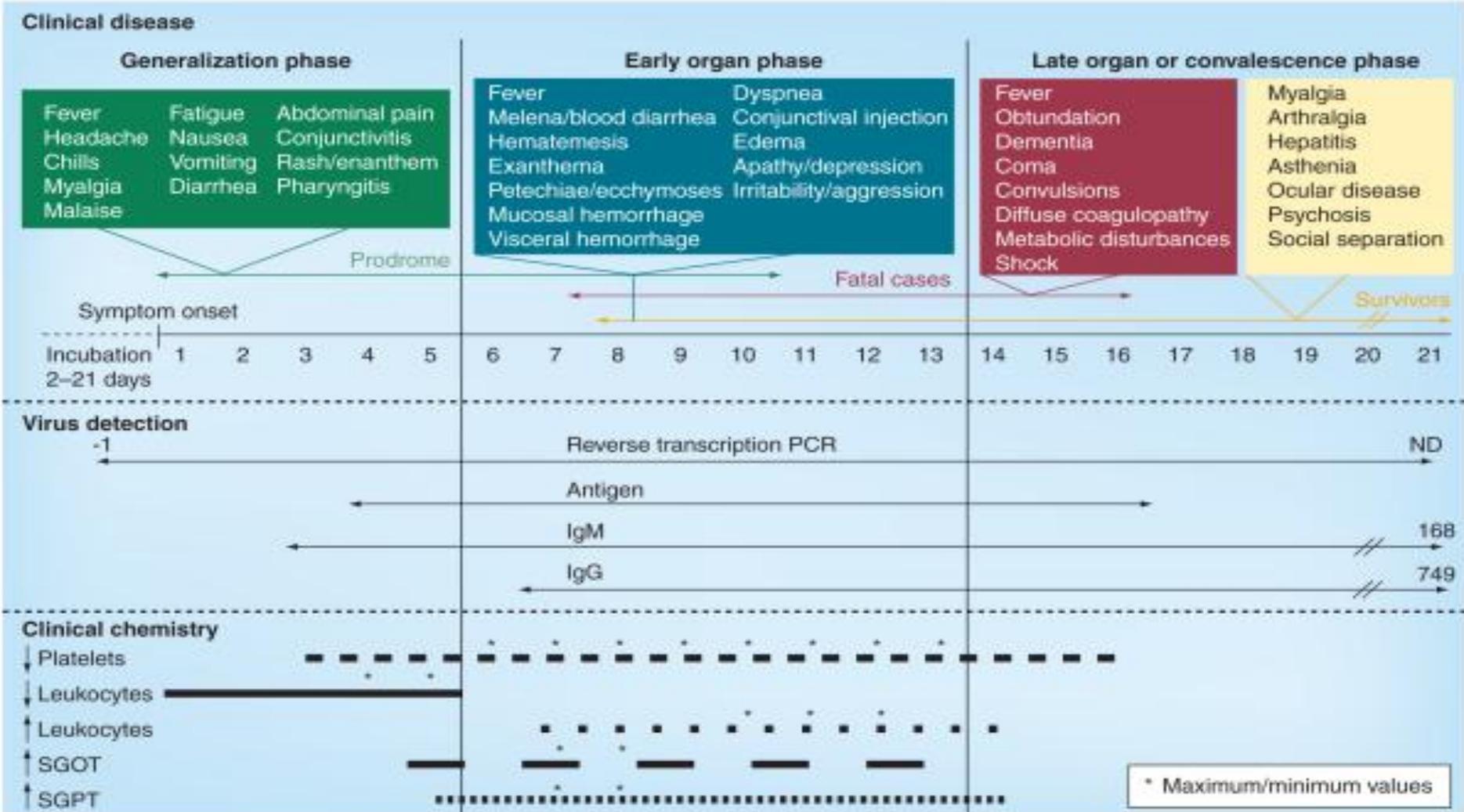


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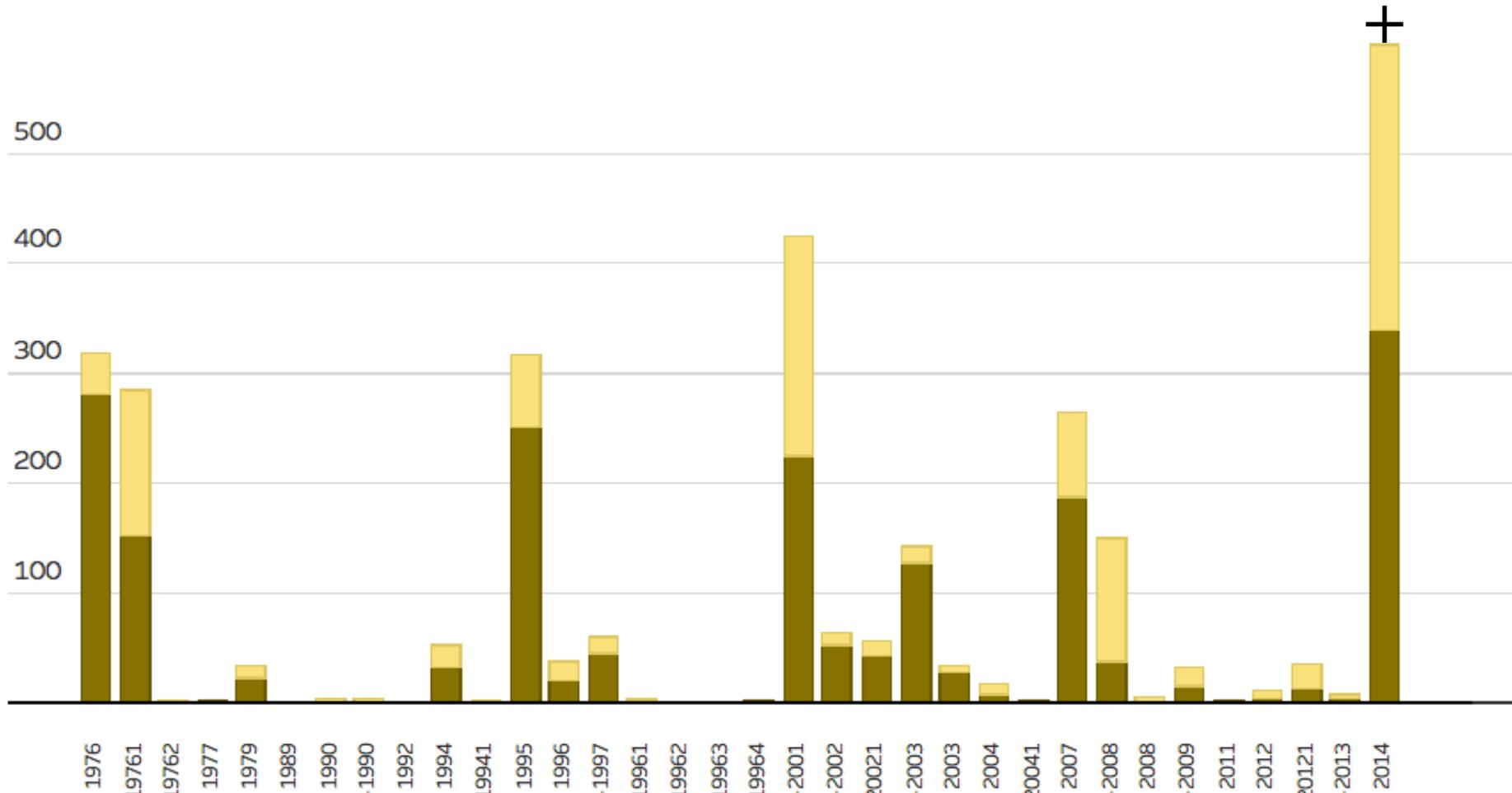
# Ebola : les trois phases cliniques chez l'homme



# Evolution clinique des patients : les trois phases de l'évolution



# Epidémies à virus Ebola de 1976 à 2014, nombre de cas et mortalité associée



# Bilan au 26 novembre 2014 (donnée OMS)

Table 1: Confirmed, probable, and suspected cases in Guinea, Liberia, and Sierra Leone

Country	Case definition	Cumulative cases	Cases in past 21 days	Cumulative deaths
Guinea	Confirmed	1850	374	1050
	Probable	210	*	210
	Suspected	74	*	0
	<b>Total</b>	<b>2134</b>	<b>374</b>	<b>1260</b>
Liberia <sup>5</sup>	Confirmed	2727	319**	‡
	Probable	1754	*	‡
	Suspected	2687	*	‡
	<b>Total</b>	<b>7168</b>	<b>319**</b>	<b>3016</b>
Sierra Leone	Confirmed	5441	1339	1189
	Probable	79	*	174
	Suspected	1079	*	35
	<b>Total</b>	<b>6599</b>	<b>1339</b>	<b>1398</b>
<b>Total</b>		<b>15 901</b>	<b>2032</b>	<b>5674</b>

Data are based on official information reported by ministries of health, through WHO country offices. These numbers are subject to change due to ongoing reclassification, retrospective investigation and availability of laboratory results. \*Not reported due to the high proportion of probable and suspected cases that are reclassified. \*\*Data available for past 20 days only. †Data not available. ‡Data missing for 23 November.

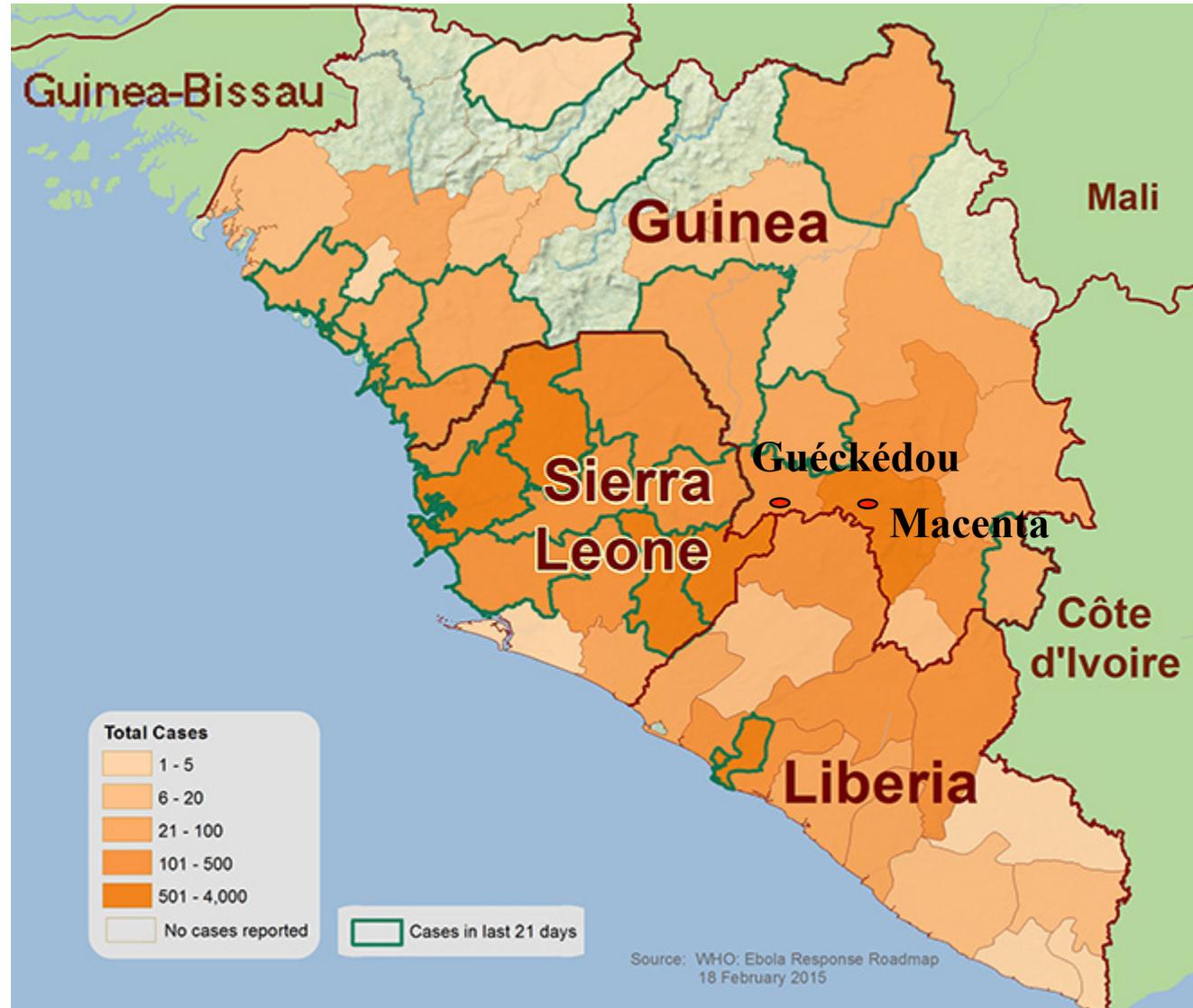
Table 5: Ebola virus disease infections in health-care workers in the three countries with intense transmission

Country	Cases	Deaths
Guinea	97	56
Liberia	342	172
Sierra Leone	136	105
<b>Total</b>	<b>575</b>	<b>333</b>

Data are based on official information reported by ministries of health. These numbers are subject to change due to ongoing reclassification, retrospective investigation and availability of laboratory results.

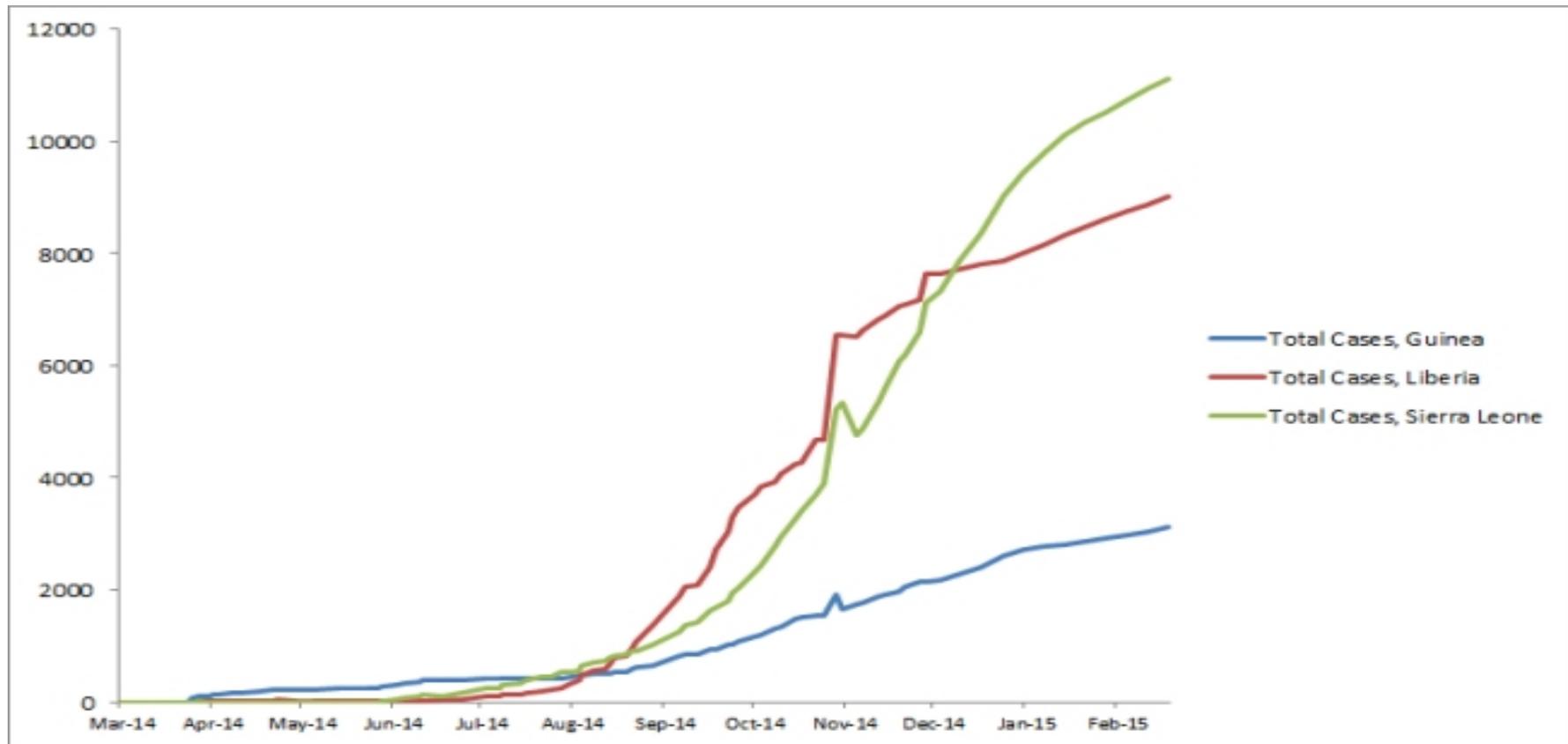
			Number of cases	Number of deaths
			Cumulative	Cumulative
<b>Guinea</b>	<b>21 February 2015</b>	<b>Confirmed</b>	2758	1699
		<b>Probable</b>	387	387
		<b>Suspected</b>	10	Not available <sup>i</sup>
		<b>Total</b>	3155	2086
<b>Liberia</b>	<b>21 February 2015</b>	<b>Confirmed</b>	3153	Not available <sup>i</sup>
		<b>Probable</b>	1888	Not available <sup>i</sup>
		<b>Suspected</b>	4188	Not available <sup>i</sup>
		<b>Total</b>	9229	4032
<b>Sierra Leone</b>	<b>17 February 2015</b>	<b>Confirmed</b>	8223	3057
		<b>Probable</b>	287	208
		<b>Suspected</b>	2645	158
		<b>Total</b>	11 155	3423
<b>All countries</b>		<b>Total</b>	23 539 <sup>i</sup>	9541 <sup>i</sup>

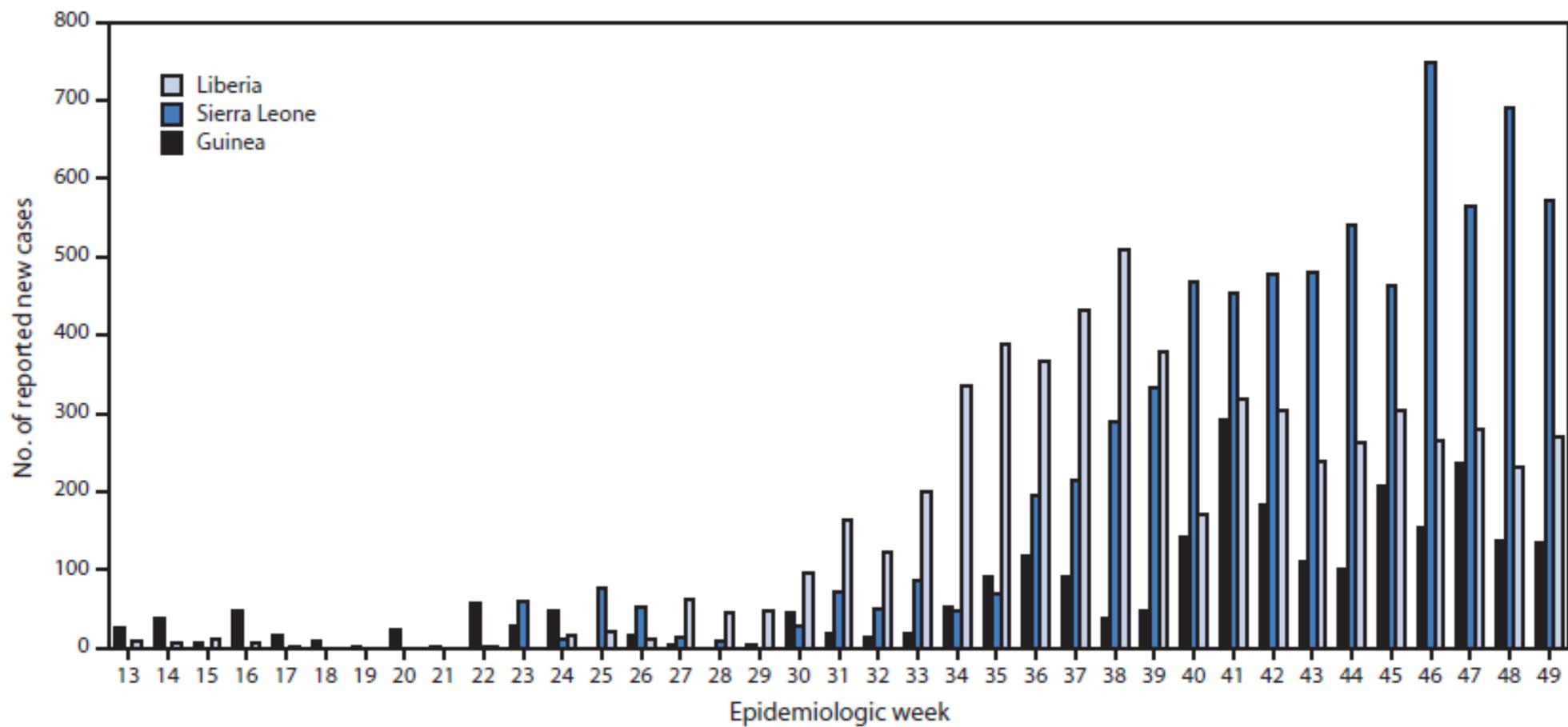
# Point de départ (Fev-Mars 2014) et situation actuelle



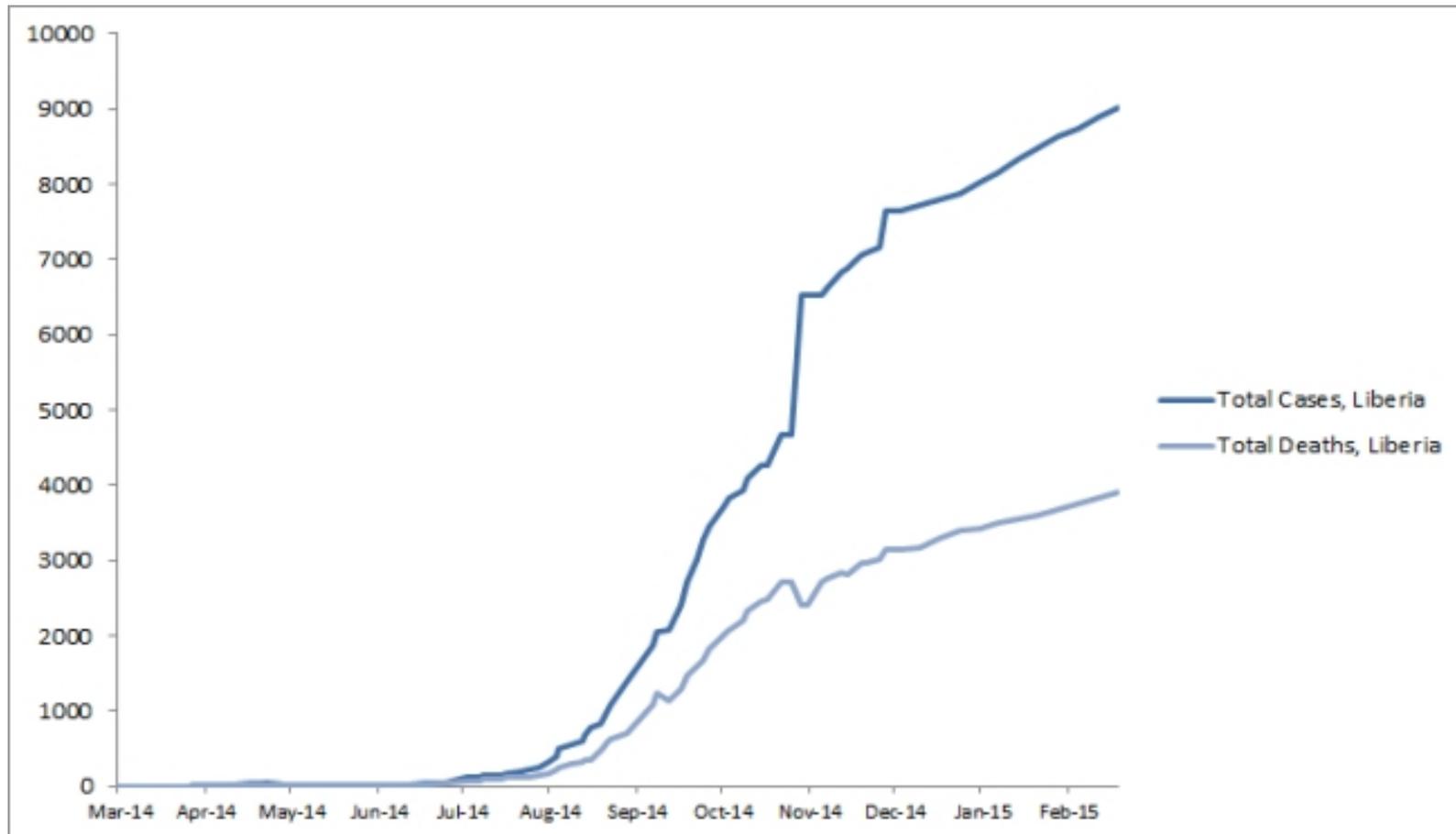


# Total cumulés des cas et depuis le 25 mars 2014 (Guinée, Libéria, Sierra Leone)

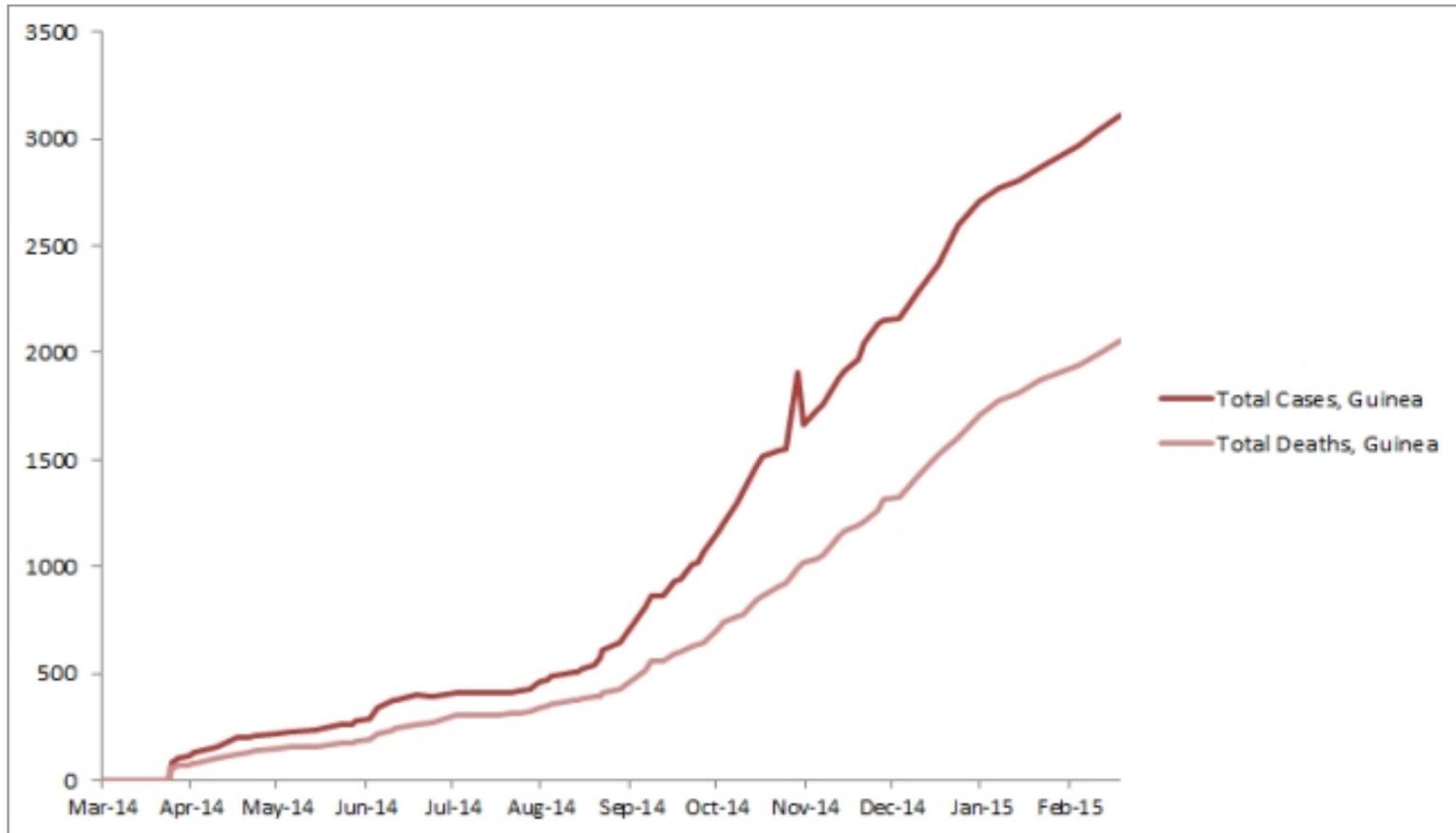




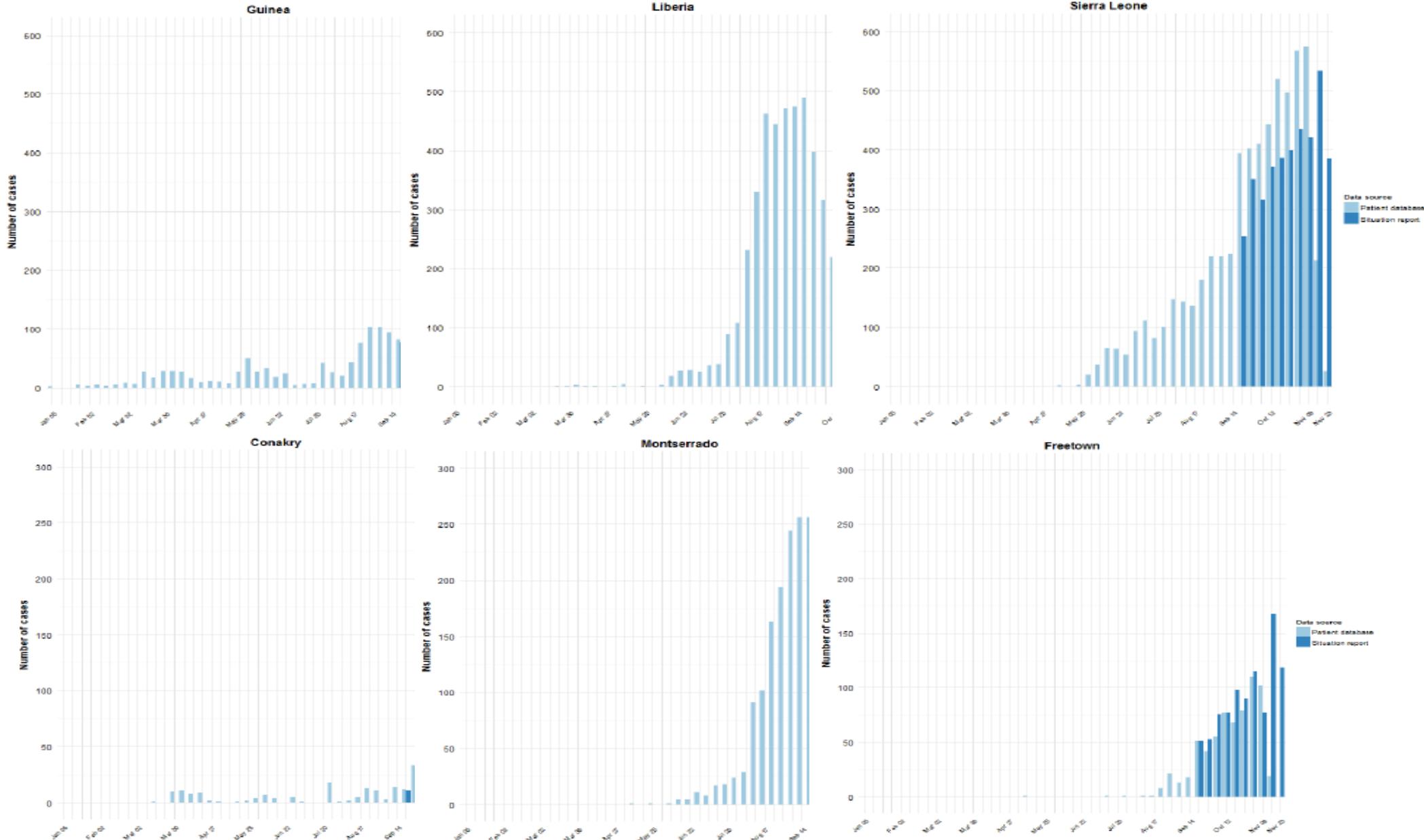
# Total cumulés des cas et des décès depuis le 25 mars 2014 (Libéria)



# Total cumulés des cas et des décès depuis le 25 mars 2014 (Sierra Leone)

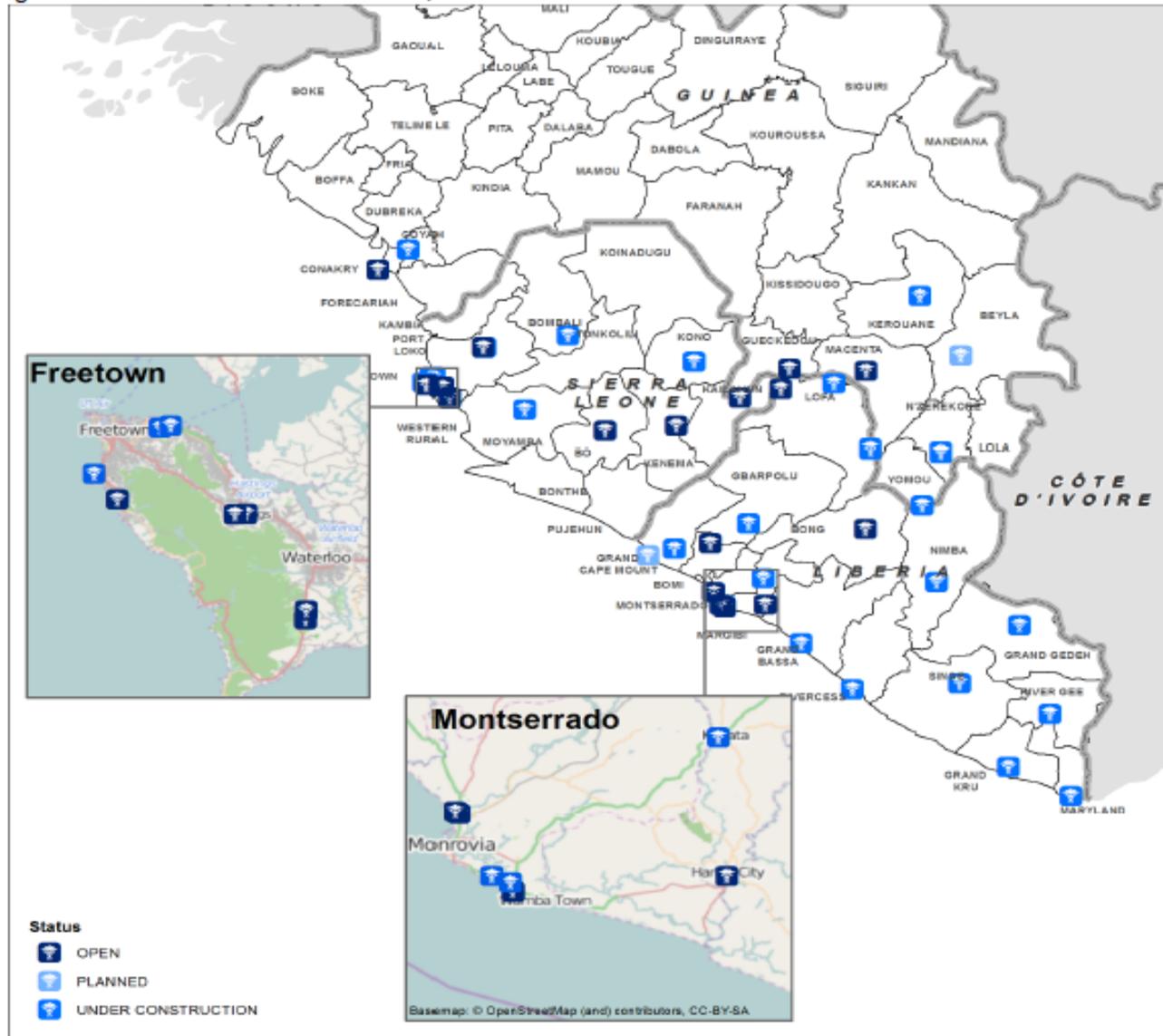


# Situation pays/capitales



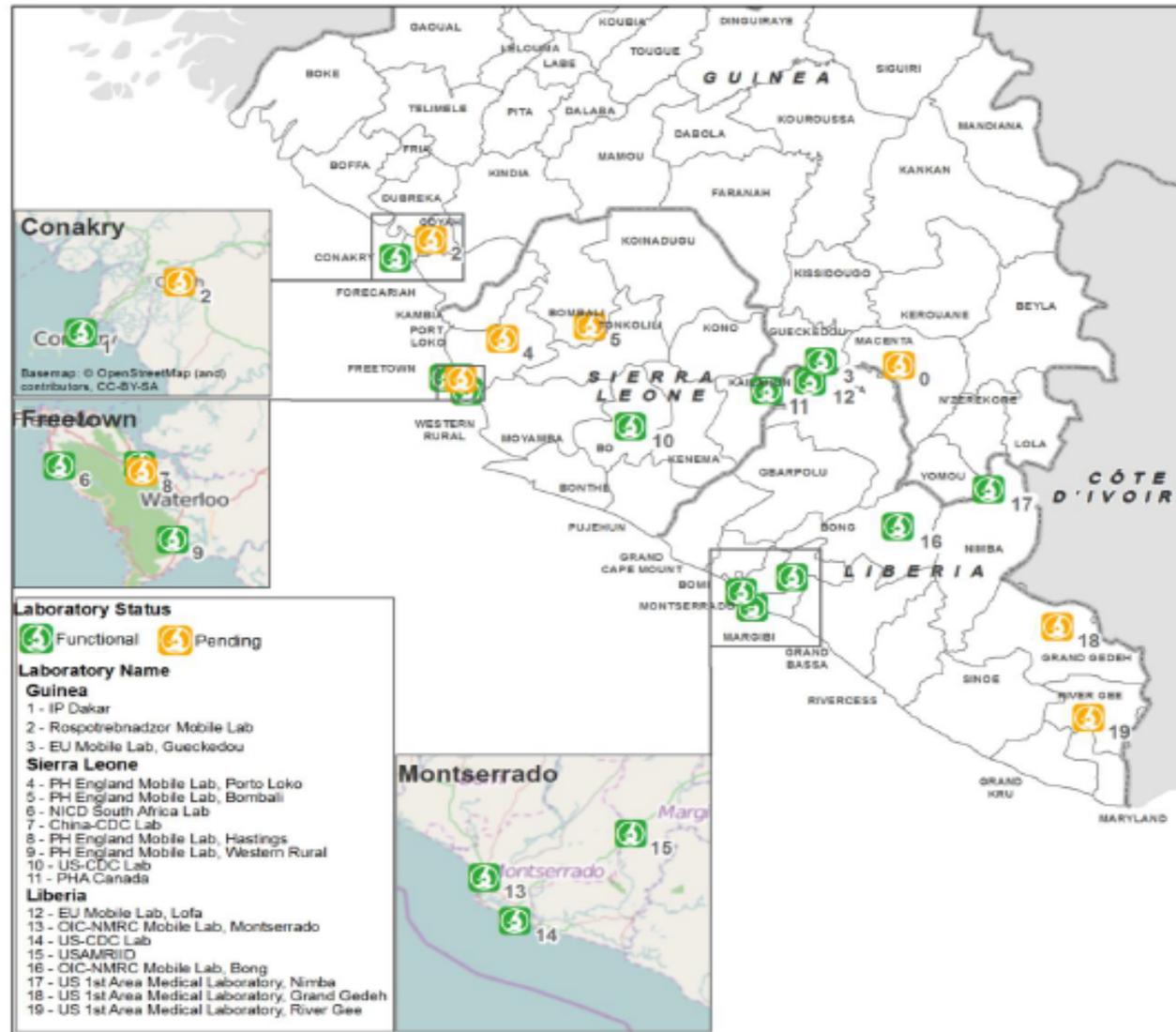
# Localisation et mise en œuvre des centres de traitement

Figure 5. Ebola Treatment Centres in Guinea, Liberia and Sierra Leone



# Localisation des laboratoires de diagnostic virologique

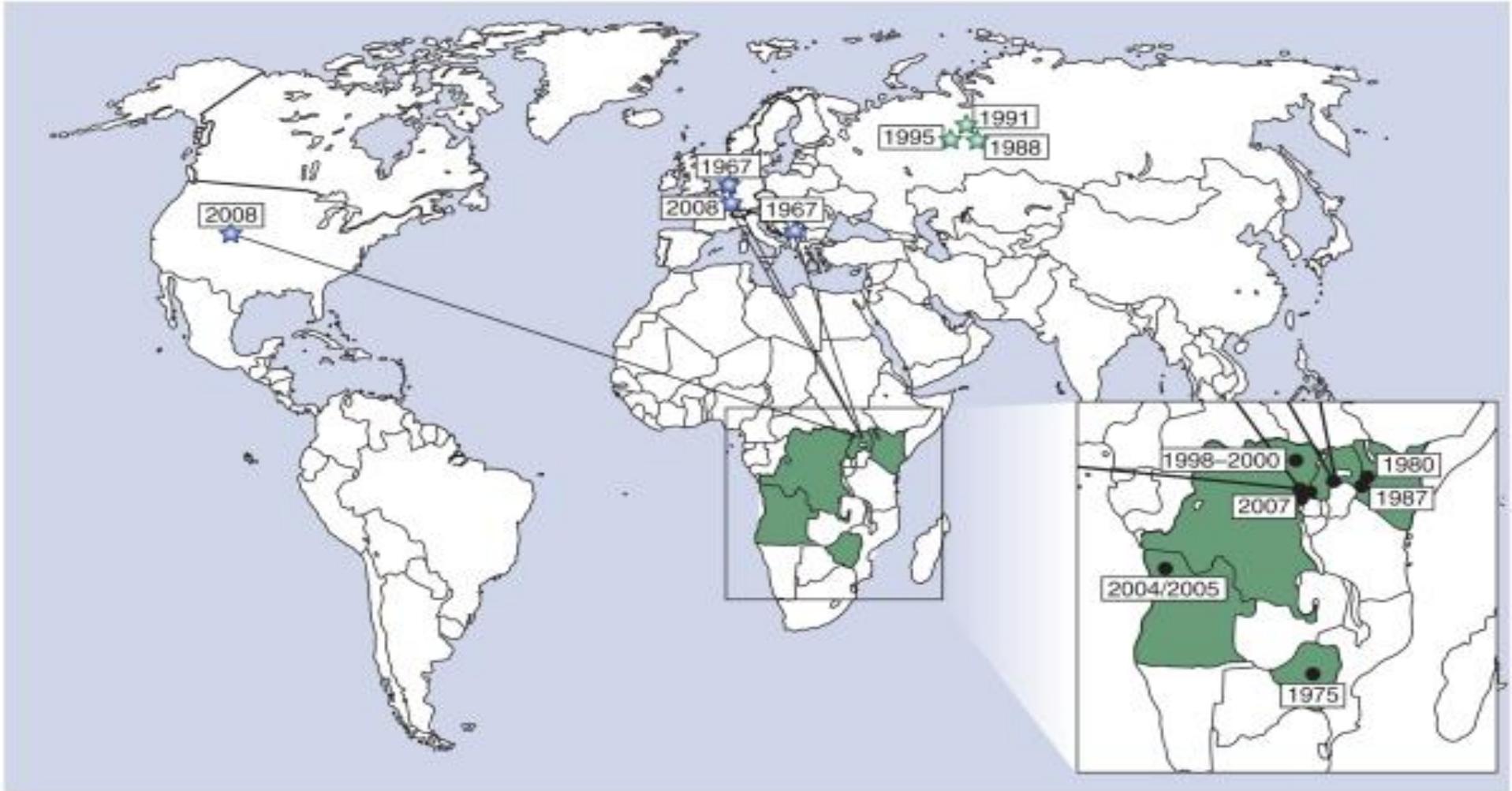
Figure 6. Status of laboratories deployed in the affected countries to support the Ebola outbreak response



# Comment lutter contre des “mythes”

- Certains prétendent que les mesures suivantes ont un effet prophylactique ou thérapeutique :
  - Macher du cola amer (*Gracinia cola* ou *G. Afzeli*)
  - Manger de l'ewedu à base de *cochorus olitorius* (un légume fréquemment utilisé dans la soupe au Nigéria)
  - Prendre des bains salés, et boire l'eau du bain
  - Prendre des bains de Kerosene
  - Prendre des bains pour blanchir la peau (hypochlorite de sodium ou eau de javel)
- Les réseaux sociaux ont été très efficaces pour véhiculer ces “mythes”
- Il a été rapporté des décès liés à la prise régulière d'eau saturée en sel au Nigéria

Ce n'est pas la première fois qu'il y a des cas d'importation :  
exemple de Marbourg :





# La protection efficace des EPI modernes



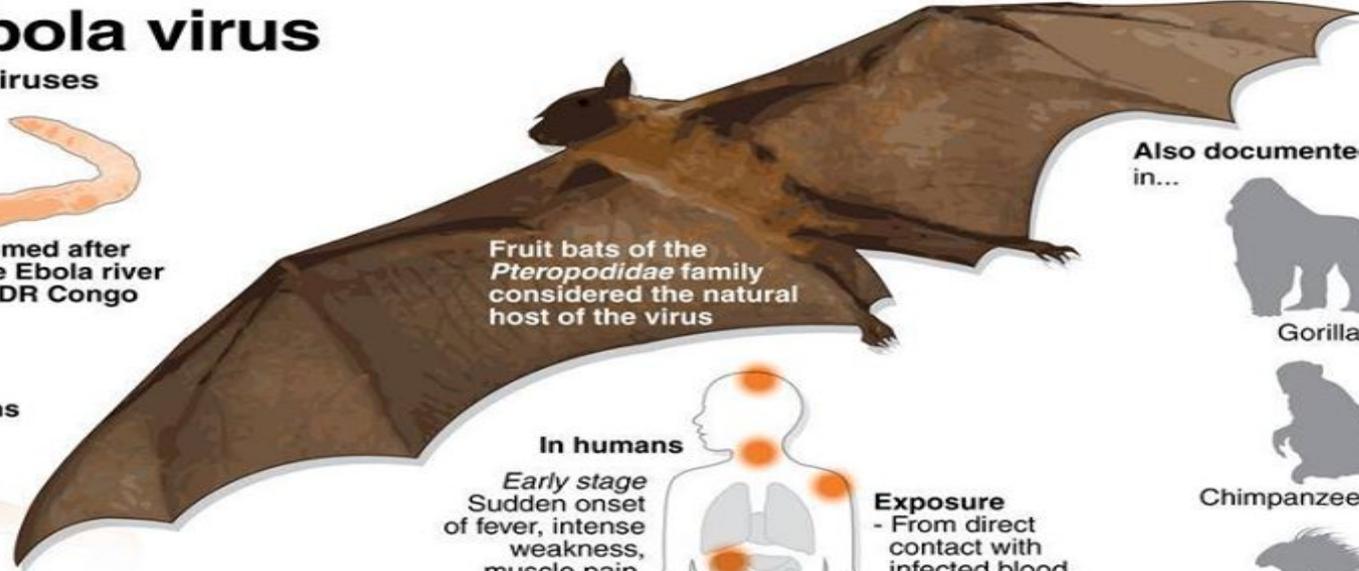
# Conclusions

- La plus grande épidémie a Ebolavirus enregistrée a ce jour (problème de la diffusion du virus en zone urbaine)
- Le nombre de cas augmente encore, mais pas de façon exponentielle.
- Les pays voisins doivent être en alerte et vigilants
- Comme toutes les épidémies liées a des virus donnant des infection aigues, elle va se terminer, mais elle recommencera
- La réponse apportée a ce jour en terme de formation, de prise en charge et de développement de thérapeutique ne peut être qu'une réponse au long cours
- La réponse pour se protéger a distance est de maitriser l'épidémie sur place
- Par l'éducation, il faut lutter contre les préjugés et les mythes
- Actuellement, il convient de passer un message d'espoir aux malades

# The deadly Ebola virus

One of the most dangerous viruses known to man

First identified in 1976 in DR Congo and Sudan



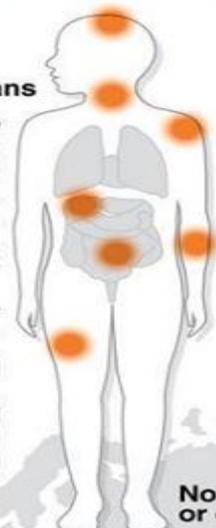
Also documented in...



## In humans

**Early stage**  
Sudden onset of fever, intense weakness, muscle pain, headache, sore throat

**Followed by...**  
Vomiting, diarrhoea, rash, impaired kidney and liver, internal and external bleeding



**Exposure**

- From direct contact with infected blood, faeces, sweat
- Sexual contact with infected person
- Unprotected handling of contaminated corpses
- Handling of contaminated objects

**No vaccine or cure**

## Major outbreaks

