MERS-COV
Implications for healthcare facilities

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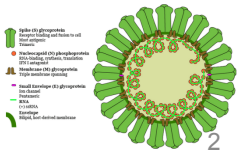
New Coronavirus - MERS-CoV

The NEW ENGLAND JOURNAL *of* MEDICINE

BRIEF REPORT

Isolation of a Novel Coronavirus from a Man with Pneumonia in Saudi Arabia

Ali Moh Zaki, M.D., Ph.D., Sander van Boheemen, M.Sc., Theo M. Bestebroer, B.Sc., Albert D.M.E. Osterhaus, D.V.M., Ph.D., and Ron A.M. Fouchier, Ph.D.



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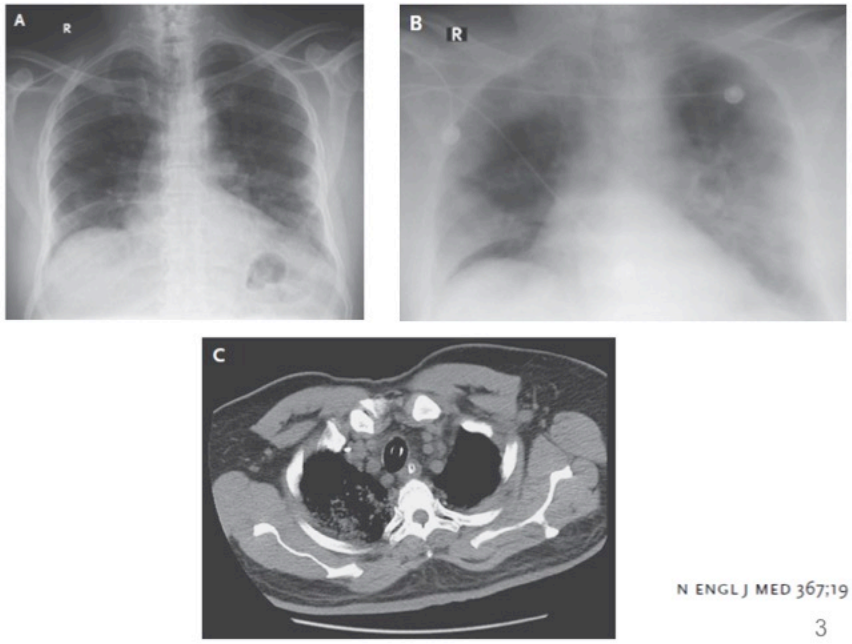

N ENGL J MED 367;19

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MERS-CoV
EPIDEMIOLOGY

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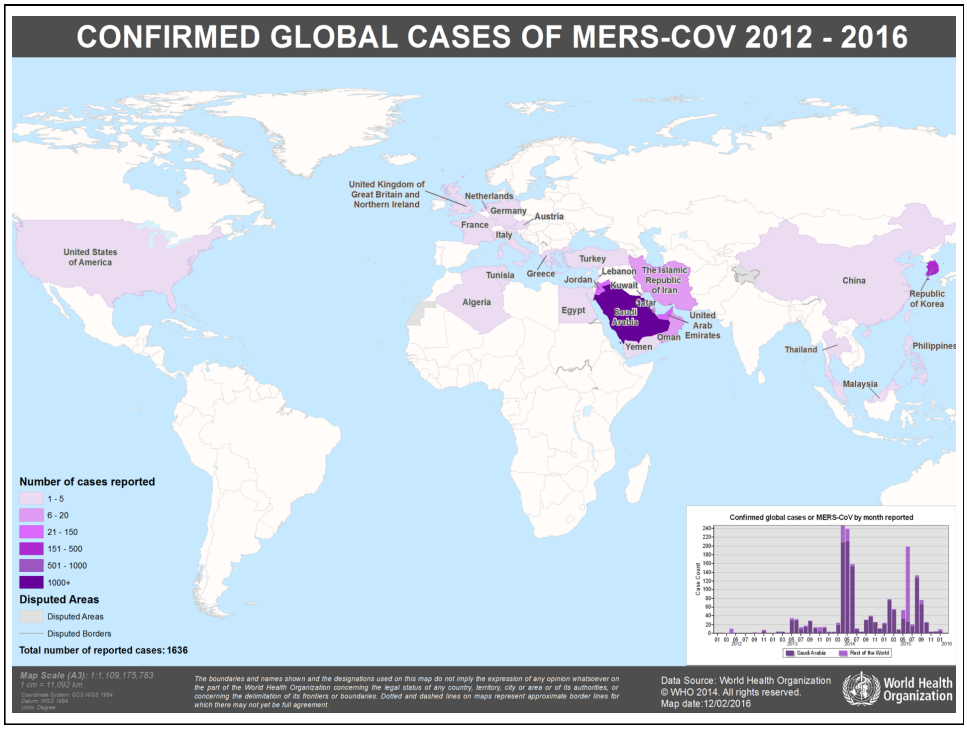
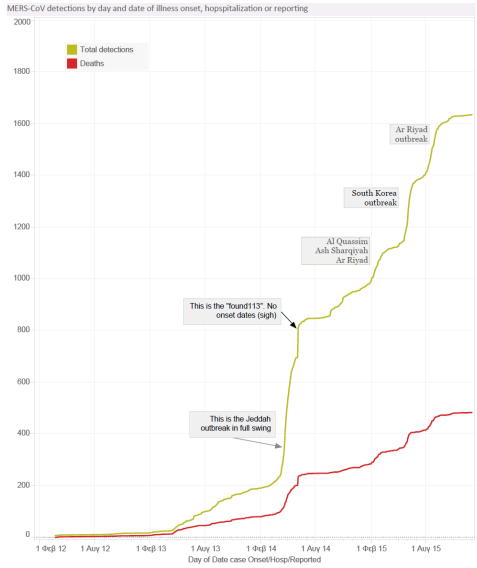


MERS 2012-2016, Epicurve



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Middle East respiratory syndrome coronavirus (MERS-CoV)

Thailand confirms MERS CoV in traveler, WHO cautions against continued risk of importation

January 2016 -- Thailand today confirmed Middle East respiratory syndrome coronavirus (MERS CoV) disease in a traveler, the second such case in the country in the last 7 months, as WHO cautioned other member states in its South-East Asia Region against the continuing risks and the need to remain vigilant.

Read the press release

WHO-SEARO/Vismita Gupta-Smith

Case fatality 35.8 %

1,638
WHO has been notified of 1,638 laboratory-confirmed cases of infection with MERS-CoV (globally).

For more: Latest disease outbreak news

587
WHO has been notified of 587 deaths related to MERS-CoV since September 2012.

For more: Coronavirus infections news

26
Since September 2012, 26 countries have reported cases of MERS-CoV.

Updates

WHO news and Feature stories

World Health Organization

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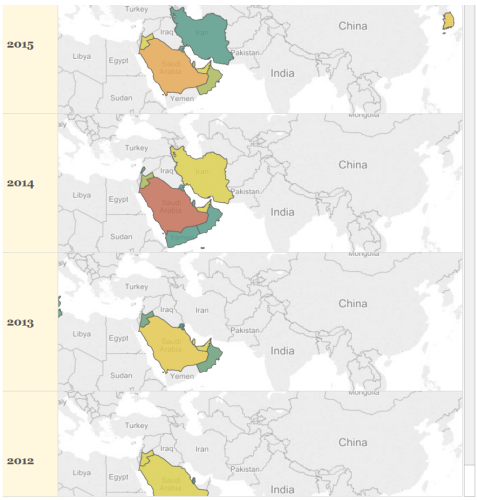
MERS-CoV cases by region of likely acquisition



Ian Mackay, www.virologydownunder.blogspot.com.au

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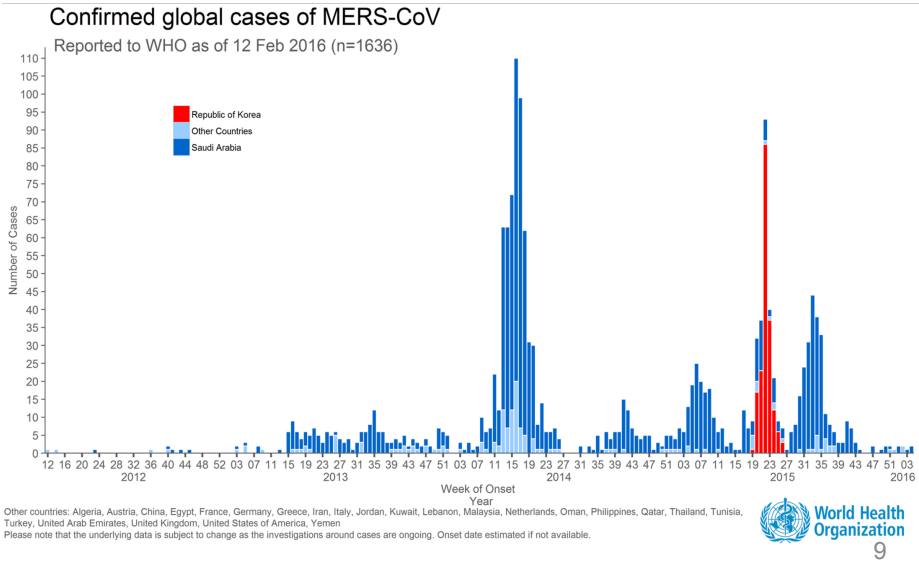
MERS 2012-2016, Epicurve



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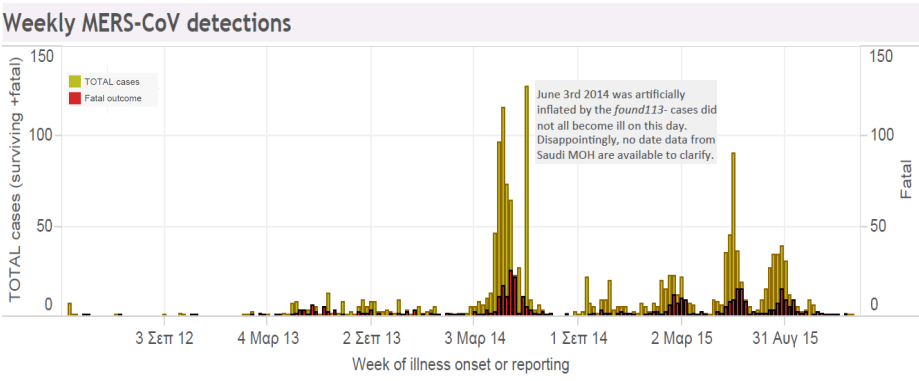
MERS – Global epi curve
n /week



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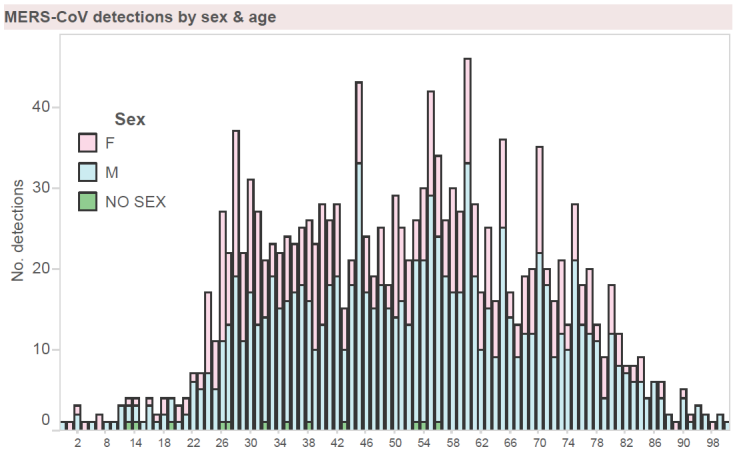
MERS – Global epi curve detections by age & gender



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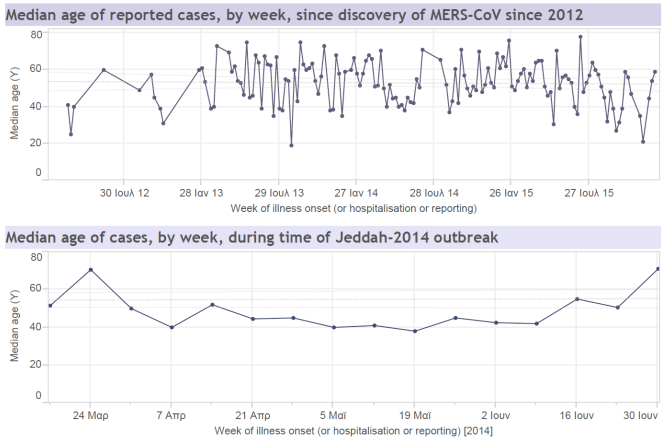
MERS – Global epi curve median age /week



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MERS by country of reporting Middle East: Mar 2012 - Oct 2015

Region	Country	Number of cases	Number of deaths
Middle East	Saudi Arabia	1 255	539
	United Arab Emirates	81	11
	Jordan	35*	14
	Qatar	13	5
	Oman	6	3
	Iran	6	2
	Kuwait	4	2
	Egypt	1	0
	Lebanon	1	0
	Yemen	1	1

77 % of cases from S Arabia

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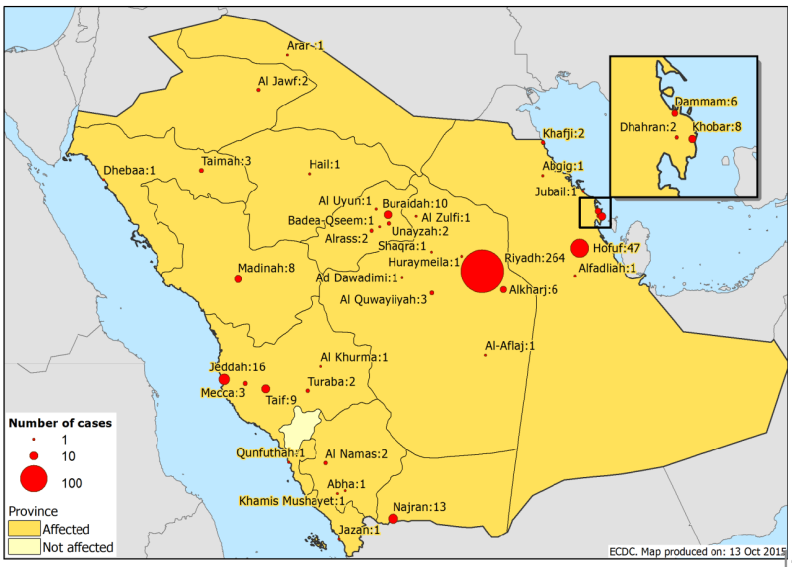
MERS – KSA 2015

Figure 4. Distribution of MERS cases by reporting city, Saudi Arabia, 1 January – 13 October 2015



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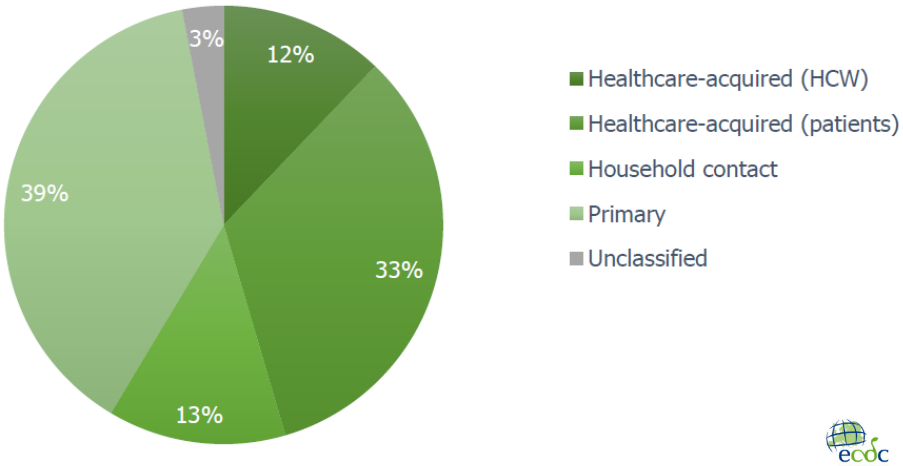
MERS – KSA 2015
Confirmed MERS by source of infection



Ministry of Health, Saudi Arabia. http://www.moh.gov.sa

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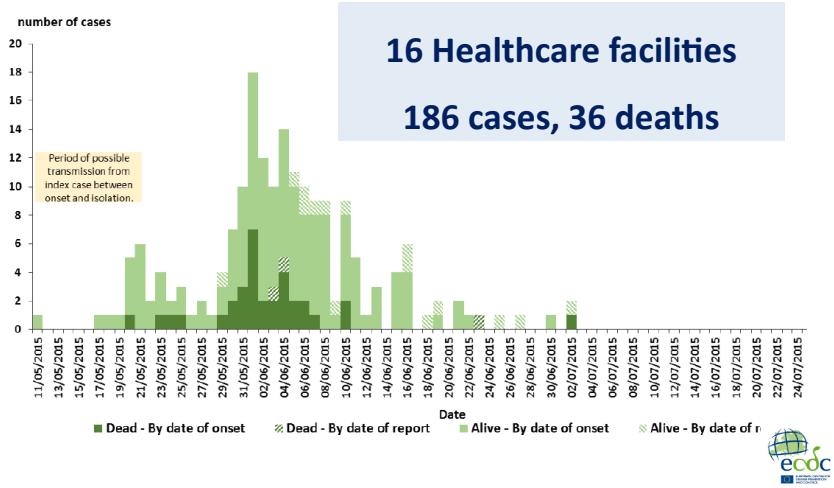
MERS-CoV, Korea & China
May - July 2015



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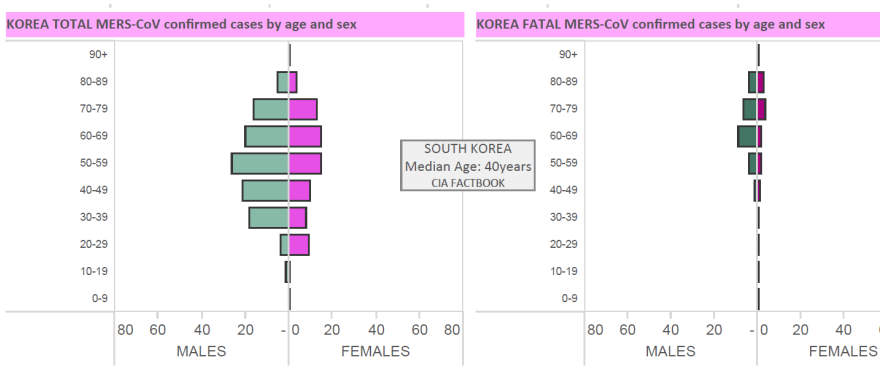
MERS-CoV, Korea & China 2015



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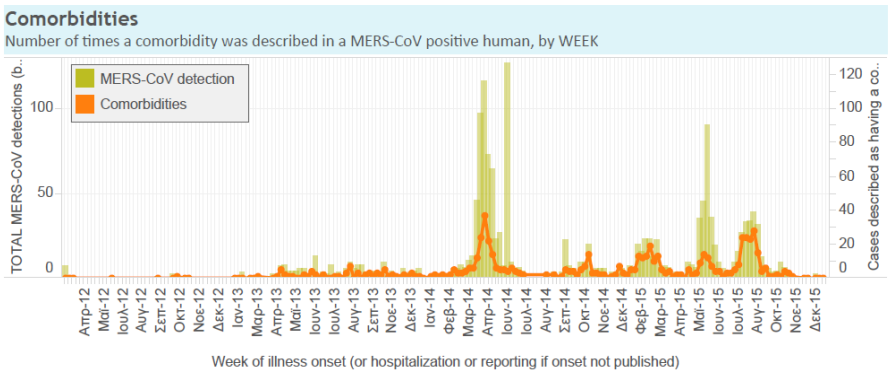
MERS-CoV, Comorbidities



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MERS - Philippines 2015

- 13 Feb 2015 → WHO notified
- 31 yr female HCW in Ryadh, S Arabia
- Onset on 26 Jan 2015 while working in hospital
- Feb 1st 2015 travel to Philippines w family member
- Feb 2nd 2015 admission to local hospital
- Isolated in special hospital February 10th 2015
- All contacts (-) to date

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Bats & … dromedary camels!!!

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Volume 19, Number 11—November 2013

Dispatch

Middle East Respiratory Syndrome Coronavirus in Bats, Saudi Arabia

Ziad A. Memish, Nischay Mishra, Kevin J. Olival, Shamsudeen F. Fagbo, Vishal Kapoor, Jonathan H. Epstein, Rafat AlHakeem, Abdulkareem Durosinloun, Mushabab Al Asmari, Ariful Islam, Amit Kapoor, Thomas Briese, Peter Daszak, Abdullah A. Al Rabeeah, and W. Ian Lipkin

Author affiliations: Ministry of Health, Riyadh, Saudi Arabia (Z.A. Memish, S.F. Fagbo, R. AlHakeem, A. Durosinloun, A.A. Al Rabeeah); Columbia University, New York, New York, USA (N. Mishra, V. Kapoor, A. Kapoor, T. Briese, W.I. Lipkin); EcoHealth Alliance, New York (K.J. Olival, J.H. Epstein, P. Daszak); Ministry of Health, Bisha, Saudi Arabia (M. Al Asmari); EcoHealth Alliance, Dhaka, Bangladesh (A. Islam)

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Middle East respiratory syndrome coronavirus (MERS-CoV) in dromedary camels, Oman, 2013

N Nowotny (Norbert.Nowotny@vetmeduni.ac.at)[1,2], J Kolodziejek[1]
1. Viral Zoonoses, Emerging and Vector-Borne Infections Group, Institute of Virology, University of Veterinary Medicine Vienna, Vienna, Austria
2. Department of Microbiology and Immunology, College of Medicine and Health Sciences, Sultan Qaboos University, Muscat, Oman

Citation style for this article:
Nowotny N, Kolodziejek J. Middle East respiratory syndrome coronavirus (MERS-CoV) in dromedary camels, Oman, 2013. Euro Surveill. 2014;19(16):pii=20781.
Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20781

Article submitted on 17 April 2014 / published on 24 April 2014

- Teams for KSA-USA
- isolated MERS-CoV from nasal swabs of dromedary camels in Saudi Arabia
- whole-genome sequences of humans and camels are indistinguishable.
- camels simultaneously infected w >1 MERS-CoV

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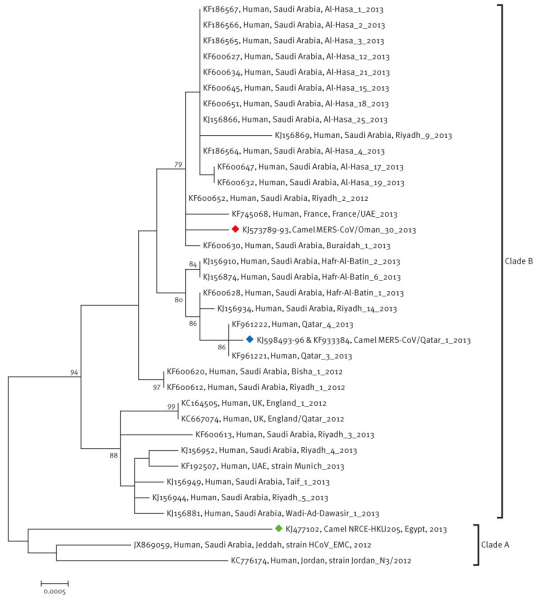
FIGURE 2
Phylogenetic analysis of three camel- and 33 human-derived Middle East respiratory syndrome coronavirus (MERS-CoV) nucleotide sequences, 2013



UAE: United Arab Emirates; UK: United Kingdom.
Each 3,754 nucleotide long sequence used to generate the tree was obtained from concatenating partial sequences of the open reading frame (ORF)1a, spike and ORF4b gene regions. Of note the different clustering of the camel-derived sequences originating from Oman (marked with a red diamond), Qatar (blue diamond) and Egypt (green diamond). The Qatari and Omani camel-derived MERS-CoV sequences cluster close to the human-derived sequences originating from the same areas.

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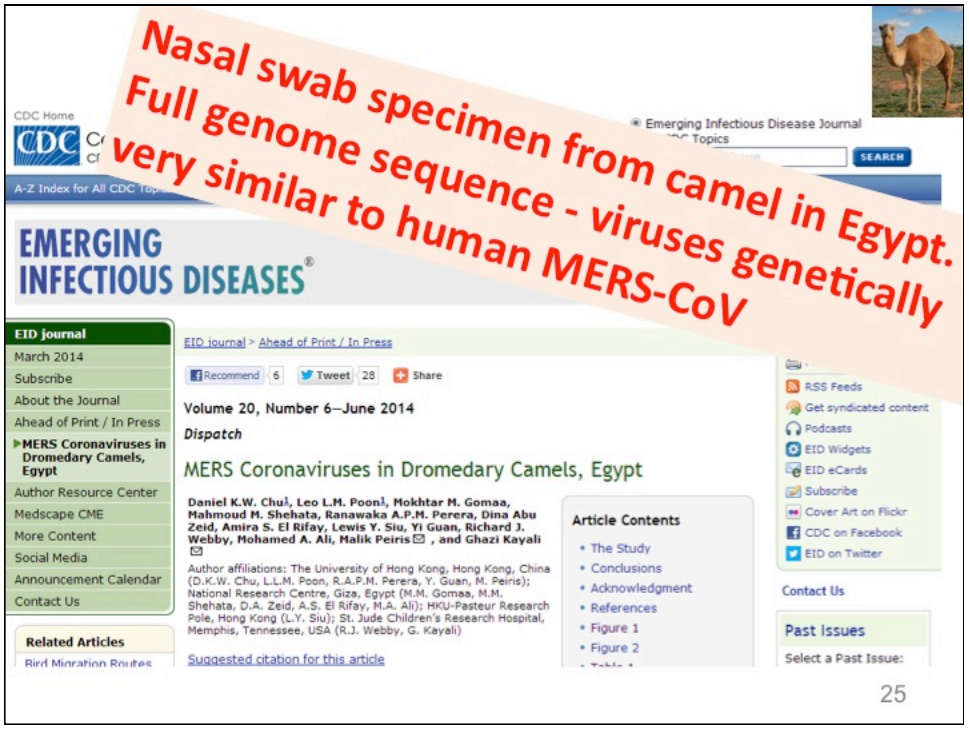
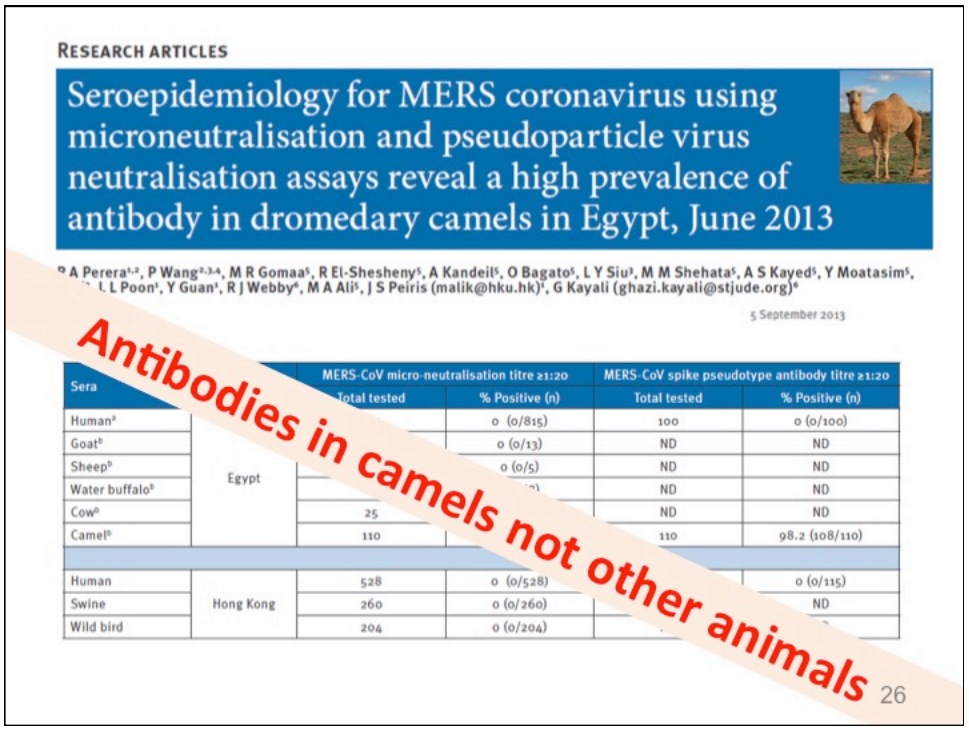
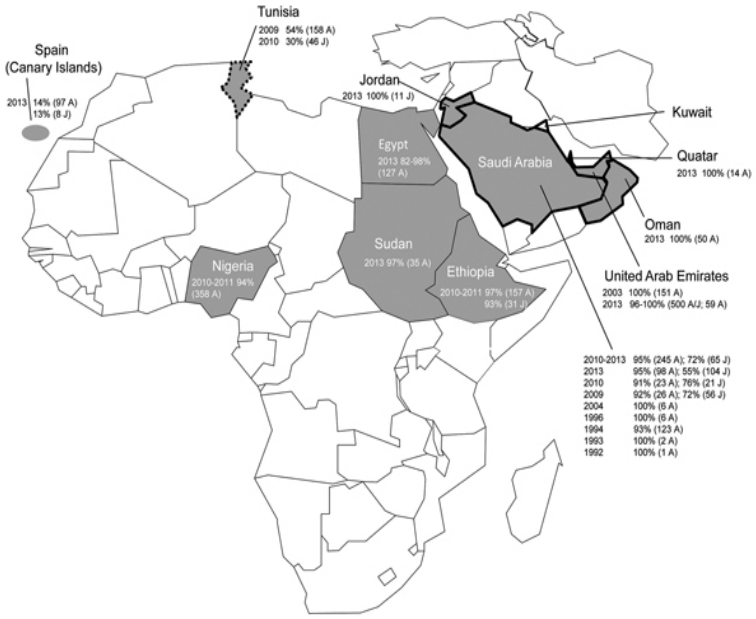




Sera		MERS-CoV micro-neutralisation titre ≥1:20		MERS-CoV spike pseudotype antibody titre ≥1:20	
		Total tested	% Positive (n)	Total tested	% Positive (n)
Human[a]	Egypt		0 (0/815)	100	0 (0/100)
Goat[b]			0 (0/13)	ND	ND
Sheep[b]			0 (0/5)	ND	ND
Water buffalo[b]				ND	ND
Cow[b]		25		ND	ND
Camel[b]		110		110	98.2 (108/110)
Human	Hong Kong	528	0 (0/528)		0 (0/115)
Swine		260	0 (0/260)		ND
Wild bird		204	0 (0/204)		



Chantal B.E.M. Reusken et al. EID 2014

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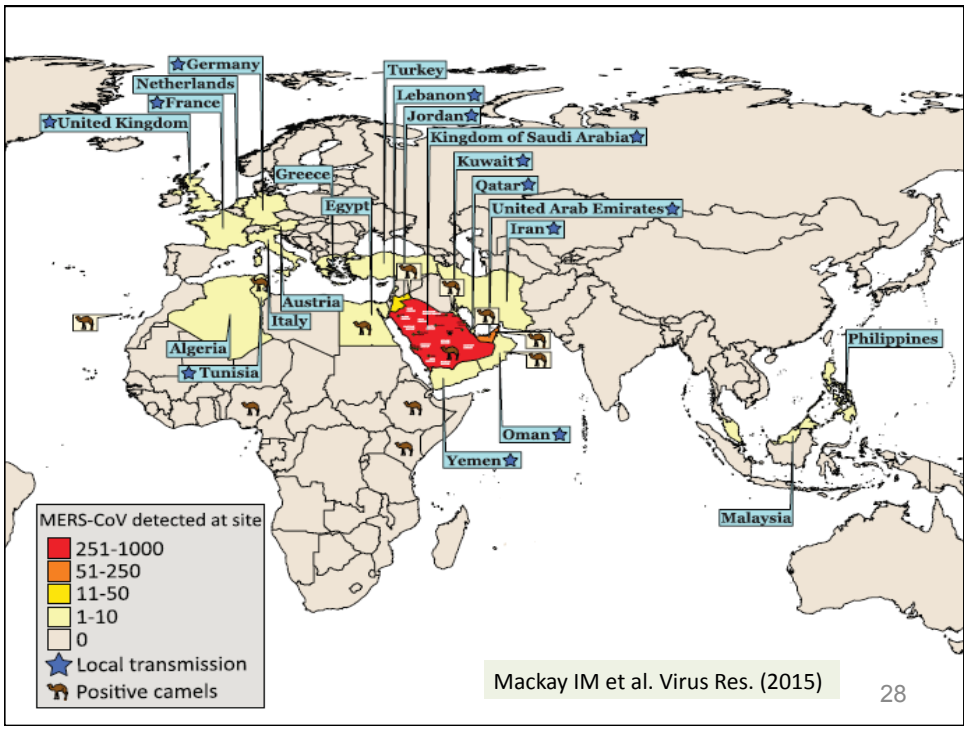

Mackay IM et al. Virus Res. (2015)

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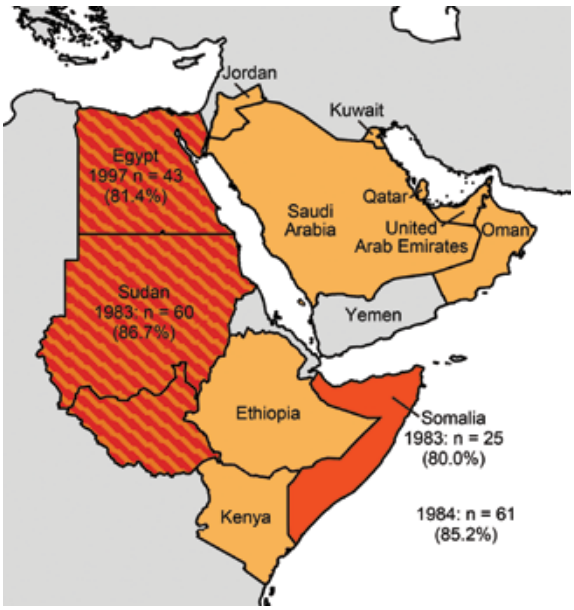

Muller et al Emerg Infect Dis. 2014 Dec;20(12):2093-5.

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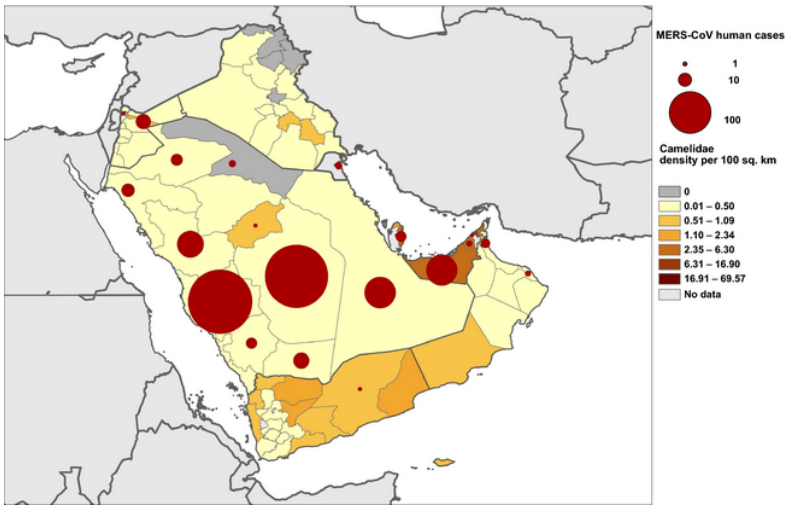
Human–Dromedary Camel Interactions and the Risk of Acquiring Zoonotic MERS-CoV Infection



Zoonoses and Public Health
27 DEC 2014 DOI: 10.1111/zph.12171
http://onlinelibrary.wiley.com/doi/10.1111/zph.12171/full#zph12171-fig-0004

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The NEW ENGLAND JOURNAL of MEDICINE

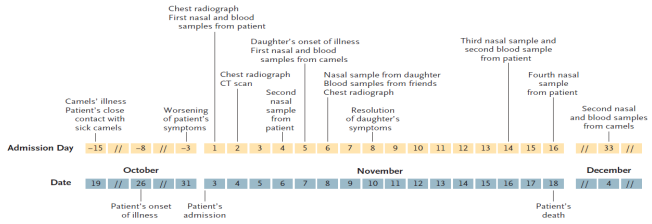
BRIEF REPORT

Evidence for Camel-to-Human Transmission of MERS Coronavirus

Esam I. Azhar, Ph.D., Sherif A. El-Kafrawy, Ph.D., Suha A. Farraj, M.Sc., Ahmed M. Hassan, M.Sc., Muneera S. Al-Saeed, B.Sc., Anwar M. Hashem, Ph.D., and Tariq A. Madani, M.D.

SUMMARY

We describe the isolation and sequencing of Middle East respiratory syndrome coronavirus (MERS-CoV) obtained from a dromedary camel and from a patient who died of laboratory-confirmed MERS-CoV infection after close contact with camels that had rhinorrhea. Nasal swabs collected from the patient and from one of his



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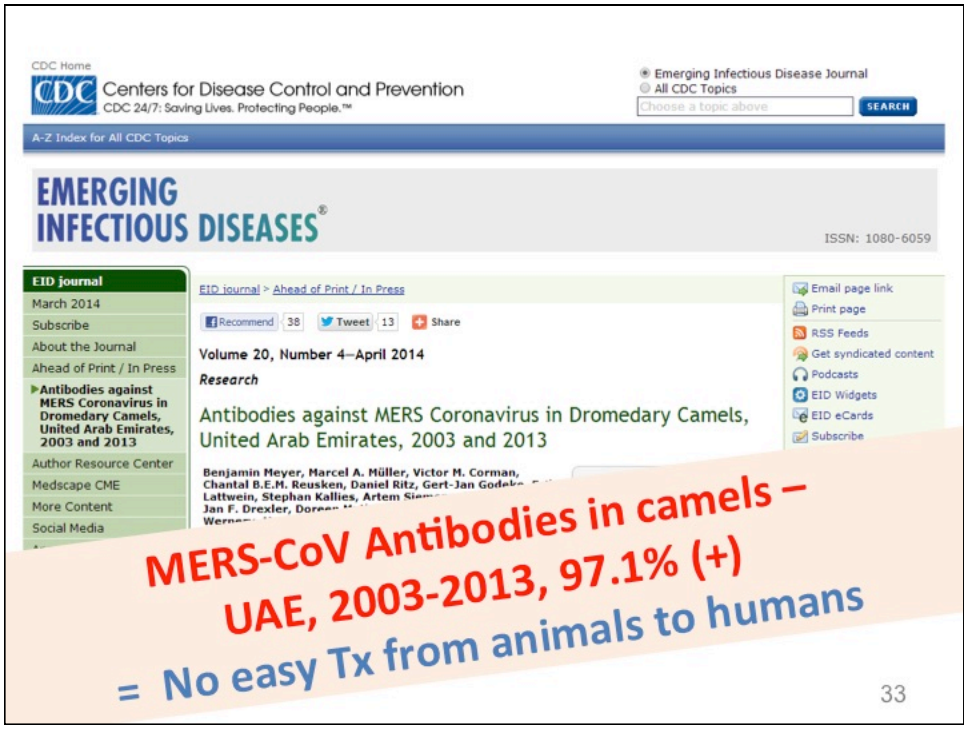
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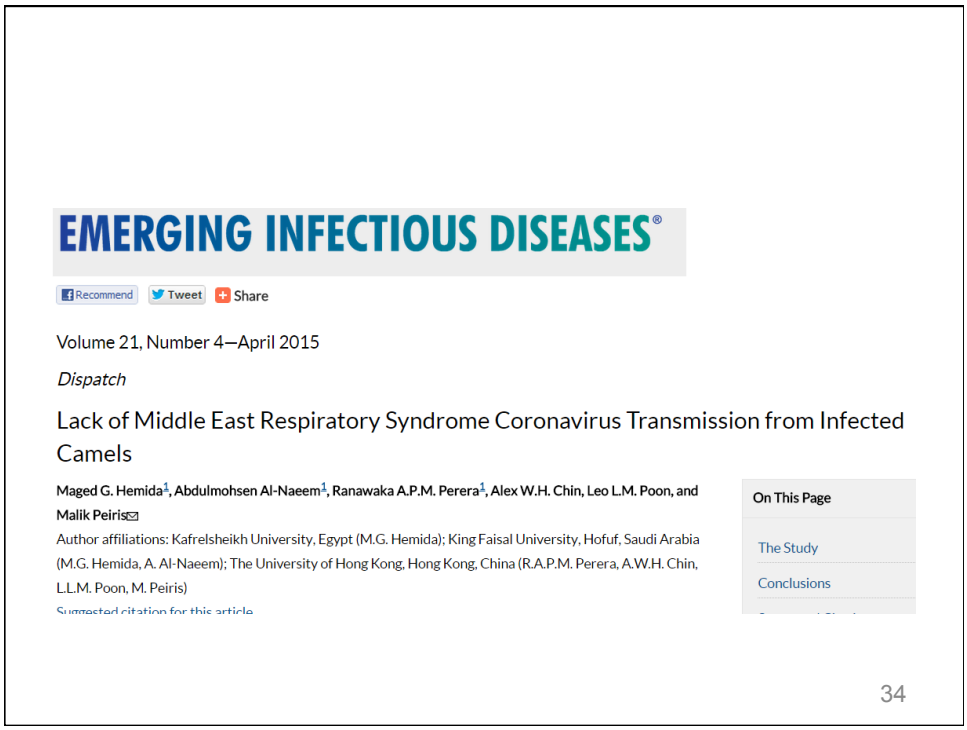
MERS-CoV Antibodies in camels –
UAE, 2003-2013, 97.1% (+)
= No easy Tx from animals to humans
33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Dispatch
Lack of Middle East Respiratory Syndrome Coronavirus Transmission from Infected Camels
Maged G. Hemida[1], Abdulmohsen Al-Naeem[1], Ranawaka A.P.M. Perera[1], Alex W.H. Chin, Leo L.M. Poon, and Malik Peiris
Author affiliations: Kafrelsheikh University, Egypt (M.G. Hemida); King Faisal University, Hofuf, Saudi Arabia (M.G. Hemida, A. Al-Naeem); The University of Hong Kong, Hong Kong, China (R.A.P.M. Perera, A.W.H. Chin, L.L.M. Poon, M. Peiris)
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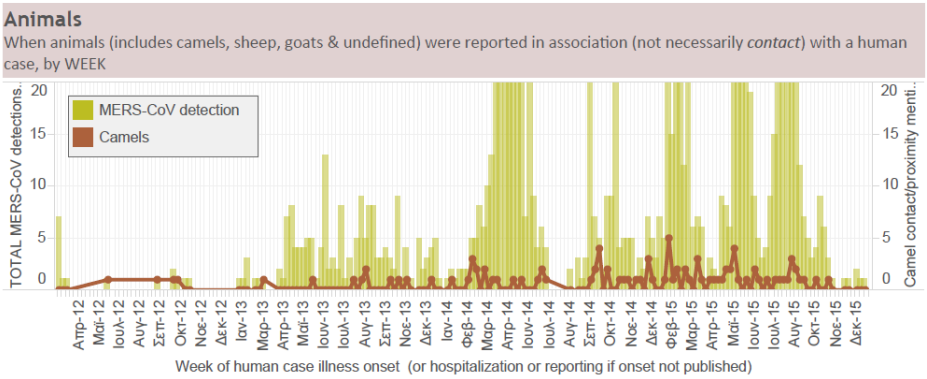
MERS-CoV, Contact w animals



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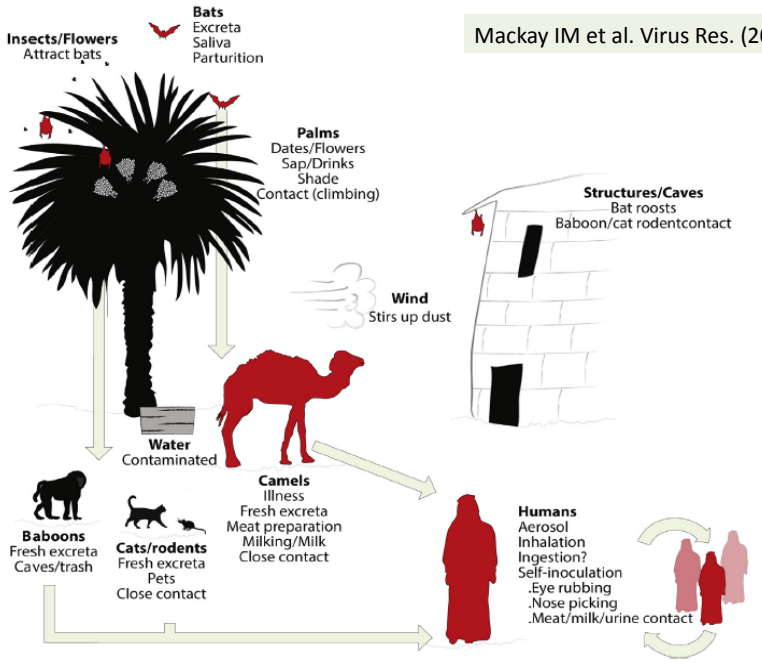

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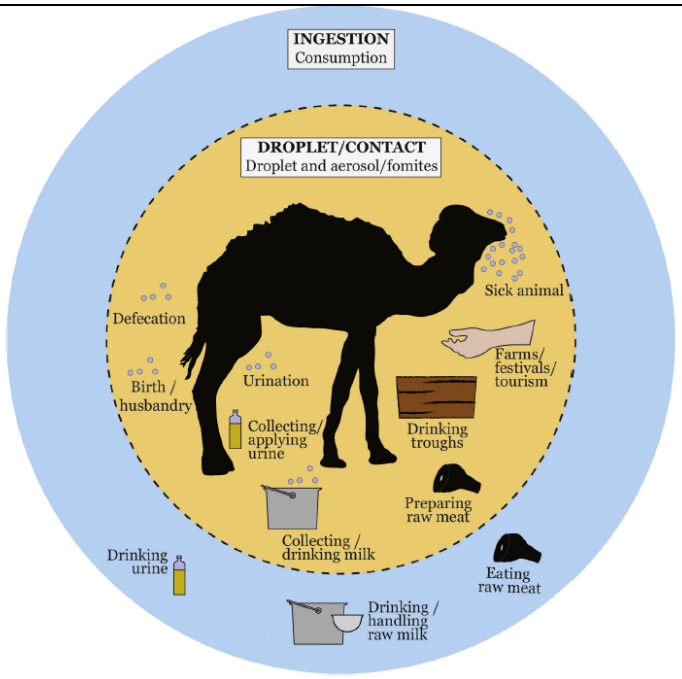

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Volume 20, Number 7—July 2014

Letter

Stability of Middle East Respiratory Syndrome Coronavirus in Milk

Suggested citation for this article

To the Editor: Middle East respiratory syndrome coronavirus (MERS-CoV) was first diagnosed in humans in 2012. Human-to-human transmission of MERS-CoV has been limited, and the transmission route is still unclear. On the basis of epidemiologic studies, involvement of an animal host has been suggested (*1*). Dromedary camels have been identified as a possible intermediate host on the basis of MERS-CoV antibodies and detection of MERS-CoV viral RNA in respiratory swab samples (*1*–*3*). Furthermore, MERS-CoV genome sequences obtained

Article Contents
- Letter
- Acknowledgments
- References
- Figure
- Suggested Citation

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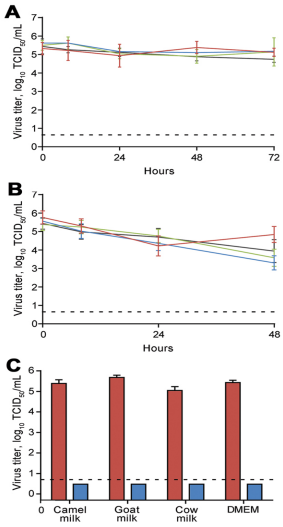
CAMEL MILK

- MERS-CoV could survive for prolonged periods in milk
- viable virus was not detectable after pasteurization

van Doremalen N, et al, EID 2014



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CAMEL MILK

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OTHER DISEASES ASSOCIATED WITH CAMELS

- **MERS-CoV**
- **Tuberculosis**
- Rift valley fever
- Brucellosis
- Adenovirus - Common Respiratory viruses
- Trypanosomiasis
- Equine Herpes virus, camelpox

- GAPS in data - NEED for further studies!!!

www.thelancet.com/infection Vol 16 January 2016 41

Evolution of MERS-CoV in camels Recent SCIENCE study

- 5 lineages in camels
- Co-circulation of multiple lineages
- At least 6 recombination events – common in RNA viruses --> ?? Increased pathogenicity
- Lineage 5, i.e. Ryadh & S. Korea/China outbreaks of recombinant origin
- Occurred between12/2013 & 6/2014

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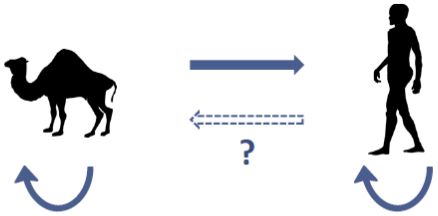
Evolution of MERS-CoV in camels
Recent SCIENCE study



Trends in Microbiology

Figure 1. Four Possible Routes for MERS-CoV Transmission. The well accepted human-to-human, human-to-camel, and camel-to-camel are labeled in solid arrows. The possible and ignored human-to-camel transmission is labeled in a dashed arrow. The camel and human images courtesy of Steven Traver and T. Michael Keesey.

Sabir, J.S. et al. (2016) Science 351, 81–84
Lin Du, GZ Han. Trends in Microbiology, February 2016, Vol. 24, No. 2

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RAPID COMMUNICATIONS

Stability of Middle East respiratory syndrome coronavirus (MERS-CoV) under different environmental conditions

N van Doremalen[1], T Bushmaker[1], V J Munster (vincent.munster@nih.gov)[1]
1. Laboratory of Virology, Division of Intramural Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Hamilton, MT, USA

Citation style for this article:
van Doremalen N, Bushmaker T, Munster VJ. Stability of Middle East respiratory syndrome coronavirus (MERS-CoV) under different environmental conditions. Euro Surveill. 2013;18(38):pii=20590. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20590

Article submitted on 10 September 2013 / published on 19 September 2013

The stability of Middle East respiratory syndrome coronavirus (MERS-CoV) was determined at 20°C – 40% relative humidity (RH); 30°C – 30% RH and 30°C – 80% RH. MERS-CoV was more stable at low temperature/low humidity conditions and could still be recovered after 48 hours. During aerosolisation of MERS-CoV, no decrease in stability was observed at 20°C – 40% RH. These data suggest the potential of MERS-CoV to be transmitted via contact or fomite transmission due to prolonged environmental presence.

Environmental stability

MERS-CoV (isolate HCoV-EMC/2012) and A/Mexico/4108/2009 (H1N1) virus were propagated and titrated by end-point titration on VeroE6 cells (for MERS-CoV) and Madin-Darby canine kidney (MDCK) cells (for A/Mexico/4108/2009 (H1N1) virus) as previously described [9,10]. To determine the environmental stability of the two viruses, 100 µl of 10^6 tissue culture infective dose 50 ($TCID_{50}$) of MERS-CoV or A/Mexico/4108/2009 (H1N1) virus was spotted in droplets of 5 µl on the surface of steel or plastic washers

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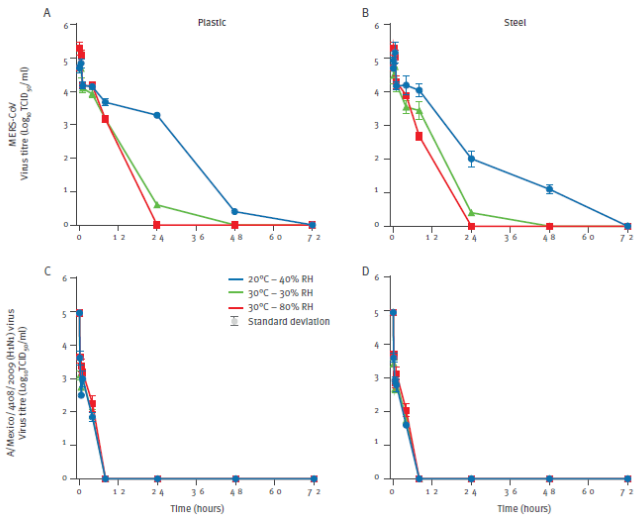
FIGURE 1
Viability over time of Middle East respiratory syndrome coronavirus (MERS-CoV) and A/Mexico/4108/2009 (H1N1) virus under different environmental conditions



N van Doremalen et al Euro Surveill. 2013;18(38)

45

MERS-CoV

Human - Human transmission

46

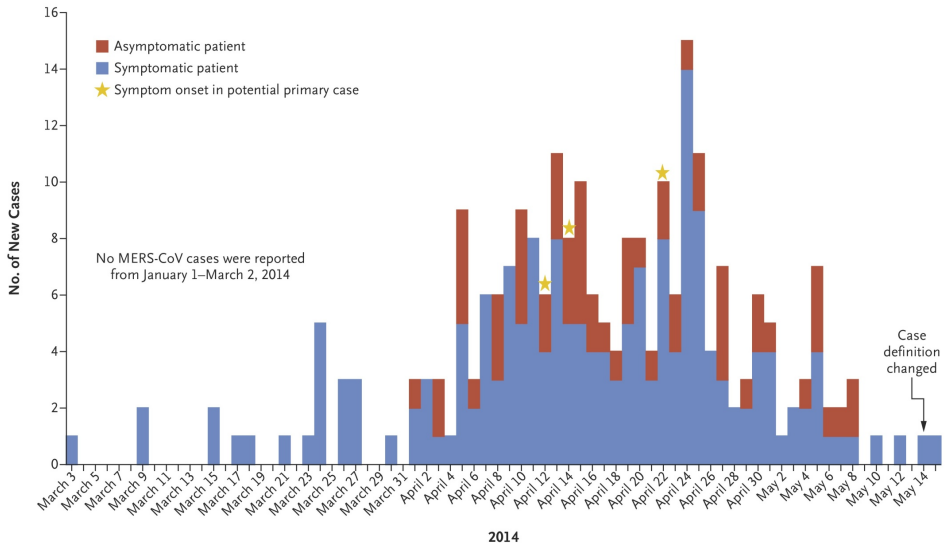
Human to human – MERS CoV

- R_0 is <1 unless NO Infection Control!!!
- Case clusters
  - UK, Tunisia, Italy, S Arabia, France
  - 2ry cases milder, asymptomatic
- > 50% of lab confirmed cases in HC settings

- 2ry transmission in households
  - 26 index → 280 contacts → 12 probable cases

N Engl J Med 2014; 371:828

47



Obono I et al. NEJM Feb 26th, 2015
Drosten C et al CID 2015:60

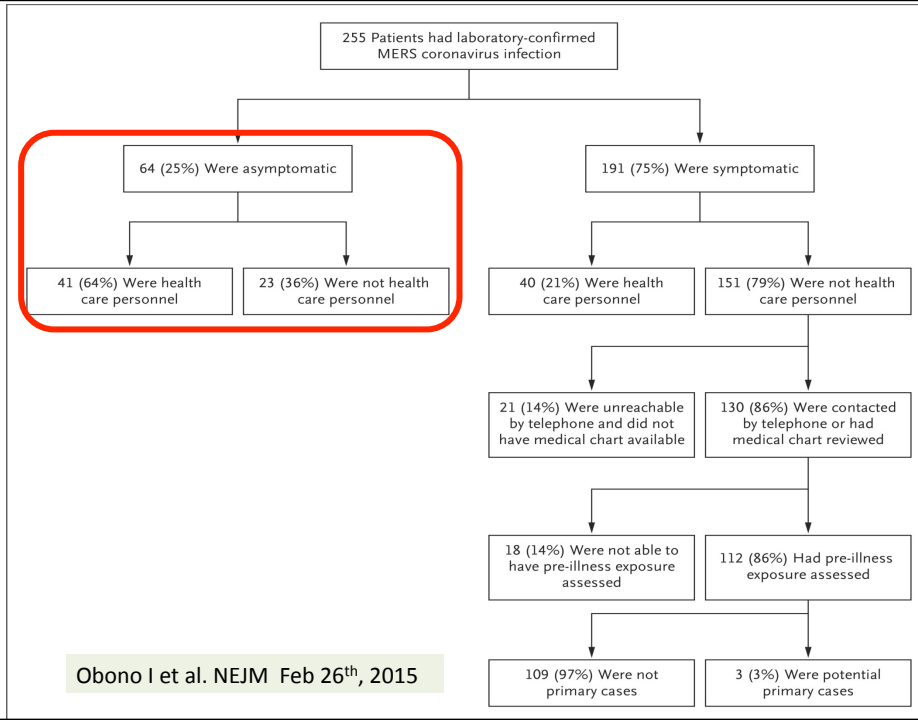
48

Source in Jeddah outbreak 2014

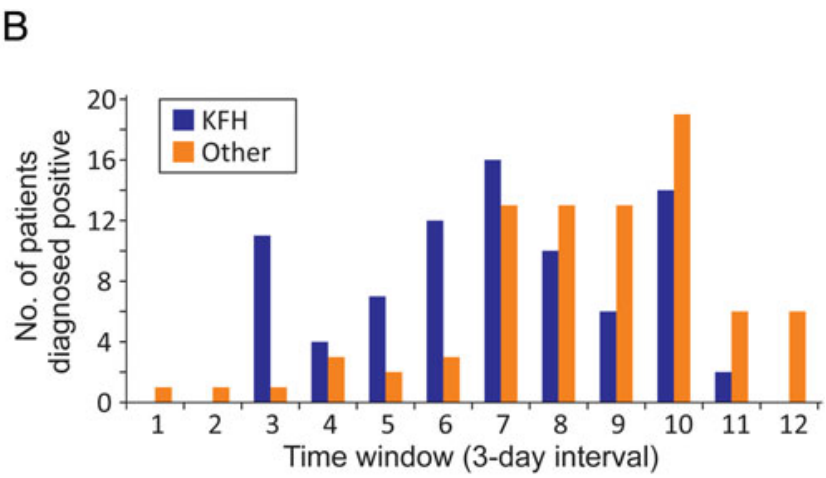
- Admission to health unit 34%
- Visit in outpatient offices 62%
- Patient visit 17%
- NO contact with healthcare 22%
- ≥ 1 sources / exposures !!!

Obono I et al. NEJM; 2015

49

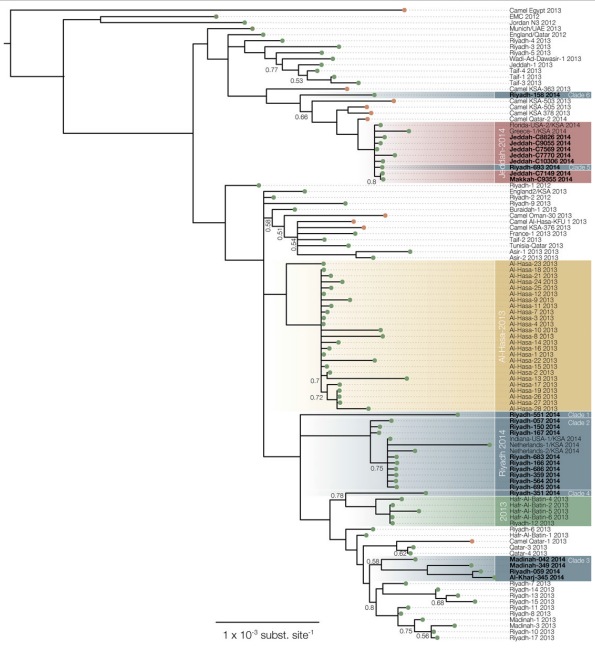


Obono I et al. NEJM Feb 26th, 2015



Drosten C et al CID 2015:60

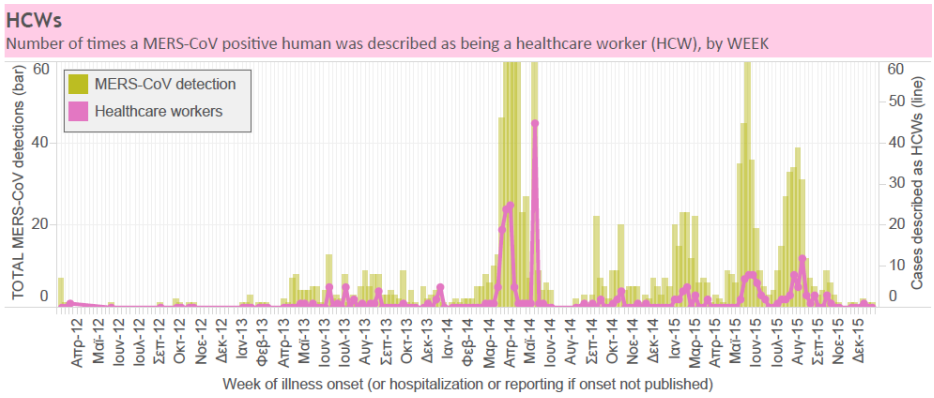
51



Drosten C et al CID 2015:60

52

MERS-CoV, HCWs / all cases



Ian Mackay, www.virologydownunder.blogspot.com.au

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MERS-CoV

Clinical Picture - Diagnosis - Rx

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Clinical picture

- Analysis 144 lab. confirmed & 17 probable
  - 63,4% -> severe respiratory disease, ARDS, MOF
  - 76% w ≥ 1 underlying condition, p<0.001
    - Renal failure, Diabetes Melitus, Heart Diseases
  - 18 asymptomatic

PLOS | CURRENTS OUTBREAKS
NOVEMBER 12, 2013
55

MERS-CoV DIAGNOSIS

- Collaboration w Reference laboratories
- rRT-PCR testing of lower respiratory specimens

World Health Organization
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MERS-CoV DIAGNOSIS

Table 1. Specimens to be collected from symptomatic patients and asymptomatic contacts

Patient	Test	Type of sample	Timing	Storage and transportation	Remarks
Symptomatic	RT-PCR	**Lower respiratory tract** - sputum - aspirate - lavage **Upper respiratory tract** - nasopharyngeal and oropharyngeal swabs - nasopharyngeal wash/nasopharyngeal aspirate **Serum** for virus detection (particularly if lower respiratory tract specimens are not available.) For monitoring the distribution of virus in the body: other sample types, stool, urine	Collect on presentation. To confirm clearance of the virus, sample collection to be repeated until the results are negative on 2 sequential samples.	If the specimen will reach the laboratory in less than 72 hours, store and ship at 4°C. If the specimen will reach the laboratory in more than 72 hours, store at -80°C and ship on dry ice or liquid nitrogen.	Follow international regulations and triple package system for transportation.

World Health Organization

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MERS-CoV DIAGNOSIS

Symptomatic	Serology	Serum for serological testing.	Paired samples are necessary for confirmation with the initial sample collected in the first week of illness and the second ideally collected 2-3 weeks later. If only a single serum sample can be collected, this should occur at least 14 days after onset of symptoms for determination of a probable case.	As above.	As above.
Asymptomatic Contact (particularly in health-care centre associated outbreaks or other situations of high-intensity contact)	PCR	Nasopharyngeal and oropharyngeal swabs; sputum if possible.	Within 14 days of last documented contact.	As above.	As above.
	Serology	Serum	Baseline serum taken within 14 days of last documented contact and convalescent serum taken 2-3 weeks later. If only a single sample is possible, collect at least 14 days after last documented contact	As above.	As above.

World Health Organization

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Diagnosis - typing MERS-CoV 2015-16

Journal of Clinical Virology 64 (2015) 83–87

Contents lists available at ScienceDirect

Journal of Clinical Virology

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

Reliable typing of *MERS-CoV* variants with a small genome fragment

Saskia L. Smits[a,b], V. Stalin Raj[a], Suzan D. Pas[a], Chantal B.E.M. Reusken[a], Khaled Mohran[c,d], Elmoubasher A.B.A. Farag[e], Hamad E. Al-Romaihi[e], Mohd M. AlHajri[e], Bart L. Haagmans[a], Marion P. Koopmans[a,f,*]

[a] *Department of Viroscience, Erasmus Medical Center, P.O. Box 2040, 3000 CA Rotterdam, Netherlands*
[b] *ViroClinics BioSciences BV, Marconistraat 16, 3029 AK Rotterdam, Netherlands*
[c] *Ministry of the Environment, Doha, Qatar*
[d] *Biotechnology Research Department, Animal Health Research Institute, Agricultural Research Center, Egypt*
[e] *Supreme Council of Health, Doha, Qatar*
[f] *Virology Division, Centre for Infectious Diseases Research, Diagnostics and Screening, National Institute for Public Health and the Environment, Bilthoven 3720BA, Netherlands*

59

Viral shedding & 2ⁿ case in Greece!

N. Spanakis et al. / International Journal of Antimicrobial Agents xxx (2014) xxx–xxx

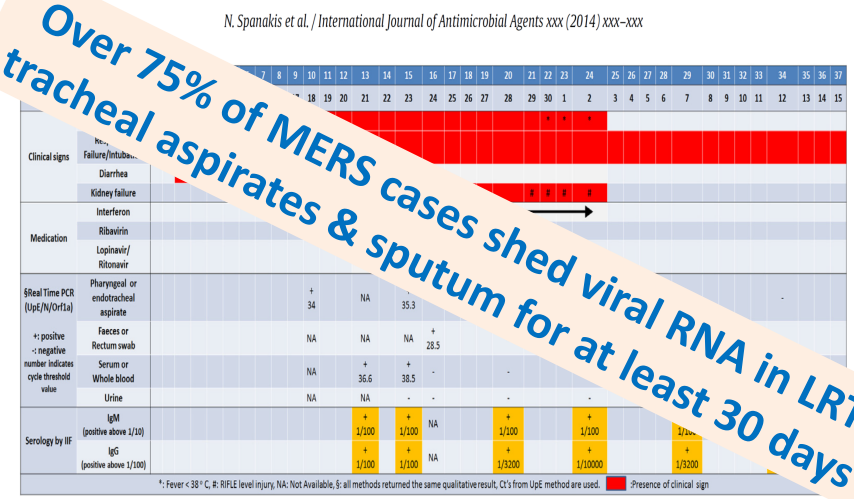
	DAY OF ILNESS	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37
	DATE (APRIL – MAY)	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Clinical signs	Fever (>38° C)																																						
	Respiratory Failure/Intubation																																						
	Diarrhea																																						
	Kidney failure																																						
Medication	Interferon																																						
	Ribavirin																																						
	Lopinavir/ Ritonavir																																						
§Real Time PCR (UpE/N/Orf1a)	Pharyngeal or endotracheal aspirate											+ 34			NA		+ 35.3	NA				+ 36.4				+ 35					-					-			
+: positve -: negative number indicates cycle threshold value	Faeces or Rectum swab											NA			NA		NA	+ 28.5				-				-					-					-			
	Serum or Whole blood											NA			+ 36.6		+ 38.5	-				-				-					-					-			
	Urine											NA			NA		-	-				-				-					-					-			
Serology by IIF	IgM (positive above 1/10)														+ 1/100		+ 1/100	NA				+ 1/100				+ 1/100					+ 1/100					+ 1/100			
	IgG (positive above 1/100)														+ 1/100		+ 1/100	NA				+ 1/3200				+ 1/10000					+ 1/3200					+ 1/3200			

*: Fever < 38 ° C, #: RIFLE level injury, NA: Not Available, §: all methods returned the same qualitative result, Ct's from UpE method are used. :Presence of clinical sign

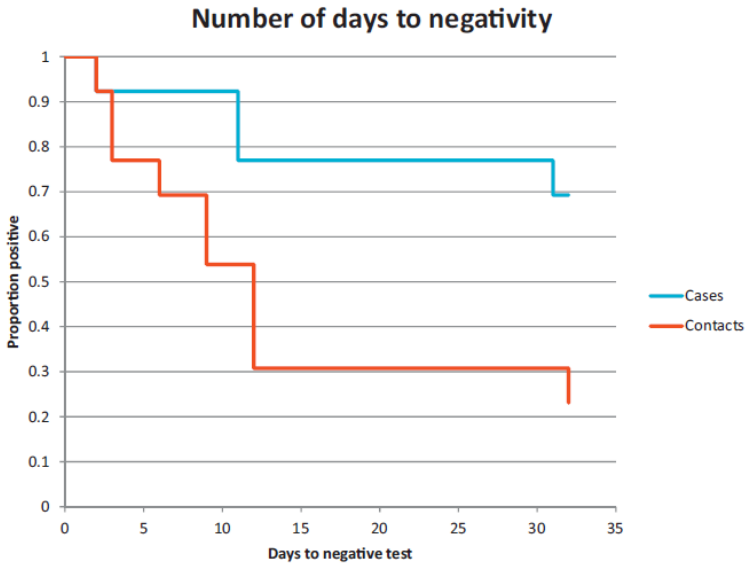
60

Viral shedding & 2η case in Greece!

Over 75% of MERS cases shed viral RNA in LRT tracheal aspirates & sputum for at least 30 days



61



International Journal of Infectious Diseases 29 (2014) 307–308

62

Rx - MERS-CoV 2016

INTERIM GUIDANCE DOCUMENT

Clinical management of severe acute respiratory infections when novel coronavirus is suspected: What to do and what not to do

11 February 2013

World Health Organization

63

Rx - MERS-CoV 2016

Public Health England

Protecting and improving the nation's health

ISARIC

Treatment of MERS-CoV: Information for Clinicians

Clinical decision-making support for treatment of MERS-CoV patients

5 September 2015
v3.0

64

Rx - MERS-CoV 2016
ISARIC & WHO

- Benefit likely to exceed risk
  - –Convalescent serum
  - –Interferons esp b
  - –Lopinavir
  - –Monoclonal & polyclonal Abs

World Health Organization

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Rx - MERS-CoV 2016

Strength of evidence

	Study Focus: *	Quality of Best Available Evidence®	Order of Recommendation¥
Convalescent plasma ≠	SIV; SA; SC; MIV	SC (Moderate)	1
Interferon	SIV; SA; SC; MIV	MIV (Low)	2
Protease Inhibitors	SIV; SA; SC	SIV (Very Low)	2
Intravenous Immunoglobulin	SIV; SA; SC; MIV	Nil	3
Nitazoxanide	Nil	Nil	3
Others e.g. Cyclosporin A	SIV; MIV	MIV (Very Low)	3
Ribavirin	SIV; SA; SC	SIV (Very Low)	4
Corticosteroids	SIV; SA; SC	SA (Low)	4
Interferon plus ribavirin	SIV; SC; MIV; MA	MA (Very Low)	4

≠ Hyperimmune globulin or human neutralising monoclonals when available. The latter were shown active in SARS animal models.

* SARS *in vitro* (SIV); SARS animal (SA); SARS clinical (SC); MERS-CoV *in vitro* (MIV); MERS animal (MA)

WHO Interim guidance, 2015

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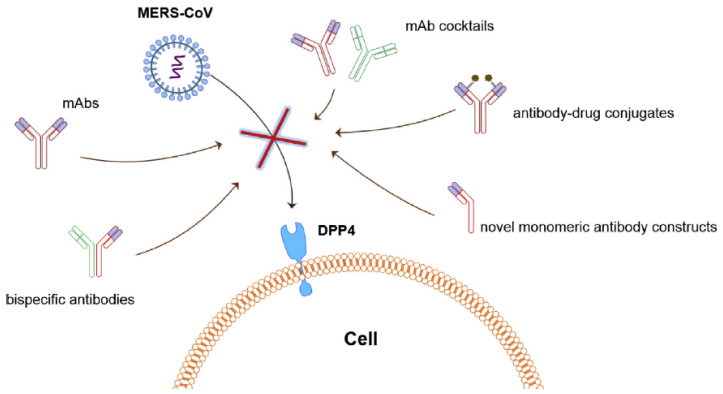
ELSEVIER
Institut Pasteur
Microbes and Infection 17 (2015) 142–148
www.elsevier.com/locate/micinf

Development of human neutralizing monoclonal antibodies for prevention and therapy of MERS-CoV infections

Tianlei Ying [a,*], Haoyang Li [a], Lu Lu [a], Dimiter S. Dimitrov [b], Shibo Jiang [a,c]

[a] Key Laboratory of Medical Molecular Virology of MOE/MOH, Shanghai Medical College, Fudan University, 130 Dong An Rd., Shanghai 200032, China
[b] Protein Interactions Section, Cancer and Inflammation Program, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Frederick, MD 21702, USA

T. Ying et al. / Microbes and Infection 17 (2015) 142–148



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Virology 490 (2016) 49–58

Contents lists available at ScienceDirect

Virology

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

ELSEVIER

VIROLOGY

3B11-N, a monoclonal antibody against MERS-CoV, reduces lung pathology in rhesus monkeys following intratracheal inoculation of MERS-CoV Jordan-n3/2012

Reed F. Johnson [a,*], Ulas Bagci [b,h], Lauren Keith [c], Xianchun Tang [d], Daniel J. Mollura [b], Larry Zeitlin [e], Jing Qin [f], Louis Huzella [c], Christopher J. Bartos [c], Natasha Bohorova [e], Ognian Bohorov [e], Charles Goodman [e], Do H. Kim [e], Michael H. Paulty [e], Jesus Velasco [e], Kevin J. Whaley [e], Joshua C. Johnson [c], James Pettitt [c], Britini L. Ork [c], Jeffrey Solomon [i], Nicholas Oberlander [c], Quan Zhu [d], Jiusong Sun [d], Michael R. Holbrook [c], Gene G. Olinger [c], Ralph S. Baric [g], Lisa E. Hensley [c], Peter B. Jahrling [a,c], Wayne A. Marasco [d]

68

Virus Research 194 (2014) 200–210

Contents lists available at ScienceDirect

Virus Research

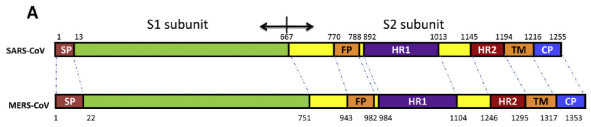
journal homepage: www.elsevier.com/locate/virusres

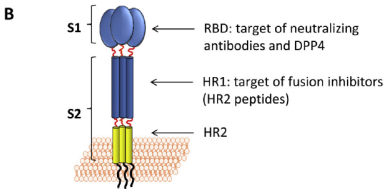
Middle East respiratory syndrome coronavirus (MERS-CoV) entry inhibitors targeting spike protein

Shuai Xia[a,1], Qi Liu[a,c,1], Qian Wang[a], Zhiwu Sun[a], Shan Su[a], Lanying Du[b], Tianlei Ying[a], Lu Lu[a,**], Shibo Jiang[a,b,*]

[a] Key Lab of Medical Molecular Virology of MOE/MOH, Shanghai Medical College, Fudan University, 130 Dong An Road, Xuhui District, Shanghai 200032, China
[b] Lindsley F. Kimball Research Institute, New York Blood Center, New York, NY 10065, USA

S. Xia et al. / Virus Research 194 (2014) 200–210





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Antiviral Research 114 (2015) 1–10

Contents lists available at ScienceDirect

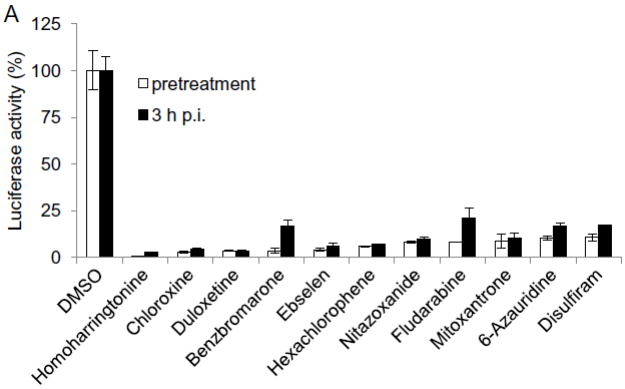
Antiviral Research

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

A screen of the NIH Clinical Collection small molecule library identifies potential anti-coronavirus drugs

Jianzhong Cao, J. Craig Forrest, Xuming Zhang *

Department of Microbiology and Immunology, University of Arkansas for Medical Sciences, Little Rock, AR 72205, United States



70

MERS – CoV
Infection control

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

State of the Science Review

Middle East respiratory syndrome coronavirus: Implications for health care facilities

Helena C. Maltezou MD, PhD [a,*], Sotirios Tsiodras MD, PhD [b]

[a] Department for Interventions in Health-Care Facilities, Hellenic Center for Disease Control and Prevention, Athens, Greece
[b] Fourth Department of Internal Medicine, University of Athens Medical School, Attikon University Hospital, Athens, Greece

American Journal of Infection Control 42 (2014) 1261-5

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MERS – CoV
Infection control

Middle East respiratory syndrome coronavirus
Case definition for reporting to WHO
Interim case definition
14 July 2015
http://www.who.int/csr/disease/coronavirus_infections/case_definition/en/

World Health Organization

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MERS-CoV / Case definition Confirmed

A person with laboratory confirmation of MERS-CoV infection[1], irrespective of clinical signs and symptoms.

World Health Organization

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MERS-CoV / Case definition Probable

Definition 1

- A febrile acute respiratory illness with clinical, radiological, or histopathological evidence of pulmonary parenchymal disease (e.g. pneumonia or Acute Respiratory Distress Syndrome); **and**
- Direct epidemiologic link[2] with a confirmed MERS-CoV case; **and**
- Testing for MERS-CoV is unavailable, negative on a single inadequate specimen[3] or inconclusive.[4]

World Health Organization

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MERS-CoV / Case definition Probable

Definition 2

- A febrile acute respiratory illness with clinical, radiological, or histopathological evidence of pulmonary parenchymal disease (e.g. pneumonia or Acute Respiratory Distress Syndrome); **and**
- The person resides or travelled in the Middle East, or in countries where MERS-CoV is known to be circulating in dromedary camels or where human infections have recently occurred; **and**
- Testing for MERS-CoV is inconclusive.[4]

World Health Organization

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MERS-CoV / Case definition Probable

Definition 3

- An acute febrile respiratory illness of any severity; **and**
- Direct epidemiologic link[2] with a confirmed MERS-CoV case; **and**
- Testing for MERS-CoV is inconclusive.[4]

World Health Organization

76

MERS – CoV
Infection control

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

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Helena C. Maltezou MD, PhD [a,*], Sotirios Tsiodras MD, PhD [b]

[a] Department for Interventions in Health-Care Facilities, Hellenic Center for Disease Control and Prevention, Athens, Greece
[b] Fourth Department of Internal Medicine, University of Athens Medical School, Attikon University Hospital, Athens, Greece

American Journal of Infection Control 42 (2014) 1261-5

77

MERS – CoV
Infection control

- Multiple events of health-care associated transmission
  - Pts w comorbidities --> severe dz
  - HCW frequently affected --> milder dz
- GAPS in infection control in all events !!!

Maltezou H, Tsiodras S. *American Journal of Infection Control 42 (2014) 1261-5*

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EMERGING INFECTIOUS DISEASES®
Volume 20, Number 4—April 2014

Contact Investigation for Imported Case of Middle East Respiratory Syndrome, Germany

Annicka Reuss ✉, Annette Litterst, Christian Drosten, Michael Seilmaier, Merle Böhmer[1], Petra Graf, Hermann Gold, Clemens-Martin Wendtner, Arina Zanuzdana, Lars Schaade, Walter Haas, and Udo Buchholz

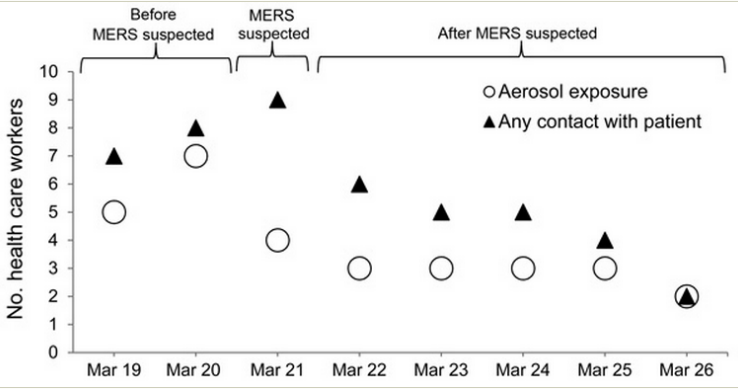

Figure 2. Daily number of health care workers who had contact with a patient infected with Middle East respiratory syndrome (MERS) coronavirus who was hospitalized in Germany, March 19–26, 2013.

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MERS-CoV / IHR EC 2015

- Recent KSA mission - 23 August 2015
- Hospital based outbreak
  - Virus transmission in the ER of the most heavily affected hospital !!!
    - Despite established triage!!!
    - overcrowded situations, movement of pts before dx, breakdowns in application of IPC measures

World Health Organization

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MERS-CoV / IPC

Infection prevention and control during health care for probable or confirmed cases of Middle East respiratory syndrome coronavirus (MERS-CoV) infection

Interim guidance

Updated 4 June 2015

WHO/MERS/IPC/15.1

World Health Organization

Background

WHO has updated the interim guidance that was published on 6 May 2013 to meet the urgent need for up-to-date information and evidence-based recommendations for the safe care of patients with probable or confirmed Middle East respiratory syndrome coronavirus (MERS-CoV) infection. The interim recommendations are informed by evidence-based guidelines WHO has published, including the *Infection prevention and control of epidemic- and pandemic-prone acute respiratory infections in health care. WHO Guidelines*[1] and review of current evidence on MERS-CoV infection. The recommendations have been reviewed by experts in infection prevention and control (IPC) and other technical areas (see Acknowledgements for names and

transmission. Health-care institutions are advised to consider reinforcing a service for the oversight of HCWs' health to ensure a safe environment for patients and HCWs. It is crucial that HCWs are provided with the best locally available protection for caring for MERS-CoV-infected patients and are followed up if exposure has occurred.

This guidance summarizes:

- Principles of IPC strategies associated with health care
- IPC precautions:
  - for providing care to all patients
  - for providing care to ARI patients. and
  - for providing care to patients wi confirmed MERS-CoV infectio

World Health Organization

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MERS - CoV / Infection control 2016

- Infection prevention & Control critical to prevent Transmission in HC facilities!!!
- Not possible to identify pts early
  - Early symptoms non specific

- HCW should apply **standard precautions** w all
- **Droplet precautions** w all URI
- **Contact & eye protection** w any care of cases of probable or confirmed infection
- **Airborne** w aerosol generating procedures

World Health Organization

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MERS-CoV / WHO 2016, HCW

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MERS-CoV / WHO 2016, HCW

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MERS-CoV / WHO 2016, HCW

World Health Organization

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MERS-CoV / WHO 2016, HCW

World Health Organization

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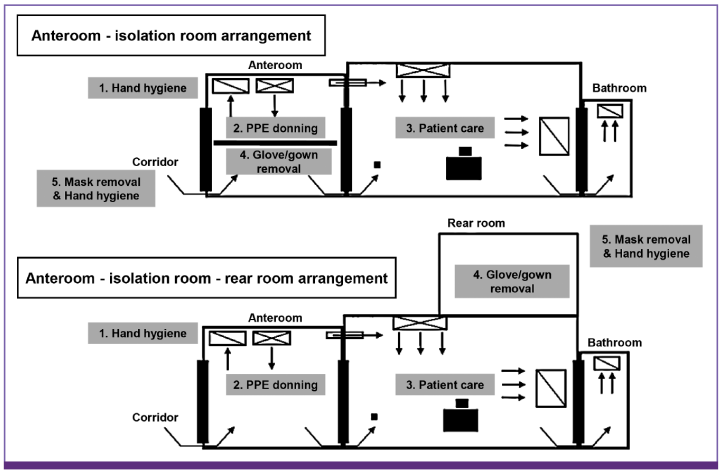
MERS-CoV / 2016 donning/doffing, S Korea



Infect Chemother 2015;47(4):278-302 87

Viral Shedding and Environmental Cleaning in Middle East Respiratory Syndrome Coronavirus Infection

Joon Young Song[1,2,3], Hee Jin Cheong[1,2], Min Joo Choi[1], Ji Ho Jeon[1], Seong Hee Kang[1], Eun Ju Jeong[1], Jin Gu Yoon[1], Saem Na Lee[1], Sung Ran Kim[3], Ji Yun Noh[1,2], and Woo Joo Kim[1,2]

[1]Division of Infectious Diseases, Department of Internal Medicine, [2]Asian Pacific Influenza Institute (APII), Korea University College of Medicine; [3]Infection Control Unit, Korea University Guro Hospital, Seoul, Korea

Viral shedding lasted 31 and 19 days from symptom onset in two patients with east respiratory syndrome coronavirus (MERS-CoV) pneumonia, respectively. Environmental real-time RT-PCR was weakly positive for bed guardrail and monitors. Even after cleaning the monitors with 70% alcohol-based disinfectant, RT-PCR was still weakly positive, and converted to negative only after wiping with diluted sodium chlorite. Further studies are required to clarify the appropriate methods to clean environments during and after treatment of patients with MERS-CoV infection.

Key Words: Virus shedding; Middle East Respiratory Syndrome; Coronavirus

Infect Chemother 2015;47(4):252-255 88

MERS-CoV/Infection prevention 2016

- People w underlying disease are high risk
  - DM, Renal failure, chronic lung dz, immunocompromised
  - Avoid contact w animals particularly camels
    - In areas w potential virus circulation
- General hygiene measures
  - Regular hand washing, avoid contact w sick animals
- Food hygiene practices
  - Avoid --> raw camel milk/urine, not properly cooked meat

World Health Organization

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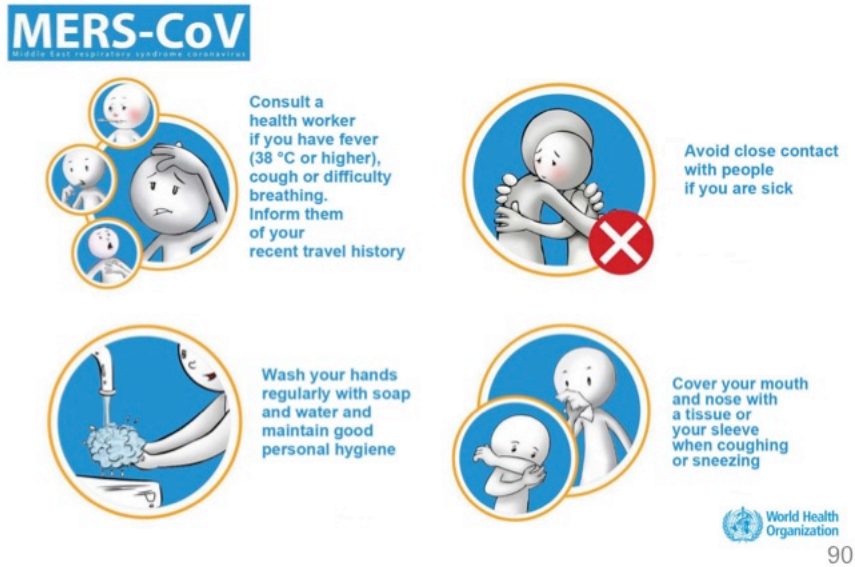
MERS-CoV WHO 2016, lay people



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MERS-CoV WHO 2016 close contacts, S Korea

Table 5. Risk assessment and recommendations for asymptomatic MERS contacts

Risk classification	Disease status of the infection source		
	Asymptomatic	Symptomatic, without pneumonia	Symptomatic, with pneumonia
High-risk close contact	Quarantine	Quarantine	Quarantine
Intermediate-risk close contact	Contact surveillance	Quarantine	Quarantine
Casual contact	No intervention	Contact surveillance	Contact surveillance

High-risk close contact: contact during an aerosol-generating procedure (e.g. nebulizer, intubation, endotracheal suction, bronchoscopy, etc.). Intermediate-risk close contact: contact within 2 m distance of a laboratory-confirmed MERS patient or a stay at the same ward/floor of a hospital exposed to laboratory-confirmed MERS patients. Casual contact: brief contact with >2 m distance from a laboratory-confirmed MERS patients.
MERS, Middle East Respiratory Syndrome.

Table 6. Control of visitors to Middle East countries or healthcare facilities affected by MERS outbreaks[a] depending on symptom manifestations

Fever	Respiratory symptoms	Assessment	Intervention plan
+	+	MERS-suspected	PCR test, hospitalization
+	-	Medical surveillance	PCR test, discharge and self-quarantine for 14 days from the last exposure[b]
-	+	Medical surveillance	PCR test, discharge and self-quarantine for 14 days from the last exposure[b]
-	-	No abnormalities	No interventions

MERS, Middle East Respiratory Syndrome; PCR, polymerase chain reaction.
[a]A healthcare facility with two or more cases of laboratory-confirmed MERS-CoV infection is regarded as being affected by MERS outbreak.
[b]In the presence of pneumonia, the patient is classified as a patient with suspected MERS-CoV infection and placed under inpatient quarantine care.

Infect Chemother 2015;47(4):278-302 91

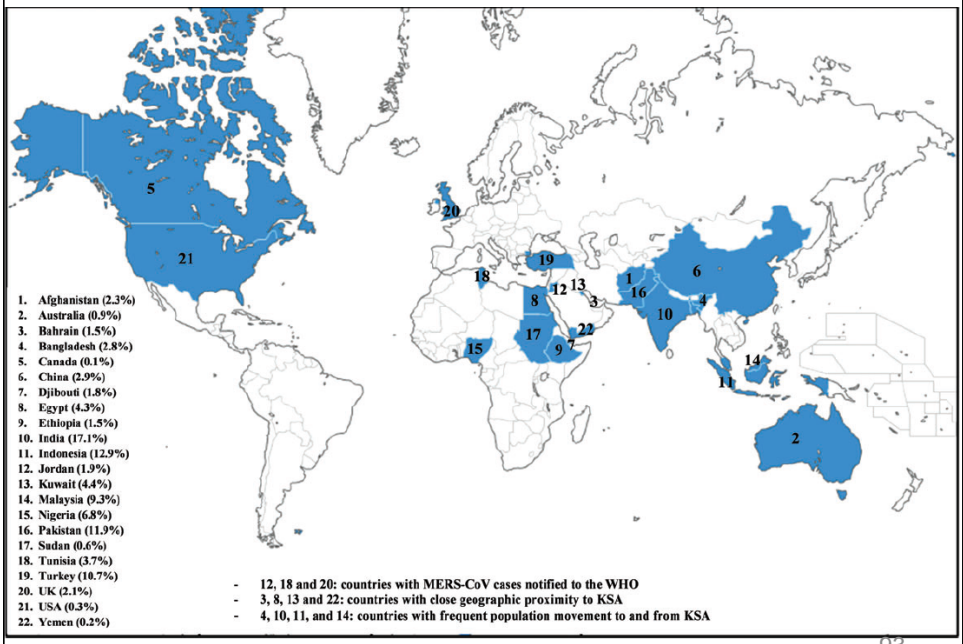
Journal of Infectious Diseases Advance Access published April 15, 2014

MAJOR ARTICLE

Prevalence of MERS-CoV Nasal Carriage and Compliance With the Saudi Health Recommendations Among Pilgrims Attending the 2013 Hajj

Ziad A. Memish,[1,2] Abdullah Assiri,[1] Malak Almasri,[1] Rafat F. Alhakeem,[1] Abdulhafeez Turkestani,[3] Abdullah A. Al Rabeeah,[1] Jaffar A. Al-Tawfiq,[4,5] Abdullah Alzahrani,[1] Essam Azhar,[6] Hatem Q. Makhdoom,[7] Waleed H. Hajomar,[8] Ali M. Al-Shangiti,[9] and Saber Yezli[1]

92



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EMERGING INFECTIOUS DISEASES®

Volume 20, Number 4—April 2014

Lack of MERS Coronavirus but Prevalence of Influenza Virus in French Pilgrims after 2013 Hajj

Philippe Gautret ✉ , Rémi Charrel, Samir Benkouiten, Khadidja Belhouchat, Antoine Nougairede, Tassadit Drali, Nicolas Salez, Ziad A. Memish, Malak al Masri, Jean-Christophe Lagier, Matthieu Million, Didier Raoult, Philippe Brouqui, and Philippe Parola

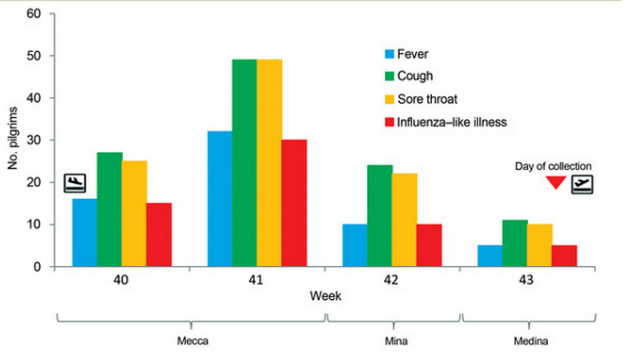

Figure. . Onset of respiratory symptoms by week, reported by 129 Hajj pilgrims from France during their stay in Saudi Arabia, October 2013.

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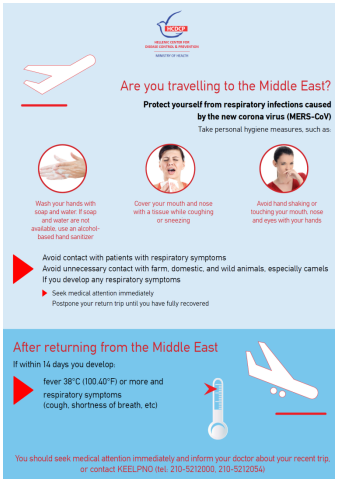
MERS - CoV / Travellers



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RAPID COMMUNICATIONS

A case of imported Middle East Respiratory Syndrome coronavirus infection and public health response, Greece, April 2014

S Tsiodras (sotirios.tsiodras@gmail.com)[1,2], A Baka[1], A Mentis[3], D Iliopoulos[1], X Dedoukou[1], G Papamavrou[1], S Karadima[1], M Emmanouil[3], A Kossyvakis[3], N Spanakis[4], A Pavli[1], H Maltezou[1], A Karageorgou[5], G Spala[1], V Pitiriga[4], E Kosmas[6], S Tsiagklis[6], S Gkatzias[6], N G Koulouris[7], A Koutsoukou[8], P Bakakos[7], E Markozanhs[7], G Dionellis[7], K Pontikis[8], N Rovina[8], M Kyriakopoulou[8], P Efstathiou[5], T Papadimitriou[1], J Kremastinou[1], A Tsakris[4], G Saroglou[1,6]

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Article submitted on 22 April 2014 / published on 24 April 2014

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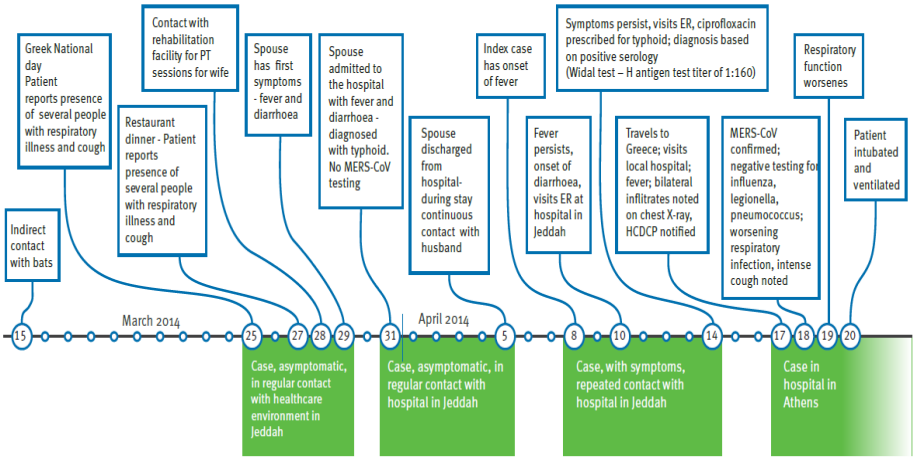
FIGURE

Timeline of possible exposure and clinical course of Middle East Respiratory Syndrome coronavirus infection case, Greece March-April 2014



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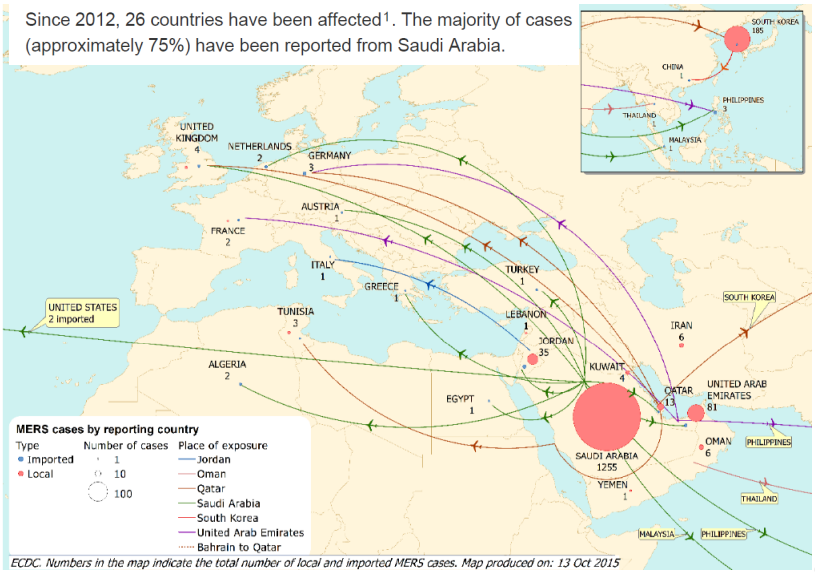
MERS-CoV in other countries

Since 2012, 26 countries have been affected[1]. The majority of cases (approximately 75%) have been reported from Saudi Arabia.



ECDC. Numbers in the map indicate the total number of local and imported MERS cases. Map produced on: 13 Oct 2015

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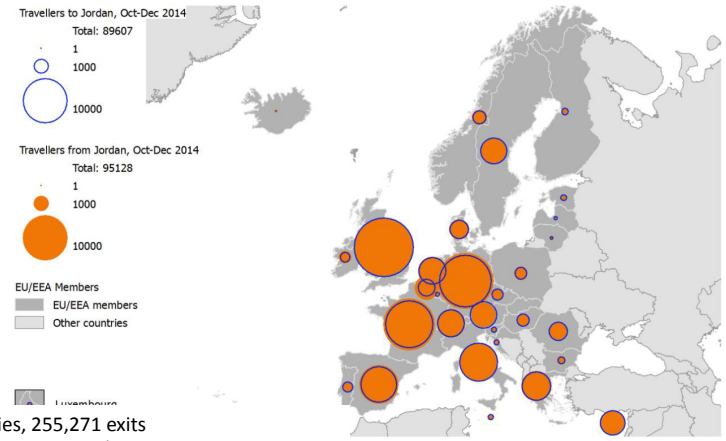
MERS-CoV in other countries the Jordan example

Figure 3. Number of travellers on commercial air carriers (excluding unscheduled charters), by EU/EEA country, to and from Jordan, October–December 2014.



251 280 entries, 255,271 exits
In 6 months 95128 to EU/EEA countries
N of border crossings from Arab countries 1,400,000
1,250,000 Jordanian passports

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2nd case in Thailand in 7 months

14/2/2016 World Health Organization, Thailand confirms MERS CoV in traveler, WHO cautions against continued risk of importation

World Health Organization
Regional Office for South-East Asia

Thailand confirms MERS CoV in traveler, WHO cautions against continued risk of importation

SEAR/PR/1618

New Delhi, 24 January 2016: Thailand today confirmed Middle East respiratory syndrome coronavirus (MERS CoV) disease in a traveler, the second such case in the country in the last seven months, as WHO cautioned other member states in its South-East Asia Region against the continuing risks and the need to remain vigilant.

"The new case of MERS CoV is a reminder of the continued risk of importation of the disease from countries where it still persists. All countries need to further enhance surveillance for severe acute respiratory infections, focus on

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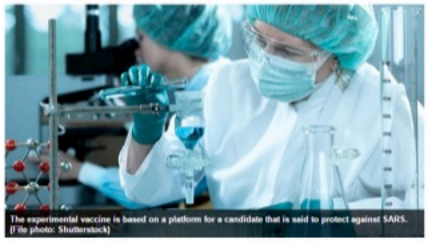
MERS - CoV / Vaccine ?

Experimental vaccine for MERS developed



NOVAVAX

Contact: John Herrmann
Vice President, General Counsel
Novavax, Inc.
240-268-2000

Novavax Produces MERS-CoV Vaccine Candidate

ELSEVIER

Vaccine
Volume 32, Issue 26, 30 May 2014, Pages 3169–3174

Purified coronavirus spike protein nanoparticles induce coronavirus neutralizing antibodies in mice

Christopher M. Coleman[a, 1], Ye V. Liu[b, 1], Haiyan Mu[b], Justin K. Taylor[a], Michael Massare[b], David C. Flyer[b], Gregory M. Glenn[b], Gale E. Smith[b, 1], Matthew B. Frieman[a, 1]

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[b] Novavax, Inc. 22 Firstfield Rd, Gaithersburg, MD 20852, USA

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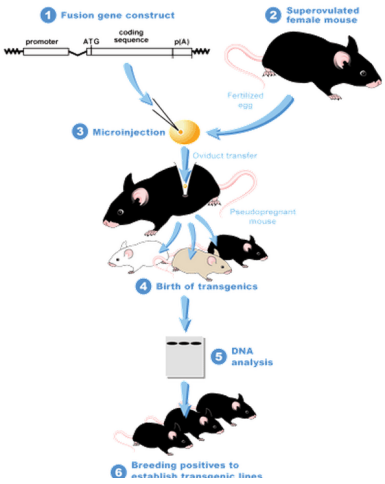
MERS - CoV Transgenic mouse



- ➢constitutive global expression of hCD26/DPP4
  - functional receptor
- ➢lung and brain prime sites for viral replication

Agrawal AS et al J Virol. 2015

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MERS – CoV / Stress in HCW

CM&R *Rapid Release*. Published online ahead of print February 4, 2016 as doi:10.3121/cmr.2016.1303

Original Research

Healthcare Workers Emotions, Perceived Stressors and Coping Strategies During MERS-CoV Outbreak

Imran Khalid, MD, FCCP; Tabindeh J Khalid, MD; Mohammed R Qabajah, RN; Aletta G Barnard, RN; and Ismael A Qushmaq, MD

Khalid et al. 2016

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MERS – CoV / Stress in HCW

Table 4. Factors that helped in reducing stress during MERS-CoV outbreak (Total n=117, Maximum Score 3)

Number	Factors that helped to reduce stress	Mean (SD)
1	Positive attitude from colleagues in your department	2.34 (0.74)
2	None of the staff getting MERS after starting strict protective measures	2.34 (0.82)
3	Improvement in patient's condition	2.30 (0.91)
4	Your colleagues who were infected getting better	2.28 (0.78)
5	Protective equipment provided to you by Hospital	2.10 (0.86)
6	Clear guidelines from Hospital for infection prevention	2.07 (1.01)
7	Your family members or friends outside hospital did not get MERS-CoV	1.97 (1.15)
8	Decrease in MERS-CoV cases reported in news	1.94 (0.99)
9	Likelihood that you would get extra compensation for your exposure to MERS-CoV	1.90 (1.18)
10	All healthcare professionals working together on front line	1.60 (1.05)
11	Confidence in the hospital staff in case you got sick from MERS-CoV	1.58 (1.12)
12	Not to do overtime	1.52 (1.08)
13	Sharing jokes or humor among colleagues	1.43 (1.04)
14	Getting free meals from the hospital in your unit	1.19 (1.16)

0= Not At All effective; 1= Mildly Effective; 2= Moderately Effective; 3= Extremely Effective in Reducing Stress

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MERS – CoV / Stress in HCW

Table 6. Motivational factors to encourage continuation of work in future outbreaks (Total n=117, Maximum Score=3)

Number	Motivational factors for future outbreaks	Importance factor Mean (SD)
1	Similar adequate personal protective equipment supply by the Hospital	2.88 (0.41)
2	Available cure or vaccine for the disease	2.85 (0.35)
3	Family support	2.71 (0.64)
4	Compensation to family if disease related death at work	2.74 (0.71)
5	Financial recognition of efforts	2.68 (0.76)
6	Disability benefits if disabled from the disease	2.64 (0.75)
7	Recognition from management and supervisors for the extra efforts	2.55 (0.77)
8	Psychiatric help and therapy made available in work place to help reduce stress and anxiety	2.27 (0.99)
9	Not forced to do overtime	1.72 (1.16)
10	Reduced working hours during outbreaks	1.67 (1.22)

0=Not important at all; 3=Most important

Khalid et al. 2016 105

MERS - CoV
Risk assessment

ecdc

RAPID RISK ASSESSMENT

Severe respiratory disease associated with Middle East respiratory syndrome coronavirus (MERS-CoV)

21st update, 21 October 2015

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MERS - CoV Risk assessment

- Majority of cases still from Middle East
- The source of the virus remains unknown, but the pattern of transmission and virological studies point towards dromedary camels in the Middle East as being a reservoir from which humans sporadically become infected through zoonotic transmission.
- Human-to-human transmission is amplified among household contacts and in healthcare settings.

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MERS - CoV Risk assessment

- Transmission in hospital settings is still one of the main sources of infection
- Sporadic importation can be expected
- Risk of nosocomial spread in other countries!!!

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MERS - CoV
Risk assessment

- Efforts to contain the nosocomial clusters in the affected countries are vital to prevent wider transmission.
- However, w appropriate IPC
  - sustained human-to-human community transmission is unlikely

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MERS - CoV
Risk assessment

- Need ↑↑ awareness among HCW and appropriate IPC activities
- No travel restrictions
- Advice for travelers especially high risk ones & HCWs !!!
- Risk of wide spread transmission remains low

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HOSPITAL LOCKDOWN!!!

Ministry of Health Portal
Kingdom of Saudi Arabia

وزارة الصحة
Ministry of Health

MOH Portal ▸ The Ministry ▸ Media Center ▸ Ministry News

Media Center Summary

- Ministry News
- Announcements
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Ministry News

MOH Closes a Private Hospital for non-Compliance with Infection Control Guidelines

23 February 2015

The Ministry of Health (MOH), represented by the Command and Control Center (CCC) of Riyadh Health Affairs General Directorate, closed a private hospital in Riyadh after failing to comply with infection control guidelines issued by the CCC to prevent the spread of infectious diseases.

The Director General of Riyadh Health Affairs, Dr. Adnan Al-Abdulkarim, said, "This nonstop step comes under direct supervision of His Excellency the Minister of Health Mr. Ahmad bin Aqeel Al-Khateeb, and in coordination with the

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Journal of Infection and Public Health (2016) 9, 1–2

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http://www.elsevier.com/locate/jiph

EDITORIAL

MERS CoV: A trigger for healthcare transformation

THANK YOU!!!

The most rec… of urgent care, prestigious tertia… n-depth analysis established Infe… nts was ongoing hospital is located in the capital of Saudi Arabia. The outbreak was associated with 82 confirmed MERS CoV cases, and more than 5000 health-care workers (HCWs) were screened for the virus. The hospital followed a written Infectious Disease because the reopening of the hospital was imminent. There was a clear sense of urgency while the leadership addressed these issues. The culture of the organization was tested by this virus outbreak.

An exposed patient that became symptomatic on

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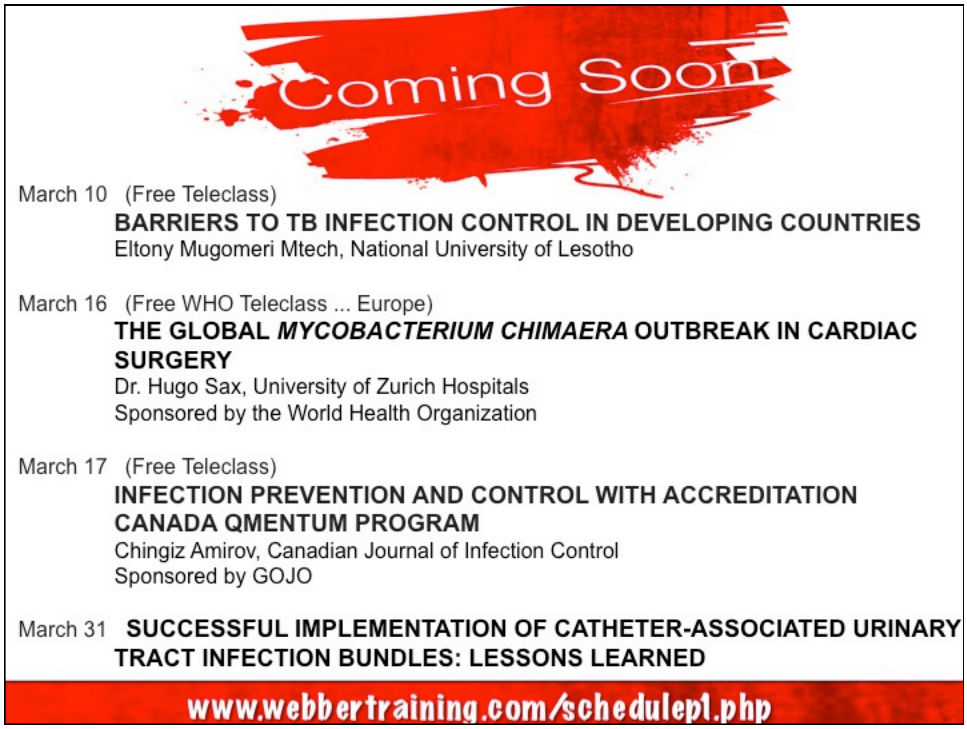
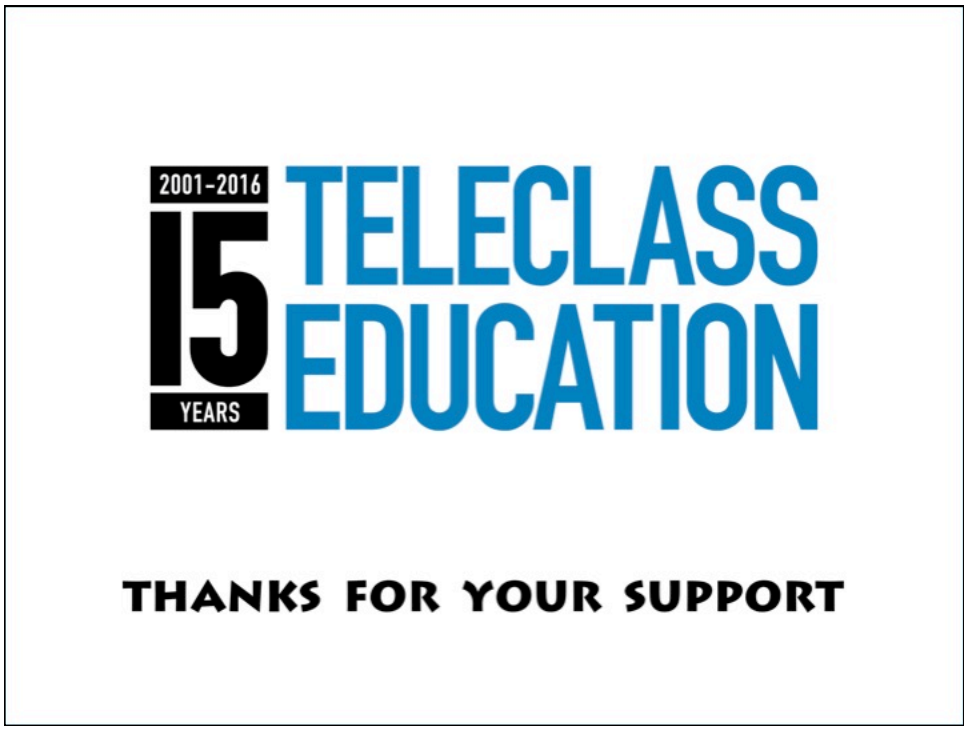
MERS-COV: Implications for Healthcare Facilities
Prof. Sotirios Tsiodras, University of Athens, Greece
A Webber Training Teleclass





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