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Editorial Li Wenliang, a face to the frontline healthcare worker? The first doctor to notify the emergence of the SARS-CoV-2, (COVID-19), outbreak Eskild Petersen a,b,c,* eskild.petersen@gmail.com ^aDirectorate General for Disease Surveillance and Control, Ministry of Health, Muscat, Oman ^bEuropean Sociaty for Clinical Microbiology and Infectious Diseases, Basel, Switzerland ^cInstitute for Clinical Medicine, Faculty of Health Sciences, University of Aarhus, Denmark *Corresponding author at: Directorate General for Disease Surveillance and Control, Ministry of Health, Muscat, Oman. David Hui Department of Medicine & Therapeutics, Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, New Territories, Hong Kong, China Davidson H. Hamer a,b ^aDepartment of Global Health, Boston University School of Public Health, Boston, MA, USA ^bSection of Infectious Disease, Department of Medicine, Boston University School of

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Dr Li Wenliang, who lost his life to the novel coronavirus, SARS-CoV-2, became the face of the threat of SARS-CoV-2 to frontline workers, the clinicians taking care of patients. Li, 34, was an ophthalmologist at Wuhan Central Hospital. On 30th December, 2019, when the Wuhan municipal health service sent out an alert, he reportedly warned a closed group of exmedical school classmates on the WeChat social media site of "Seven cases of severe acute".

respiratory syndrome (SARS) like illness with links with the Huanan Seafood Wholesale Market" at his hospital. He was among eight people reprimanded by security officers for "spreading rumours". In a tragic turn of events, he subsequently contracted SARS-CoV-2 and, after a period in intensive care, died on the morning of Friday 7th February, 2020. This case is a stark reminder of the risks of emerging disease outbreaks for healthcare workers (HCWs). Dr Li Wenliang's name is added to the long list of HCW that were at the forefront of outbreaks of SARS, Ebola, MERS and now SARS-CoV-2. It is important to recognise that it was the clinicians in Wuhan who sounded the alarm about the emergence of SARS-CoV-2 which was rapidly identified after these clinicians sent samples to a reference laboratory for next generation sequencing (NGS) (Zhou et al., 2020). Global public health security is of primary importance to prevent outbreaks of diseases with epidemic potential and every effort to detect, report, and institute infection prevention and control measures should be made. Astute clinicians, access to laboratories with state of the art tools, and openness, transparency and quick reporting are crucial components of this response (Kavanagh, 2020). This requires an open flow of information and collaboration between laboratory experts and clinicians on the frontline who may be the first to observe unusual

clustering of cases or uncommon clinical presentations, both of which should be reported immediately.

Healthcare workers are also one of the groups most at risk from outbreaks due to reemerging and novel pathogens. This has been seen in the current SARS-CoV-2 outbreak in China where as many as 1716 health workers have been reported to be infected by the virus with 6 deaths as on 14th February, 2020 (WHO, 2020a). In a single center case series of SARS-CoV-2 from Wuhan published recently, almost 29% of all patients were healthcare workers presumed to have been infected in the hospital (Wang et al., 2020b). The preliminary sequence data on the case cluster were obtained by NGS of specimens collected on 26th December 2019 through 7 January 2020 (Lu et al., 2020). The Chinese authorities ruled out SARS-CoV and MERS-CoV, and confirmed a novel coronavirus as the probable cause on 9th January, 2020 (Hui et al., 2020; Wang et al., 2020a). The first genome sequence was released on virological.org the 12th January 2020, seventeen days after obtaining the first specimen and several additional genomic sequences were then shared on GISAID (Wang et al., 2020c). This is an impressive rapid progression from initial outbreak

notification to identification of a novel pathogen.

The rapid identification of the SARS-CoV-2 virus by NGS illustrates the advances in molecular identification since the SARS-CoV (2003) and MERS-CoV (2012) outbreaks, where both viruses were initially identified by in vitro cell culture. Thus, clinician of the possibility of a new infectious disease coupled with NGS can serve to quickly identify novel pathogens and allow for the rapid initiation of control measures to reduce further spread and potentially prevent large-scale outbreaks.

The SARS-CoV outbreak originating from China in 2003 was first reported to the global health community by ProMED (ProMED, 2003; Carrion and Madoff, 2017; Hamer et al., 2017). It took six weeks for the authorities to acknowledge the outbreak had spread significantly from Guangdong throughout China after cases were reported from Hong Kong, Hanoi, Singapore, and Toronto.

In reporting the existence of a new respiratory disease to the WHO on December 31 st, the

Chinese authorities formally acknowledged the outbreak much sooner this time, perhaps in

part because of the ongoing spread of information on informal social media networks.

ProMED posted the initial report of the unknown pneumonia outbreak in Wuhan on 30

December 2019 (ProMED, 2019). Since then, transmission of information has been relatively transparent, with the prompt sharing of the sequence of the virus and actual numbers of cases

reported on a daily basis. The case figures have demonstrated the upward trajectory of the rapid spread of SARS-CoV-2 from Wuhan and Hubei Province to all of China.

On 13th February 2020 the Chinese authorities changed the case definition and the number of newly reported cases over the prior 24 h jumped to 14,886 from a previous high of 4370 on 6th February 2020. This was not a real increase, but reflected the addition of the cumulative number of clinically diagnosed cases (without laboratory confirmation) to the reported number of laboratory confirmed cases and demonstrates how easily a case definition can influence numbers. On 19 February 2020, the Chinese authorities changed the case definition to include laboratory confirmed cases only and designating clinically diagnosed cases as suspected cases. This resulted in a rapid drop of daily newly confirmed cases, again demonstrating the impact of case definition on reported case numbers. As of 23 February 2020, WHO has reported a total of 78,007 cases with 2,462 deaths globally with reports of cases from 29 countries (WHO, 2020a,b).

A key question remains "what is the real number of people infected since many cases may be mild or asymptomatic?" A recent modelling estimated the population attack rate to be between 0.75 per 100,000 to 15.8 per 100,000 analysing rates down to prefecture level in China (Yang et al., 2020). Any determination of incidence will likely be an underestimate

since it will not include mild and asymptomatic cases. Accuracy of such estimates will depend on the development of sensitive and specific serologic tests.

Recognizing disease in travelers is a particularly important aspect of surveillance for the importation of emerging infections. Multi-site collaborations such as the GeoSentinel Surveillance Network (Wilder-Smith and Boggild, 2018) can act as sentinel systems to recognize new patterns of disease in travelers from specific areas. Previous GeoSentinel data showed that despite receiving care at specialized post-travel medicine sites, up to 40% of returning ill travellers with febrile illness do not have a confirmed etiology; frequently no specific diagnostic testing is available to identify a cause (Freedman et al., 2006; Wilson et al., 2007; Leder et al., 2013). The current large-scale outbreak of a novel pathogen, SARS-CoV-2, highlights the critical importance of prioritizing the identification of disease etiology through clinician awareness and modern laboratory techniques such as NGS. There has been widespread mourning of the sad demise of Dr Li from COVID-2019. Dr Li Wenliang's example as an astute clinician should inspire all of us to be vigilant, bold and courageous in reporting unusual clinical presentations. The SARS-CoV-2 outbreak underscores the responsibilities and the vulnerabilities of frontline health care workers in tackling novel and highly transmissible pathogens. We must use our knowledge and skills,

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with the backup of laboratory support, to rapidly detect and report any suspicion of emerging

infections. Rapid, transparent communication is paramount when infectious diseases emerge.

This is the only way to prevent major outbreaks and will save many lives.

Conflict of interests

The authors declare that they have no conflict of interests.

Uncited reference

South China Morning Post (2020).

References

Carrion and Madoff, 2017 Carrion M, Madoff LC, ProMED-mail: 22 years of digital

surveillance of emerging infectious diseases. Int Health. 2017;9:177-183.

Freedman et al., 2006 Freedman DO, Weld LH, Kozarsky PE, Fisk T, Robins R, von

Sonnenburg F, et al. 2006. Spectrum of disease and relation to place of exposure among ill

returned travelers. N Engl J Med 354:119–130.

Hamer et al., 2017 Hamer DH, Khan K, German M, Madoff LC. Non-traditional infectious

diseases surveillance systems. Peterson E, Chen LH, Schlagenhauf P, Infectious diseases: a

geographic guide, 2nd ed., Wiley Blackwell 2017.

Commented [AB8]: The citations "Wang et al., 2020a; Wang et al., 2020b; Wang et al., 2020c; Carrion and Madoff, 2017; WHO, 2020a,b; Wilder-Smith and Boggild, 2018" have been changed to match the author name/date in the reference list. Please check and correct if precessary.

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11

Hui et al., 2020 Hui DS, Azhar EI, 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;91:264-266 [Published online 14 January 2020. https://www.ijidonline.com/article/S1201-9712(20)30011-4/fulltext] Kavanagh, 2020 Kavanagh MM. Authoritarianism, outbreaks, and information politics. Lancet 2020. [Published 13 February 2020; online ahead of print]. DOI: https://doi.org/10.1016/S2468-2667(20)30030-X. Leder et al., 2013 Leder K, Torresi J, Libman MD, Cramer JP, Castelli F, Schlagenhauf P, et al. GeoSentinel surveillance of illness in returned travelers, 2007-2011. Ann Intern Med. 2013;<mark>158</mark>:456-468 Lu et al., 2020 Lu R, Zhao X, Ni P, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet 2020; [Published online 29 January]. https://doi.org/10.1016/S0140-6736(20)30251-8. ProMED, 2003 ProMED. Pneumonia — China (Guangdong): request for information. https://promedmail.org/promed-post/?id=20030210.0357. 2003. 10 February. [Accessed 23 February 2020].

Commented [AB11]: Please note that as per the journal style, if there are more than six authors, the first six author names are listed followed by 'et al.'; please provide names of first six authors followed by 'et al.' for all the relevant references.

ProMED, 2019 ProMED, Undiagnosed pneumonia — China (Hubei): request for

information. https://promedmail.org/promed-post/?id=20191230.6864153. 2019. 30

December. [Accessed 23 February 2020]

South China Morning Post, 2020 South China Morning Post, Li Wenliang: an 'ordinary hero'

at the centre of the coronavirus storm 2020. 15 February. [Accessed 23 February 2020]

https://www.scmp.com/news/china/society/article/3050733/li-wenliang-ordinary-hero-centre-

coronavirus-storm.

Wang et al., 2020a Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak

of global health concern. Lancet 2020; [Published online 24 January]

https://doi.org/10.1016/S0140-6736(20)30185-9.

Wang et al., 2020b Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J et al. Clinical

characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia

in Wuhan, China. JAMA [Published online 7 February]. 2020. DOI:

10.1001/jama.2020.1585.

Wang et al., 2020c Wang L-F, Anderson DE, Mackenzie JS, Merson MH. From Hendra to

Wuhan: what has been learned in responding to emerging zoonotic viruses. Lancet, February,

2020 https://doi.org/10.1016/S0140-6736(20)30350-0.

Commented [AB12]: Please check the presentation of Refs. South China Morning Post, 2020 and ProMED, 2019, and correct if necessary.

WHO, 2020a WHO. WHO Director-General's remarks at the media briefing on COVID-2019

Commented [AB13]: Please check the year that has been inserted for the Refs. WHO, 2020a, and Yang et al., 2020 and correct if necessary.

outbreak on 14 February 2020 2020. https://www.who.int/dg/speeches/detail/who-director-

general-s-remarks-at-the-media-briefing-on-covid-2019-outbreak-on-14-february-2020

[Accessed 24 February 2020]

WHO, 2020bWHO. Coronavirus disease 2019 (COVID-19) situation report — 23. WHO,

Geneva 2020. 12 February. [Accessed 23 February 2020]

Wilder-Smith and Boggild, 2018 Wilder-Smith A, Boggild A. Sentinel surveillance in travel

medicine: 20 years of GeoSentinel publications (1999-2018). J Travel Med 2018;25:1-7.

Wilson et al., 2007 Wilson ME, Weld LH, Boggild A, Keystone JS, Kain KC, von

Sonnenburg F, et al. 2007. Fever in returned travelers: results from the GeoSentinel

Surveillance Network. Clin Infect Dis 44:1560–1568

Yang et al., 2020 Yang Y, Lu Q-B, Liu M-J, Wang Y-X, Zhang AR, Jalali N et al.

Epidemiological and clinical features of the 2019 novel coronavirus outbreak in China.

medRxiv preprint 2020 doi: https://doi.org/10.1101/2020.02.10.20021675 [Accessed 23]

February 2020]

Zhou et al., 2020 Zhou P, Yang X-L, Wang X-G, Hu B, Zhang L, Zhang W et al. Discovery

of a novel coronavirus associated with the recent pneumonia outbreak in humans and its

Commented [AB14]: Please provide the volume number and page range for the bibliography in Refs. Kavanagh, 2020; Lu et al., 2020; Wang et al., 2020a; Wang et al., 2020b.

potential bat origin. bioRxiv. 2020. January

https://www.biorxiv.org/content/10.1101/2020.01.22.914952v2. [Accessed 24 February

2020].