COVID-19 AND THE GREAT CHINESE PUZZLE

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The <u>pandemic</u> is spreading like wildfire. What started surreptitiously sometime in late 2019 in Wuhan, China, has engulfed 172 countries and regions by March 25, 2020. Globally over 4,35,000 have been reported as confirmed infected, over 19,500 have died, and around 1,11,000 have recovered.

The virus is SARS-CoV-2; the clinical illness is COVID-19. When not specified, reported numbers may pertain to either infection or disease or a mix, misleading decision-makers to conflate the two.

Coronavirus | China to lift travel curbs on 50 million people in Hubei

The numbers of test results put out from China, the 'index country', have helped the world World Health Organization (WHO) and affected countries get a sense of the seriousness of <u>COVID-19</u> and <u>SARS-CoV-2</u> infection. In China, about 81,600 had confirmed disease; there were about 3,100 deaths. The crude estimate of case fatality was 3.7%. All diseased are infected, the reverse is not true. Not all infected are sick or tested. Hence, information from China is unhelpful to confidently project the probabilities/proportions that will get infected; get COVID-19 symptoms; develop pneumonia; die.

Virus spread in China reportedly stopped by the end of the third week of March, with no new SARS-CoV-2 infections arising locally since then. China is now gearing up to prevent virus transmission from citizens returning from other countries. If only 90,000 were infected among a 1.4 billion population, the proportion was only 0.0065%. Here is the puzzle: for any epidemic, its downturn consequent to high herd immunity requires about 70% infected and immune. Every second person in the community will then be a dead-end for virus spread. What proportion of the Chinese was actually infected? The proportion of 0.0065% is unrealistically low for the visible shift in epidemiology. If 70% were infected, there were 980 million infections. This extraordinary range is the puzzle.

The story began unfolding in December 2019 with cases of pneumonia without an identifiable cause. One astute physician saw this and alerted his colleagues. He was reprimanded by the authorities for spreading fear, rather like 'anti-national activity' in contemporary Indian parlance. Soon they realised that the alarm was true. Among the first 41 cases, most were workers in, or had direct contact with, the Hunan Seafood Wholesale Market, where several species of wildcaught animals were stocked and sold. On December 31, health officials informed the WHO of the outbreak of a suspected zoonosis (vertebrate-to-human transmitted infectious disease). That market and all other similar markets nationally were closed the next day. On January 7, WHO was notified that the pathogen was a novel coronavirus. Soon Chinese scientists mapped its full genome sequence and gene sequence for primers needed for diagnostic tests and made these data publicly available. The International Committee on Taxonomy of Viruses re-named it SARS-CoV-2 because of its close genetic similarity to the SARS coronavirus that had caused the SARS epidemic in 2002-03. Also the new disease was clinically SARS-like. By mid-January, several countries (Thailand, Japan, Taiwan, South Korea, Viet Nam, USA, France, Australia, Singapore, Malaysia and Nepal) reported COVID-19. This was a globalising disease, no longer China's problem alone. It was no longer zoonosis but had become anthroponosis (person-toperson transmitted infectious disease). But when did this epidemic actually start in Wuhan? How long did it remain unrecognised? The number of cases at a given time could reflect the duration of the outbreak. Since amplification of infection is a function of time, the higher the number of

cases at a time when laboratory testing was in full swing, the longer the virus had circulated in China as anthroponosis. The necessary numbers are just not available, which is a problem.

Editorial | China's zero

Only on January 11 did China record the first death from COVID-19. Considering that the test had just become available, any earlier death would not have been attributed to SARS-CoV-2 infection. More than a week later China counted 26 deaths among 830 diagnosed with COVID-19. By January 20, Wuhan was placed under lockout; Hubei province followed shortly. China alerted the world by end-January, it alerted the world that COVID-19 was widely prevalent in all 31 provinces. The WHO declared the disease a 'public health emergency of international concern' on January 30. The very next day Philippines, India, Russia, Spain, Sweden and the U.K. documented virus importation through infected travellers. A pandemic (global epidemic) is declared by the WHO 'when the world's population would likely be exposed to a new infection with potential to make a proportion sick'. By February 2, the infection had already spread to 24 countries outside China-Hong Kong-Macau. Given time this contagious anthroponosis was more than likely to expose the whole world and was already a pandemic by definition. But WHO declared a pandemic only on March 11: 38 precious days were lost. Did WHO get misled by the 0.0065% risk? Countries like India that depend heavily on WHO guidance for public health action had apparently mistaken the non-declaration as a signal that it was short-lived or nonserious. Was not the likelihood of universal spread low if it was not pandemic? On March 12, fear gripped India as it had not done homework to face the pandemic and invoked the Epidemic Diseases Act giving the state extraordinary powers.

Coronavirus | China sees drop in imported cases

On June 11, 2009, WHO had declared influenza H1N1 as a pandemic. It was relatively mild with a case-fatality of about 0.1%. The low fatality rate was probably, partly, because it was not an entirely new virus. The 1918 Spanish flu pandemic was H1N1 virus, replaced by the 1957 Asian flu pandemic of H2N2. People aged 53 and above in 2009 had a high probability of having some immune memory for H1N1. In addition, the 2009 H1N1 strain had lower virulence than earlier pandemics. The pandemic alert was clearly warranted based on defined virological and epidemiological criteria. Yet there were allegations that WHO had declared a 'false pandemic' as a pandemic on account of pharmaceutical industry pressure to sell more pharmacological products. Might WHO have delayed the declaration of COVID-19 as a pandemic until it was too obvious to avoid criticism?

This infection shows an exponential growth pattern typical of contagious anthroponosis. Epidemiologists have estimated the transmissibility of SARS-CoV-2. The term basic reproduction number (R0) denotes the number of new infections that an infected person could seed, during the infective period, if all contacts exposed were non-immune and susceptible. For this infection, R0 has been estimated to be between 1.5 and 3.5. If we accept conservatively R0=2, one infected person will, on an average, infect two other people; next generation will be 4, then 8, 16, 32 and so on. When a large proportion is infected, hence immune, the scene changes. An infected person will encounter a majority of immune and a minority of non-immune among contacts, and virus transmission will slow down.

Coronavirus | China's high-tech battle against COVID-19

Experts outside China are projecting infection to reach 30-70% of the world's population in the coming months. Data from China indicate that 80% of the infected are likely to be not very ill, and hence require little or no medical attention. Around 14% would develop severe disease, and around 6% would require critical care. Consider these figures against a total of 90,000 reported

infected in all of China and extrapolate to a probable 980 million infected. If countries use these estimates to plan resource demand in terms of hospital beds, personnel, ICU beds, ventilators, equipment and trained personnel, no country in the world can claim to be prepared to meet these requirements. This is why the Chinese puzzle needs exploration. If only <1 % will be infected when the numbers begin to fall, countries like India have reason for optimism.

Or does this puzzle indicate that although 70% of Chinese were actually infected with SARS-COV-2 by the third week of March, only about 90,000 of the 980 million infected (0.0092%) developed COVID-19? This could also provide reason for optimism, but is highly speculative without necessary information. Why are the data missing? Has the world at large and WHO particularly missed a massive elephant in China? For infection rate to decline, the proportion of immune, hence non-susceptible people among the whole population should be fairly high. We define herd immunity as the proportion immune in the population and herd effect as the reduction of infection incidence in the non-immune segment of the population on account of the high herd immunity slowing down the circulation of the virus. To determine how large the COVID-19 epidemic was in China is information that we need urgently. The only way to get it is by careful antibody prevalence surveys, which we hope WHO will be demanding from China.

Coronavirus | Wuhan closes makeshift hospital as new cases in China drop sharply

China claimed success in interrupting transmission because Hubei province was under lockdown fairly early in the course of the epidemic, and China also imposed travel restrictions on other provinces. Is its claim credible? What if the epidemic had actually started, say, in August?

Since the lockdown occurred later than it should have, travellers attending the Chinese Lunar New Year celebrations transmitted the infection wherever they went. Most countries have focussed on identifying infections brought by travellers from such high-risk countries but the majority with COVID-19 infections now are showing increasing rates of local transmission. The signal from the Chinese puzzle could be that widespread infection is not inevitable and with stringent public health measures infection rate could be brought down to zero. That scenario does not make epidemiological sense. We have to conclude that China does not know, or is not revealing, the magnitude of infection in all of China.

All countries that expected very small numbers to be at risk of infection based on the China puzzle must anticipate about 70% to be infected in the first wave of the epidemic. If summer heat dampens transmission, we may not reach 70% until autumn or winter. After that, the infection may stay on as endemic and seasonal. We are better off to learn lessons from other countries. We must also learn our own lessons real-time, as and when events happen. We have to catch up for lost time because of our optimistic reading of data that were not verified or even checked for plausibility.

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