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2019 novel coronavirus (2019-nCoV) outbreak: A new challenge

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ABSTRACT

Objectives: Following the public-health emergency of international concern (PHEIC) declared by the World Health Organization (WHO) on 30 January 2020 and the recent outbreak caused by 2019 novel coronavirus (2019-nCoV) [officially renamed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)] in China and 29 other countries, we aimed to summarise the clinical aspects of the novel*Betacoronavirus* disease (COVID-19) and its possible clinical presentations together with suggested therapeutic algorithms for patients who may require antimicrobial treatment.

Methods: The currently available literature was reviewed for microbiologically confirmed infections by 2019-nCoV or COVID-19 at the time of writing (13 February 2020). A literature search was performed using the PubMed database and Cochrane Library. Search terms included 'novel coronavirus' or '2019-nCoV' or 'COVID-19'.

Results: Published cases occurred mostly in males (age range, 8–92 years). Cardiovascular, digestive and endocrine system diseases were commonly reported, except previous chronic pulmonary diseases [e.g. chronic obstructive pulmonary disease (COPD), asthma, bronchiectasis] that were surprisingly underreported. Fever was present in all of the case series available, flanked by cough, dyspnoea, myalgia and fatigue. Multiple bilateral lobular and subsegmental areas of consolidation or bilateral ground-glass opacities were the main reported radiological features of 2019-nCoV infection, at least in the early phases of the disease.

Conclusion: The new 2019-nCoV epidemic is mainly associated with respiratory disease and few extrapulmonary signs. However, there is a low rate of associated pre-existing respiratory co-morbidities.

1. Introduction

During December 2019, a novel *Betacoronavirus* provisionally named 2019 novel coronavirus (2019-nCoV), and subsequently officially renamed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses (ICTV), causing coronavirus disease 2019 (or COVID-19), was associated with a cluster of respiratory tract infections in Wuhan, Hubei Province, China [1] and has rapidly spread across continents [2,3]. At 17 February 2020, according to surveillance by the European Centre for Disease Prevention and Control (ECDC) and the US Centers for Disease Control and Prevention (CDC) [2,3], 71 333 cases have been reported among 29 countries on five main continents, and the number of deaths was 1775, almost all occurring in China (N = 1770; with 1 case in each of the Philippines, Hong Kong, France, Taiwan and Japan), with a currently reported fatality rate of between 2–2.3% [2,3]. In this short report, we aimed to summarise the clinical aspects of the novel *Betacoronavirus* infection and its possible manifestations.

2. Materials and methods

A literature search was performed using the PubMed database and Cochrane Library. Search terms included 'novel coronavirus' and '2019-nCoV'. The MeSH terms were 'novel' [all fields] AND ('coronavirus' [MeSH terms] OR '2019-nCoV' [all fields]) OR 'COVID-19' [all fields]). The defined search period from 30 November 2019 to 13 February 2020 was selected to compare studies regarding the first outbreaks and findings. Given the nature of the review, no ethical approval was required. The search was performed by two investigators (SC and TL). A total of 225 studies were identified (PubMed, n = 225; Cochrane Library, n = 0). Two investigators then reviewed these articles, initially by title and

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abstract and then in detail, using a customised data abstraction form. Studies were excluded if they had an incorrect subject matter or were duplications or reviews. Only studies in English were included. Twelve studies were identified for full-text review as they contained original data.

3. Results

3.1. Patients characteristics

Most of the patients were male (Table 1) with an age range of 8–92 years: interestingly, in the first period of this global epidemic there have been few cases in young people aged <15 years [1,4–15]. Nevertheless, among known infected subjects outside of China, the prevalence of males and the age distribution at the time of diagnosis resemble those in the Chinese epidemic [4,6,15]. Although past medical histories were not always available [1,4–15], hypertension was the most reported underlying condition [1,4–15] in as many as 80% and 31.2%, respectively, in the case series from Ren et al. [9] and Wang et al. [12]. Chen et al. [10] described mostly cardiovascular and cerebrovascular diseases (40%) in their population. Furthermore, Ren et al. [9] have reported underlying chronic liver disease in their whole population (n = 5) and this feature differs, at least so far, from the other cases of COVID-2019 [1,4–8,10–15].

Huang et al. [1] and Wang et al. [12] have shown a rate of chronic obstructive pulmonary disease (COPD) of approximately 2% and 2.9%, respectively. Subsequently, Chen et al. [10] have reported a rate of approximately 1% for respiratory system diseases, different from an estimated COPD prevalence of between 1.2–8.9% in different regions of China [16]. Moreover, interstitial lung disease, history of smoking, bronchiectasis or asthma were underreported [1,4–15]. Diabetes was first mentioned by Huang et al [1] and represented the main co-morbidity in their cohort (8/41; 20%), and thereafter other authors [11,12] reported diabetes in approximately 10% of subjects. Furthermore, among cases outside Asia, Holshue et al. [4] have mentioned hypertriglyceridemia as the sole chronic illness of the first US case of COVID-2019; on the other hand, German cases [6] were overall healthy.

3.2. Signs and symptoms

Patients with confirmed 2019-nCoV infection mostly had respiratory signs and symptoms [1,4–11]. Fever was reported in all of the case series available, flanked by cough, mostly dry (Table 1). Dyspnoea was not uncommon and was reported in the entire cohort by Ren et al. (n = 5; 100%) [9]. A significant proportion of patients complained of gastrointestinal symptoms such as nausea, vomiting and diarrhoea, also appearing during the course of illness, a distinct feature [1,4–15]: Holshue et al. [4] meticulously described the evolution of the first US case, complaining first of respiratory symptoms (i.e. dry cough) followed by abdominal discomfort and self-limiting nausea, vomiting and diarrhoea. There was myalgia or fatigue in 44–60% of Asian case series [1,9].

3.3. Chest radiographic abnormalities

Multiple bilateral lobular and subsegmental areas of consolidation or bilateral ground-glass opacities were the main reported radiological features of COVID-2019 [1,4–15]. In the 41 patients in the case series reported by Huang et al. [1], all had plain chest radiography (CXR) or computed tomography (CT) findings of pneumonia. Although CT is the best method to define the extension and typology of lung parenchyma involvement, CXR was mostly employed as a first investigation, probably because of the associated need to comply with infection control procedures [5].

3.4. Laboratory abnormalities

Leukopenia was the most common abnormality [1,4–9], reported in up to 63% of subjects in the study by Huang et al. [1]. Thrombocytopenia occurred in the reports by Holshue et al. [4] and Chen et al. [10] but is rarely reported in other series [1,5–15], although low platelets counts were found in up to 45% of severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) infections [17,18]. Nevertheless, abnormalities in hepatic [e.g. slight increase in aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels] and muscle (e.g. slight increase in creatine kinase or lactate dehydrogenase) enzymes were seen in early cases and later reported (Table 1) [1,4–15]. As one might expect, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were frequently abnormal and, in contrast, most of the patients had normal procalcitonin (PCT) levels at admission: in the cohort of Huang et al. [1] up to 69% of patients had a PCT level of <0.1 ng/mL. Interestingly in the case series of Wang et al. [12] a prolonged prothrombin time was reported in approximately 58% of adults.

3.5. Complications and mortality

In one of the larger cohorts available by Huang et al. [1] with 41 patients, 4 (10%) had a superinfection and the risk increased with the intensity of care [intensive care unit (ICU) care 31% vs. no ICU care 0%; P = 0.0014], with almost all patients being treated with empirical antibiotic coverage during the acute phase. Furthermore, the risk of acute respiratory distress syndrome, with or without specific bacterial superinfection, complicated the clinical course of up to 29% of patients (12/41) [1]. In the same large cohort by Huang et al. [1], in up to 12% of cases an increase in troponin I count occurred, and five patients complained of an acute cardiac injury: this finding requires further study to assess the heart tropism of 2019-nCoV and the cardiovascular risk of infected patients during acute illness.

Chen et al. [10] reported a low rate (4%) of fungal isolates with a clinical need for empirical antifungal treatment, with one case of *Candida glabrata*, three cases of *C. albicans* and one case, more important, of *Aspergillus flavus* isolation. Moreover, the authors reported a lower rate of bacterial respiratory isolates, mostly *Acinetobacter baumannii* and *Klebsiella pneumoniae* [10]; according to that, microbiological data are poor to represent all of the 2019-nCoV-infected population, and the follow-up time reported in the literature is too short to define the real burden of post-viral infectious complications.

The first wave of 2019-CoV has caused 1775 deaths despite the severity of illness being mild in most of cases [1,4–9,12,14,15]. Wang et al. [19] have interestingly reviewed the underlying diseases and demographic characteristics of deaths occurring in the Wuhan epidemic and found that older adults (>70 years) presented a shorter period between the first symptom and death compared with younger persons [11.5 (range 6–19) days vs. 20 (range 10–41) days; P = 0.033], as previously reported for other betacoronaviruses [17,18]: this confirms the increased severity in the elderly for coronavirus illness [1,4–15]. Furthermore, according to Wang et al. [19], 2019-CoV has developed a median period between the symptomatic phase to death (median 14 days) somewhat similar to MERS-CoV (median 14 days) and SARS-CoV (median 17.4 days) [12,17,18] (Table 2).

4. Discussion

We are daily assessing the real extent of the 2019-CoV epidemic and the scientific turmoil that is trying to keep up. We have learned, at least scientifically, the lesson from previous epidemics

Table 1
Clinical and laboratory features of confirmed infection by 2019 novel coronavirus (2019-nCoV) currently (as of 13 February 2020) reported in the literature.[a]

Author	Date of publication	Continent	State	No. of cases	Age (range) (years)	Sex (male rate)	Past medical history	Signs at admission	Symptoms at admission	Laboratory abnormalities	CXR abnormalities	Ward of admission	Treatment	Outcome
COVID-19 National Incident Room Surveillance Team [15]	12 February 2020	Oceania	Australia	15	43 (8–66)	10 males (67%)	N/A	Fever and/or chills (93%)	Cough (73%)	N/A	Pneumonia	Internal medicine, ICU	N/A	Favourable
Kim et al. [14]	10 February 2020	Asia	Incheon, Korea	1	35	Female (N/A)	Obesity	Fever	Myalgia	Leukopenia, thrombocytopenia and hepatic abnormalities	Multiple ground-glass opacities located in both subpleural spaces	N/A	Support, lopinavir/ritornavir	Favourable
Wang et al. [13]	09 February 2020	Asia	Shanghai, China	4	19–63	3 males (75%)	Fatty liver (1 patient); no underlying medical conditions in other three	Fever (100%), rhonchi (100%)	Cough, dizziness, fatigue	Lymphopenia (25%)	Ground-glass opacities and consolidations, bilateral or monoliteral	Internal medicine	Lopinavir/ritornavir, Shufeng Jiedu capsule, Arbidol (umifenovir)	Favourable
Wang et al. [12]	07 February 2020	Asia	Wuhan, Hubei, China	138	56 (22–92)	75 males (54.3%)	Hypertension (31.2%), CD (14.5%), DM (10.1%), malignancy (7.2%), COPD (2.9%), CKD (2.9%)	Fever (98.6%)	Fatigue (69.6%), dry cough (59.4%), diarrhoea (10.1%)	Lymphopenia (70.3%), prolonged PT time (58%), elevated LDH (39.9%)	Bilateral patchy shadows or ground-glass opacitie in the lungs	ICU, internal medicine	Support, empirical antibiotics and antiviral therapy	6 died (4.3%)
Lui et al. [11]	07 February 2020	Asia	Wuhan, Hubei, China	137	57 (20–83)	61 males (44.5%)	DM (10.2%), hypertension (9.5%), CD (7.3%), COPD (1.5%), malignancy (1.5%)	Fever (81.8%)	Cough (48%), myalgia or fatigue (32.1%), heart palpitations, diarrhoea and headache	Lymphopenia (72.3%)	Multiple, bilateral, peripheral ground-glass opacities and consolidations or cord-like shadows (CT imaging)	Internal medicine, ICU	Empirical antibiotics (86.9%), antiviral therapy (76.6%), immunoglobulin G, systemic CTS	16 died (11.7%)
Holshue et al. [4]	31 January 2020	America	Snohomish County, Washington	1	35	Male (100%)	Hypertriglyceridaemia	Fever, tachycardia, lung rhonchi, dry mucous membrane	Dry cough, nausea and vomiting, abdominal discomfort, diarrhoea, fatigue, rhinorrhoea	Leukopenia, thrombocytopenia, elevated creatine kinase and lactate dehydrogenase, hepatic abnormalities	Lower lobe pneumonia, bilateral basilar streaky opacities	Internal medicine	Support; vancomycin plus cefepime (from Day 9); remdesivir	Favourable
Lei et al. [5]	31 January 2020	Asia	Lanzhou, China	1	33	Female (N/A)	N/A	Fever, coarse breath sounds	Cough	Leukopenia, elevated CRP, elevated ESR	Multiple, bilateral, peripheral ground-glass opacities and consolidations or cord-like shadows (CT imaging)	Internal medicine	Support, IFN	N/A
Rothe et al. [6]	30 January 2020	Europe	Munich, Germany	4	33	Males (100%)	Healthy	Fever	Productive cough	N/A	N/A	Internal medicine	N/A	Favourable
Ren et al. [9]	11 February 2020	Asia	Wuhan, China	5	52 (41–65)	3 males (60%)	Chronic liver disease (100%), hypertension (80%)	Fever (100%)	Cough (100%), dyspnoea (100%), myalgia (60%)	Leukopenia (20%), slightly increased ALT (40%)	Bilateral ground-glass opacities (100%), consolidations (80%) on CXR	ICU (100%)	Support, empirical antibiotics	1 died (20%)

Chen et al. [10]	30 January 2020	Asia	Wuhan, China	99	55 (42–68)	67 males (68%)	CD and cerebrovascular disease (40%), digestive system disease (11%), endocrine system disease (11%)	Fever (83%),	Cough (82%), shortness of breath (31%), confusion (9%), headache (8%)	Lymphopenia (35%), thrombocytopenia (12%), AST increased (35%), ALT increased (28%)	Bilateral consolidations (75%) on CXR or CT	N/A	Support, empirical antibiotics, antiviral and antifungal	11 died (11%)
Li et al. [7]	29 January 2020	Asia	Wuhan, China	425	59 (15–89)	240 males (56%)/	NA	Respiratory S/s and less frequently GI	Respiratory and less frequently GI	N/A	N/A	N/A	N/A	N/A
Huang et al. [1]	24 January 2020	Asia	Wuhan, China	41	49 (41–48)	30 males (73%)	DM (20%), hypertension (15%), CD (15%), COPD (2%)	Fever (98%)	Cough (76%), productive cough (28%), myalgia or fatigue (44%), dyspnoea (55%), headache (8%), haemoptysis (5%), diarrhoea (3%)	Leukopenia (63%), increased AST (37%), increased troponin I (12%)	41 (100%) CXR or CT findings of pneumonia; bilateral multiple lobular and subsegmental areas of consolidation or bilateral ground-glass opacities	13 (32%) ICU	Empirical antibiotics, oseltamivir (93%), steroids (22%)	6 died (15%)
Zhu et al. [8]	24 January 2020	Asia	Wuhan, China	3	49 (32–61)	2 males (67%)	N/A	Fever	Cough	N/A	N/A	N/A	N/A	N/A

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CD, cardiovascular disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; CT, computed tomography; CTS, corticosteroids; CXR, chest radiography; DM, diabetes mellitus; ESR, erythrocyte sedimentation rate; GI, gastrointestinal; ICU, intensive care unit; IFN, interferon; LDH, lactate dehydrogenase; N/A, not available; PT, prothrombin time.

[a] Officially renamed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses (ICTV).

Table 2
Differences in pathogenicity and virulence of different coronaviruses currently reported in literature.

Main features	2019-nCoV (COVID-19)	SARS	MERS
Possible natural reservoir	Bat	Bat	Bat
Mean incubation time in humans (days)	3–6	5	5
Origin	Wuhan, China	Guangdong Province, China	Arabian Peninsula
Case number (period)	71 333 (as of 17 February 2020)	8098 (2002–2003)	2254 (2012–2013)
Type of illness	Acute respiratory syndrome	Severe acute respiratory syndrome	Severe acute respiratory syndrome
Severity of symptoms	Mild to moderate	High	High compared with SARS
Fatality rate (%)	2–2.3	>10	>35

2019-nCoV, 2019 novel coronavirus [officially renamed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)]; COVID-19, coronavirus disease 2019; SARS, severe acute respiratory syndrome; MERS, Middle East respiratory syndrome.

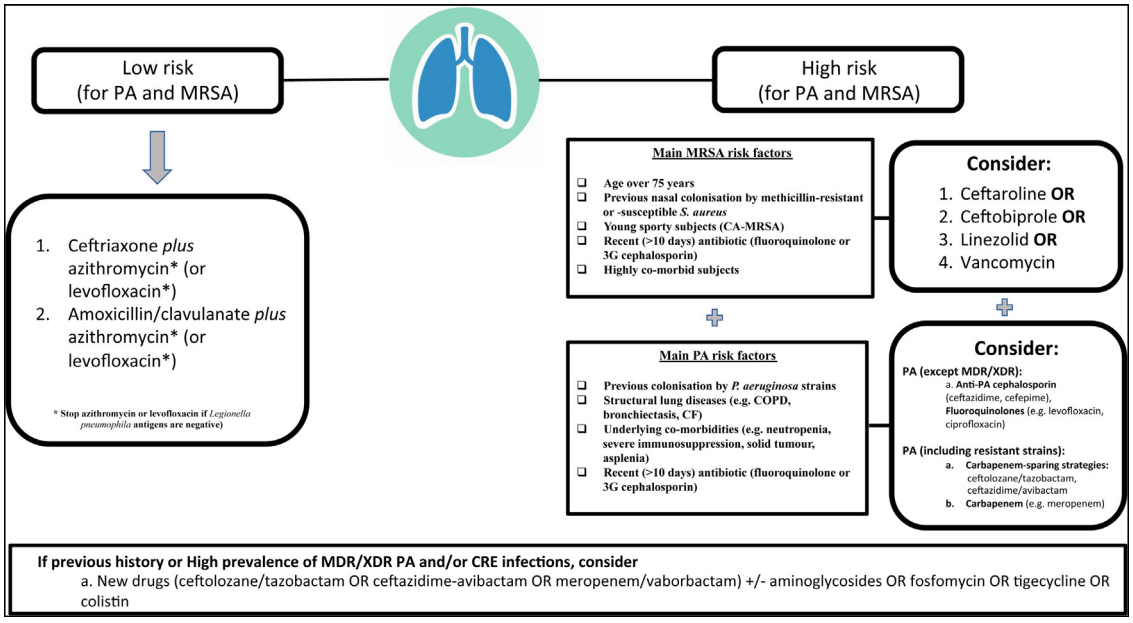

Fig. 1. Positive reverse transcription PCR (RT-PCR) for 2019-nCoV (SAR-CoV-2) and clinical and/or radiological suspicion of bacterial superinfection. 3G, third-generation; CA, community-acquired; CF, cystic fibrosis; COPD, chronic obstructive pulmonary disease; CRE, carbapenem-resistant Enterobacteriaceae; MDR, multidrug-resistant; MRSA, methicillin-resistant *Staphylococcus aureus*; PA, *Pseudomonas aeruginosa*; XDR, extensively drug-resistant.

of SARS-CoV and MERS-CoV [17,18,20,21]; therefore, we are awaiting the true extent of this new disease with its features, notably outside Chinese lands. The lack of specific clinical features, the diagnostic microbiological challenge [e.g. reverse transcription PCR (RT-PCR) on nasal or rhinopharyngeal swabs] along with the 2019-nCoV outbreak occurring during the delayed peak of the seasonal influenza make the definition of COVID-19 a difficult task [22]. On one hand, clinical symptoms such as high rate of fever and respiratory symptoms resemble previous features of coronavirus infection; on the other hand, systemic symptoms such as chills and rigors seen, respectively, in 87% and in up to 73% of cases during MERS-CoV and SARS-CoV epidemics, respectively, were an unusual phenomenon among 2019-nCoV infection [17,18,20,21]. The usual pattern of presentation of the novel coronavirus is quite unspecific and is similar to many viral infections: most of the co-morbidities in the past MERS-CoV epidemic had included cardiovascular diseases (e.g. hypertension), history of smoking, and diabetes: although the number of chronic illnesses is low and underreported despite that, we are probably not that far to have a more precise overview [17,18,20,21]. The high rate of radiological and clinically suspicious pneumonia reported in the reviewed cohorts of patients [1,4–15] call for a reflection, notably with a perspective view, on the need for empirical antibiotic coverage in the setting of possible bacterial superinfection, as in influenza virus outbreaks. As reported in 2003 for the SARS-CoV epidemic, there was an increased rate of methicillin-resistant *Staphylococcus aureus* (MRSA) from 3.53% (3.53 cases per 100 admissions) during the pre-SARS period to 25.3% during the SARS period ($P < 0.001$), with an increased rate of ventilator-acquired pneumonia in ICUs, mostly (47.1%) caused by MRSA [23]. Giving the number of common points between 2019-nCoV and previous coronavirus infection, anti-MRSA empirical treatment needs to be considered also with 2019-nCoV to reduce the risk of superinfection. Therefore, assessing the risk of MRSA and other difficult-to-treat bacterial superinfections such as *Pseudomonas aeruginosa* and multidrug-resistant Gram-negative bacilli colonisation, according to cardiovascular co-morbidities, lung abnormalities or systemic diseases, the severity of pneumonia and the risks of adverse events or drug-related toxicity are crucial points for all suspected cases of 2019-nCoV. A treatment algorithm is proposed and based on common risk factors for MRSA and/or *P. aeruginosa* (Fig. 1). The risk of fungal co-infection appears to be low [10], despite the fact that viral infections such as influenza and a large number of classical risk factors (e.g. haematological patients, solid-organ and haematopoietic stem cell transplant recipients, HIV patients) have been described as a favourable environment for invasive fungal infections, especially for invasive pulmonary aspergillosis [24]. Empirical antifungal treatment should only be considered in critically patients with new pulmonary infiltrate superimposed on a viral pneumonitis pattern, with the aim of confirming the

diagnosis by invasive techniques and/or the use of fungal biomarkers. So far, data on the efficacy of specific antiviral treatments are inconclusive, and the current series have reported a wide range of management options [1,4–15]. Holshue et al. [4] have resorted to compassionate use of remdesivir with a favourable outcome; on the other hand, Chen et al. [10] in their population (99 patients) described antiviral treatment in 75 patients (76%) with a median duration of 3 days (interquartile range, 3–6 days). In conclusion from an infectious diseases perspective, based on the lessons learned from the previous well-known coronavirus outbreaks (e.g. MERS-CoV and SARS-CoV), we have to be ready for further outbreaks and must focus our attention to the prompt diagnosis of cases and infection control procedures with isolation of suspected cases, and to anticipate those that may be the complications and evolutions in the course of the 2019-nCoV epidemic.

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Competing interests

None declared.

Ethical approval

Not required.

References

[1] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497–506, doi:http://dx.doi.org/10.1016/S0140-6736(20)30183-5.
[2] European Centre for Disease Prevention and Control (ECDC). Situation update worldwide. https://www.ecdc.europa.eu/en/geographical-distribution-2019-ncov-cases.
[3] US Centers for Disease Control and Prevention (CDC). Coronavirus disease 2019 (COVID-19). Locations with confirmed COVID-19 cases. Global map. https://www.cdc.gov/coronavirus/2019-ncov/locations-confirmed-cases.html.
[4] Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, Bruce H, et al. First case of 2019 novel coronavirus in the United States. N Engl J Med 2020;382:929–36, doi:http://dx.doi.org/10.1056/NEJMoa2001191.
[5] Lei J, Li J, Li X, Qi X. CT imaging of the 2019 novel coronavirus (2019-nCoV) pneumonia. Radiology 2020;(January)200236, doi:http://dx.doi.org/10.1148/radiol.2020200236 [Epub ahead of print].
[6] Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, et al. Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. N Engl J Med 2020;382:970–1, doi:http://dx.doi.org/10.1056/NEJMc2001468.
[7] Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med 2020 (January), doi:http://dx.doi.org/10.1056/NEJMoa2001316 [Epub ahead of print].
[8] Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. China Novel Coronavirus Investigating and Research Team. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020;382:727–33, doi:http://dx.doi.org/10.1056/NEJMoa2001017.
[9] Ren LL, Wang YM, Wu ZQ, Xiang ZC, Guo L, Xu T, et al. Identification of a novel coronavirus causing severe pneumonia in human: a descriptive study. Chin Med J (Engl) 2020(February), doi:http://dx.doi.org/10.1097/CM9.0000000000000722 [Epub ahead of print].
[10] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395:507–13, doi:http://dx.doi.org/10.1016/S0140-6736(20)30211-7.
[11] Lui K, Fang YY, Deng Y, Liu W, Wang MF, Ma JP, et al. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. Chin Med J (Engl) 2020(February), doi:http://dx.doi.org/10.1097/CM9.0000000000000744 [Epub ahead of print].
[12] 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 2020(February), doi:http://dx.doi.org/10.1001/jama.2020.1585 [Epub ahead of print].
[13] Wang Z, Chen X, Lu Y, Chen F, Zhang W. Clinical characteristics and therapeutic procedure for four cases with 2019 novel coronavirus pneumonia receiving combined Chinese and Western medicine treatment. Biosci Trends 2020 (February), doi:http://dx.doi.org/10.5582/bst.2020.01030 [Epub ahead of print].
[14] Kim JY, Choe PG, Oh Y, Oh KJ, Kim J, Park SJ, et al. The first case of 2019 novel coronavirus pneumonia imported into Korea from Wuhan, China: implication for infection prevention and control measures. J Korean Med Sci 2020;35:e61, doi:http://dx.doi.org/10.3346/jkms.2020.35.e61.
[15] COVID-19 National Incident Room Surveillance Team. COVID-19, Australia: epidemiology report 2 (reporting week ending 19:00 AEDT 8 February 2020). Commun Dis Intell (2018) 2020;44:, doi:http://dx.doi.org/10.33321/cdi.2020.44.14.
[16] Zhu B, Wang Y, Ming J, Chen W, Zhang L. Disease burden of COPD in China: a systematic review. Int J Chron Obstruct Pulmon Dis 2018;13:1353–64, doi:http://dx.doi.org/10.2147/COPD.S161555.
[17] de Wit E, van Doremalen N, Falzarano D, Munster VJ. SARS and MERS: recent insights into emerging coronaviruses. Nat Rev Microbiol 2016;14:523–34, doi:http://dx.doi.org/10.1038/nrmicro.2016.81.
[18] Bassetti M, Vena A, Giacobbe DR. The novel Chinese coronavirus (2019-nCoV) infections: challenges for fighting the storm. Eur J Clin Invest 2020;50:e13209, doi:http://dx.doi.org/10.1111/eci.13209.
[19] Wang W, Tang J, Wei F. Updated understanding of the outbreak of 2019 novel coronavirus (2019-nCoV) in Wuhan, China. J Med Virol 2020;92:441–7, doi:http://dx.doi.org/10.1002/jmv.25689.
[20] Oh MD, Park WB, Park SW, Choe PG, Bang JH, Song KH, et al. Middle East respiratory syndrome: what we learned from the 2015 outbreak in the Republic of Korea. Korean J Intern Med 2018;33:233–46, doi:http://dx.doi.org/10.3904/kjim.2018.031.
[21] Feng D, Jia N, Fang LQ, Richardus JH, Han XN, Cao WC, et al. Duration of symptom onset to hospital admission and admission to discharge or death in SARS in mainland China: a descriptive study. Trop Med Int Health 2009;14 (Suppl 1):28–35, doi:http://dx.doi.org/10.1111/j.1365-3156.2008.02188.x.
[22] European Centre for Disease Prevention and Control (ECDC). Weekly influenza update, week 4, January 2020. https://www.ecdc.europa.eu/en/publications-data/weekly-influenza-update-week-4-january-2020. [Accessed 6 March 2020].
[23] Yap FH, Gomersall CD, Fung KSC Ho PL, Ho OM, Lam PKN, et al. Increase in methicillin-resistant *Staphylococcus aureus* acquisition rate and change in pathogen pattern associated with an outbreak of severe acute respiratory syndrome. Clin Infect Dis 2004;39:511–6, doi:http://dx.doi.org/10.1086/422641.
[24] Donnelly JP, Chen SC, Kauffman CA, Steinbach WJ, Baddley JW, Verweij PE, et al. Revision and update of the consensus definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium. Clin Infect Dis 2019 (December), doi:http://dx.doi.org/10.1093/cid/ciz1008 pii: ciz1008 [Epub ahead of print].