

Editorial

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The novel coronavirus (2019-nCoV) outbreak: think the unthinkable and be prepared to face the challenge

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A new and threatening viral outbreak, originating from the Chinese city of Wuhan, has been declared. According to the most recent updates of the World Health Organization (WHO), this outbreak – sustained by a newly identified strand of coronavirus – has already been confirmed in 581 patients in six different countries, causing 95 critically ill cases and 17 deaths, as of January 23, 2020, and with number of contagion events (and deaths) rapidly escalating [1]. A first case has been announced by the Centers for Disease Control and Prevention (CDC) in the United States, on January 21, 2020 [2]. The responsible pathogen has been isolated on January 7, 2020, and has been temporarily named 2019 novel coronavirus (2019-nCoV). The identification of this specific microorganism follows that of two similar viruses, causing quite similar epidemics, i.e. the severe acute respiratory syndrome (SARS-CoV) in 2002 and the Middle East respiratory syndrome (MERS-CoV) in 2012. Overall, the former condition has involved 8437 people, causing as many as 813 SARS-CoV-associated deaths in 32 different countries, whilst 2494 laboratory-confirmed cases of infection with MERS-CoV have been identified so far, leading to 858 deaths in 27 different countries [3, 4] (Table 1). There are some major and most obvious similarities among these three outbreaks, encompassing the virus (i.e. all three belong to the Coronavirus family), the narrow geographical origin (i.e. Middle East and China), as well as the biological and clinical characteristics of human involvement (Table 1). Regarding the former aspect, all these conditions can be classified as zoonoses (i.e. diseases caused by microorganisms spreading from animals to humans). As concerns the clinical manifestations, although more accurate information would be needed to precisely portend the 2019-nCoV epidemic (the outbreak has apparently originated from a fish and wild animal market in Wuhan, China, traceable to snake origin), clinical symptoms and complications seem nearly overlapping among the three syndromes, as one would expect from diseases caused by viruses belonging

to the same family [5]. Another important analogy is the capability of these viruses to spread from person to person, thus producing secondary cases among nearby contacts, including relatives and healthcare operators [6].

Coronaviruses encompass a large family of single-strand, positive-sense RNA viruses, with a ~26–32 kilobase genome, which usually causes mild disease, mostly mimicking influenza, though some specific strains (such as SARS-CoV, MERS-CoV and 2019-nCoV) may be associated with a more severe pathology, which can then evolve toward severe acute respiratory distress syndrome and death [7, 8]. Looking at the recent epidemiology of these outbreaks, what emerges clearly is that nearly 10 years have passed between SARS and MERS, whilst the period between MERS and 2019-nCoV epidemics is limited to approximately 7 years. Although it would be inappropriate to draw definitive conclusions from this limited evidence, the 3-year shorter period characterizing the origin of MERS-CoV and 2019-nCoV outbreaks would lead to speculate that the frequency of appearance of novel and divergent coronavirus outbreaks in humans is narrowing, thus leading the way to some important reflections.

The first important consideration concerns the causes of the relatively frequent recombination events occurring in coronaviruses. Some theories have been elaborated on this matter. Coronaviruses are characterized by a moderate-to-high mutation rate compared to other single-stranded RNA viruses (i.e. average substitution rate: $\sim 10^{-4}$ substitutions per year per site) [8]. Despite the precise genetic recombination mechanisms remaining almost unclear, template switching leading to homologous recombination in similar genes from different lineages of coronaviruses or other viruses has been proposed, a process that is probably amplified in these microorganisms by their large circulation in multiple animal reservoirs [8]. Notably, climate has a considerable impact on most living organisms, including viruses [9]. The recently developing climate changes may hence press the viruses to adapt dynamic responses to a changing environment, inducing natural adaptation, and ultimately promoting

Table 1: Main characteristics of severe acute respiratory syndrome (SARS-CoV), Middle East respiratory syndrome (MERS-CoV) and new 2019 coronavirus (2019-nCoV) outbreaks.

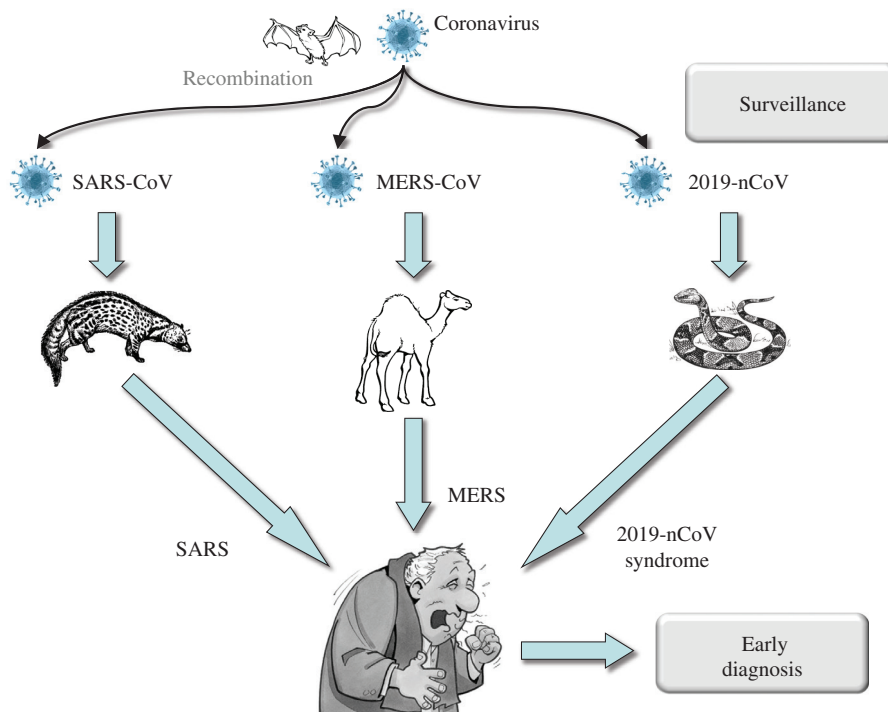
Characteristics	SARS-CoV	MERS-CoV	2019-nCoV
Pathogen	Coronavirus	Coronavirus	Coronavirus
Period	2002–2004	2012–	2019–
Likely origin	China	Middle East	China
Vector	Bats, civet cats	Dromedary camels	Snakes
Human-to-human transmission	Yes	Yes	Likely
Laboratory-confirmed cases ^a	8437	2494	278
Deaths ^a	813	858	6
Incubation	2–10 days	2–14 days	2–14 days
Symptoms	Fever, malaise, myalgia, headache, diarrhea, shivering, cough, shortness of breath	Fever, myalgia, diarrhea, cough, shortness of breath	Fever, myalgia, cough, shortness of breath
Major complications	Pneumonia, severe acute respiratory distress syndrome, death	Pneumonia, severe acute respiratory distress syndrome, death	Pneumonia, severe acute respiratory distress syndrome, death

^aLast WHO update: 21 January, 2020.

the generation of new and potentially virulent strands. Another, less credible – but worthwhile mentioning – theory involves genetic engineering, for either clinical or unfair purposes [10]. A deliberate release of SARS-CoV [11] and MERS-CoV [12] has been hypothesized as a possible cause of these two recent viral outbreaks, whereby some inconsistencies have been found in the epidemiology of SARS and MERS, more strictly fitting sporadic

than epidemic patterns. This evidence would persuade us to report here Julia Rosen’s thought, that “thinking the unthinkable” may be occasionally reasonable when facing some unpredictable and unexpected natural hazards [13].

Irrespective of the underlying nature of these three recent coronavirus outbreaks, the most reasonable steps for preventing and/or mitigating the unfavorable consequences of viral epidemics (or pandemics) on mankind

**Figure 1:** Natural history and management of recent coronavirus outbreaks in humans.

CoV, coronavirus; SARS, severe acute respiratory syndrome; MERS, Middle East respiratory syndrome; 2019-nCoV, new 2019 coronavirus.

entail the development of active surveillance programs, coupled with laboratory preparedness to face new environmental and biological challenges (Figure 1) [14, 15]. In case of serious biohazards, such as viral outbreaks, laboratory medicine plays a pivotal role in rapid and accurate identification of new microorganisms by means of molecular diagnostic assays [16], which represent a cornerstone in diagnostic virology [17]. This would hence entail widespread diffusion of molecular epidemiology, specifically aimed at detecting new viral strands in animal reservoirs, such as bats for most of the virulent mammalian coronaviruses [18], as well as the introduction of molecular diagnostic techniques in reference medical laboratories, which would thus enable rapid identification, isolation and treatment of affected cases (Figure 1). This demonstrates, once more, that laboratory medicine is integral to most care pathways [19], and will perhaps remain so for many years to come.

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References

- World Health Organization. Disease outbreak news. Available at: <https://www.who.int/csr/don/en/>.
- Centers for Disease Control and Prevention. Situation summary. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/index.html>.
- World Health Organization. Middle East respiratory syndrome coronavirus (MERS-CoV). Available at: <https://www.who.int/emergencies/mers-cov/en/>.
- World Health Organization. Severe acute respiratory syndrome (SARS). Available at: https://www.who.int/csr/don/archive/disease/severe_acute_respiratory_syndrome/en/.
- Hui DS, I Azhar E, Madani TA, Ntoumi F, Kock R, Dar O, et al. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health – The latest 2019 novel coronavirus outbreak in Wuhan, China. *Int J Infect Dis* 2020;91:264–6.
- To KK, Hung IF, Chan JF, Yuen KY. From SARS coronavirus to novel animal and human coronaviruses. *J Thorac Dis* 2013;5(Suppl 2):S103–8.
- Geller C, Varbanov M, Duval RE. Human coronaviruses: insights into environmental resistance and its influence on the development of new antiseptic strategies. *Viruses* 2012;4:3044–68.
- Su S, Wong G, Shi W, Liu J, Lai AC, Zhou J, et al. Epidemiology, genetic recombination, and pathogenesis of coronaviruses. *Trends Microbiol* 2016;24:490–502.
- Caminade C, McIntyre KM, Jones AE. Impact of recent and future climate change on vector-borne diseases. *Ann NY Acad Sci* 2019;1436:157–73.
- van Aken J, Hammond E. Genetic engineering and biological weapons. New technologies, desires and threats from biological research. *EMBO Rep* 2003;4 Spec No:S57–60.
- Weber SG, Bottei E, Cook R, O'Connor M. SARS, emerging infections, and bioterrorism preparedness. *Lancet Infect Dis* 2004;4:483–4.
- MacIntyre CR. The discrepant epidemiology of Middle East respiratory syndrome coronavirus (MERS-CoV). *Environ Syst Decis* 2014;34:383–90.
- Rosen J. Thinking the unthinkable. *Science* 2016;353:232–7.
- Lippi G, Favaloro EJ, Plebani M. Laboratory medicine and natural disasters: are we ready for the challenge? *Clin Chem Lab Med* 2010;48:573–5.
- Lippi G, Mattiuzzi C, Plebani M. Laboratory preparedness to face infectious outbreaks. Ebola and beyond. *Clin Chem Lab Med* 2014;52:1681–4.
- Song Z, Xu Y, Bao L, Zhang L, Yu P, Qu Y, et al. From SARS to MERS, thrusting coronaviruses into the spotlight. *Viruses* 2019;11. pii: E59. doi: 10.3390/v11010059.
- Parreira R. Laboratory methods in molecular epidemiology: viral infections. *Microbiol Spectr* 2018;6. doi: 10.1128/microbiolspec.AME-0003-2018.
- Smith I, Wang LF. Bats and their virome: an important source of emerging viruses capable of infecting humans. *Curr Opin Virol* 2013;3:84–91.
- Plebani M, Laposata M, Lippi G. A manifesto for the future of laboratory medicine professionals. *Clin Chim Acta* 2019;489:49–52.

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