Severe acute respiratory syndrome vs. the Middle East respiratory syndrome

David S. Hui[a], *Ziad A. Memish*[b], *and Alimuddin Zumla*[c,d]

Purpose of review
This review compares the clinical features, laboratory aspects and treatment options of severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS).

Recent findings
Bats are the natural reservoirs of SARS-like coronaviruses (CoVs) and are likely the reservoir of MERS coronavirus (MERS-CoV). Although a small number of camels have been found to have positive nasal swabs by real-time polymerase chain reaction and to carry antibody against MERS-CoV, the transmission route and the intermediary animal source remain uncertain amongst the sporadic primary cases. Both SARS-CoV and MERS-CoV may cause severe respiratory failure and extrapulmonary features such as diarrhoea, whereas mild or asymptomatic cases also occur in both conditions. In comparison with SARS, patients with MERS are older with male predominance, more comorbid illness and relatively lower human-to-human transmission potential. Although the viral kinetics of MERS-CoV remain unknown, nosocomial infections of MERS occur early within the first week of illness of the index case, whereas those of SARS occurred mainly in the second week of illness when the patient's upper airway viral load peaks on day 10 of illness. In-vitro data suggest that interferon (IFN) with or without ribavirin and mycophenolic acid may inhibit MERS-CoV, whereas protease inhibitors and IFN have inhibitory activity against SARS-CoV.

Summary
Although there are some similarities in the clinical features, MERS progresses to respiratory failure much more rapidly than SARS. The higher case fatality rate of MERS is likely related to older age and comorbid illness. More studies are needed to understand MERS-CoV in order to guide public health infection control measures and treatment.

Keywords
clinical features, MERS, MERS-CoV, pathogenesis, respiratory tract infections, SARS, treatment

INTRODUCTION

Severe acute respiratory syndrome (SARS) first emerged in 2012 in Guangdong, China, and spread globally through Hong Kong in 2003 [1,2]. In November 2002, an unusual epidemic of atypical pneumonia occurred in Foshan, Guangdong Province in China, with a high rate of nosocomial transmission to healthcare workers (HCWs) [3,4]. A retrospective analysis of 55 patients hospitalized with atypical pneumonia in Guangzhou between January and February 2003 revealed positive SARS coronavirus (CoV) in their nasopharyngeal aspirates (NPAs), while 48 (87%) patients had positive serology to SARS-CoV in their convalescent sera. Genetic analysis showed that the SARS-CoV isolates from Guangzhou shared the same origin with those in other countries, with a phylogenetic pathway that matched the spread of SARS to other parts of the world [5].

The Middle East respiratory syndrome CoV (MERS-CoV) was initially reported in September 2012 when a novel β CoV was isolated from a Saudi Arabian patient who died of severe pneumonia and multiorgan failure in June 2012 [6▪▪]. Retrospective

[a]Department of Medicine & Therapeutics, Stanley Ho Center for Emerging Infectious Diseases, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong, [b]Ministry of Health, Al-Faisal University, Riyadh, Kingdom of Saudi Arabia, [c]Division of Infection and Immunity, Department of Infection, Centre for Clinical Microbiology, University College London and [d]NIHR Biomedical Research Centre, University College London Hospitals, London, UK

Correspondence to David S. Hui, Department of Medicine & Therapeutics, Stanley Ho Center for Emerging Infectious Diseases, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, New Territories, Hong Kong. Tel: +852 2632 3128; fax: +852 2648 9957; e-mail: dschui@cuhk.edu.hk

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KEY POINTS

- Bats appear to be the common natural source of both SARS and MERS.
- The clinical features are similar, but MERS progresses to respiratory failure much more rapidly than SARS.
- Although the estimated pandemic potential of MERS-CoV is lower than that of SARS-CoV, the case fatality rate of MERS is much higher and likely related to older age and comorbid illness of the sporadic cases.
- More studies are needed to understand the pathogenesis, viral kinetics, mode of disease transmission, any intermediary source and treatment options of MERS in order to guide public health infection control measures and treatment.

analysis of a cluster of hospital cases dated back to April 2012 in Jordan confirmed MERS-CoV as the cause of the outbreak [7▪]. Globally, from September 2012 to early January 2014, WHO has been informed of 178 laboratory-confirmed cases of infection with MERS-CoV, with 75 deaths [8].

In this article, we compare and contrast the clinical and laboratory features, pathogenesis and potential treatment modalities of SARS and MERS.

THE VIRUS AND ITS ORIGIN

In February 2003, a novel CoV was confirmed to be the causative agent for SARS, thus referred to as SARS-CoV [9–12]. Retrospective serologic survey suggested that cross-species transmission of SARS-CoV or its variants from animal species to humans might have occurred frequently in the wet market, where a high seroprevalence was detected amongst asymptomatic animal handlers [13]. Masked palm civets were initially suspected to play a role in transmitting SARS-CoV to humans following the detection of a close variant of SARS-CoV from palm civets in Dongmen market, Shenzhen, in 2003 [14]. During the small-scale SARS outbreaks in late 2003 and early 2004, three of the four patients had direct or indirect contact with palm civets [15,16]. However, sequence analysis showed that the SARS-CoV-like virus had not been circulating amongst masked civets in markets for long. Coronaviruses highly similar to SARS-CoV were isolated in horseshoe bats in 2005 [17,18]. These bat SARS-like CoVs shared 88–92% sequence homology with human or civet isolates and the data suggest that bats could be a natural reservoir of a close ancestor of SARS-CoV [19].

In a study screening the faecal specimens of bats from Ghana and four European countries for β coronaviruses, viruses related to the novel human β CoV (EMC/2012 which was later renamed as MERS-CoV) were detected in 46 (24.9%) of 185 *Nycteris* bats and 40 (14.7%) of 272 *Pipistrellus* bats [20]. Out of 1100 bat samples tested in another study, one fragment of MERS-CoV was found in one *Taphozous* bat, with close matching to a human isolate of MERS-CoV [21▪]. Their genetic relatedness indicates that MERS-CoV has originated from bats. Camels from the Spanish Canary Islands, Oman and Egypt were found to have high neutralizing antibody levels against MERS-CoV, but no viral genetic material was detected in camel sera and faecal samples [22▪]. A study conducted in a Qatari farm has provided virological confirmation of an outbreak of MERS-CoV involving three camels and two humans. However, it is puzzling whether the people on the farm were infected by the camels or vice versa, or if another source was responsible [23▪▪].

On the basis of a variety of analytical tools with different statistical assumptions, whole-genome sequences and individual genes derived from human infections at different timepoints, the data suggest the emergence of MERS-CoV in mid-2011, with the possible dates ranging broadly from November 2009 to April 2012 [24▪▪].

EPIDEMIOLOGY

A 64-year-old nephrologist who came from southern China to Hong Kong on 21 February 2003 was the index case causing subsequent outbreaks of SARS in Hong Kong and many other countries [1,2,25,26]. At least 16 hotel guests and visitors were infected by the physician whilst they were staying or visiting friends on the same floor of the hotel M, where the physician had stayed. Through international air travel, these visitors spread the infection to 29 countries and regions with a total of 8098 cases and a mortality rate of 774 (9.6%) by the end of the epidemic in July 2003 [27].

SARS appears to have spread by close person-to-person contact via droplet transmission or contact with fomite [28]. The high infectivity of SARS was reflected by the super-spreading event at the Prince of Wales Hospital (PWH) in Hong Kong, where 138 individuals (many of whom were HCWs and previously healthy) were infected within 2 weeks following exposure to one single patient (a visitor of hotel M), who was hospitalized with community-acquired pneumonia to a general medical ward [1,29]. This super-spreading event was likely caused by several factors, including the use of a jet nebulizer for delivering bronchodilator to the index case, overcrowding and poor ventilation in

the hospital ward [1,30]. SARS-CoV was also detected in the respiratory secretions, faeces, urine and tears of infected individuals [30].

In addition, SARS might have spread by opportunistic airborne transmission in a major community outbreak in a private residential complex, Amoy Gardens, in Hong Kong [31,32]. On the basis of the analysis of all confirmed cases, airborne spread was the most likely explanation in the Amoy Gardens outbreak, and the SARS-CoV could have spread over 200 m to nearby residential complexes [33▪▪]. Air samples obtained from a room occupied by a SARS patient and swab samples taken from frequently touched surfaces in rooms and in a nurses' station in Toronto were positive by PCR testing [34]. In addition, the temporal–spatial spread of SARS amongst inpatients in the index medical ward of the PWH in Hong Kong was consistent with airborne transmission [35].

All the cases of MERS confirmed so far have had a direct or indirect link with the Middle East [8]. Since its first discovery in September 2012, the relatively small number of MERS cases with very limited global spread outside the Middle East countries highlights the very low human-to-human transmissibility of MERS-CoV, in contrast to SARS-CoV. The transmission mode of the primary and sporadic cases of MERS is unknown, although it is suspected that contact with an intermediary animal or contaminated source other than bats is involved. Overall, the median age of MERS-CoV patients was 50 years (range 14 months to 94 years), while the majority of patients were men (Table 1). Most patients experienced severe respiratory disease, while 30% had less severe disease, including 18 asymptomatic cases [36▪▪].

In contrast to SARS, about 75% of patients with MERS had at least one comorbid illness, and fatal cases were more likely to have an underlying condition (86% amongst fatal cases vs. 42% amongst recovered or asymptomatic cases, $P < 0.001$). Index and sporadic cases were older (median age 59 vs. 43 years, $P < 0.001$) and more likely to suffer from severe disease requiring hospitalization (94 vs. 59%, $P < 0.001$) in comparison with the secondary cases. Cases specifically reported as 'mild disease' or 'asymptomatic' occurred only amongst secondary cases [36▪▪]. Most (90%) of the index and sporadic cases had severe disease, while a higher proportion of patients with renal failure was noted amongst secondary cases, because of the nosocomial outbreak involving the haemodialysis units in hospitals in Al Hasa [37▪▪]. Amongst the secondary cases of MERS, 13 cases appear to have been infected in household settings, 60 in healthcare settings (HCS), with one in another workplace. The specific routes of exposure leading to transmission are unknown [36▪▪].

A minority of confirmed and probable cases of MERS have information related to exposure to animals. Amongst these, index and sporadic cases reported exposure to animals more often than secondary cases (17.9 vs. 9.5%, respectively). Direct contact with camels in the 10 days before symptom onset was reported in 80% (4 of 5) of index and sporadic cases vs. 50% (1 of 2) of secondary cases [36▪▪].

Transmission to close contacts amongst clusters outside the Middle East has been limited, and secondary attack rates amongst the family members of patients in other clusters appear rather low. Good infection control measures in reported clusters involving HCS probably limited onward transmission to HCWs and hospitalized patients [36▪▪].

Few HCWs infected by exposure to patients with MERS had underlying comorbid illness, whereas the majority had mild disease. Nevertheless, three died, while 32.1% experienced severe disease. In contrast, amongst 19 patients who were initially hospitalized for other conditions but acquired noscomial MERS-CoV infection in HCS, all had underlying conditions and developed severe disease, and 17 (89.5%) died [36▪▪].

CLINICAL FEATURES

The estimated mean incubation period of SARS was 4.6 days [95% confidence interval (CI) 3.8–5.8 days], while the mean time from symptom onset to hospitalization varied between 2 and 8 days, decreasing over the course of the epidemic. The mean time from onset to death was 23.7 days (95% CI 22.0–25.3 days) [40].

As the exposure leading to sporadic infection of MERS is unknown, it is impossible to estimate the incubation period in the primary cases. However, based on the data related to human-to-human transmission in several clusters, the incubation period has been estimated to be over 5 days, but could be as long as 2 weeks (median 5.2 days [95% CI 1.9–14.7]) [37▪▪]. The median times from symptom onset of MERS to hospitalization, admission to an ICU or to death were 4.0 (range 0–16, $n = 62$), 5.0 (range 1–15, $n = 35$) and 11.5 days (range 4–298, $n = 40$), respectively [36▪▪].

The major clinical features of SARS on presentation include persistent fever, chills/rigor, myalgia, dry cough, headache, malaise and dyspnoea. Sputum production, sore throat, coryza, nausea and vomiting, dizziness and diarrhoea were less common [1,2,25,26] (Table 1). Watery diarrhoea

Table 1. Comparison of demographic, clinical and laboratory features between MERS-CoV and SARS-CoV outbreaks

	MERS-CoV [8,36▪▪–39▪▪]	SARS-CoV [1,28,40]
Date of first case report (place)	April 2012 (Jordan) June 2012 (first KSA case)	November 2002 (China)
Incubation period	Mean: 5.2 days (95% CI: 1.9–14.7) Range: 2–13 days	Mean: 4.6 days (95% CI: 3.8–5.8) Range: 2–14 days
Serial interval	7.6 Days	8.4 Days
Age group		
Adults	Adults (98%)	Adults (93%)
Children	Children (2%)	Children (5–7%)
Age (years): range, median	Range: 1–94; median: 50	Range: 1–91; mean: 39.9
Mortality		
Case fatality rate (CFR)–overall	41.8%	9.6%
CFR in patients with comorbidities	13.3%	1–2%
Time from onset to death	Median 11.5 days	Mean 23.7days
Sex (M, F)	M: 64.5%, F: 35.5%	M: 43%, F: 57%
Presenting symptoms		
Fever >38°C	98%	99–100%
Chills/rigors	87%	15–73%
Cough	83%	62–100%
Dry	56%	29–75%
Productive	44%	4–29%
Haemoptysis	17%	0–1%
Headache	11%	20–56%
Myalgia	32%	45–61%
Malaise	38%	31–45%
Shortness of breath	72%	40–42%
Nausea	21%	20–35%
Vomiting	21%	20–35%
Diarrhoea	26%	20–25%
Sore throat	14%	13–25%
Rhinorrhoea	6%	2–24%
Comorbidities	76%	10–30%
Diabetes	10%	24%
Chronic renal disease	13%	2–6%
Chronic heart disease	7.5%	10%
Malignancy	2%	3%
Hypertension	34%	19%
Obesity	17%	N/A
Smoking	23%	17%
Viral hepatitis	Not known	27%
Laboratory results		
CXR abnormalities	100%	94–100%
Leukopenia ($<4.0 \times 10^9$/l)	14%	25–35%
Lymphopenia ($<1.5 \times 10^9$/l)	32%	68–85%
Thrombocytopenia ($<140 \times 10^9$/l)	36%	40–45%
Elevated LDH	48%	50–71%
Elevated ALT	11%	20–30%
Elevated AST	14%	20–30%
Ventilatory support required	80%	14–20%

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; CXR, chest X-ray; KSA, Kingdom of Saudi Arabia; LDH, lactate dehydrogenase; MERS-CoV; Middle East respiratory syndrome coronavirus; SARS-CoV, severe acute respiratory syndrome coronavirus.

became prominent in 40–70% of patients with SARS 1 week down the clinical course of the illness [9,41]. SARS-CoV was detected in the cerebrospinal fluid and serum samples of two cases with status epilepticus [42,43]. Elderly patients with SARS might present with decrease in general condition, poor feeding, fall or fracture [44] and delirium, without the typical febrile response. In contrast, young children (<12 years of age) often ran a benign clinical course, whereas teenagers tended to have a clinical course similar to those of adults [45]. There was no reported fatality in young children and teenage patients [45], but SARS in pregnancy carried a significant risk of mortality [46]. A meta-analysis has shown overall seroprevalence rates of 0.1% for the general population and 0.23% for HCWs, although the true incidence of asymptomatic infection remains unknown [47].

The clinical course of SARS generally followed a typical pattern [1,48–50]: phase 1 (viral replication) was associated with increasing viral load and characterized by fever, myalgia and other systemic symptoms that generally improved after a few days; phase 2 (immunopathological injury) was characterized by recurrence of fever, hypoxaemia and radiological progression of pneumonia with falls in viral load, with about 20% of patients progressing into acute respiratory distress syndrome (ARDS) necessitating invasive ventilatory support [1,49]. As there was progressive decrease in the rates of viral shedding from nasopharynx, stool and urine from day 10 to day 21 after symptom onset, clinical worsening during phase 2 was likely the result of immune-mediated lung injury because of an over-exuberant host response [50].

The clinical presentation of MERS-CoV infection ranges from asymptomatic to very severe pneumonia with ARDS, septic shock and multiorgan failure resulting in death. In contrast to SARS, the clinical course of MERS is more severe in immunocompromised patients and generally mild in individuals without comorbid illness [36▪▪]. Few cases have been reported in children less than 5 years of age. Typically, MERS begins with fever, cough, chills, sore throat, myalgia and arthralgia, followed by dyspnoea and rapid progression to pneumonia within the first week (in contrast to SARS), often requiring ventilatory and other organ support [7▪,36▪▪–38▪▪]. Most patients have presented with respiratory illness; however, one immunocompromised patient in France was initially hospitalized with fever, chills and diarrhoea and later developed pneumonia because of MERS-CoV [51]. At least one-third of patients also had gastrointestinal symptoms, such as vomiting and diarrhoea [7▪, 36▪▪–39▪▪,51].

LABORATORY FEATURES

Lymphopenia, disseminated intravascular coagulation, elevated lactate dehydrogenase and creatinine kinase were the common laboratory features of SARS [1,52,53]. The CD4 and CD8 T lymphocyte counts fell early in the course of SARS, and low counts of CD4 and CD8 at presentation were associated with adverse clinical outcome [54].

Similar to SARS and other severe viral illness, common laboratory findings of MERS include leucopoenia, particularly lymphopenia [6▪▪,7▪,39▪▪,51]. Reports from several cases found viral RNA in blood, urine and stool, but at much lower viral loads than in the respiratory tract [51,55▪]. The viral load in the upper respiratory tract specimens is generally lower than in the lower respiratory specimens. There were some cases with a consumptive coagulopathy [36▪▪]. Co-infection with other respiratory viruses (e.g. parainfluenza, rhinovirus, influenza A(H1N1)pdm09, herpes simplex, and influenza B) has been reported, whereas nosocomial bacterial infections (including *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Acinetobacter* spp., and *Candida* spp.) occurred in patients receiving invasive mechanical ventilation [6▪▪,36▪▪,55▪].

RADIOLOGICAL FEATURES

Common radiographic features of SARS included the predominant involvement of lung periphery and the lower zone in addition to absence of cavitation, hilar lymphadenopathy or pleural effusion [1,56]. Radiographic progression from unilateral focal air-space opacity to either multifocal or bilateral involvement occurred during the second phase of the disease, followed by radiographic improvement with treatment [1,52,56]. In a case series, 12% of patients developed spontaneous pneumomediastinum, whereas 20% of patients developed ARDS over a period of 3 weeks [50]. Common HRCT features included ground-glass opacification (GGO), sometimes with consolidation, and interlobular septal and intralobular interstitial thickening, with predominantly a peripheral and lower lobe involvement [56].

Radiographic findings of MERS are consistent with viral pneumonitis and ARDS, with bilateral hilar infiltration, unilateral or bilateral patchy densities or infiltrates, segmented or lobar opacities, GGO and small pleural effusions in some cases. Lower lobes are affected more than upper lobes early in the course of illness with more rapid radiographic progression than SARS [1,6▪▪,52,56]. Chest computed tomography scans have shown interstitial infiltrates and consolidation compatible with ARDS in severe cases [36▪▪].

PATHOGENESIS

The route of entry for SARS-CoV in humans was through the respiratory tract mainly by droplet transmission. Although human intestinal cells were proven to be susceptible to SARS-CoV replication, the role of the intestinal tract as a portal of entry remains uncertain [57]. The surface envelop spike protein (S protein) of SARS-CoV plays an important role in establishing infection and determining the cell and tissue tropism. Entry of the virus requires receptor binding, followed by conformational change of the S protein, and then cathepsin L-mediated proteolysis within the endosome [58]. The angiotensin-converting enzyme 2 (ACE2) is the host receptor mediating the entry of SARS-CoV [59] and is expressed on a wide variety of body tissues. The presence of ACE2 may not be the sole determinant for tropism of SARS-CoV. SARS-CoV was found in colonic enterocytes and hepatocytes that lacked ACE2, whereas SARS-CoV was not detected in the endothelial cells of blood vessels and smooth muscle cells of intestine despite their expression of ACE2 [41,60].

Several mechanisms of direct injury in infected lungs with SARS have been revealed. Firstly, ACE2 probably contributes to the diffuse alveolar damage (DAD). ACE2 is a negative regulator of the local renin–angiotensin system and data from animal study support that the DAD seen in SARS is mediated by S protein–ACE2–renin–angiotensin pathway [61]. In addition, the SARS-CoV-encoded 3a and 7a proteins were shown to be strong inducers of apoptosis in cell lines derived from different organs, including lungs, kidneys and liver [62,63].

The dipeptidyl peptidase 4 (DPP4, also known as CD26) has been identified as the functional cellular receptor for MERS-CoV [64▪▪,65]. DPP4 homologues permitting MERS-CoV infection are present in a variety of cell lines [66,67]. Cell-based studies have revealed that MERS-CoV evades innate immune response and this may explain the large number of severe cases [68▪,69▪,70]. However, MERS-CoV was noted to have higher sensitivity to pegylated interferon (IFN) treatment than SARS-CoV [68▪]. This may be because of the lack of a SARS-CoV ORF6 homologue in MERS-CoV, which can inhibit the nuclear translocation of p-STAT1 and activation of downstream antiviral genes [71,72]. MERS-CoV can induce a more severe dysregulation of the host cellular transcriptome and more rapidly after infection than SARS-CoV, resulting in profound apoptosis of surrounding cells, through greater suppression of the antigen presentation pathway than SARS-CoV [70,73,74].

TREATMENT OF SEVERE ACUTE RESPIRATORY SYNDROME

Ribavirin, a nucleoside analogue, was widely used for treating SARS patients in 2003, but ribavirin alone had no significant in-vitro activity against SARS-CoV [75] and it caused significant haemolysis in many patients [1,26,52].

Lopinavir and ritonavir in combination is a boosted protease inhibitor regimen widely used for the treatment of human immunodeficiency virus infection. In-vitro activity against SARS-CoV was demonstrated for lopinavir and ribavirin at 4 and 50 μg/ml, respectively, whereas inhibition of in-vitro cytopathic effects was achieved down to a concentration of 1 μg/ml of lopinavir combined with 6.25 μg/ml of ribavirin [76]. A retrospective analysis showed that the addition of lopinavir 400 mg and ritonavir 100 mg (LPV/r) as initial therapy was associated with lower overall death rate (2.3 vs. 15.6%) and intubation rate (0 vs. 11%) than a matched historical cohort that received ribavirin alone as the initial antiviral therapy [77]. However, the outcome of a subgroup that had received LPV/r as late rescue therapy after receiving pulsed methylprednisolone for worsening respiratory symptoms was not better than the matched cohort [76,77].

Type I IFNs are produced early as part of the innate immune response to virus infections. There are in-vitro and limited animal and observational data that IFN, particularly early use, has efficacy against SARS-CoV [75,78,79]. In experimentally infected cynomolgus macaques, prophylactic treatment with pegylated IFN-α significantly reduced viral replication and excretion, viral antigen expression by type 1 pneumocytes and lung damage, vs. untreated macaques, whereas postexposure treatment with pegylated IFN-α yielded intermediate results [80]. Use of IFN-α1 and systemic corticosteroids was associated with improved oxygen saturation, more rapid resolution of radiographic lung opacities and lower levels of creatine phosphokinase than systemic corticosteroids alone in an uncontrolled study of SARS patients [81].

During the second week of SARS illness, there was evidence of bronchiolitis obliterans organizing pneumonia (BOOP) radiologically [1,52], and histopathologically in some cases [82], while the progression of the pulmonary disease was mediated by the host inflammatory response [50]. Systemic corticosteroids significantly reduced interleukin-8 (IL-8), monocyte chemoattractant protein-1 (MCP-1) and IFN-γ inducible protein-10 (IP-10) concentrations from 5 to 8 days after treatment in 20 adult SARS patients at PWH in an uncontrolled study [83]. Induction of IP-10 is thought to be a

critical event in the initiation of immune-mediated lung injury and lymphocyte apoptosis [84]. The use of rescue pulsed methylprednisolone during clinical progression was associated with favourable clinical improvement in some patients, with resolution of fever and radiographic lung opacities within 2 weeks [1,52,85]. However, a retrospective analysis showed that the use of pulsed methylprednisolone was associated with an increased risk of 30-day mortality (adjusted odds ratio 26.0, 95% CI 4.4–154.8) [86]. In addition, disseminated fungal disease and avascular osteonecrosis occurred following prolonged systemic corticosteroids therapy [87,88]. A randomized placebo-controlled study showed that plasma SARS-CoV RNA concentrations in the second and third weeks of illness were higher in patients given initial hydrocortisone ($n = 10$) than those given normal saline as control ($n = 7$) during the early clinical course of illness. Despite the small sample size, the data suggest that pulsed methylprednisolone given in the earlier phase might prolong viraemia [89].

Convalescent plasma, donated by patients including HCWs at PWH who had recovered from SARS, contained high levels of neutralizing antibody and appeared clinically useful for treating other SARS patients. Amongst 80 nonrandomized patients with SARS who were given convalescent plasma at PWH, the discharge rate at day 22 was 58.3% for patients ($n = 48$) treated within 14 days of illness onset vs. 15.6% for those ($n = 32$) treated beyond 14 days [90].

TREATMENT OF MIDDLE EAST RESPIRATORY SYNDROME

In the absence of specific antiviral therapy and lack of knowledge of viral kinetics, clinical management of MERS largely depends on supportive treatment and prevention of complications. Lung-protective ventilatory strategies for ARDS, inotropic support, antimicrobial therapy for co-infections and renal replacement therapy for acute renal failure have been used [6▪▪,36▪▪,38▪▪,51]. Some patients with severe disease have been treated with systemic corticosteroids, but unsuccessfully [36▪▪]. Several agents have shown inhibitory effects against MERS-CoV in cell cultures, including IFNs, ribavirin, cyclosporin A and mycophenolic acid [68▪,69▪,73,91▪]. A combination of IFNα2b and ribavirin appears to have beneficial effects in reducing lung injury and inflammation when given to rhesus macaques within 8 h of inoculation with MERS-CoV [92▪▪]. This treatment combination was given to several severely ill patients with unfortunately fatal outcome, likely because of late administration [93]. Currently, there are insufficient clinical data supporting the routine use of these agents, and randomized controlled trials are needed if supported by favourable response in animal models. Convalescent plasma to be donated by patients who have fully recovered from MERS-CoV infection would be a good treatment option.

CONCLUSION

Bats appear to be the common natural source of both SARS and MERS. The clinical features are similar, but MERS progresses to respiratory failure much more rapidly than SARS. Although the estimated pandemic potential of MERS-CoV is lower than that of SARS-CoV [94], the case fatality rate of MERS is much higher and likely related to older age and comorbid illness of the sporadic cases. Lots of knowledge gaps remain since the first discovery of MERS-CoV in 2012 [36▪▪,95]. More studies are needed to understand the pathogenesis, viral kinetics, mode of disease transmission and the intermediary source of MERS in order to guide public health infection control measures and treatment.

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Conflicts of interest

There are no conflicts of interest.

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