Severe acute respiratory syndrome: a vanished evil?

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The year 2013, the 10th anniversary of epidemics of severe acute respiratory syndrome (SARS), an evil that has swept the world leading to significant death tools and rendered global alert, heralds an emerging era of prevention and treatment against viral communicable diseases. SARS has, unlike avian or swan influenza (1), vanished from the public perspective with exception of scattered cases reported in 2004 (2). This seems reasonable to lead us to assume that global alert of potential epidemics, with well-practised protocols for disease management, is anything but necessary.

Similar with miscellaneous viral communicable diseases, SARS is a well-recognized highly infectious zoonotic disease that has been evidenced to originate from intimate contact with the wildlife, in particular, civet cats (3-6). The blossom of wildlife market and exotic enjoy for food (7) has contributed considerably to SARS outbreak in Guangdong, China (3,8). The strong enactment of Guangdong government against rearing, sales, slaughter and transport of wildlife proved effective for the crackdown of wildlife markets and spread of SARS. Unfortunately, following remission of epidemics, the wildlife markets resumed to thrive, a consequence possibly stemming from the lack of subsequent governance and reduced public health awareness. Potential infection of SARS variants, i.e. the recently reported emerging SARS-like coronavirus (9), is likely and therefore deserves persistent global alert.

The SARS coronavirus (SARS-CoV) has been recognized as an RNA virus coated by spike and membrane proteins, the culprit responsible for autoimmune reactions presented as acute lung injury and respiratory distress (10). These proteins, the selective molecules that potently bind airway epithelial cells leading to progressive structural damage, are governed by the expression of core RNA that could readily mutate owing to the nature of RNA recombination (11). The consequence, frequently labeled as antigen shift, has been linked to the generation of novel viral species with surprisingly unaffected pathogenicity associated with immune escape (12). Wildlife, the pivotal carriers of SARS-CoV, could have harbored highly contagious mutants that readily provoke a new wave of epidemics following an epidemiologically silent period. That SARS-like virus (9), an emerging member of coronavirus family, has claimed six mortality cases worldwide urgently calls for stringent administrative management of the blossom of market driven by human's exotic desire to complement their vitality. The fatality of zoonotic SARS-CoV should never be underestimated, regardless of the currently low incidence reported.

To abrogate potential threats from wildlife contact, the government and healthcare institutions are responsible to endeavor effective preventative measures against SARS outbreak. Wildlife markets, in conjunction with the personnel involving in transaction, slaughter and transportation, should be made illegal and are subjected to punishment and serious warning. The laws are strongly recommended to be enforced periodically under stringent supervision. Importantly, disclosure of up-to-date information regarding the incidence, death tools and administrative measures will definitively improve public trust and confidence that have been evidenced to safeguard from social chaos and panic, based on a survey undertaken among the Singaporean (13). The mass public is also expected to acquire knowledge on disease prevention and environmental disinfection. Public lectures and television education programs should be held constantly, on the basis of community healthcare schedules. This may contribute to a preferable hygiene condition associated with reduced risks of infectious diseases.

Effective preventative measures and raised public trust and knowledge, however, do not adequately constitute the prerequisite for eliminating the possible crisis of SARS outbreak. This is because that the virus mutants could be derived from aerosols and poultry (14) that have much to correlate with daily

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life. The cryptogenic causative factors have virtually rendered it impossible for human to keep away from potential threats. As the rescue measures, development of effective regimens for treatment is conceivably and understandably indicated, particularly among the neonates and pregnant women who are at increased risk of being severe cases. Akin to those less pathogenic viruses, specific treatment targeting at complete elimination of SARS-CoV *in vivo* is lacking, although corticosteroids have been shown to effectively reduce mortality and shorten the length of hospital stay (15). Most of the treatments, to our knowledge, aim at resolving the symptoms and averting acute lung injury before the humanized specific antibodies are produced. While pharmaceutical agents eliciting antibody secretion may offer promise for the treatment of SARS, the constant variation in viral epitopes arisen from RNA recombination could have inevitably led to treatment failure. Minute molecules, i.e. small interference RNA, has been increasingly recognized as an effective prophylactic and therapeutic regimen for SARS-CoV in Rhesus *macaque* models (16), suggesting that potentially competitive surrogate would clinically avert the progression of airway injury and systemic inflammatory responses. However, clinical trials are necessary to confirm the efficacy and safety of novel molecules in human.

There are remaining issues, apart from the aforementioned approaches, that need to be further addressed. First, dismissing the officials who are responsible for the accident and administrative disclosing are indispensible for securing public trust and confidence. Second, the freedom to remark and comment and an open access to the latest information should be legally protected and enforced, thus allowing the news to be timely covered without impacts of authoritative instructions and citizens to update knowledge whenever possible. Underreporting, influenced by administrative forces, has been related to increased public mistrust resulting in adverse social impacts. Third, medical institutions should take initiatives to refine the current treatment and research, based on the principle of "four earliness", namely, early identification, early report, early isolation and early management (8,17). Finally, a brainstorm of the view that the war against SARS should be persistently held is necessary. Mutants of SARS-CoV, the Nemesis to human, may strike the world claiming a higher mortality and should frequently deserve sufficient awareness and effective measures for the prevention.

In conclusion, the potential pathogenicity of SARS-CoV mutants arisen from gene recombination should not be underestimated. Regular enforcement of laws against wildlife markets, development of effective therapy, administrative refinements and retaining public awareness are essential to safeguard from subsequent outbreaks. These algorithms may be extrapolated to miscellaneous contagious communicable diseases that would constitute major threat to our health.

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