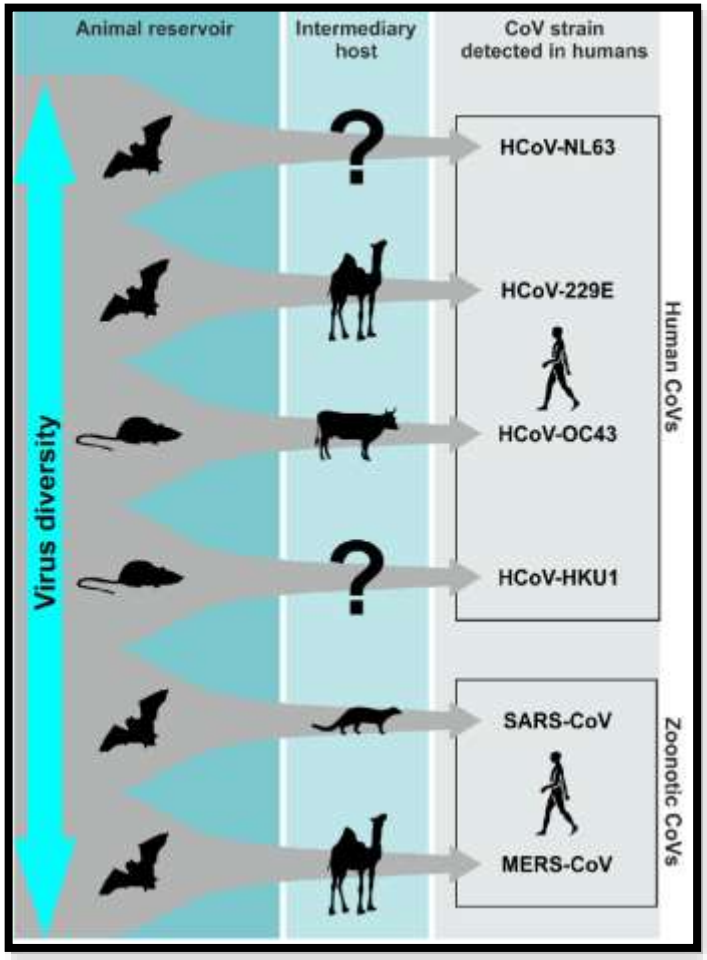
MERS-CoV: Epidemiology, Burden and Risk Factors of the Infection

Ziad A Memish, MD, FRCPC, FRCPL, FRCPE, FACP, FFPH
Senior Infectious Diseases Consultant & Director Research & Innovation Center
King Saud Medical City
Ministry of Health &
Professor, College of Medicine
AlFaisal University
Riyadh, KSA

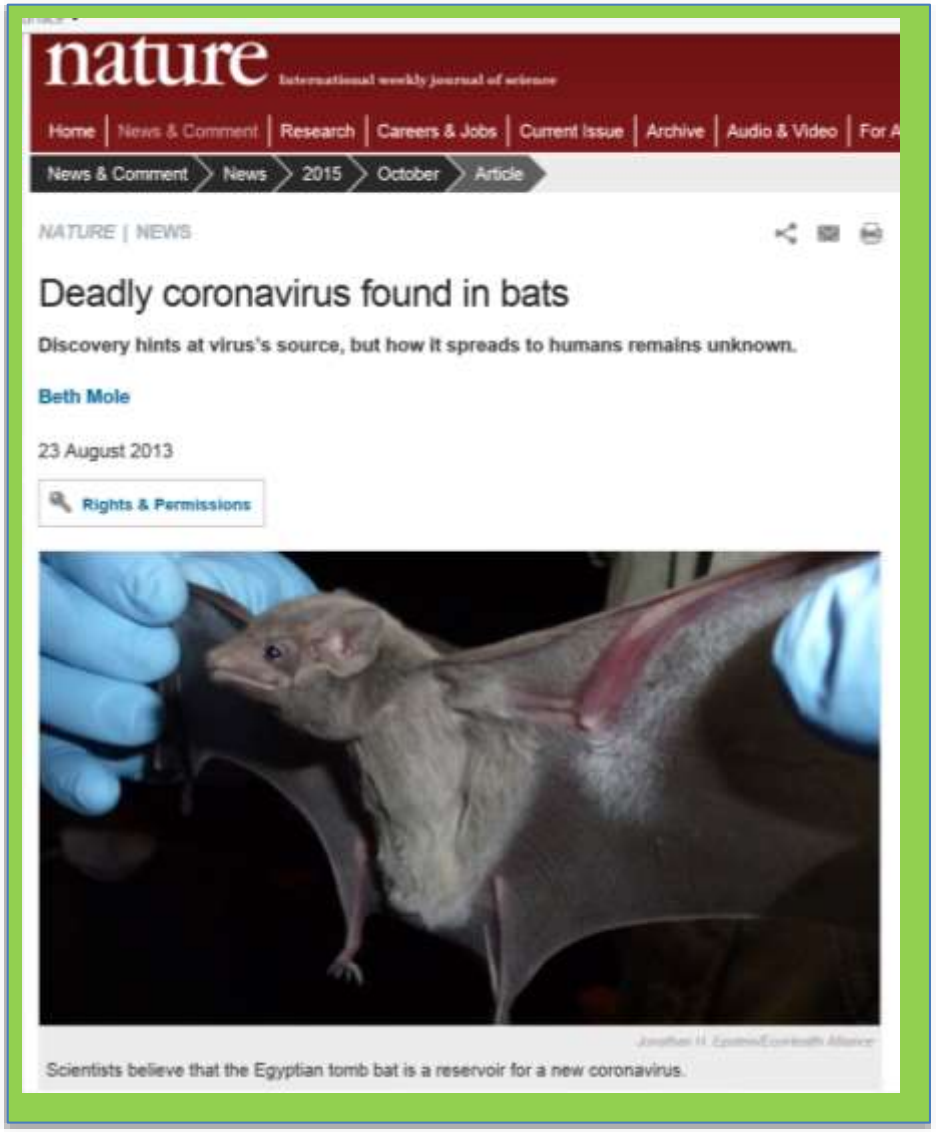
zmemish@yahoo.com

The Animal Groups Representing Natural Hosts & the Putative Intermediate Hosts for the Six Human CoVs



Victor M. Corman, et al. Hosts and Sources of Endemic Human Coronaviruses. Advances in Virus Research, 2018

Scientists Believe that Egyptian Tomb Bat is a Reservoir for MERS-CoV

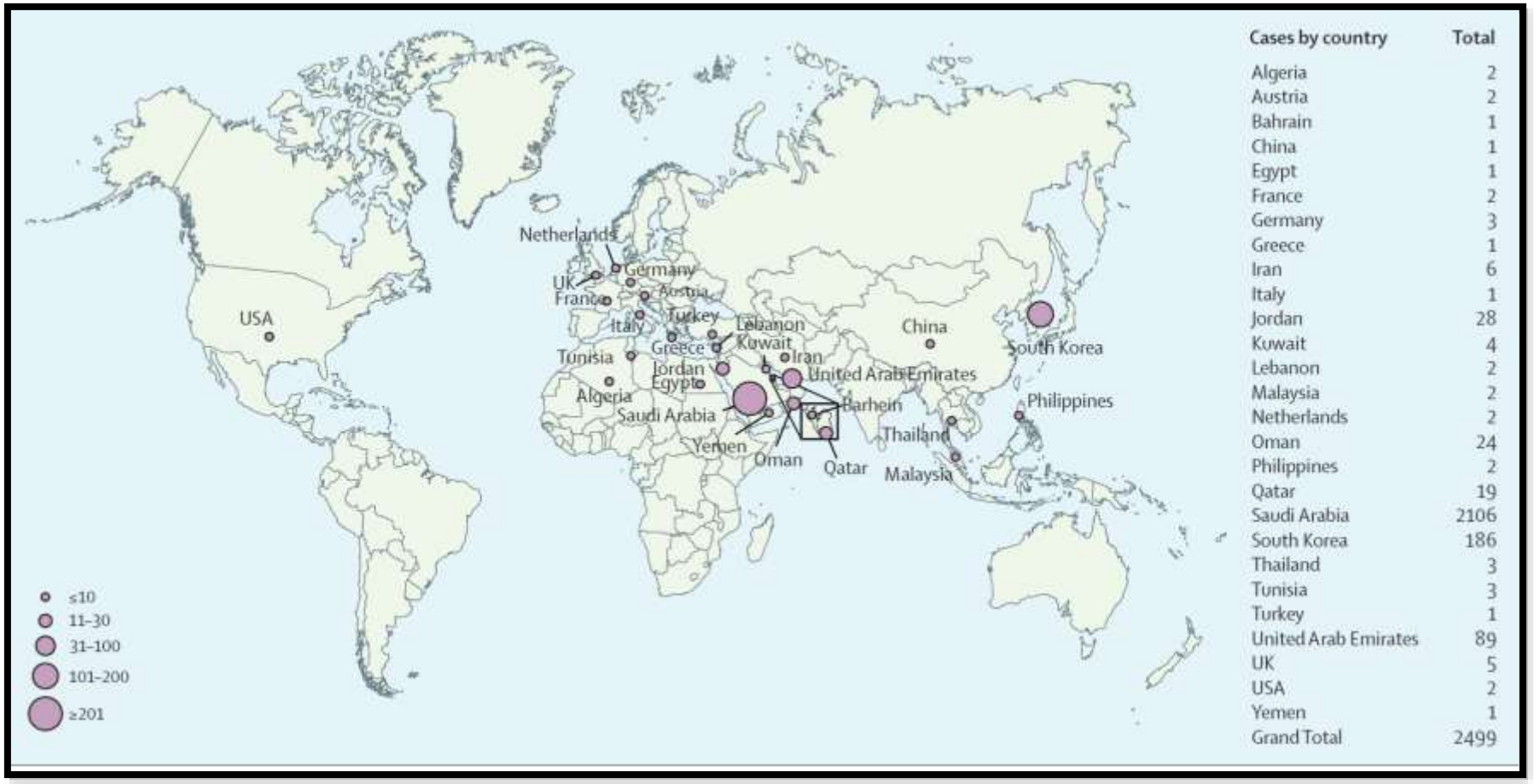


Beth Mole Nature 23 Aug 2013

Memish, Z. et al. EID 2013

Abeer N. Alshukairi, et al. High Prevalence of MERS-CoV Infection in Camel Workers in Saudi Arabia. mBio September/October 2018 Volume 9 Issue 5 e01985-18

Geographical Distribution of Reported Human Infections of MERS-CoV



Cases by country	Total
Algeria	2
Austria	2
Bahrain	1
China	1
Egypt	1
France	2
Germany	3
Greece	1
Iran	6
Italy	1
Jordan	28
Kuwait	4
Lebanon	2
Malaysia	2
Netherlands	2
Oman	24
Philippines	2
Qatar	19
Saudi Arabia	2106
South Korea	186
Thailand	3
Tunisia	3
Turkey	1
United Arab Emirates	89
UK	5
USA	2
Yemen	1
Grand Total	2499

Memish ZA, Perlman S, Van Kerkhove MD, Zumla A. Middle East respiratory syndrome coronavirus. Lancet 2020; 395: 1063–77
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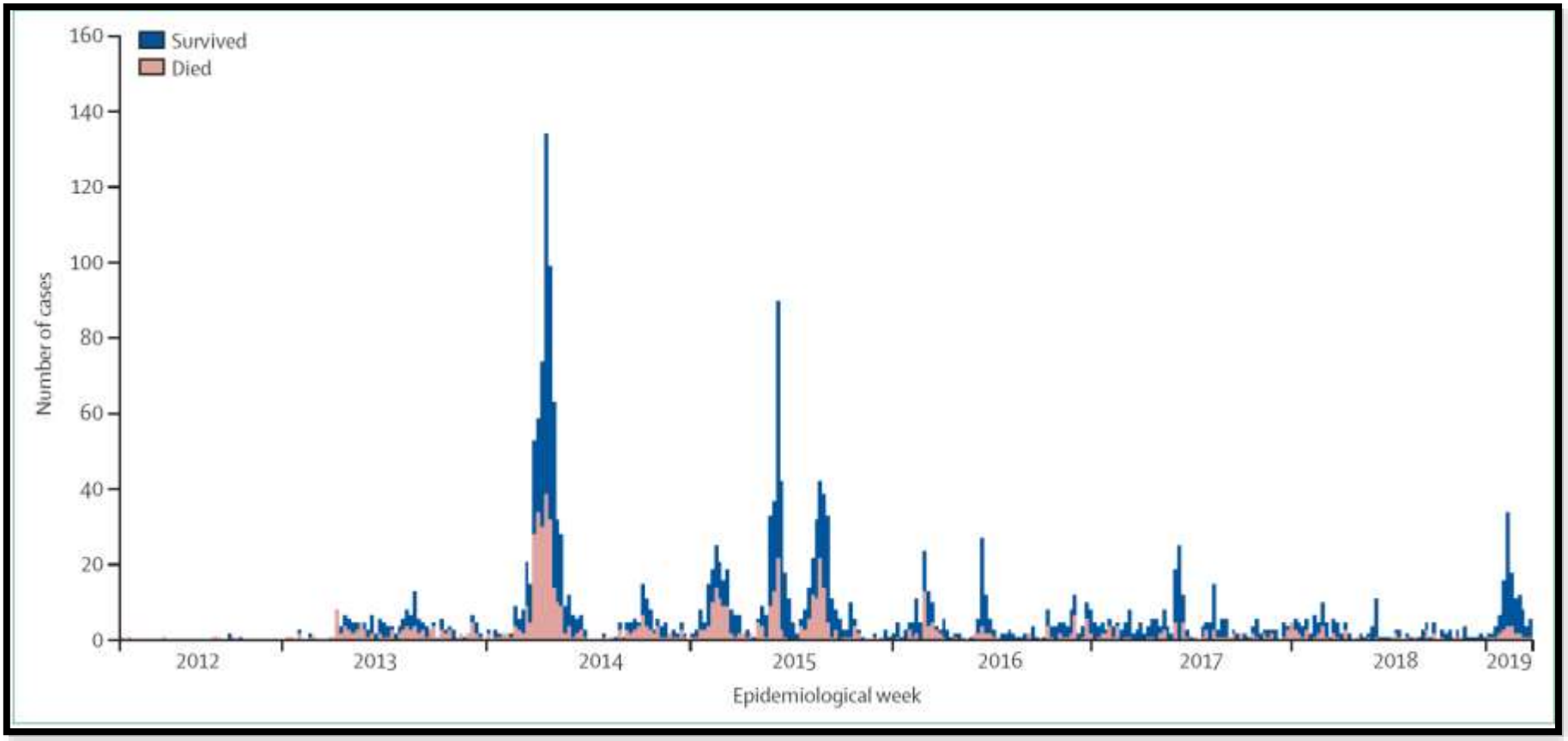
Global MERS Reported to WHO by Week, 2012–19



Memish ZA, Perlman S, Van Kerkhove MD, Zumla A. Middle East respiratory syndrome coronavirus. Lancet 2020; 395: 1063–77

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Epidemiological, Clinical, & Laboratory Features of MERS

A Sources of MERS-CoV

Animal and environmental sources

MERS-CoV-infected camels
- Camel nasal secretions
- Camel excreta (urine, saliva and faeces)
- Camelid birth products (amniotic fluid, fetal membranes and placenta)
- Camel food products (milk, meat)
- Other unknown?

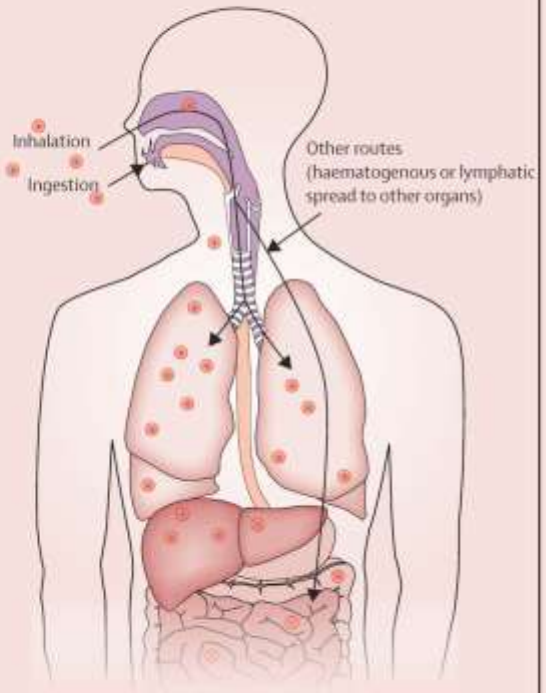
Human sources

Symptomatic and subclinical MERS-positive individuals in:
- The community
- Family households
- Family compounds
- Hostels
- Health-care facilities and hospitals
- Camel farms

Up to 25% report direct or indirect contact with camels and approximately 50% are the result of human-to-human transmission

B Probable MERS-CoV routes of entry, circulation, and organ involvement

MERS-CoV host cell DPP4 receptor found in:
broncial epithelium, lung parenchyma, interstitium (endothelial cells), kidneys, intestines, liver, thymus, haemopoetic cells (leukocytes, macrophages, dendritic cells, mononuclear lymphoid cells)



C Clinical, imaging, and laboratory features

Presenting symptoms

General
- Fever (>38°C)
- Chills or rigours
- Lethargy
- Anorexia
- Malaise, lethargy
- Myalgia
- Body aches

CNS
- Headache
- Confusion

Upper respiratory tract
- Runny nose
- Sneezing
- Sore or tickly throat

Lower respiratory tract
- Cough (dry or productive with sputum)
- Shortness of breath
- Chest pain
- Haemoptysis

Gastrointestinal tract
- Decreased appetite
- Nausea
- Vomiting
- Diarrhoea
- Abdominal pain
- Abdominal discomfort

Incubation period
Mean: 5·2 days
(95% CI 1·9–14·7)
Range 2–14 days

Sex distribution
Males 64%, females 36%

Abnormal investigations
Imaging: chest x-ray and CT changes
- Leucopenia
- Lymphopenia
- Thrombocytopenia
- Elevated LDH
- Elevated ALT
- Elevated AST

Complications
- Severe acute respiratory syndrome
- Respiratory failure
- Liver failure
- Renal failure
- Multiorgan failure
- Septic shock

Factors associated with increased mortality

Comorbidities:
- Diabetes
- Chronic lung disease (COPD, asthma)
- Chronic kidney disease
- Chronic liver disease
- Chronic heart disease
- Malignancies
- Immunosuppressive drugs
- Age >65 years
- Presence of pleural effusion
- Low serum albumin

Case fatality rate
Overall (global): 36·0%
Saudi arabia: 41·8% (22%–69%)
South korea: 20·4% (14·5–47%)

Memish ZA, Perlman S, Van Kerkhove MD, Zumla A. Middle East respiratory syndrome coronavirus. Lancet 2020; 395: 1063–77

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What we Learned so far About: HCA MERS Transmission & Effective IC Measures

Table 1. Characteristics of Health Care Workers with Confirmed MERS-CoV Infection.*

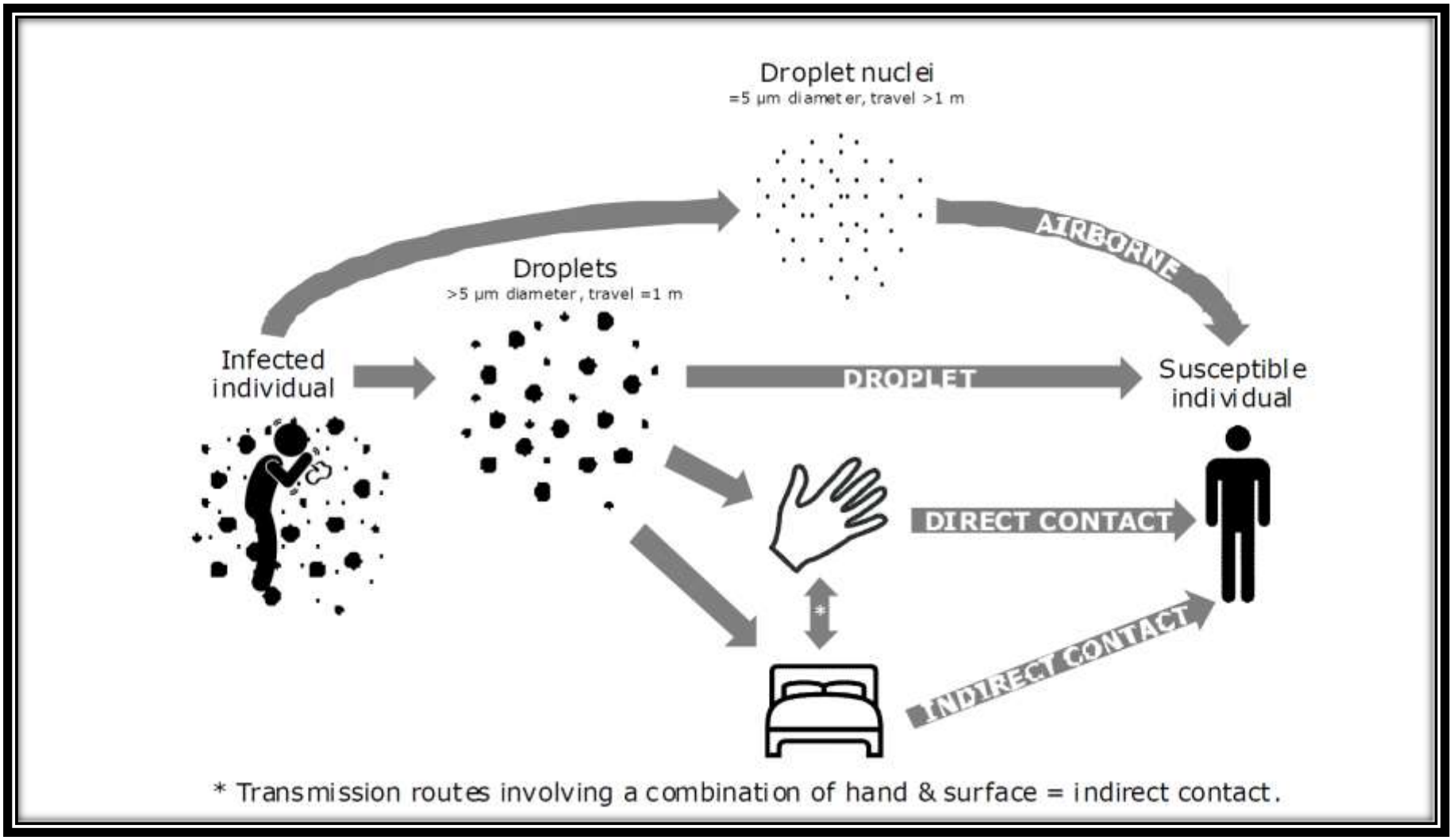
Characteristic	Health Care Worker						
	1	2	3	4	5	6	7
Age (yr)	42	29	46	39	59	28	56
Sex	Female	Female	Female	Female	Female	Female	Female
Result of chest radiography	Normal	Normal	Normal	Normal	Normal	Normal	Normal
MERS-CoV PCR test	Positive	Positive	Positive	Positive	Positive	Positive	Positive
Viral load (Ct value)	33	37	38	34	35	30	37
Coexisting condition							
Diabetes mellitus	Yes	No	No	No	No	No	No
Other	No	No	No	No	No	No	No
Symptoms							
Feverish feeling	Yes	No	Yes	No	No	Yes	Yes
Fever, measured	Yes	No	No	No	No	No	No
Cough	Yes	No	No	No	No	No	Yes
Sore throat	Yes	No	Yes	No	No	Yes	Yes
Runny nose	No	No	Yes	No	Yes	Yes	Yes
Muscle aches	Yes	No	Yes	No	No	No	Yes
History of exposure	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Memish ZA, Zumla AI, Assiri A. Middle East respiratory syndrome coronavirus infections in health care workers. N Engl J Med. 2013 Aug 29;369(9):884-

Exposure history							
Total Duration of exposure/s:							
<1 hr	+	-	-	+	+	-	+
1-2 hr	-	-	-	-	-	-	-
3-4 hr	-	-	-	-	-	-	-
>5 hr	-	+	+	-	-	+	+
Type of exposure/s to patient:							
Change linen	-	+	+	-	-	+	+
Feeding	-	+	+	-	-	+	+
Bathing	-	-	+	-	-	+	+
Lifting	-	-	+	-	+	+	+
Give meds	-	+	+	-	-	+	+
Place IV or other catheters	-	+	+	+	-	+	+
Presence during high risk procedure (aerosol generating)							
Intubation	+	+	+	+	-	-	+
Airway suctioning	-	+	+	-	-	+	+
Sputum induction	-	-	-	-	-	+	+

Memish ZA, Zumla AI, Assiri A. Middle East respiratory syndrome coronavirus infections in health care workers. N Engl J Med. 2013 Aug 29;369(9):884-6.

Transmission routes: Droplet, Airborne, Direct Contact, and Indirect Contact



Otter J, et al. Transmission of SARS and MERS coronaviruses and influenza virus in healthcare settings: the possible role of dry surface contamination.J Hosp Infect Oct 2015

Role of the Environment

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

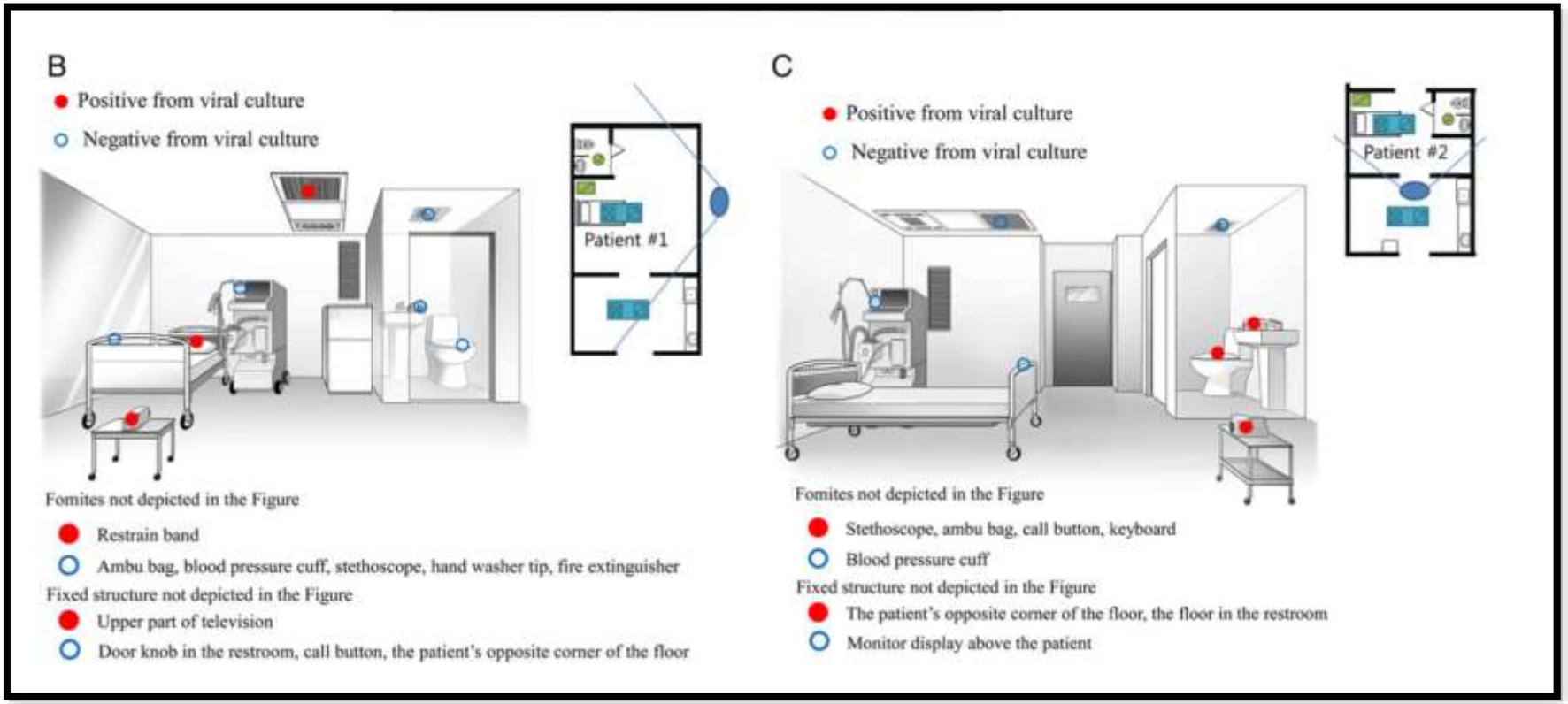
- **Plastic & steel surfaces did not affect the stability of MERS-CoV differentially:**
  ~48 hrs at the (20°C – 40% RH)
  ~8 hrs (30°C – 80% RH)
  ~24 hrs (30°C – 30% RH)
- **MERS-CoV very stable in aerosol form at 20°C – 40% RH.**
- **MERS-CoV decreased only 7% in viability at 40% RH, whereas the viability at 70% RH decreased significantly 89%.**

Frequency of Environmental Sample Positivity for MERS-CoV in RT PCR or Viral Culture

Swab Site	PCR Results (Positivity Percent, %)	Culture Results (Positivity Percent, %)
Bed sheet	3/15 (20.0)	1/15 (6.7)
Bedrails	4/15 (26.7)	1/15 (6.7)
Bed tables	2/5 (40.0)	0/5 (0.0)
Bed controllers	5/15 (33.3)	0/15 (0.0)
Shelves	0/14 (0.0)	0/14 (0.0)
Door buttons	1/10 (10.0)	0/10 (0.0)
Bathroom door knobs	1/10 (10.0)	0/10 (0.0)
Patient room floor	0/7 (0.0)	0/7 (0.0)
Patient monitor buttons	0/5 (0.0)	0/5 (0.0)
Thermometers	1/5 (20.0)	0/5 (0.0)
IV fluid hangers	5/14 (35.7)	2/14 (14.3)
Portable X-rays	1/5 (20.0)	0/5 (0.0)
Computed radiography cassette	1/1 (100.0)	1/1 (100.0)
Anteroom floors	2/14 (14.3)	0/14 (0.0)
Anteroom tables	3/7 (42.8)	1/7 (14.3)
Entrances of air-ventilating equipment	1/6 (16.7)	0/6 (0.0)

Seo Yu Bin, et al. Clin Infect Dis 2016

Results of Viral Cultures of Air & Swabs from Two Patient Rooms



Sung-Han Kim, et al. Extensive Viable Middle East Respiratory Syndrome (MERS) Coronavirus Contamination in Air and Surrounding Environment in MERS Isolation Wards. Clin Infect Dis. 2016 Aug 1;63(3):363-9

Heat Inactivation of the MERS-CoV

Table 1. $TCID_{50}$ per ml values obtained at 56 and 65°C

	56°C					65°C				
Time (minute)	**0·5**	**15**	**30**	**60**	**120**	**0·5**	**15**	**30**	**60**	**120**
Sample 1	$10^{5.5}$	$10^{0.67}$	ND	ND	ND	$10^{4.67}$	ND	ND	ND	ND
Sample 2	$10^{6.17}$	$10^{1.0}$	$10^{0.67}$	ND	ND	$10^{2.00}$	ND	ND	ND	ND
Sample 3	$10^{4.67}$	ND	$10^{1.33}$	ND	$10^{0.67}$	$10^{3.67}$	ND	ND	ND	ND

Time zero values were $10^{5.59}$ $TCID_{50}$ per ml for each sample. ND: not detected (below the limit of virus detection which corresponded to $10^{0.67}$ $TCID_{50}$ per ml). The whole experiment was performed twice with similar results (data not shown).

India Leclercq et al.(2014) Influenza and Other Respiratory Viruses 8(5), 585-586.

Virucidal Activity of PVP-I Skin Cleanser, Surgical Scrub & Gargle/Mouthwash Against MERS-CoV

Test product	Dilution	Log_{10} reduction factor (95% CI[a])							
		Clean conditions[b]				Dirty conditions[b]			
		MERS-CoV	MVA			MERS-CoV	MVA		
		15 s	15 s	30 s	60 s	15 s	15 s	30 s	60 s
PVP-I surgical scrub[c] (7.5 g/L available iodine)	Undiluted	**4.64**	**≥4.00**	**≥4.00**	**≥4.00**	**4.64**	**≥4.17**	**≥4.17**	**≥4.17**
	1:10	n.d.	**≥5.50**	**≥5.50**	**≥5.50**	n.d.	**≥5.67**	**≥5.67**	**≥5.67**
	1:100	n.d.	3.83 (±0.65)	**4.17** (±0.58)	**4.50** (±0.58)	n.d.	1.00 (±0.70)	1.67 (±0.70)	1.83 (±0.71)
PVP-I skin cleanser[c] (4 g/L available iodine)	Undiluted	**4.97**	**≥4.17**	**≥4.17**	**≥4.17**	**4.97**	**≥4.00**	**≥4.00**	**≥4.00**
	1:10	n.d.	**4.50** (±0.54)	**≥4.67**	**≥4.67**	n.d.	**4.33** (±0.56)	**≥4.50**	**≥4.50**
	1:100	n.d.	3.33 (±0.56)	3.67 (±0.47)	3.67 (±0.47)	n.d.	0.33 (±0.56)	1.00 (±0.63)	1.00 (±0.63)
PVP-I gargle and mouthwash (1 g/L available iodine)	Undiluted	**4.30**	**6.50** (±0.45)	**6.50** (±0.45)	**6.50** (±0.45)	**4.30**	**6.50** (±0.45)	**6.50** (±0.45)	**6.50** (±0.45)
	1:10	n.d.	**4.83** (±0.71)	**5.83** (±0.71)	**5.83** (±0.61)	n.d.	3.50 (±0.45)	**4.00** (±0.63)	**4.00** (±0.63)
	1:100	n.d.	0.67 (±0.56)	0.67 (±0.56)	0.67 (±0.70)	n.d.	0.50 (±0.65)	0.67 (±0.70)	1.00 (±0.63)

Marren Eggers et al. Infect Diseases & Therapy 2015 Dec;4(4):491-501

What we Learned so far About: Patterns of Transmission

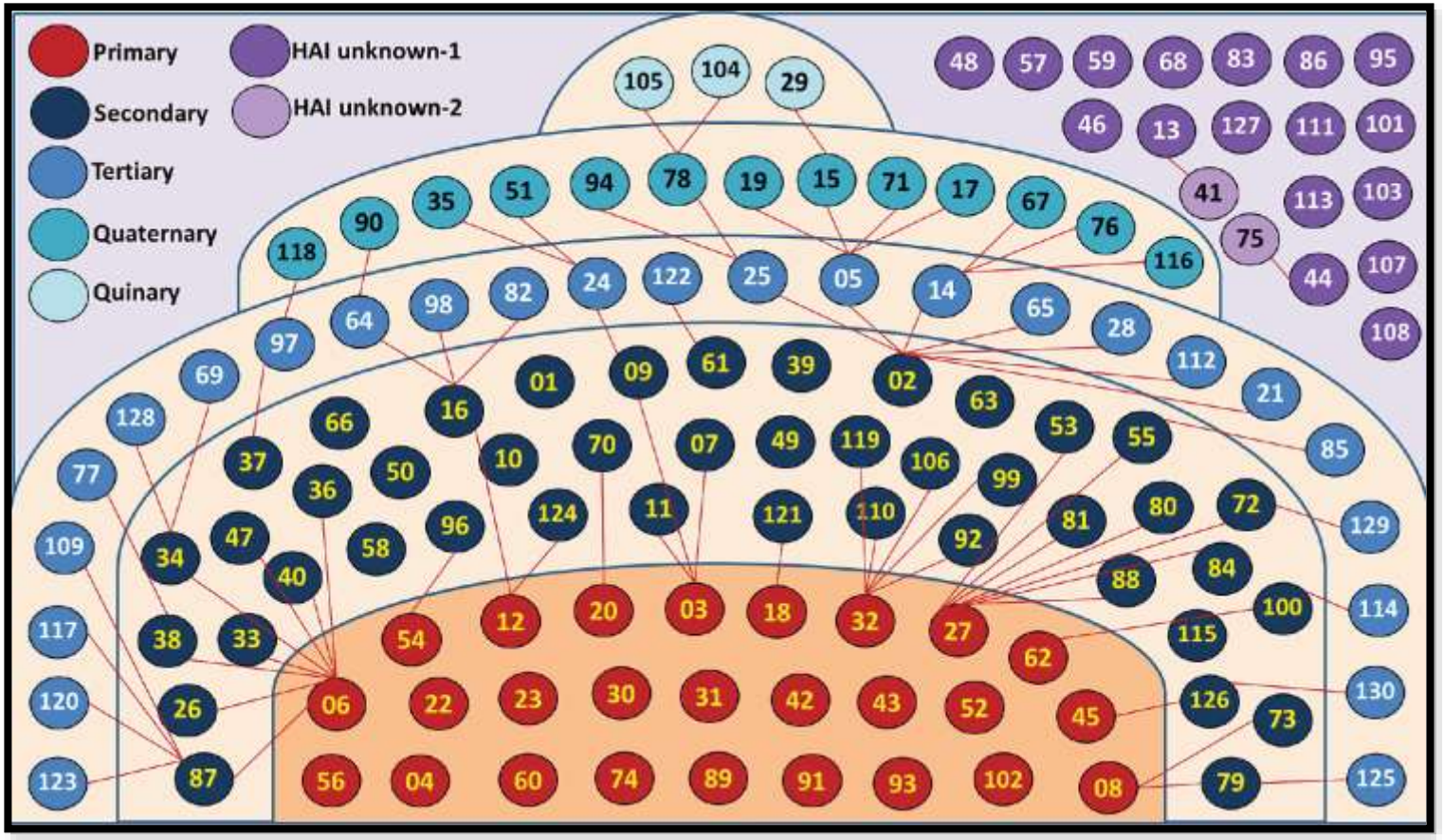
What we Learned so far About Patterns of Transmission

The virus behaves differently when compared to SARS with selective transmission, but to date 3 patterns exist:

- Sporadic community cases: with presumed non-human exposure
- Family clusters: contact with infected family members
- Health care acquired: between patients and from patient to health care workers

Risk of HCA Transmission & Superspreading Events in MERS

Identified Transmission Dynamics of MERS-CoV Infection During an Outbreak: Implications of an Overcrowded Emergency Department (N=130)



Thamer H. Alenazi, et al. Identified Transmission Dynamics of MERS-CoV Infection During an Outbreak: Implications of an Overcrowded Emergency Department. CID 2017:65 (15 August)

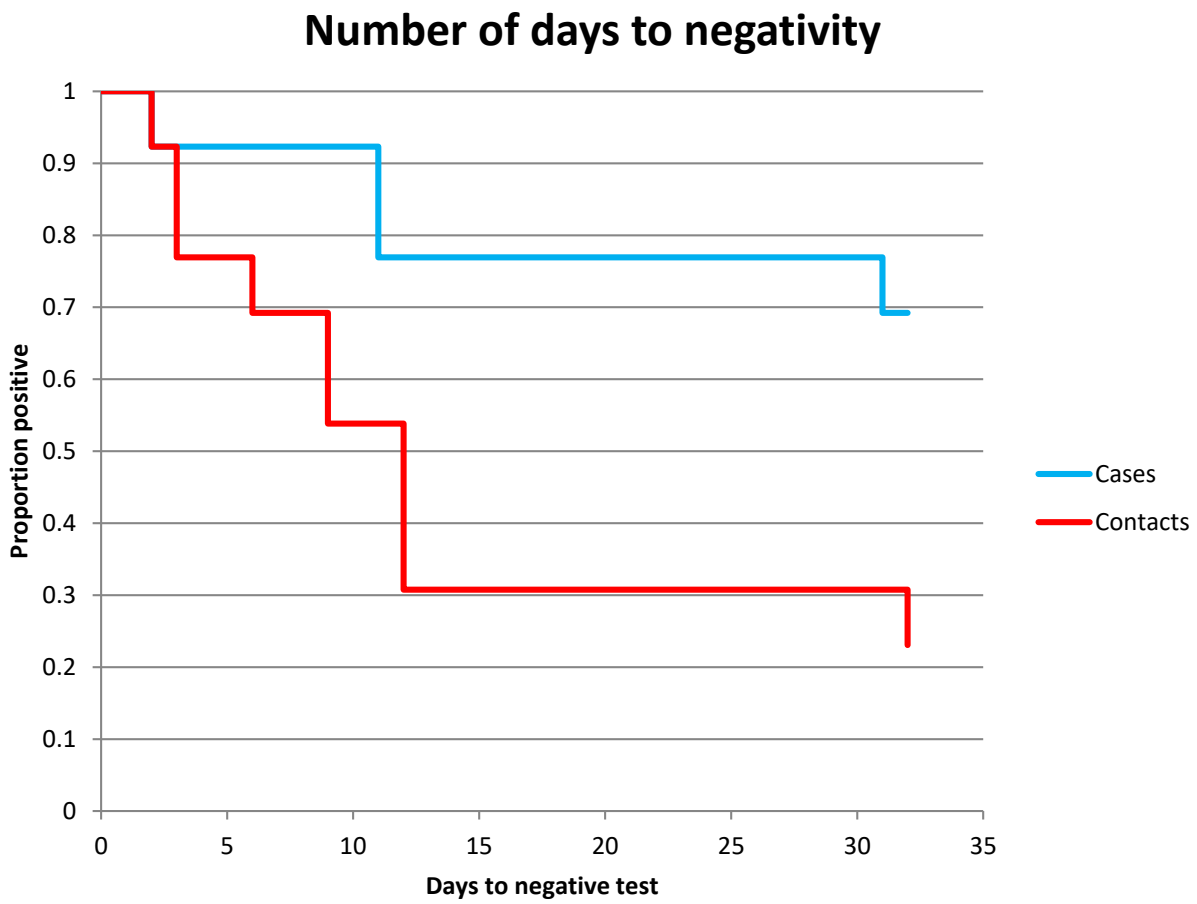
What we Learned so far About: HCA MERS Transmission & Effective IC Measures

Enhanced Infection Control Measures that were Effective in Controlling Nosocomial Outbreaks

- Hand hygiene, and droplet and contact precautions for febrile patients with a fever before testing these patients for MERS-CoV
- Putting surgical masks on all patients undergoing haemodialysis, and ensuring health-care workers wear N95 filtering facepiece respirators when managing any patient with a confirmed MERS-CoV infection who is undergoing an aerosol-generating procedure
- Patients with suspected MERS-CoV infection admitted to dialysis or intensive care units should be placed in isolation rooms with a portable dialysis machine
- Increasing environmental cleaning, and preventing non-essential staff and visitors from coming into contact with patients infected with MERS-CoV

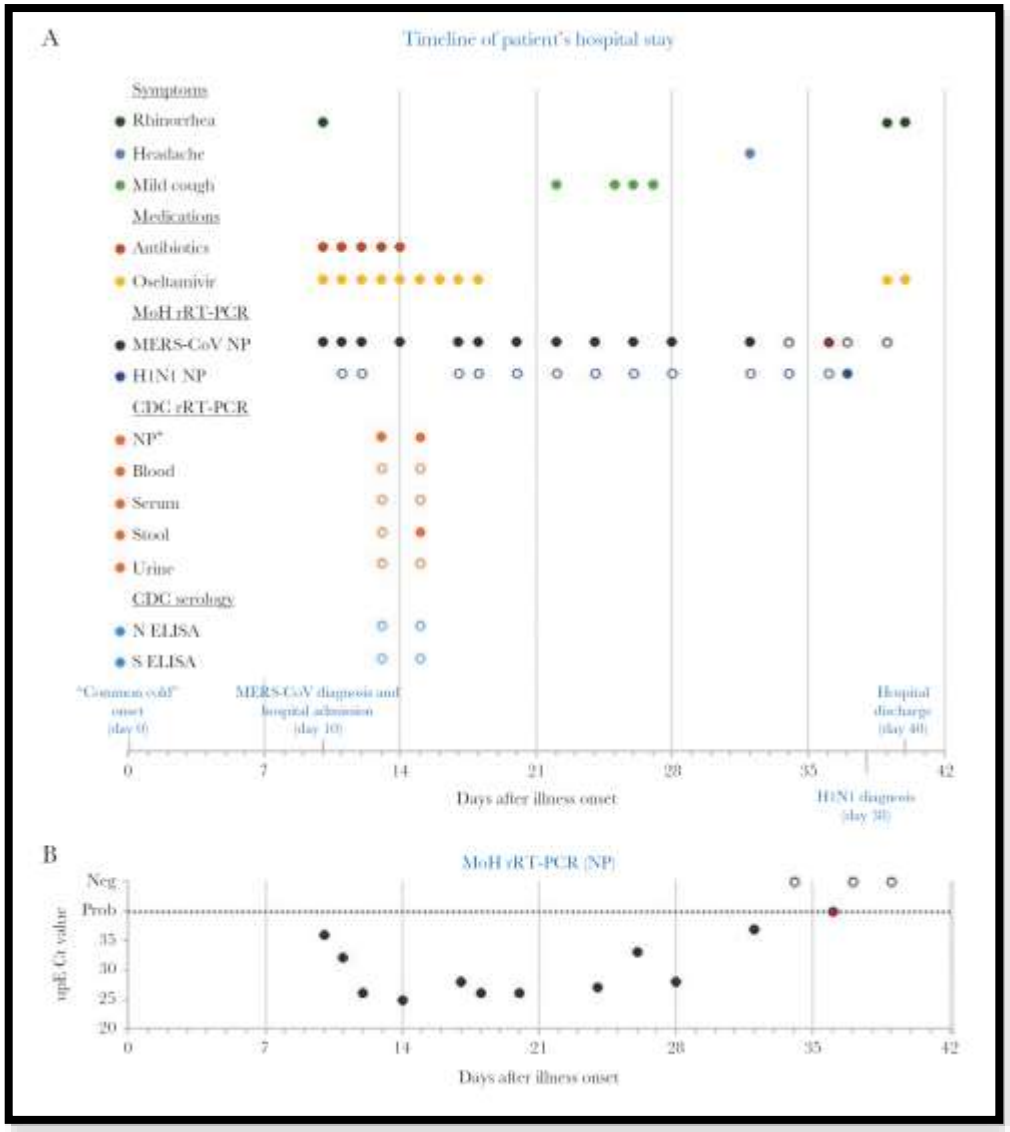
Hui DS, Azhar EI, Kim YJ, Memish ZA, Oh MD, Zumla A. Middle East respiratory syndrome coronavirus: risk factors and determinants of primary, household, and nosocomial transmission. Lancet Infect Dis. 2018 Aug;18(8):e217-e227

Time to Negative Test Curve in Cases and Contacts (26/20)



Memish ZA, et al. Middle East respiratory syndrome coronavirus (MERS-CoV) viral shedding in the respiratory tract: an observational analysis with infection control implications. International Journal of Infectious Diseases 29 (2014) 307–308

Infectious MERS-CoV Isolated From Mildly Ill Patient, Saudi Arabia



Hail M. Al-Abdely, et al. Infectious MERS-CoV Isolated From a Mildly Ill Patient, Saudi Arabia. OFID May 2018

American Journal of Infection Control 47 (2019) 290–293

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

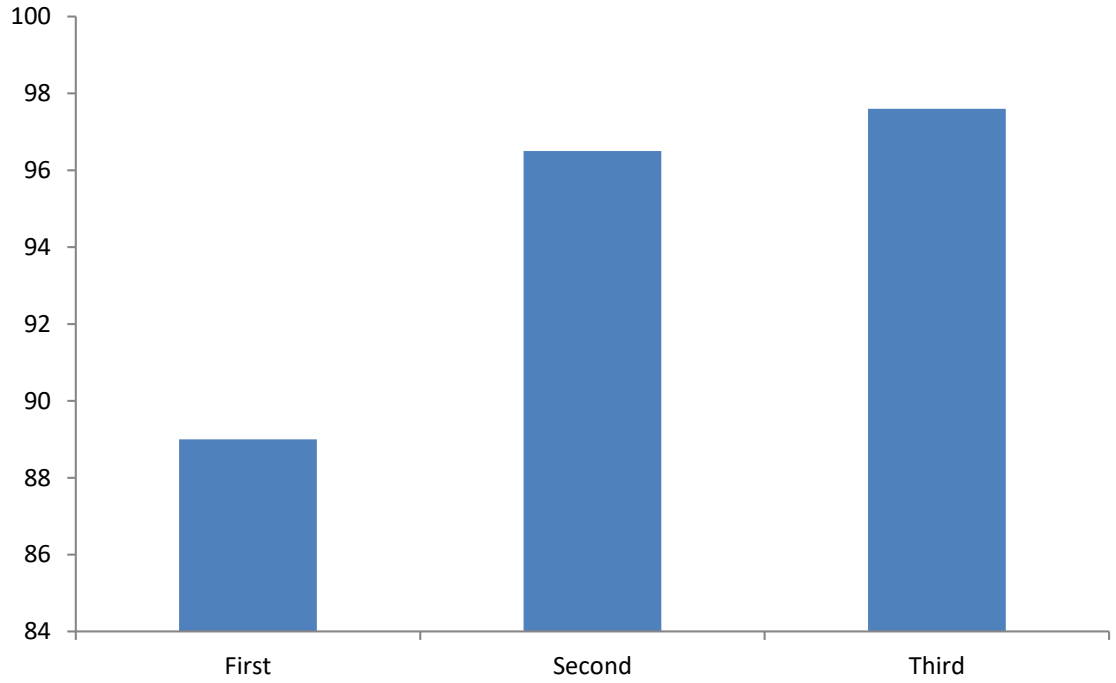
Major Article

Middle East respiratory syndrome coronavirus intermittent positive cases: Implications for infection control

Sarah H. Alfaraj MD [a,b], Jaffar A. Al-Tawfiq MD [c,d,e], Ziad A. Memish MD, FRCPC, FACP, FRCPE, FRCPL [f,g,h,*]

[a] Corona Center, Infectious Diseases Division, Department of Pediatrics, Prince Mohamed Bin Abdulaziz Hospital, Ministry of Health, Riyadh, Saudi Arabia
[b] University of British Columbia, Vancouver, BC, Canada
[c] Johns Hopkins Aramco Healthcare, Dhahran, Saudi Arabia
[d] Indiana University School of Medicine, Indianapolis, IN
[e] Johns Hopkins University School of Medicine, Baltimore, MD
[f] College of Medicine, Alfaisal University, Riyadh, Saudi Arabia
[g] Infectious Diseases Division, Department of Medicine, Prince Mohamed Bin Abdulaziz Hospital, Ministry of Health, Riyadh, Saudi Arabia
[h] Hubert Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, GA

Cumulative Positivity Rate of Nasopharyngeal Swabs



Alfaraj S, Memish ZA, et al. MERS-CoV intermittent positive cases: Implications for infection control. Am J Infect Control 2018 in press

Conclusions

Conclusion (1)

- MERS-CoV transmission pattern has been consistent with sporadic community cases leading to sizable health care facility outbreaks.
- Pattern of disease is wide and considerable asymptomatic/mild cases exist.
- Diagnosis still relies on rt-PCR & LRT samples and repeat sampling have much higher yield.
- The biggest challenge to identify MERS-CoV patients early.
- Need for improvement in infection control in HCF (early detection & proper isolation (Droplet & Contact).

Conclusion (2)

- HCWs continue to be at risk
- Urgent need for POC testing
- We need to apply the WHO updated guidance in quarantining HCWs exposed to index cases .
- A minimum of two samples are needed to exclude diagnosis in suspected patients and 2 samples are needed to clear positive cases from isolation.