Collège De Maladies Infectieuses, Parasitologie Et Microbiologie

CAS CLINIQUE

Pr Ag Fahmi Dachraoui (Monastir)

Pr Amine Slim (Tunis)

Tunis 6 -12- 2013

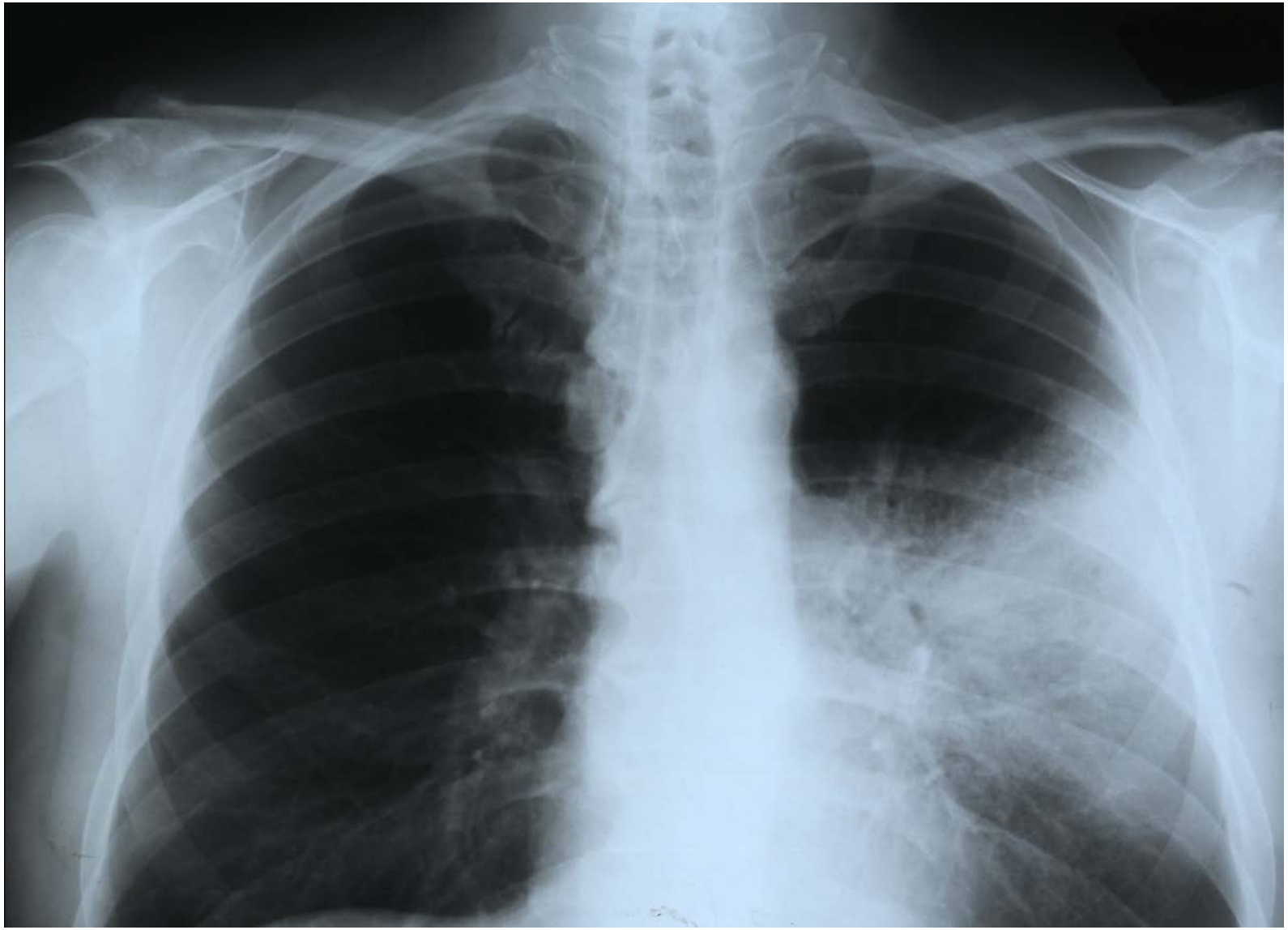
Mr R. A

- Âgé de 66 ans, transféré du service de pneumologie le 8 mai 2013 pour **Insuffisance Respiratoire Aigue**
- ATCD :
  - DNID
  - Bronchite chronique
- Retraité de la fonction publique
- Père d'un IDE du service de réanimation

Anamnèse

- Le 01/05/2013: installation d'une fièvre à 40°C avec toux sèche.
- Le 04/05/2013: Il a consulté aux urgences d'un hôpital régional où il a été traité pour une grippe.
- Le 06/05/2013: il a été hospitalisé au service de pneumologie

Radio thorax Pneumologie



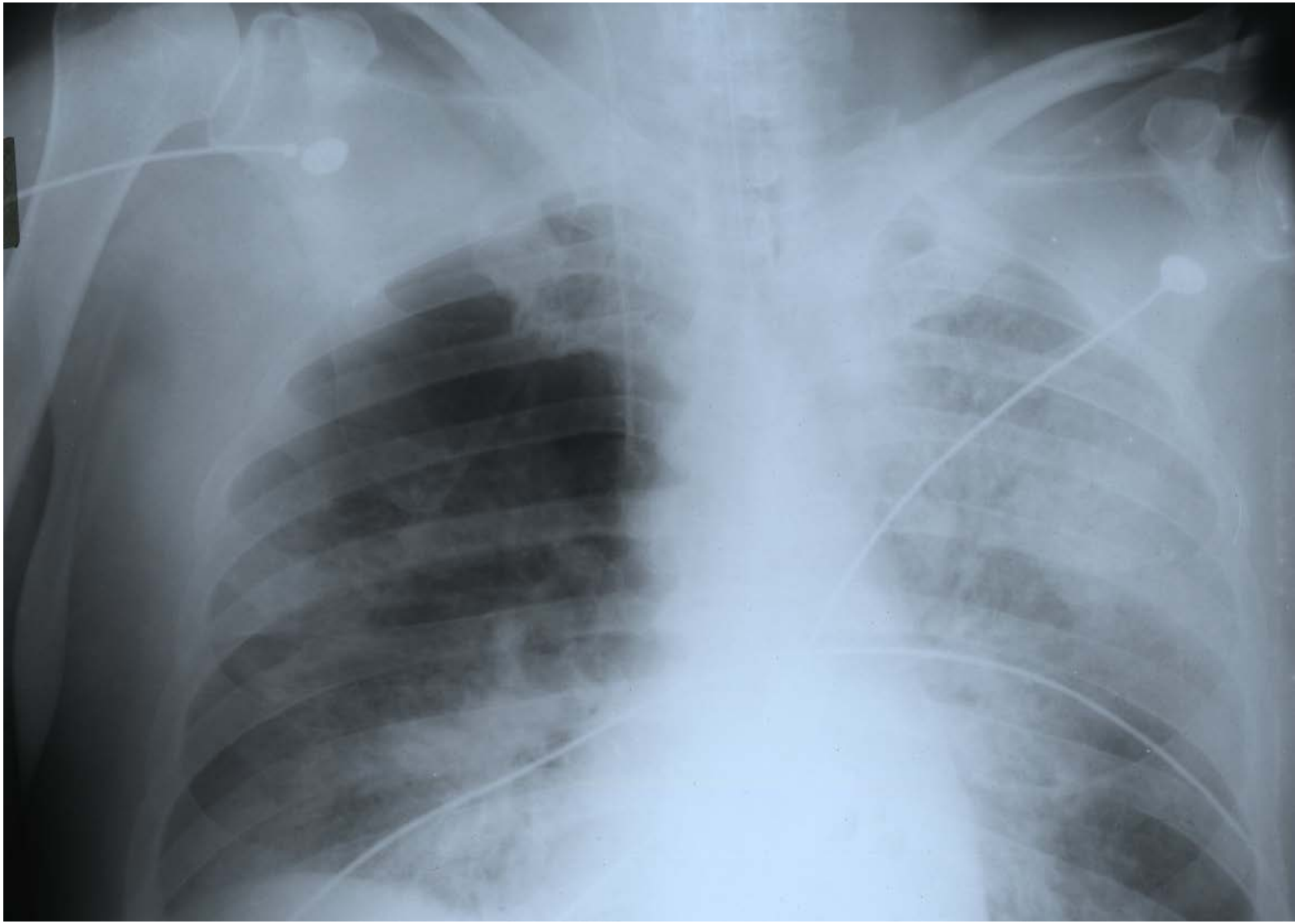
En pneumologie

- Diagnostic : PFLA
- Antibiothérapie: amox-ac clav + Ofloxacine
- Evolution : signes d'IRA
- Le 08/05/2013 :hospitalisation en réanimation Médicale

En réanimation

- T°= 38.5°c
- FR= 40 cpm
- Tirage intercostal
- SaO_2 = 80% sous MHC 10l/min
- Auscultation pulmonaire : râles crépitants diffus
- TA = 140/66mmHg
- FC = 110 bpm
- Marbrures , froideur des extrémités
- Score de Glasgow à 15/15.

Radio thorax Réanimation



Quelle sont vos hypothèses diagnostiques ?
Quelle est votre attitude ?

- **Sepsis sévère /pneumopathie communautaire bilatérale hypoxemiante**
- « VNI » : prudemment !!!!
- IOT
- Remplissage vx : oui mais ….
- Antibiothérapie
- Bilan biologique : «standard» + étiologique
- Echocardiographie
- Surveillance

Examens complémentaires

- CRP: 595mg/l
- GB =9100 /mm3 plaq=159000/mm3
- Na+ :123 mmol/L K+ : 3.26mmol/L
- TP : 81%
- Créat : 223µmol/L
- CPAP (10cm H2O) pH = 7.5 ; $PaCO_2$ = 3.36 KPa ; PaO_2 = 7.95 KPa ; HCO_3^- = 20.7 mmol/l ; SaO_2 = 93.5%

Recherche bactériologique

- Sérologies des germes atypiques
- AT : Examen direct +culture
- « Mini »-LBA

Notre attitude …

- VNI …puis qq heures après : Intubation
- Conditionnement : cathéter central + artériel
- Mesures standards de la prise en charge des états septiques

http://www.survivingsepsis.org

Surviving Sepsis Campaign

Notre attitude …

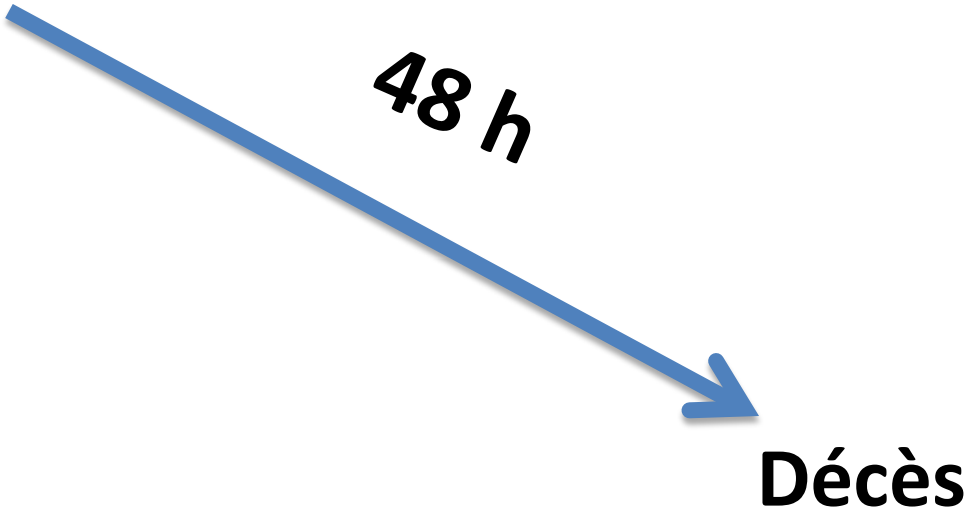
- Ventilation protectrice /SDRA : 6ml/kg/IBW
- PEP
- amox-ac clav + Ofloxacine puis Rifampicine
- Décubitus ventral
- Corticoïdes :stress dose
- « Mini»-LBA

Echocardiographie

- FEVG à 50%
- Pas d’ argument en faveur de l’augmentation des pressions de remplissage gauches
- VG non dilaté
- VG non hypertrophié
- VD non dilaté de fonction systolique conservée

Evolution

- SDRA - Choc septique refractaire
- SDMV
- Noradrénaline (dose +++)

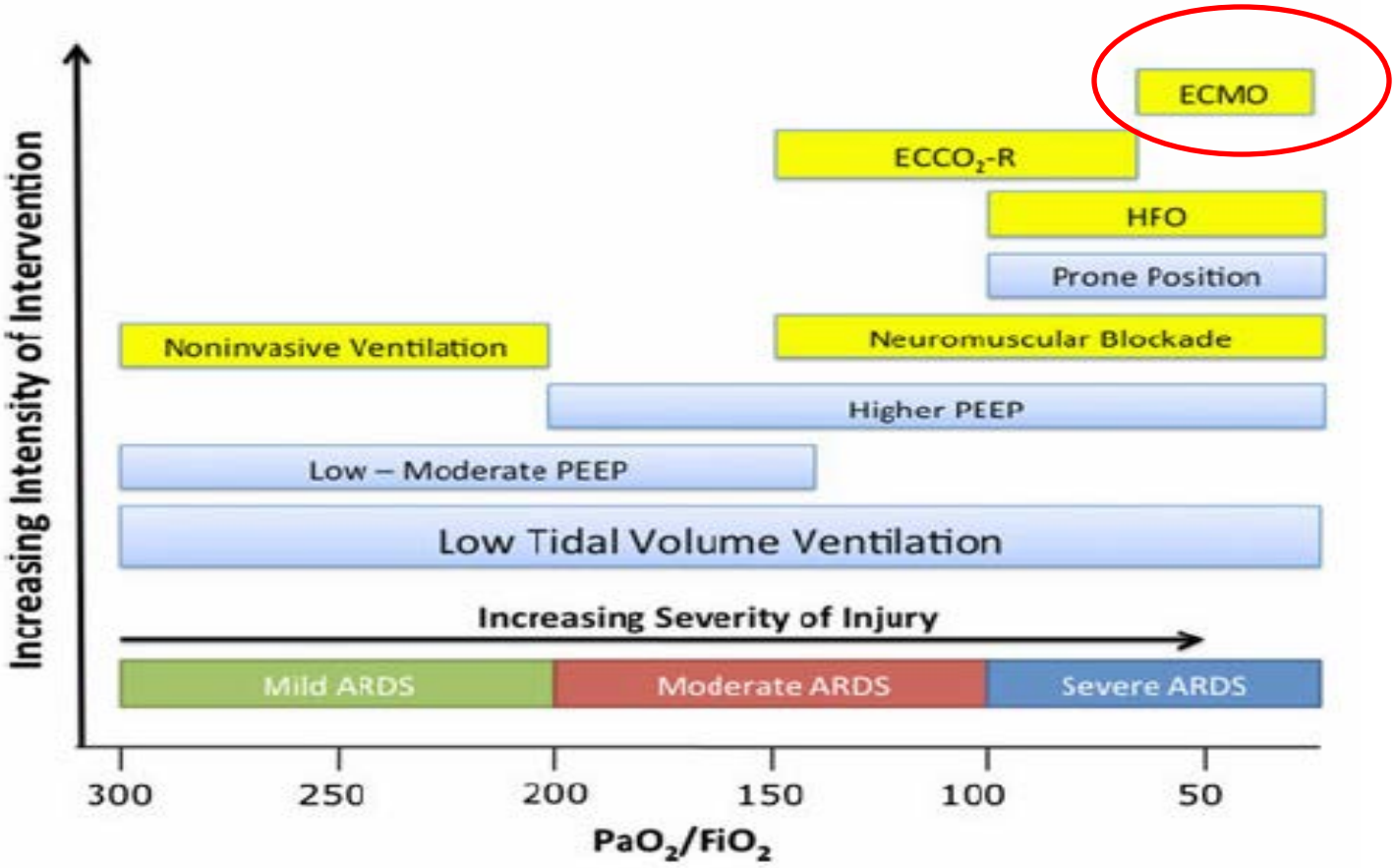


Intensive Care Med (2012) 38:1573–1582
DOI 10.1007/s00134-012-2682-1

SPECIAL ARTICLE

Niall D. Ferguson
Eddy Fan
Luigi Camporota
Massimo Antonelli
Antonio Anzueto
Richard Beale
Laurent Brochard
Roy Brower
Andrés Esteban
Luciano Gattinoni
Andrew Rhodes
Arthur S. Slutsky
Jean-Louis Vincent
Gordon D. Rubenfeld
B. Taylor Thompson
V. Marco Ranieri

The Berlin definition of ARDS: an expanded rationale, justification, and supplementary material

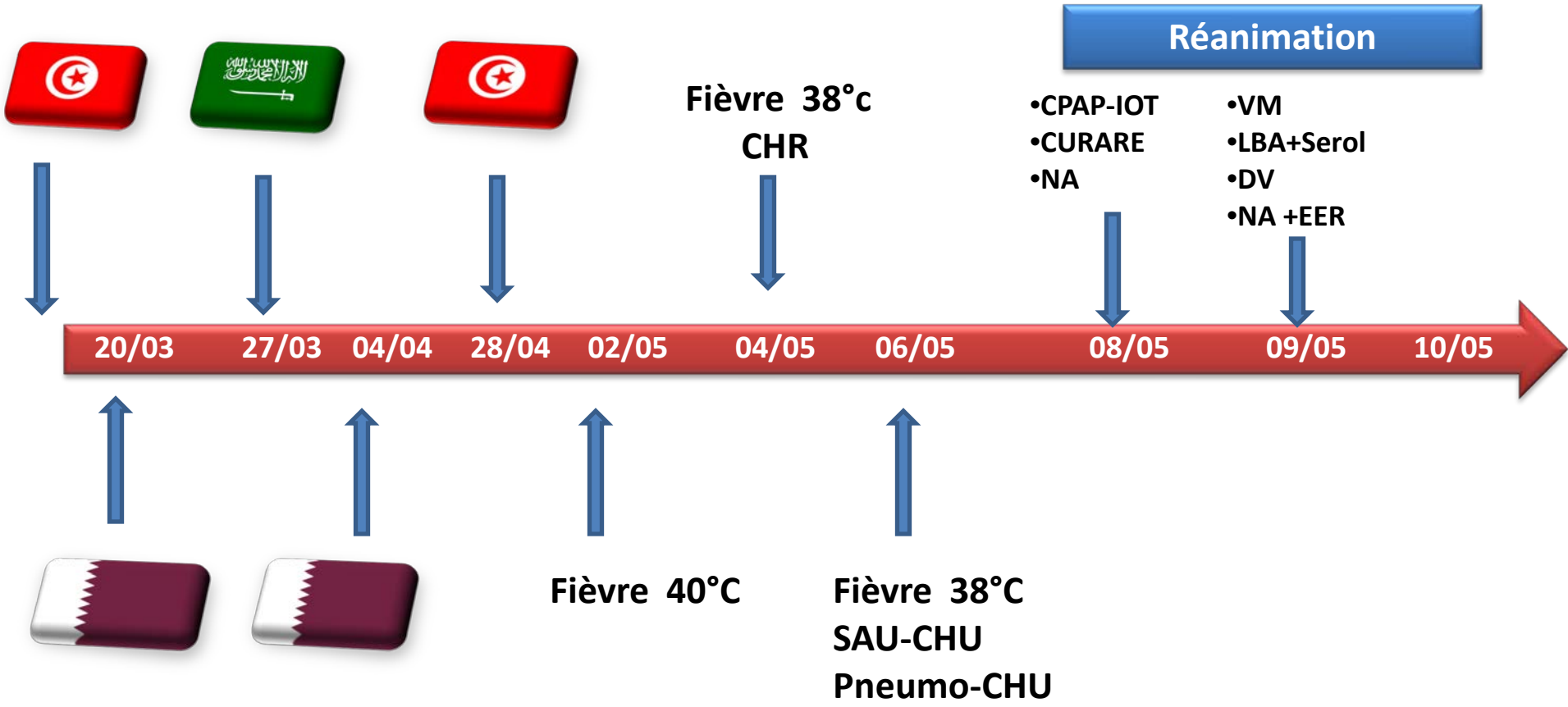


Mais ….

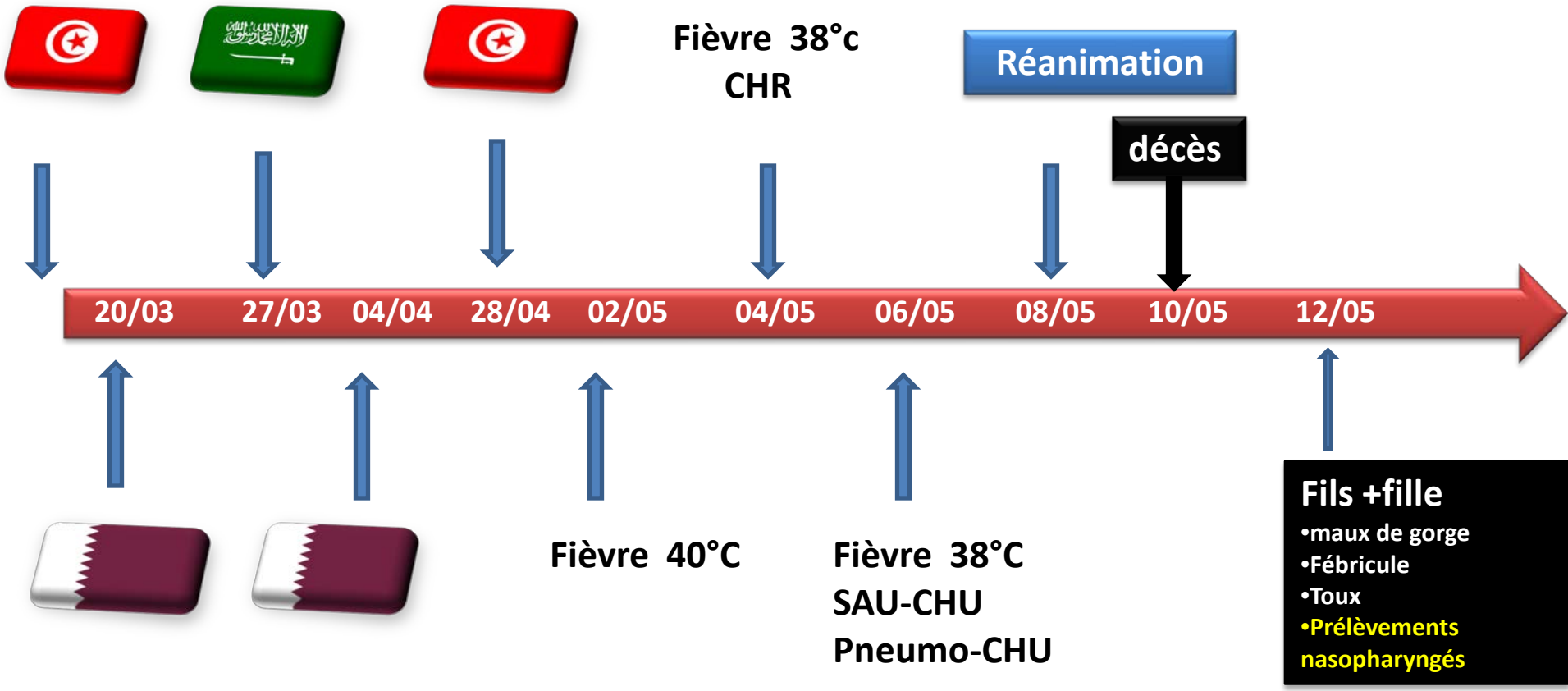
À la reprise de l'interrogatoire

Notion de retour d'un voyage récent : Qatar et Arabie Saoudite (chez sa fille)

Mr R. A
Mars-Avril-Mai 2013



Mr R. A
Mars-Avril-Mai 2013



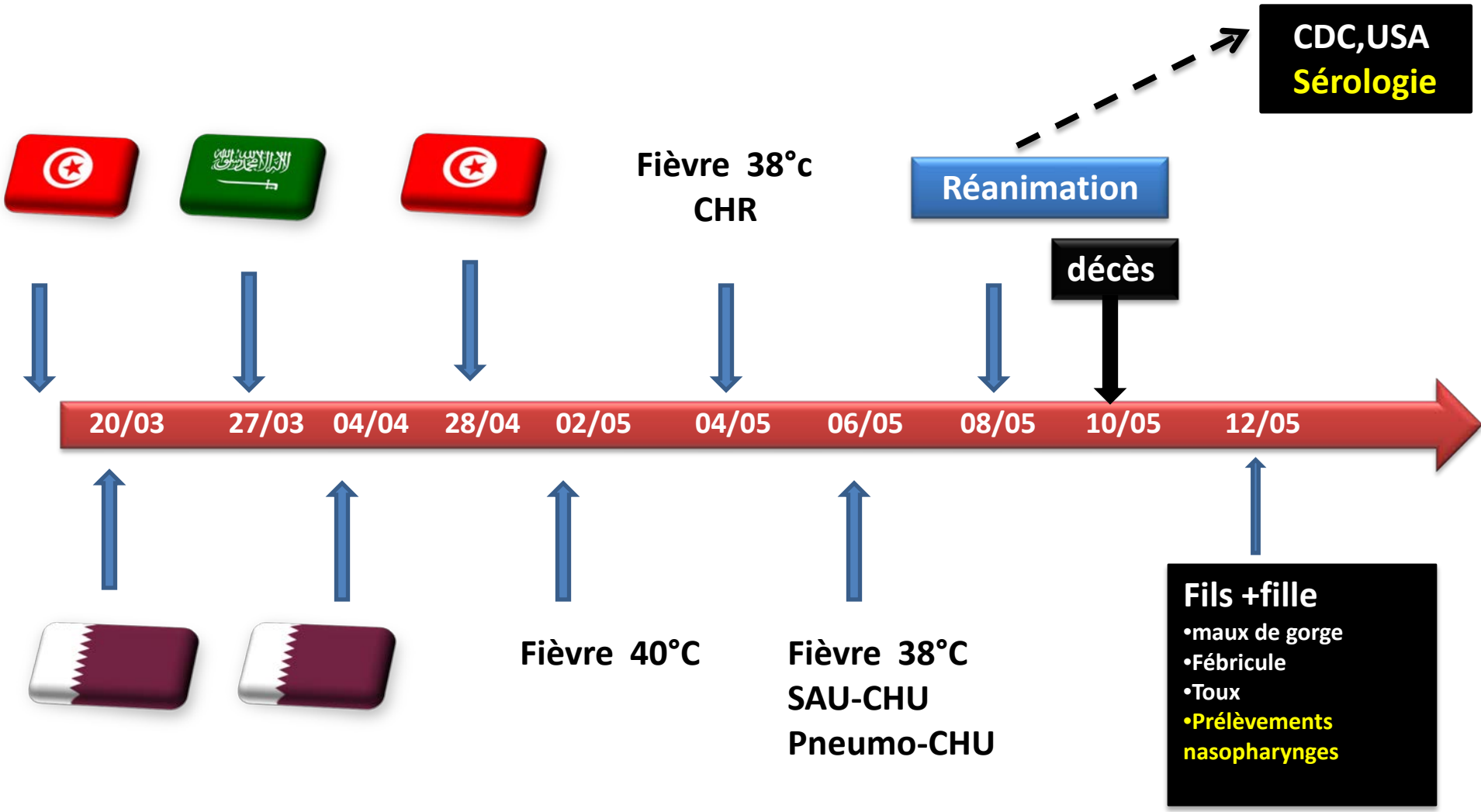
Des idées ?

Résultats

- Les 2 enfants du patient: prélèvements nasopharyngés :***positifs en rt-PCR au CoronaVirus***

- Middle East respiratory syndrome corona virus **(MERS-CoV).**
- It was named by the Corona virus Study Group of the International Committee on Taxonomy of Viruses in May 2013.

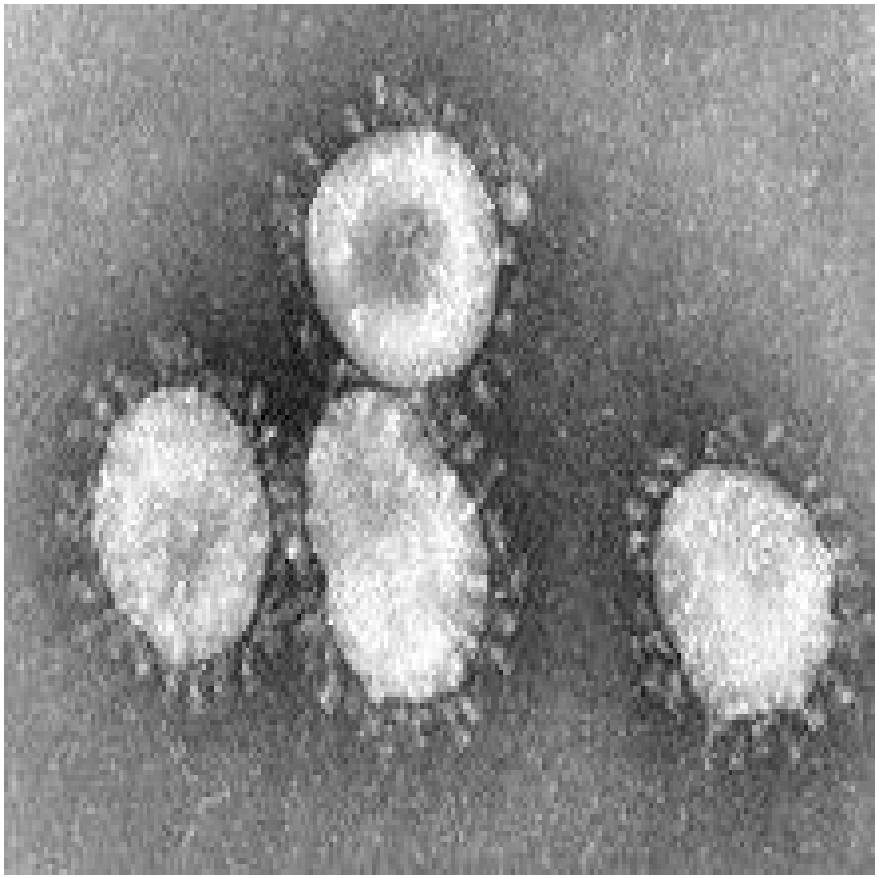
Mr R. A
Mars-Avril-Mai 2013

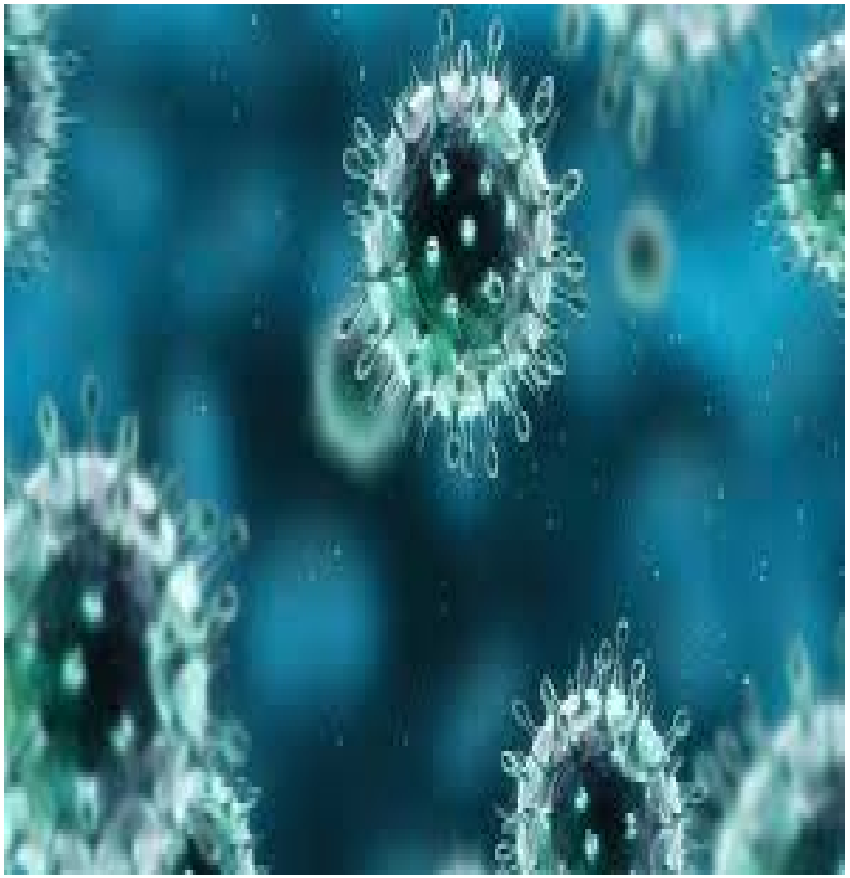


Diagnostic virologique

- Les séquences complètes du nucléocapside du virus ont montré une signatures unique par rapport aux séquences publiées dans la littérature.
- La recherche de contacts effectuée auprès des membres restants de la **famille**, et du **personnel** de santé ayant été en contact avec le cas index étaient négatifs par RT- PCR .

Corona Virus



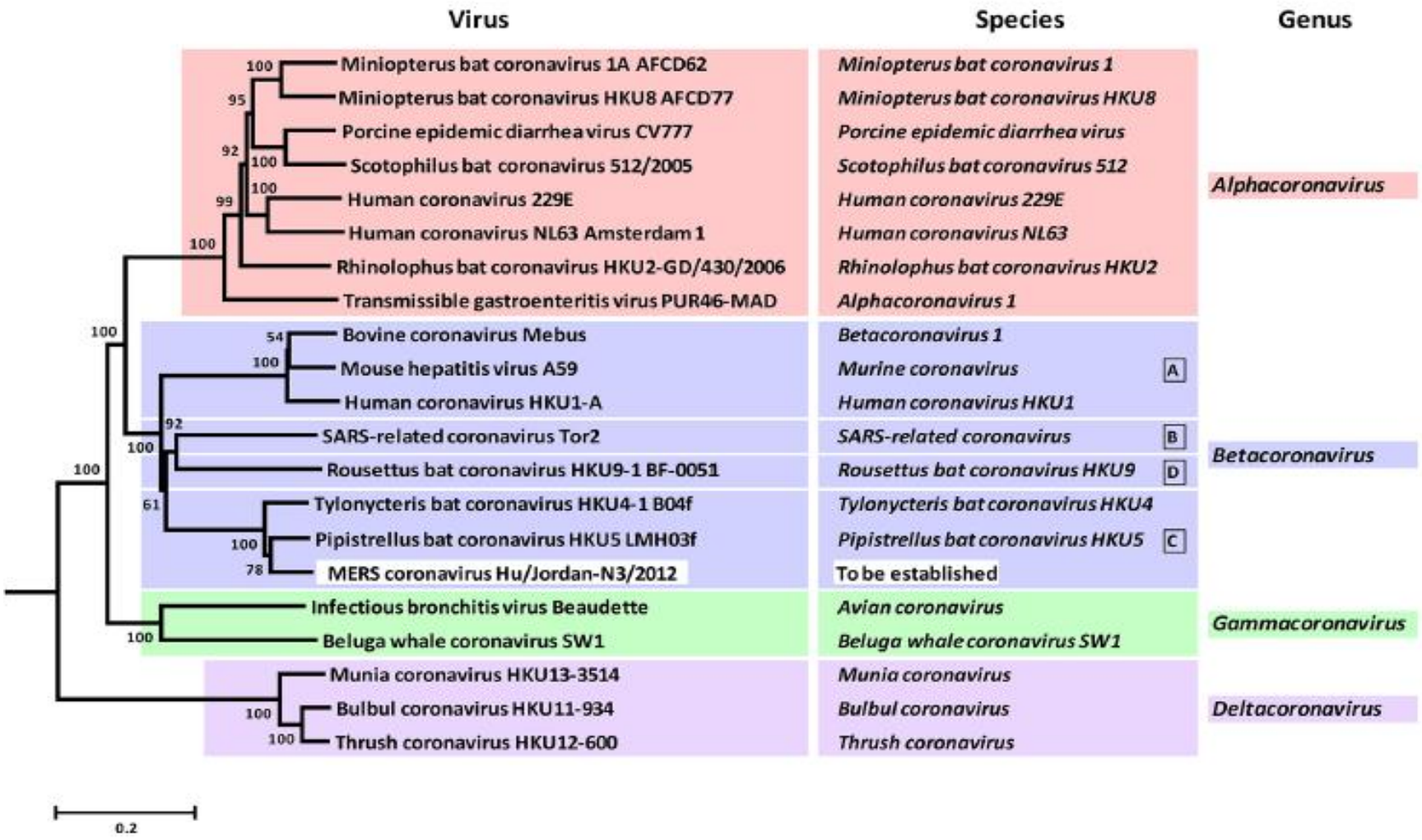


Coronaviruses (CoVs)

- Enveloped positive strand RNA virus
- Human CoVs isolated in the 1960s
- 6 human CoVs (HCoVs) have been identified to date:

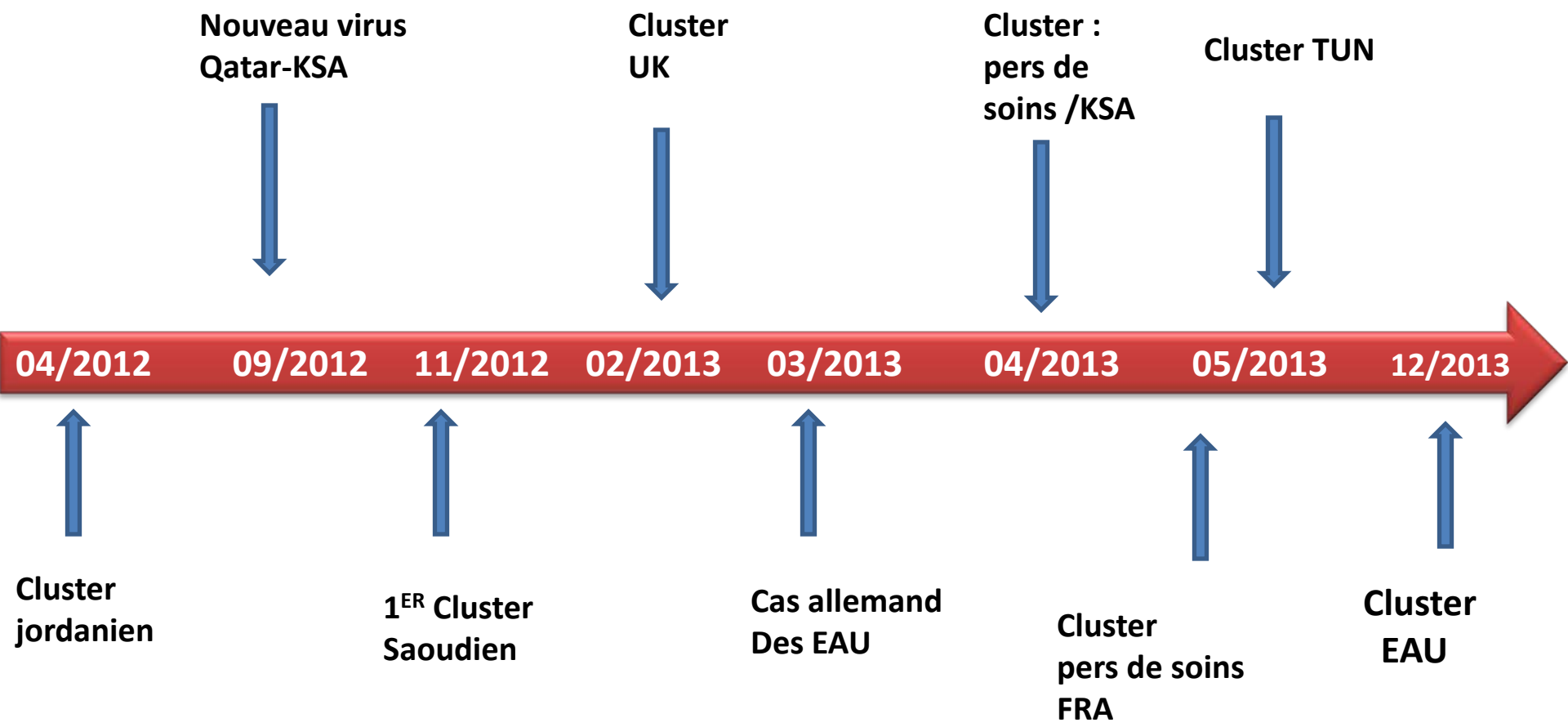
1. HCoV 229E
2. HCoV OC43
3. HCoV NL63
4. HCoVHKU1
5. **SARS CoV**
6. **Middle East Respiratory Syndrome Coronavirus (MERS-CoV)**

Coronavirus



L’étude des clusters publiés « les enseignements »

Les clusters d'infection/MERS-CoV



International Journal of Infectious Diseases 17 (2013) e668–e672

Contents lists available at SciVerse ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

A family cluster of Middle East Respiratory Syndrome Coronavirus infections related to a likely unrecognized asymptomatic or mild case

Ali S. Omrani [a], Mohammad Abdul Matin [b], Qais Haddad [c], Daifullah Al-Nakhli [d], Ziad A. Memish [e,*], Ali M. Albarrak [a]

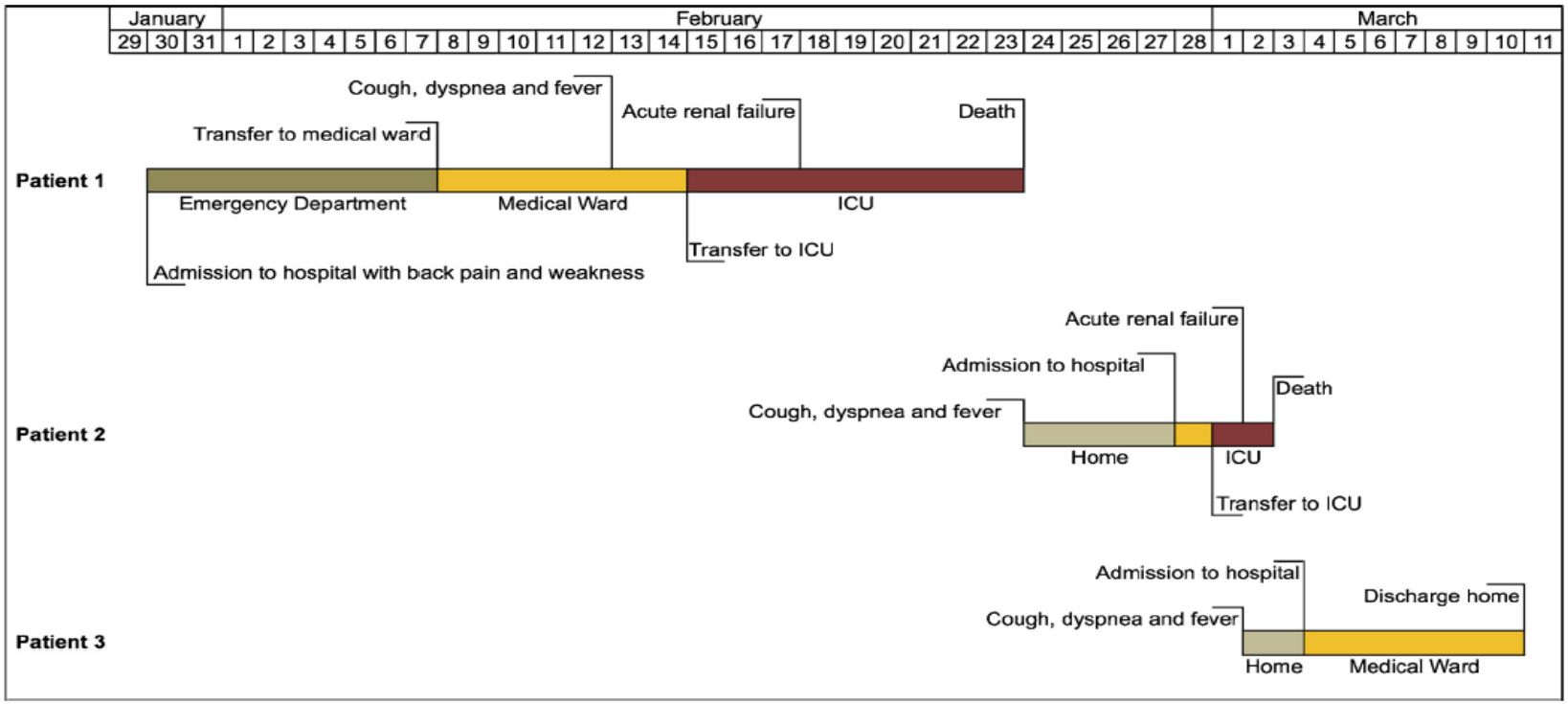


Figure 3. Clinical timelines for three patients with definite or probable Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection.

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Les signes cliniques

Table 1
Clinical and investigational features of a family cluster of 3 patients with Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infections from Riyadh, Saudi Arabia and from previously reported cases.[a]

	Patient 1	Patient 2	Patient 3	Data from previous MERS-CoV reports[b]
Fever	Yes	Yes	Yes	30/33 (90.9%)
Cough	Yes	Yes	Yes	30/33 (90.9%)
Dyspnea	Yes	Yes	Yes	20/33 (60.6%)
Gastrointestinal symptoms	No	No	No	12/33 (36.4%)
Chest x-ray infiltrates	Yes	Yes	Yes	25/33 (75.8%)
Lymphopenia	Yes	Yes	Yes	9/9 (100%)
Thrombocytopenia	Yes	Yes	Yes	11/32 (34.4%)
Creatinine kinase rise	Yes	Yes	Yes	2/2 (100%)
Alanine transaminase rise	Yes	Yes	Yes	3/7 (42.9%)
Lactate dehydrogenase rise	Not available	Yes	Yes	3/6 (50%)
Acute renal failure	Yes	Yes	No	7/10 (70%)
ICU[c] admission	Yes	Yes	No	26/33 (78.8%)
Mechanical ventilation	Yes	Yes	No	26/33 (78.8%)

[a] Data collated from reports in which clinical details of patients with MERS-CoV infection were made available.[1,7,8,10,19,24,27]
[b] Numerator indicates number of patients in whom a particular characteristic was present; denominator indicates the total number in which the presence or absence of the particular characteristic was reported.
[c] ICU denotes intensive care unit.

The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

Family Cluster of Middle East Respiratory Syndrome Coronavirus Infections

Ziad A. Memish, M.D., Alimuddin I. Zumla, M.D., Ph.D., Rafat F. Al-Hakeem, M.D., Abdullah A. Al-Rabeeah, M.D., and Gwen M. Stephens, M.D.

- A cluster of 4 respiratory illnesses in a family who lived in an apartment
- All males; ages 16-70y
- All hospitalized
- 3 of 4 confirmed with MERS-CoV
- 3 of 4 patients with gastrointestinal symptoms: diarrhea, abdominal pain, anorexia
- 2 deaths

The NEW ENGLAND JOURNAL of MEDICINE

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Transmission interhumaine?

Table 1. Level of Contact among Family Members of Patients with MERS-CoV Infection before and after Hospital Admission.*

Family Member	Close Contact with Patient 1 before Admission	Close Contact with Patient 1 after Admission	Close Contact with Patient 2 before Admission	Close Contact with Patient 4 before Admission	Clinical Diagnosis of MERS-CoV Infection
Wife of Patient 1	Frequent	No	Infrequent	Infrequent	No
Patient 2	Frequent	Frequent	NA	Frequent	Yes
Wife of Patient 2	No	No	Frequent	No	No
Patient 3	Infrequent	Infrequent	Frequent	Frequent	Yes
Patient 4	Frequent	Frequent	Frequent	NA	Yes
Wife of Patient 4	No	No	No	Frequent	No

* NA denotes not applicable.

UK Cluster: Public Health Implications

- Evidence of person-to-person transmission
- **Coinfection with influenza** (index case) and **parainfluenza type 2** (both secondary cases)
- No sustained chains of transmission
- **Incubation period may be 1-9 days**

HPA UK Novel Coronavirus Investigation Team; Eurosurv 2013; 18(11)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 1, 2013 VOL. 369 NO. 5

Hospital Outbreak of Middle East Respiratory Syndrome Coronavirus

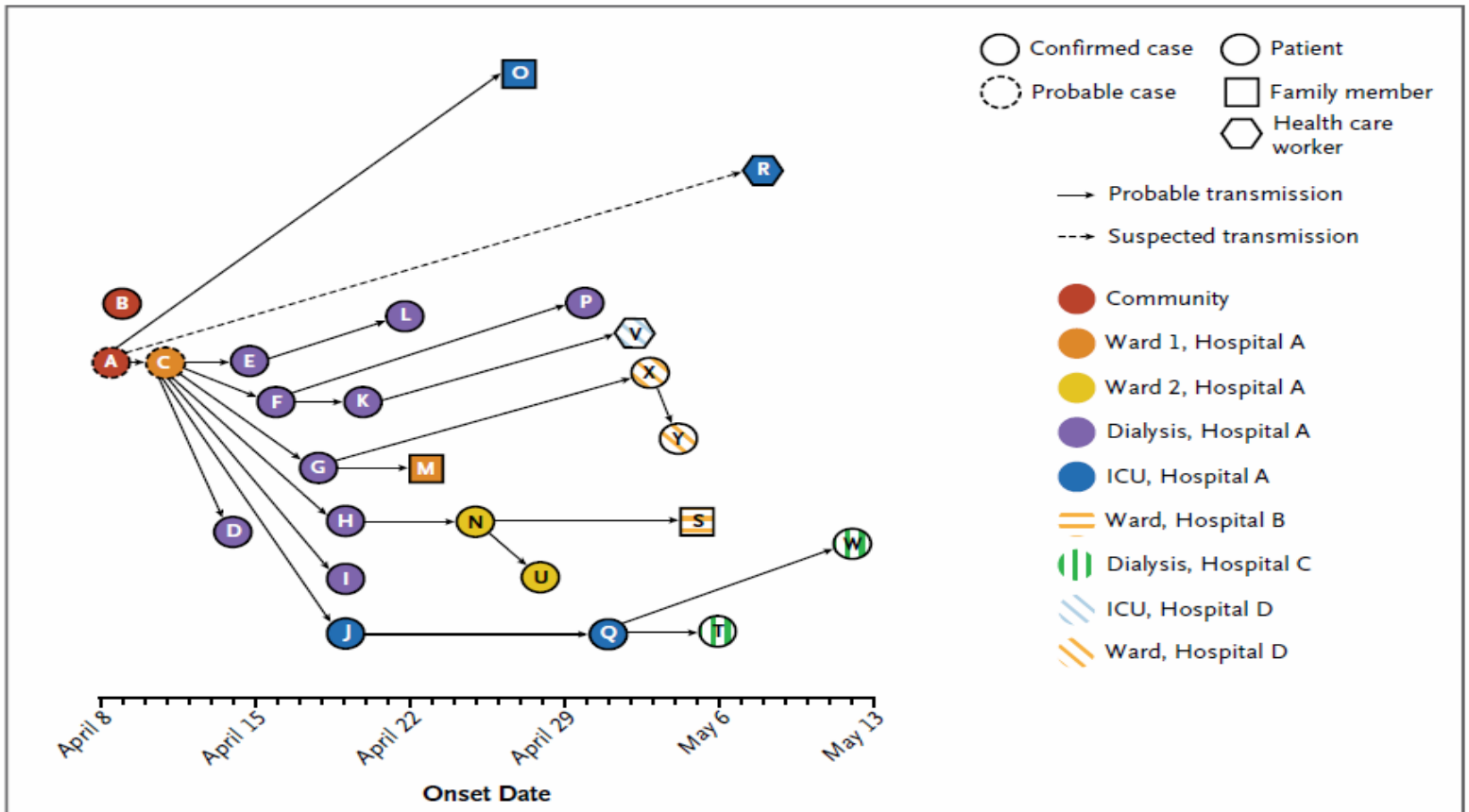

Figure 2. Transmission Map of Outbreak of MERS-CoV Infection.

All confirmed cases and the two probable cases linked to transmission events are shown. Putative transmissions are indicated, as well as the date of onset of illness and the settings. The letters within the symbols are the patient identifiers (see Fig. S2 in the Supplementary Appendix).

EMHJ • Vol. 19 Supplement 1 2013 Eastern Mediterranean Health Journal
La Revue de Santé de la Méditerranée orientale

Country experience

Novel coronavirus infections in Jordan, April 2012: epidemiological findings from a retrospective investigation

B. Hijawi,[1] M. Abdallat [2] A. Sayaydeh,[2] S. Alqasrawi,[2] A. Haddadin,[3] N. Jaarour,[2] S. Alsheikh[2] and T. Alsanouri[3]

العدوى بالفيروس التاجي الجديد في الأردن نيسان 2012: النتائج الوبائية للتقصيات الاستعادية

بسام حِجَّاوي، محمد العبدلاّت، أيوب صيايده، سلطان الكسراوي، أكثم حدادين، نجوى جعروري، سامح الشيخ، طارق السانوري

الخلاصة: في نيسان/ أبريل 2012، اندلعت فاشية من المرض التنفسي الحادّ في إحدى المستشفيات العمومية في مدينة الزرقاء في الأردن، وأصيب خلالها ثمانية من العاملين في الرعاية الصحية من بين أحد عشر مصاباً، ومات أحدهم بعد ذلك. ولم يكن سبب الفاشية معروفاً آنذاك، فالنتائج التي أسفرت عنها التقصيات الوبائية والتي تضمَّنت اختبارات مختبرية أجريت فور اندلاع الفاشية لم تكن قاطعة. وبعد اكتشاف العدوى بالفيروس التاجي الجديد في الجزيرة العربية في أيلول/ سبتمبر 2012، أجريت الاختبارات مجدداً على العينات التنفسية والمصلية التي تم تخزينها من المرضى في تلك الفاشية، فتأكَّد تشخيص العدوى بالفيروس التاجي الجديد لدى مريضَيْن متوفيَيْن. وتصف هذه الدراسة النتائج الوبائية للتقصيات الاستعادية التي أجريت في تشرين الثاني/ نوفمبر 2012، وتُلقي الضوء على احتمال سراية عدوى المستشفيات بالفيروس التاجي في مواقع الرعاية الصحية. فقد تم كشف حالتَيْن مؤكَّدتَيْن مختبرياً وإحدى عشرة حالة محتملة في تلك الفاشية، وكان من بين المصابين بها عشرة من العاملين في الرعاية الصحية واثنان من أفراد أُسَر المصابين بالحالات.

Jordan Cluster, April, 2012

- 2 confirmed cases reported retrospectively
- Both cases fatal
- Occurred at the same time as a cluster of severe respiratory illness among **healthcare workers, N=13**

Hijawi et al. EMHJ 2013; 19: Suppl 1: S12-S18

Country experience

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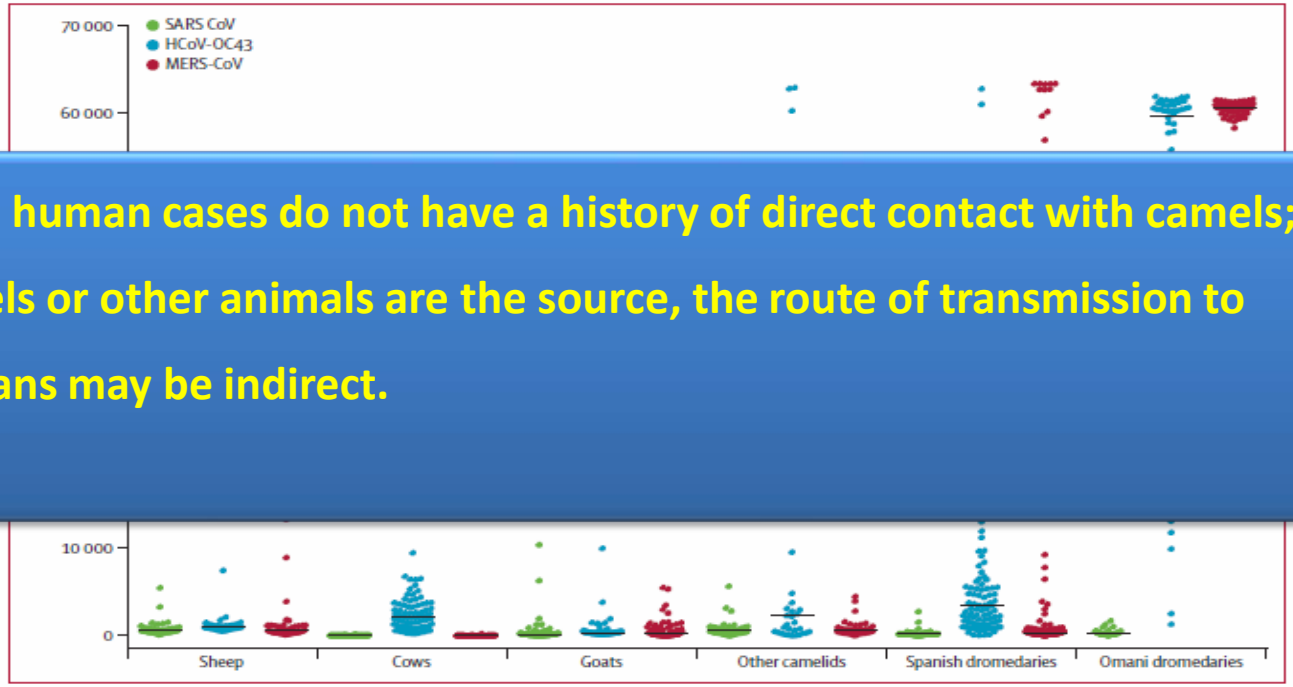
B. Hijawi,[1] M. Abdallat [2] A. Sayaydeh,[2] S. Alqasrawi,[2] A. Haddadin,[3] N. Jaarour,[2] S. Alsheikh[2] and T. Alsanouri[3]

	(years)		onset	admission	discharge/ death			
1	25	Male	21 Mar	4 Apr	25 Apr	Student	Deceased	Confirmed case
2	30	Male	30 Mar	8 Apr	23 Apr	Nurse	Alive	Probable case
3	40	Female	2 Apr	9 Apr	19 Apr	Nurse	Deceased	Confirmed case
4	60	Male	2 Apr	Refused admission	–	Physician, internist	Alive	Probable case
5	29	Male	11 Apr	15 Apr	21 Apr	Nurse	Alive	Probable case
6	33	Male	12 Apr	14 Apr	21 Apr	Nurse	Alive	Probable case
7	28	Male	13 Apr	17 Apr	21 Apr	Nurse	Alive	Probable case
8	45	Male	14 Apr	17 Apr	24 Apr	Road technician (brother of case 3)	Alive	Probable case
9	46	Male	15 Apr	16 Apr	21 Apr	Nurse	Alive	Probable case
10	25	Male	15 Apr	18 Apr	21 Apr	Nurse	Alive	Probable case
11	53	Male	18 Apr	21 Apr	23 Apr	Physician, internist	Alive	Probable case
12	28	Female	19 Apr	Refused admission	–	Nurse	Alive	Probable case
13	60	Female	26 Apr	1 May	5 May	Housewife (mother of case 2)	Alive	Probable case

Middle East respiratory syndrome coronavirus neutralising serum antibodies in dromedary camels: a comparative serological study

Chantal B E M Reusken, Bart L Haagmans*, Marcel A Müller*, Carlos Gutierrez, Gert-Jan Godeke, Benjamin Meyer, Doreen Muth, V Stalin Raj, Laura Smits-De Vries, Victor M Corman, Jan-Felix Drexler, Saskia L Smits, Yasmin E El Tahir, Rita De Sousa, Janko van Beek, Norbert Nowotny, Kees van Maanen, Ezequiel Hidalgo-Hermoso, Berend-Jan Bosch, Peter Rottier, Albert Osterhaus, Christian Gortázar-Schmidt, Christian Drosten, Marion P G Koopmans*



Most human cases do not have a history of direct contact with camels; if camels or other animals are the source, the route of transmission to humans may be indirect.

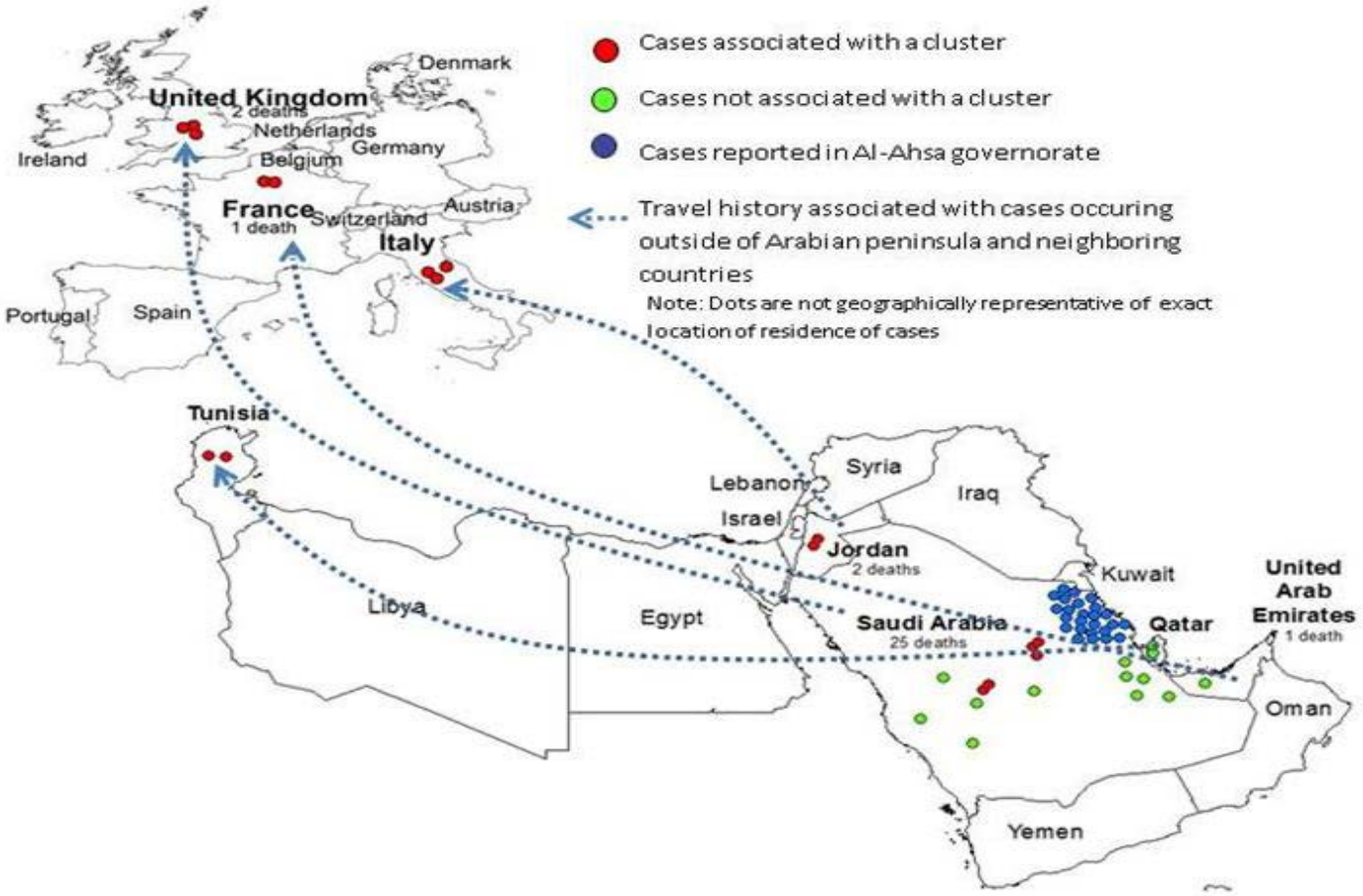
Figure 1: **Reactivity of livestock sera with three coronavirus S1 antigens**
Fluorescent intensities per antigen at a serum dilution of 1/20. Black lines indicate median. Dashed line is cutoff of the assay. RFU=relative fluorescence units.

THE LANCET Infectious Diseases

Vol 13 October 2013

Situation épidémiologique actuelle

MERS-CoV



Organisation mondiale de la Santé

- L'OMS a été informée de 3 cas supplémentaires, confirmés en laboratoire, d'infection MERS CoV aux EAU
- À l'échelle mondiale, de septembre 2012 jusqu'à présent, l'OMS a été informée au total de **163 cas confirmés** en laboratoire d'infection par le MERS-CoV, parmi lesquels il y a eu **71 décès**.

Au 5 Décembre 2013 – 23h

http://www.who.int/csr/don/2013_12_02/en/index.html

Recommandations

Centers for Disease Control and Prevention Atlanta, Georgia, USA

CDC Case Definition

- **A Patient Under Investigation (PUI):**
  - –infection respiratoire aigue :fievre (≥ 38°C) +toux

    ET

    -atteinte pulmonaire parenchymateuse (pneumonia /ARDS)

    ET
  - –voyage en peninsule Arabe ou pays voisins (14 j);

    ET
  - –non entierement expliquée par une autre infection ou etiologie(incluant celles de PAC) en reference aux recommendations locales.

CDC Definition: Close Contact

Close contact is defined as:

–Any person who **provided care** for the patient, including a healthcare worker or **family** member, or had similarly **close physical contact.**

–Any person who **stayed at the same place** (e.g. lived with, visited) as the patient while the **patient was ill.**

CDC Definition :Probable Case toute personne:

- **Critères** du “Patient Under Investigation” + signes cliniques +radiol ou histopathologiques d’une atteinte parenchymateuse, **MAIS** pas de possibilité de confirmation au labo (pas d’echantillions / pas de test)

ET

- Close contact avec un cas confirmé au labo ,

ET

- Symptomatologie non expliqueé par une PCA (en reference aux guidelines locaux)

- **OU toute personne :**

- Atteinte respiratoire severe , **ET**
- Relation epidémiologique à un cas confirmé d’infection par MERS-cov

CDC Definition :Confirmed Case

- A person with laboratory confirmation of infection with MERS-CoV.

Laboratory Testing

- Novel Coronavirus 2012 Real-time RT-PCR Assay (NCV-2-12 rRT-PCR Assay) is used to conform MERS- CoV in respiratory, blood and stool samples.
- Lower respiratory tract specimens should be a priority for collection and PCR testing.
- Stool specimens are of lower priority.

Journal of the Formosan Medical Association (2013) 112, 372–381

Available online at www.sciencedirect.com
SciVerse ScienceDirect

journal homepage: www.jfma-online.com

REVIEW ARTICLE

The emerging novel Middle East respiratory syndrome coronavirus: The "knowns" and "unknowns"

Jasper Fuk-Woo Chan [a,b,c], Susanna Kar-Pui Lau [a,b,c], Patrick Chiu-Yat Woo [a,b,c,*]

Traitement : Pistes

- Interférons types I :↓ réplication virale ex vivo poumon humain (>> SARS-CoV)
- interferon-α2b a + ribavirin :↓ replication MERS-CoV in Vero and LLC-MK2
- type II transmembrane serine proteases (TMPRSS2) +endosomal cathepsins

MERS-CoV S protein activation: virus-cell fusion

- Identification du domaine de fixation de MERS-CoV S protein :développement du vaccin?

Traitement :Autres pistes

- Convalescent plasma
- Intravenous Immunoglobulin
- Cyclosporin A
- Corticosteroids
- …

Conclusions: “more questions than answers”

- Animal Reservoirs Of The Virus
- Evolutionary Process
- Transmissibility
- Prognostic Factors
- Optimal Treatment

Merci