fever, cough, and sputum (83). Hence, the clinicians must be on the look-out for the possible occurrence of atypical clinical manifestations to avoid the possibility of missed diagnosis. diagnosis. The early transmission ability of SARS-CoV-2 was found to be similar to or slightly higher than that of SARS-CoV, reflecting that it could be controlled despite moderate to high transmissibility (84).

Increasing reports of SARS-CoV-2 in sewage and wastewater warrants the need for further investigation due to the possibility of fecal-oral transmission. SARS-CoV-2 present in environmental compartments such as soil and water will finally end up in the wastewater and sewage sludge of treatment plants (328). Therefore, we have to reevaluate the current wastewater and sewage sludge treatment procedures and introduce advanced techniques that are specific and effective against SARS-CoV-2. Since there is active shedding of SARS-CoV-2 in the stool, the prevalence of infections in a large population can be studied using wastewater-based epidemiology. Recently, reverse transcription-quantitative PCR (RT-qPCR) was used to enumerate the copies of SARS-CoV-2 RNA concentrated from wastewater collected from a wastewater treatment plant (327). The calculated viral RNA copy numbers determine the number of infected individuals. The

Prevention [21, 30]

Since at this time there are no approved treatments for this infection, prevention is crucial. Several properties of this virus make prevention difficult namely, non-specific features of the disease, the infectivity even before onset of symptoms in the incubation period, transmission from asymptomatic people, long incubation period, tropism for mucosal surfaces such as the conjunctiva, prolonged duration of the illness and transmission even after clinical recovery.

Isolation of confirmed or suspected cases with mild illness at home is recommended. The ventilation at home should be good with sunlight to allow for destruction of virus. Patients should be asked to wear a simple surgical mask and practice cough hygiene.

prongs, face mask, high flow nasal cannula (HFNC) or non-invasive ventilation is indicated. Mechanical ventilation and even extra corporeal membrane oxygen support may be needed. Renal replacement therapy may be needed in some. Antibiotics and antifungals are required if coinfections are suspected or proven. The role of corticosteroids is unproven; while current international consensus and WHO advocate against their use, Chinese guidelines do recommend short term therapy with low-to-moderate dose corticosteroids in COVID-19 ARDS [24, 25]. Detailed guidelines for critical care management for COVID-19 have been published by the WHO [26]. There is, as of now, no approved treatment for COVID-19. Antiviral drugs such as ribavirin, lopinavir-ritonavir have been used based on the experience with SARS and MERS. In a historical

(173, 174). Hence, knowledge and understanding of S protein-based vaccine development in SARS-CoV will help to identify potential S protein vaccine candidates in SARS-CoV-2. Therefore, vaccine strategies based on the whole S protein, S protein subunits, or specific potential epitopes of S protein appear to be the most promising vaccine candidates against coronaviruses. The RBD of the S1 subunit of S protein has a superior capacity to induce neutralizing antibodies. This property of the RBD can be utilized for designing potential SARS-CoV vaccines either by using RBD-containing recombinant proteins or recombinant vectors that encode RBD (175). Hence, the superior genetic similarity existing between SARS-CoV-2 and SARS- CoV can be utilized to repurpose vaccines that have proven in vitro efficacy against SARS-CoV to be utilized for SARS-CoV-2. The possibility of cross- protection

in COVID-19 was evaluated by comparing the S protein sequences of SARS-CoV-2 with that of SARS-CoV. The comparative analysis confirmed that the variable residues were found concentrated on the S1 subunit of S protein, an important vaccine target of the virus (150). Hence, the possibility of SARS-CoV-specific neutralizing antibodies providing cross-protection to COVID-19 might be lower. Further genetic analysis is required

this emerging virus will establish a niche in humans and coexist with us for a long time166. Before clinically approved vaccines are widely available, there is no better way to protect us from SARS-CoV-2 than personal preventive behaviours such as social distancing and wearing masks, and public health measures, including active testing, case tracing and restrictions on social gatherings. Despite a flood of SARS-CoV-2 research published every week, current knowledge of this novel coronavirus is just the tip of the iceberg. The animal origin and cross-species infection route of SARS-CoV-2 are yet to be uncovered. The molecular mechanisms of SARS-COV-2 infection pathogenesis and virus-host

Interestingly, disease in patients outside Hubei province has been reported to be milder than those from Wuhan [17]. Similarly, the severity and case fatality rate in patients outside China has been reported to be milder [6]. This may either be due to selection bias wherein the cases reporting from Wuhan included only the severe cases or due to predisposition of the Asian population to the virus due to higher expression of ACE2 receptors on the respiratory mucosa [11].

Disease in neonates, infants and children has been also reported to be significantly milder than their adult counterparts. In a series of 34 children admitted to a hospital in Shenzhen, China between January 19th and February 7th, there were 14 males and 20 females. The median age was 8 y 11 mo and in 28 children the infection was linked to a family member and 26

or even die, whereas most young people and children have only mild diseases (non-pneumonia or mild pneumonia) or are asymptomatic 9,81,82. Notably, the risk of disease was not higher for pregnant women. However, evidence of transplacental transmission of SARS-CoV-2 from an infected mother to a neonate was reported, although it was an isolated case 83,84. On infection, the most common symptoms are fever, fatigue and dry cough13,60,80,81. Less common symptoms include sputum production, headache, hemoptysis, diarrhea, anorexia, sore throat, chest pain, chills and nausea and vomiting in studies of patients in China 13,60,80,81. Self-reported olfactory and taste disorders were also reported by patients in Italy 85. Most people showed signs of diseases after an incubation period of 1-14 days (most commonly around 5 days), and dyspnoea and pneumonia developed within a median time of 8 days from illness onset 9.

In a report of 72,314 cases in China, 81% of the cases were classified as mild, 14% were severe cases that required ventilation in an intensive care unit (ICU) and a 5% were critical (that is, the patients had respiratory failure, septic shock and/or multiple organ dysfunction or failure)9,86. On admission, ground-glass opacity was the most common radiologic finding on chest computed tomography (CT) 13,60,80,81. Most patients also developed marked lymphopenia, similar to what was observed in patients with SARS and MERS, and non-survivors developed severer lymphopenia over time 13,60,80,81. Compared with non-ICU patients, ICU patients had higher levels

in Yunnan. This novel bat virus, denoted ‘RmYN02, is 93.3% identical to SARS-CoV-2 across the genome. In the long lab gene, it exhibits 97.2% identity to SARS-CoV-2, which is even higher than for RaTG13 (REF.28). In addition to RaTG13 and RmYN02, phylogenetic analysis shows that bat coronaviruses ZC45 and ZXC21 previously detected in Rhinolophus pusillus bats from eastern China also fall into the SARS-CoV-2 lineage of the subgenus Sarbecovirus36 (FIG. 2). The discovery of diverse bat coronaviruses closely related to SARS-CoV-2 suggests that bats are possible reservoirs of SARS-CoV-2 (REF.37). Nevertheless, on the basis of current findings, the divergence between SARS-CoV-2 and related bat coronaviruses likely represents more than 20 years of sequence evolution, suggesting that these bat coronaviruses can be regarded only as the likely evolutionary precursor of SARS-CoV-2 but not as the direct progenitor of SARS-CoV-2 (REF.38).

Beyond bats, pangolins are another wildlife host probably linked with SARS-CoV-2. Multiple SARS-CoV-2- related viruses have been identified in tissues of Malayan pangolins smuggled from Southeast Asia into southern China from 2017 to 2019. These viruses from pangolins independently seized by Guangxi and Guangdong provincial customs belong to two distinct sublineages39-41 The Guangdong strains, which were isolated or sequenced by different research groups from smuggled pangolins, have 99.8% sequence identity with each other11. They are very closely related to SARS-CoV-2, exhibiting 92.4% sequence similarity. Notably, the RBD of Guangdong pangolin coronaviruses is highly similar to that of SARS-CoV-2. The receptor-binding motif (RBM; which is part of the RBD) of these viruses has only one amino acid variation from SARS-CoV-2, and it is identical to that of SARS-CoV-2 in all five critical

identified angiotensin receptor 2 (ACE2) as the receptor through which the virus enters the respiratory mucosa [11].

The basic case reproduction rate (BCR) is estimated to range from 2 to 6.47 in various modelling studies [11]. In comparison, the BCR of SARS was 2 and 1.3 for pandemic flu H1N1 2009 [2].

Clinical Features [8, 15-18]

The clinical features of COVID-19 are varied, ranging from asymptomatic state to acute respiratory distress syndrome and multi organ dysfunction. The common clinical features include fever (not in all), cough, sore throat, headache, fatigue, headache, myalgia and breathlessness. Conjunctivitis has also been described. Thus, they are indistinguishable from other respiratory infections. In a subset

Origin and Spread of COVID-19 [1, 2, 6]

In December 2019, adults in Wuhan, capital city of Hubei province and a major transportation hub of China started presenting to local hospitals with severe pneumonia of unknown cause. Many of the initial cases had a common exposure to the Huanan wholesale seafood market that also traded live animals. The surveillance system (put into place after the SARS outbreak) was activated and respiratory samples of patients were sent to reference labs for etiologic investigations. On December 31st 2019, China notified the outbreak to the World Health Organization and on 1st January the Huanan sea food market was closed. On 7th January the virus was identified as a coronavirus that had >95% homology with the bat

infections clinically or through routine lab tests. Therefore travel history becomes important. However, as the epidemic spreads, the travel history will become irrelevant.

Treatment [21, 23]

Treatment is essentially supportive and symptomatic.

The first step is to ensure adequate isolation (discussed later) to prevent transmission to other contacts, patients and healthcare workers. Mild illness should be managed at home with counseling about danger signs. The usual principles are maintaining hydration and nutrition and controlling fever and cough. Routine use of antibiotics and antivirals such as oseltamivir should be avoided in confirmed cases. In hypoxic patients, provision of oxygen through nasal prongs, face mask, high flow nasal

(entertainment parks etc). China is also considering introducing legislation to prohibit selling and trading of wild animals [32].

The international response has been dramatic. Initially, there were massive travel restrictions to China and people returning from China/ evacuated from China are being evaluated for clinical symptoms, isolated and tested for COVID-19 for 2 weeks even if asymptomatic. However, now with rapid world wide spread of the virus these travel restrictions have extended to other countries. Whether these efforts will lead to slowing of viral spread is not known. A candidate vaccine is under development.

Practice Points from an Indian Perspective

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pandemic flu where patients were asked to resume work/school once afebrile for 24 h or by day 7 of illness. Negative molecular tests were not a prerequisite for discharge.

At the community level, people should be asked to avoid crowded areas and postpone non-essential travel to places with ongoing transmission. They should be asked to practice cough hygiene by coughing in sleeve/ tissue rather than hands and practice hand hygiene frequently every 15-20 min. Patients with respiratory symptoms should be asked to use surgical masks. The use of mask by healthy people in public places has not shown to protect against respiratory viral infections and is currently not recommended by WHO. However, in China, the public has been asked to wear masks in public and especially in crowded places and large scale gatherings are prohibited (entertainment parks etc). China is also

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exponentially in other countriesincluding South Korea, Italy and Iran. Of those infected, 20% are in critical condition, 25% have recovered, and 3310 (3013 in China and 297 in other countries) have died [2]. India, which had reported only 3 cases till 2/3/2020, has also seen a sudden spurt in cases. By 5/3/2020, 29 cases had been reported; mostly in Delhi, Jaipur and Agra in Italian tourists and their contacts. One case was reported in an Indian who traveled back from Vienna and exposed a large number of school children in a birthday party at a city hotel. Many of the contacts of these cases have been quarantined.

These numbers are possibly an underestimate of the infected and dead due to limitations of surveillance and testing. Though the SARS-COV-2 originated from bats, the intermediary

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themselves while examining such patients and practice hand hygiene frequently.

• Suspected cases should be referred to government designated centres for isolation and testing (in Mumbai, at this time, it is Kasturba hospital). Commercial kits for testing are not yet available in India.

• Patients admitted with severe pneumonia and acute respiratory distress syndrome should be evaluated for travel history and placed under contact and droplet isolation. Regular decontamination of surfaces should be done. They should be tested for etiology using multiplex PCR panels if logistics permit and if no pathogen is identified, refer the samples for testing for SARS- CoV-2.

specimens, like bronchoalveolar lavage fluid, sputum, nasal swabs, fibrobronchoscope brush biopsy specimens, pharyngeal swabs, feces, and blood (246).

The presence of SARS-CoV-2 in fecal samples has posed grave public health concerns. In addition to the direct transmission mainly occurring via droplets of sneezing and coughing, other routes, such as fecal excretion and environmental and fomite contamination, are contributing to SARS-CoV-2 transmission and spread (249-252). Fecal excretion has also been documented for SARS-CoV and MERS-CoV, along with the potential to stay viable in situations aiding fecal-oral transmission. Thus, SARS-CoV-2 has every possibility to be transmitted through this mode. Fecal-oral transmission of SARS- CoV-2, particularly in regions having low standards of hygiene and poor sanitation, may have grave consequences with regard to the high spread of this virus. Ethanol and disinfectants containing chlorine or bleach are effective against coronaviruses (249-252). Appropriate precautions need to be followed strictly while handling the stools of patients infected with SARS-CoV-2. Biowaste materials and

sewage from hospitals must be adequately disinfected, treated, and disposed of properly. The significance of frequent and good hand hygiene and