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The Executive Summary is produced weekly and contains in-depth analysis. International SOS publishes a COVID-19 [Daily Case Summary](#).

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SECOND WAVE IN BEIJING SEMINAL IN CORONAVIRUS PANDEMIC

Beijing is experiencing China's most significant outbreak of COVID-19 since February. The outbreak can probably be classified as the first true "second wave" in the COVID-19 pandemic. This is because Beijing had had 51 COVID-free days prior to this outbreak.

The new outbreak has occurred despite rigorous testing, control, and quarantine measures. For this reason, this outbreak has worrying implications for the control of coronavirus globally.

Outbreak details and viral strain

The current outbreak began when a man with no history of recent travel visited a doctor on 10 June with a fever and chills. He tested positive for SARS-CoV-2, the virus that causes COVID-19, and was hospitalized the following day. Officials think he, or a close contact, was infected at the Xinfadi Agricultural Wholesale Market.

Since then, more than 356,000 people have been tested and 137 cases confirmed. Thirty-one new cases were diagnosed on 17 June, four more than the day before.

Genomic sequencing shows the viral variant causing the new outbreak is related to strains China has found in people returning from Europe.

Link to Xinfadi Wholesale Food Centre

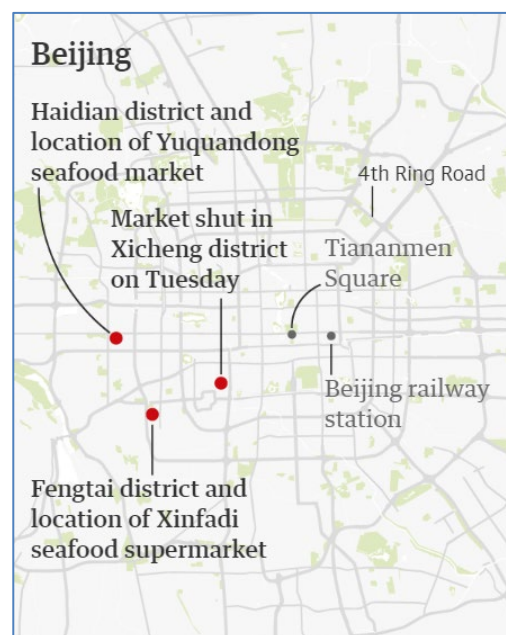
The recently confirmed cases have been traced to the huge Xinfadi Agricultural Wholesale Market in Beijing's south-west, where thousands of tonnes of vegetables, fruit and meat change hands each day.

Over 200,000 people are thought to have visited the market since 30 May. More than 8,000 market workers have been tested and quarantined.

Authorities have reported that several surfaces in the market tested positive for SARS-CoV-2, including a cutting board in a booth handling imported salmon.

There is no evidence coronaviruses infect fish, but one hypothesis is that infected workers in Europe contaminated the fish or its packaging during processing.

Chinese and Norwegian authorities have since concluded that Norwegian salmon was unlikely to be the source of the new outbreak. If this had been true, we would have expected more than one salmon-related outbreak around the world. China had halted salmon imports from Norway.



Graphic: The Guardian

It is still uncertain how the virus was introduced to the market area.

Nuanced response

Beijing has adopted a targeted approach to control the outbreak. The city has applied different degrees of restrictions on people from different areas based on their risk level. This contrasts with the sweeping lockdown imposed on Wuhan and more recently cities in the north-east.

Beijing's public health emergency response level was increased from three to two, the second highest. Under the level-two restrictions, the city's roads and highways remain open, companies and factories, in the main, can continue work, and there is no blanket restriction on residential compounds.

Some more details:

- Twenty-eight neighborhoods and districts in Beijing have been designated "medium" or "high risk"
- People from "medium" or "high risk" neighborhoods are banned from leaving Beijing and all residents should avoid "non-essential travel" out of the capital
- Taxi- and ride-hailing services are prohibited from carrying passengers out of the city
- Anyone leaving Beijing must have a negative reading on a nucleic acid test taken within seven days prior to departure
- Non-residents and outside vehicles are prohibited from entering high and medium risk areas
- Several residential compounds have been locked down
- Schools across the capital, many of which have been gradually reopening since March, have reverted to online classes
- Certain businesses have been closed, soon after they had reopened
- Companies should use flexible work arrangements such as teleworking, where possible
- Libraries, museums, art galleries and parks are limited to 30% capacity
- All indoor sports and entertainment venues have been shut
- 100,000 community workers have been sent door-to-door to trace about 200,000 people who have been to the Xinfadi Market
- Interprovincial travel has been restricted: 40% of flights in and out of Beijing have been cancelled and several interprovincial bus services suspended

Mass testing

- Mass testing and tracing is underway. The city has the capacity to perform 90,000 tests per day. 70,000 tests were performed last Sunday

PCR testing for people and market workers at a football stadium.

Source: NPR



Cases probably exported to other cities and provinces

- Hebei, Liaoning and Sichuan provinces have discovered new coronavirus cases in recent days probably linked to the Beijing outbreak
- A 36-year-old businessman at the Beijing market has developed COVID-19 in the city of Taizhou, 1,500 kilometers (932 miles) from Beijing

Travel to other parts of China

- Other parts of China (including Shanghai) have imposed restrictions on people entering from the capital, however normal travel is allowed for those with a green “health code” on their smartphone
- Some other cities across China have warned they would quarantine arrivals from the capital
- Officials are tracking people from Beijing who have travelled to other parts of China

The future

- Gao Fu, the head of China’s Center for Disease Control and Prevention (CDC), said ([link in Chinese](#)) the new outbreak may have begun “one month earlier” than the previously suggested period of late May or early June (meaning April)
- Wu Zunyou, Chief Epidemiologist with China’s CDC has said that the trend of confirmed cases in the next few days will be crucial for determining the course of the outbreak. “Those who have contracted the virus should display symptoms in around two days, and if cases aren’t surging by then, it’s safe to say the outbreak has basically stabilized. There have been no clear signs of family clusters or cross-infection between patients”

Macau introducing quarantine for travellers from Beijing

Authorities in Macau, the world's biggest casino hub, said people who have been to Beijing within two weeks of arriving in Macau will be quarantined for 14 days at a designated location.

INTERNATIONAL SOS DISCUSSION

It is accepted that COVID-19 outbreaks often start in an area well before being detected. This was the case in Lombardy and New York where, because of late control efforts, ICU's later became overwhelmed.

This outbreak in Beijing, which probably started in April or May, clearly demonstrates how a previously virus-free area can quickly become an epidemic centre if the virus is introduced (or re-introduced) and is not quickly detected.

FOCUS ON NEW TREATMENTS

STERIOD DRUG DEXAMETHASONE HAILED AS A 'MAJOR BREAKTHROUGH' IN TREATING CORONAVIRUS

On Tuesday 16 June, [Oxford University](#) released the results of its double-blind trial using dexamethasone to treat over 2,000 COVID-19 patients.

The results showed dexamethasone to be the first drug to significantly reduce the risk of death among severe COVID-19 cases. Among those who could only breathe with the help of a ventilator, dexamethasone reduced deaths by one-third, and by one-fifth in other patients receiving oxygen only, according to preliminary results.



Graphic: ABC Australia

POSSIBLE HORMONAL CAUSE OF BLOOD CLOTS TO BE TARGETED IN TRIAL

About one in three patients with COVID-19 develop dangerous blood clots. [A trial](#), funded by the British Heart Foundation, will test the theory the blood clots are caused by a hormone imbalance triggered by coronavirus infection. The drug to be tested is TRV027 which apparently "rebalances hormones involved in blood pressure, water and salt.

This approach is different from many therapeutic trials based on reducing the body's inflammatory response.

TWO COMPANIES TRIALING MONOCLONAL ANTIBODY TREATMENT BEGINS CLINICAL TRIALS

Giving antibodies to a patient is called "passive immunisation". Both companies are making synthetic antibodies, unlike treatment with convalescent plasma, which comes from recovered COVID-19 patients.

1. [Tychan](#), a biotechnology company based in Singapore, will begin Phase 1 clinical trials of the first monoclonal antibody treatment (TY027) treatment for COVID-19. TY027 binds to a specific epitope of the spike (S) protein found on the surface of the virus. The trial will evaluate the ability to treat as well as to prevent COVID-19, for example after a person has been exposed to the SARS-CoV-2 virus. Phase 1 will involve 23 volunteers and take about six weeks.
2. [Eli Lilly and Company](#) has also started human trials of an antibody therapy designed to treat COVID-19. Phase 1 results are expected in late June. The first COVID-19 patients to be treated are hospitalized at New York University's Grossman School of Medicine in New York, Cedars-Sinai in Los Angeles and Emory University in Atlanta.

US HUMAN TRIALS BEGIN FOR FIRST ANTIBODY COCKTAIL THAT MIGHT TREAT AND PREVENT COVID-19

Biotechnology company Regeneron [announced](#) that it is trialing an “antibody cocktail” to both prevent and treat COVID-19. The placebo-controlled trials of REGN-COV2 will be at multiple sites and will test four populations:

- People who are hospitalized with COVID-19
- People who have symptoms of the disease, but are not hospitalized
- People who are healthy but are at high risk of getting sick, and
- Healthy people who have come into close contact with a person who is sick.

Regeneron's scientists picked two antibodies against COVID-19 and mass-produced them.

ARTICLE / JOURNAL ROUNDUP

FDA STOPS RECOGNIZING HYDROXYCHLOROQUINE AND CHLOROQUINE AS EMERGENCY TREATMENTS FOR COVID-19.

The US Food and Drug Administration (FDA) is no longer recognizing hydroxychloroquine and chloroquine as emergency treatments for COVID-19. Despite early small studies that showed some positive results, more recent larger, [more carefully designed studies](#) have failed to confirm this benefit.

TOILETS MAY CAUSE AEROSOLS THAT CONTRIBUTE TO COVID-19 SPREAD

SARS-CoV-2 has been shown to be present in stool of infected patients, and therefore stool could potentially be infectious. A study published today in the journal [Physics of Fluids](#) examined whether flushing a toilet could contribute to transmission of COVID-19 through aerosolising of virus. The study simulated flushing the toilet and found that virus-sized particles could reach above the toilet seat.

The authors suggest some simple measures to reduce the potential risk:

- Put the toilet lid down before flushing, which can basically prevent virus transmission.
- Clean the toilet seat before using it, since floating virus particles could have settled on its surface.
- Wash hands carefully after flushing, since virus particles may be present on the flush button and door handle.



Image: new.engineering.com

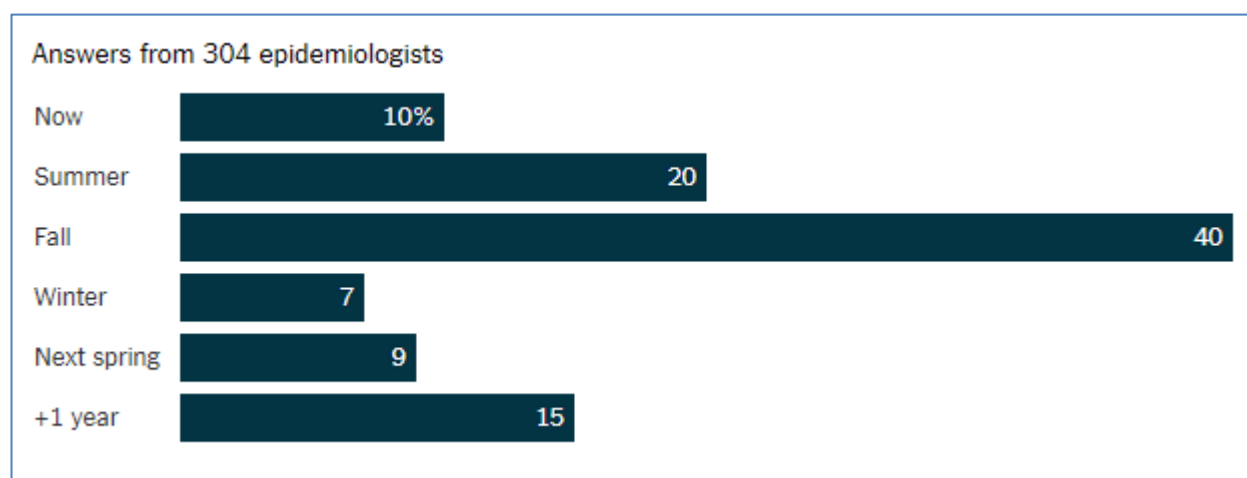
HOW 132 EPIDEMIOLOGISTS ARE DECIDING WHEN TO SEND THEIR CHILDREN TO SCHOOL

The New York Times conducted a [survey](#) of more than 500 epidemiologists and infectious disease experts. One question was about when they would send their children back to school, school camp or childcare:

- 70% said they do this right now or later in the summer or fall
- 30% said they would wait for a vaccine.

CHART 1: When Would You Send Your Children to School, Camp or Day Care?

Source: [New York Times](#)



CASES REDUCING IN DHARAVI, MUMBAI'S SLUM

We have previously discussed the [risk of COVID-19 to Dharavi](#), India's most crowded slum within Mumbai. However, the management of COVID-19 may provide a model to less-developed nations.

Authorities have been going door-to-door to locate cases of COVID-19, screening by measuring temperature and oxygen saturation. So far over 700,000 people have been screened. Fever clinics have also been set up.

Due to the overcrowding, safe quarantine within Dharavi is virtually impossible, so those with symptoms have been isolated in nearby schools and sports clubs converted into quarantine centres. Daily new infections are now down to a third compared with early May, half the sick are recovering, and the number of deaths this month has been significantly reduced.



Image: Mumbai Times

This contrasts with total cases in India which have been rapidly increasing.

Dharavi's "chase the virus" (aka "track and trace") approach is based on cluster management in both Wuhan, South Korea and now Beijing.

EFFECT OF OBESITY

A [BBC article](#) examines the increased risk of severe COVID-19 due to obesity.

The statistics are clear:

- A [UK study](#) of 17,000 hospital patients with a body mass index (BMI) of more than 30 had a 33% greater risk of dying than those who were not obese
- A [study of NHS electronic health records](#) found obesity caused a doubling of the risk of dying from COVID-19
- A [study of critically ill patients](#) in UK intensive care units found that nearly 34.5% were overweight, 31.5% were obese and 7% morbidly obese (a total of 73%), compared to 26% with a healthy BMI

Various hypotheses are given for the effect of obesity

- Lower lung capacity / greater oxygen requirement due to being obese
 - More likely to need assistance with breathing and support with kidney function
- Adipose tissue (fatty tissue) may have higher levels of ACE2
 - ACE is the main way the virus enters the body
- Inflammation caused by the macrophages that “invade” our fat cells
 - A specific type of fat tissue more common in people from black, African and minority ethnic (BAME) backgrounds. This may partly explain higher diabetes rates and vulnerability to COVID-19
- Other problems?
 - Obesity is often associated with decreased heart, lung or kidney function and Type 2 diabetes

PUZZLING COVID CLUSTER AT FORT BENNING, USA

The [US Army](#) tested 640 new recruits for COVID-19 on their arrival at Fort Benning. Four were +ve and were isolated. The other recruits were monitored for 14 days.

Eight days after the monitoring period ended, one recruit reported COVID-19 symptoms. The recruits were re-tested and 142 positive cases (22%) were identified.

International SOS comment

The number of cases that evolved means that it is likely that several of the recruits were in the pre-symptomatic phase of COVID-19 and tested negative. We know that [false negative PCR tests are common](#) in this early phase of the disease.

UPDATE ON TEXAS

This is our seventh weekly report on the number of cases per day in Texas since “re-opening” in stages began on 1 May.

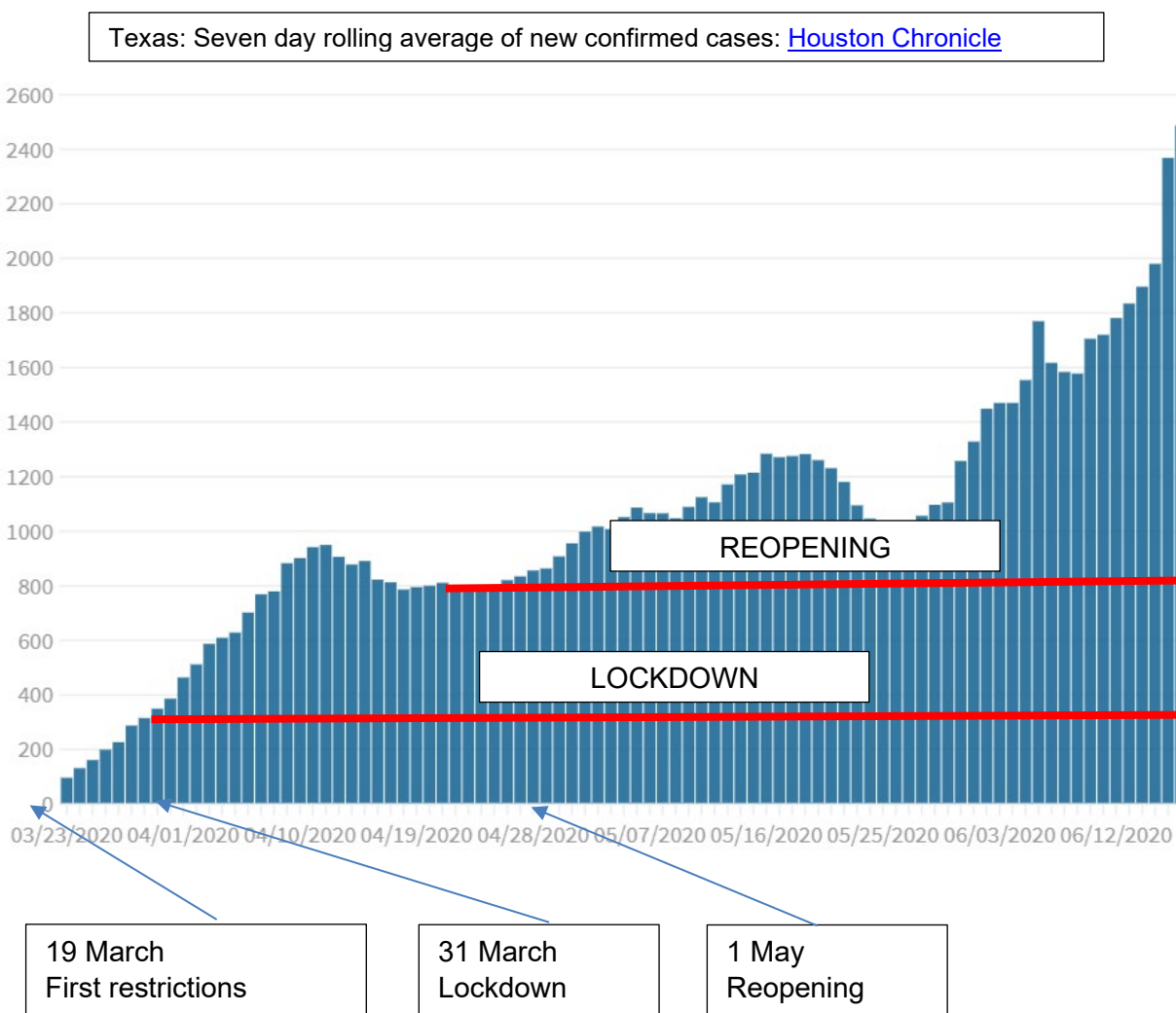
- Cases per day continue to increase
- COVID-related hospitalizations continue to increase
- COVID-related ICU admissions continue to increase

NEW CASES PER DAY

The graph below from the Houston Chronicle shows a sharp increase in new coronavirus cases. The rate remains a multiple of both when lockdown occurred and when re-opening began on 1 May.

Cases per day

Lockdown	31 March 2020	325 cases per day
Re-opening	1 May 2020	785 cases per day
	10 June 2020	1,575 cases per day
	17 June	2,634 cases per day

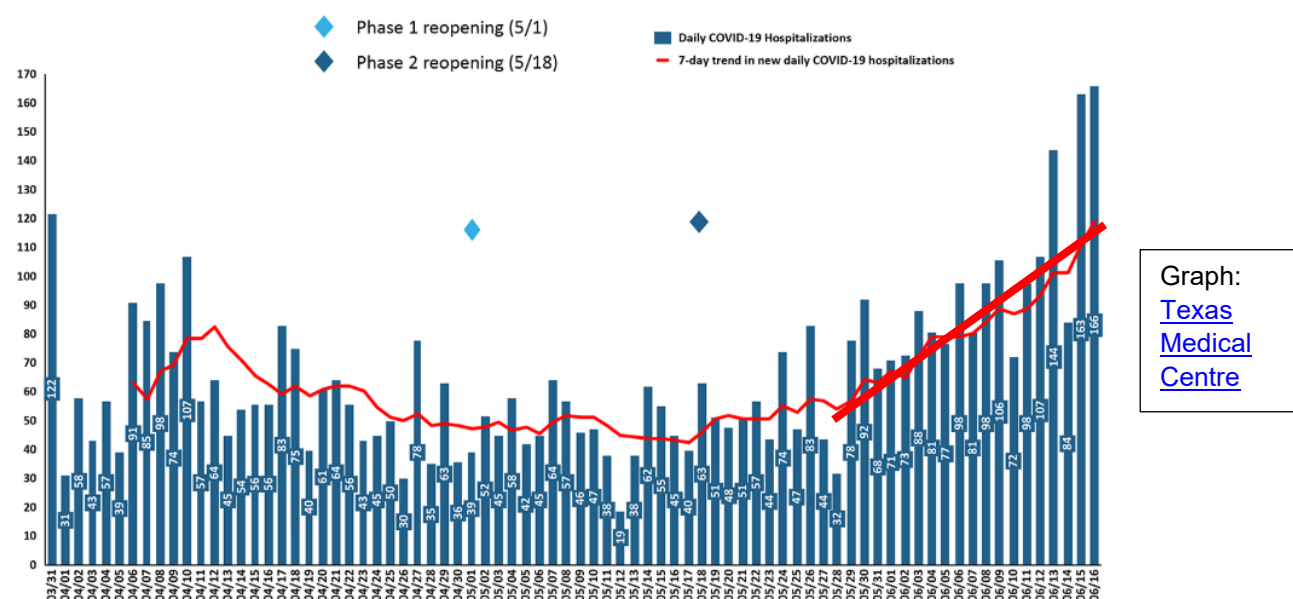


HOSPITALIZATIONS IN TEXAS

The State of Texas does not report daily state-level hospitalizations, however Texas Medical Centre (Houston) does. The graph shows a continued increase in new COVID hospitalizations in recent weeks.

Date	TMC average daily growth in hospitalizations
4 June	2.1% daily growth
11 June	3.5% daily growth
17 June	4.4% daily growth

ICU & Med Surg hospitalizations

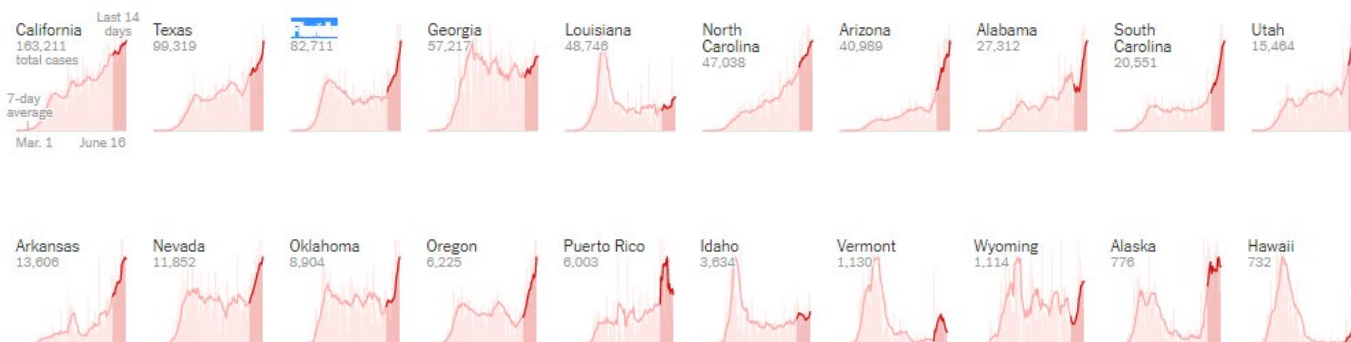


Source: TMC institution clinical census

TMC TEXAS MEDICAL CENTER

"TMC" refers to the group of individual hospitals and institutions that make up Texas Medical Center

WHERE CASES ARE INCREASING IN THE USA

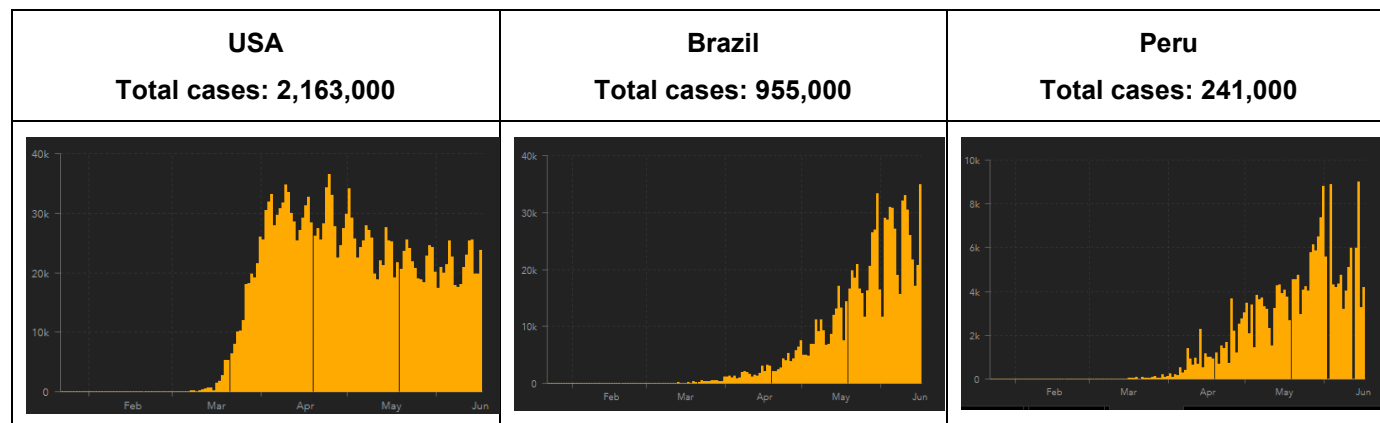


Data: New York Times

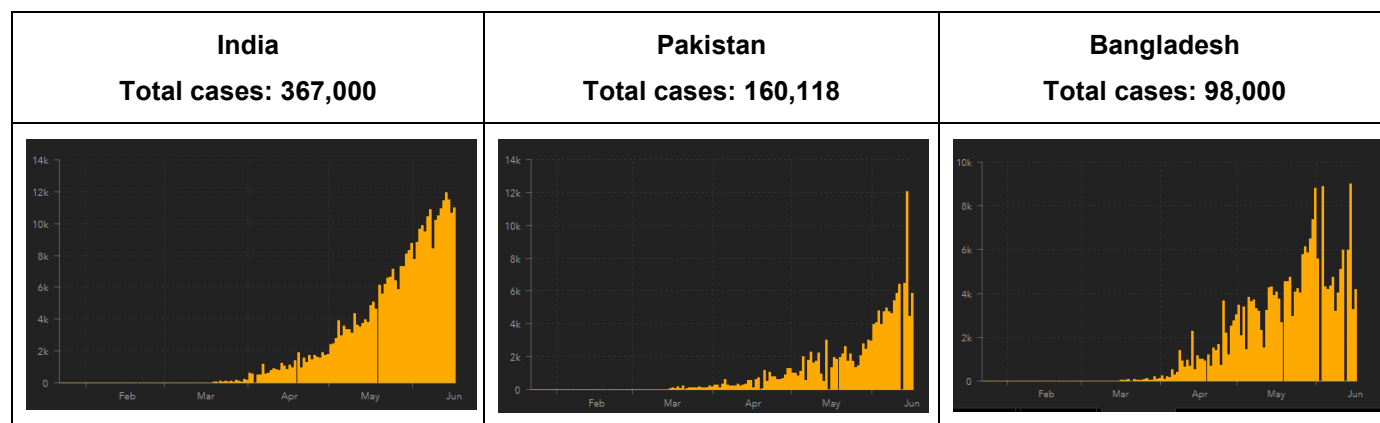
GLOBAL HOTSPOT ROUNDUP

Defined as countries with highest case counts in the region which have not passed their first peak of new cases

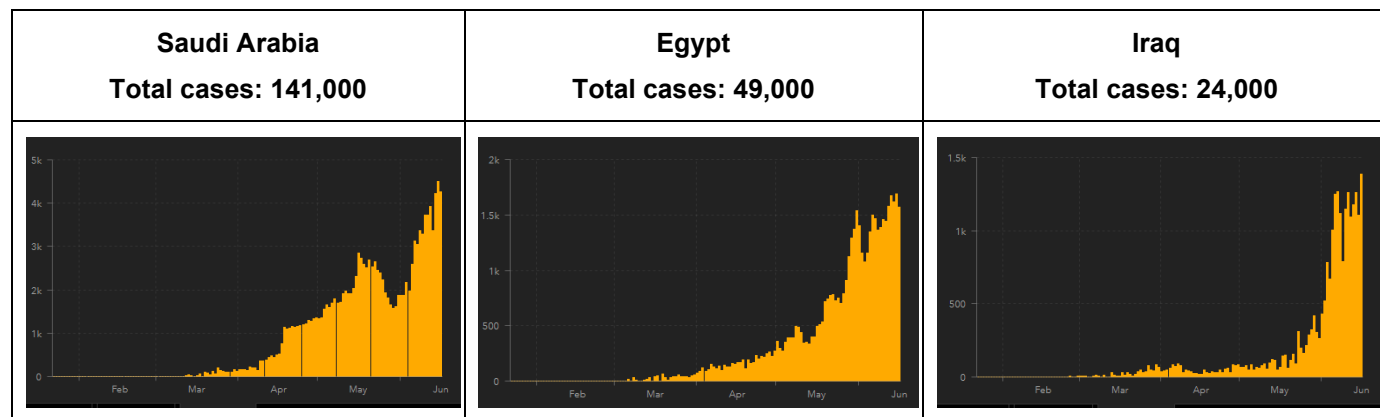
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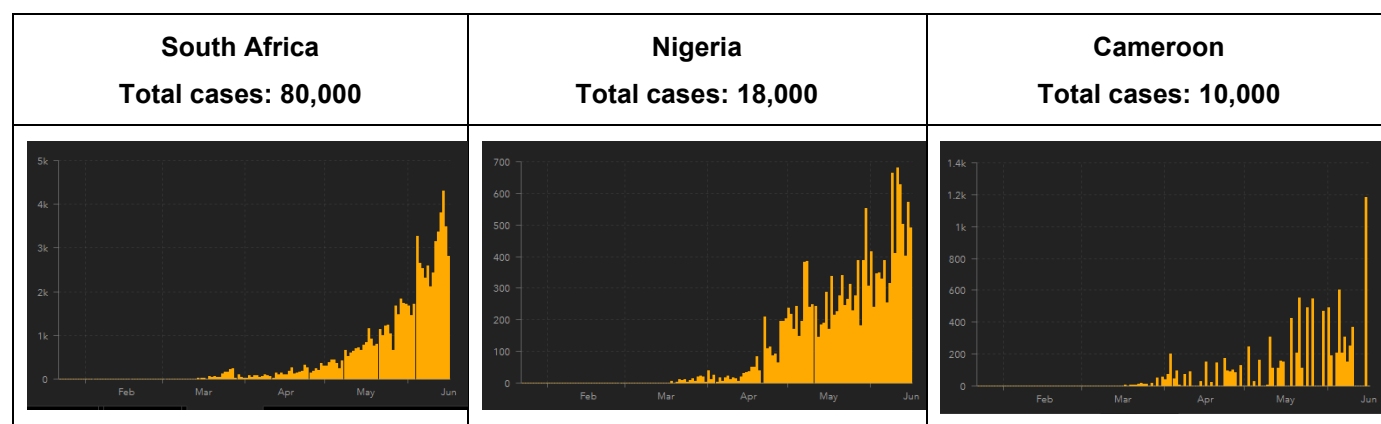
INDIAN SUB-CONTINENT



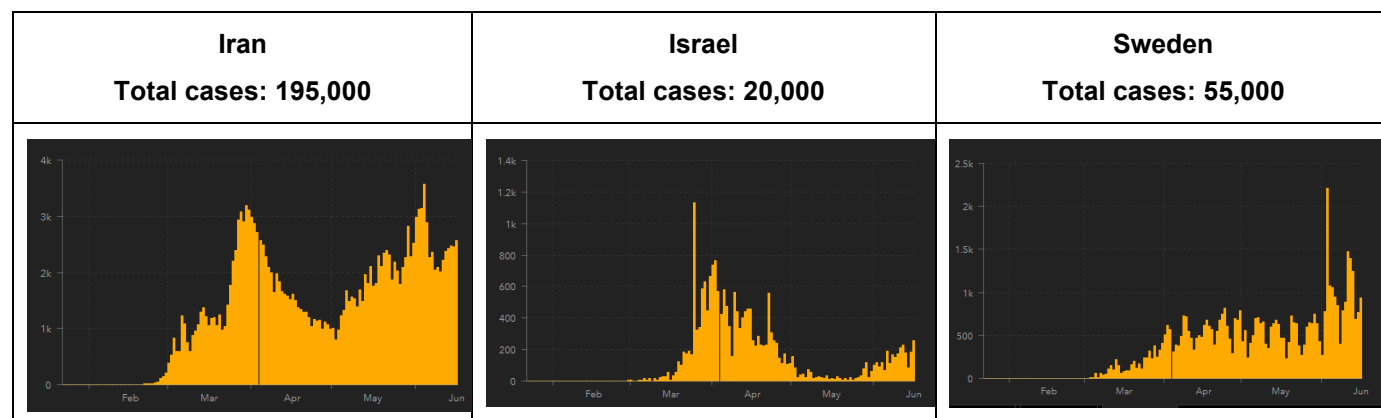
MIDDLE EAST



AFRICA



COUNTRIES WITH SECOND PEAKS IN THE FIRST WAVE



A VIEW FROM THE LABORATORY: PROFESSOR JOHN OXFORD

The dominant route of transmission of COVID-19 is by air; masks play an important role

A [new study in PNAS by Zhang et al](#) showed that airborne transmission is “highly virulent and dominant” in the three epicentres they studied. **They concluded face covering protective measures are “the determinant that shapes the pandemic”**. Social distancing, at least in the USA, was insufficient to protect the public.

The centres studied were New York, Wuhan and Italy. They conclude face masks in public, along with social distancing, quarantine and contact tracing, represent the most likely fighting opportunities to stop the COVID-19 pandemic. **They also note data showing that the peak of infectiousness is on or before symptom onset.**

In the USA social distancing measures in NYC were to stay 6 feet (about two meters) away from people, to avoid mass gatherings and stay away from crowded places. The rise in the infections in the USA cast doubt on these measures alone. It is difficult to disentangle the various measures used in China because they were introduced simultaneously. However, in the USA and Italy face coverings were introduced later. Their calculations were that face masks reduced the number of infections by over 78,000 in Italy from 6 April – 9 May and by over 66,000 in NYC from 17 April to 9 May. “Sound science should be effectively communicated to policy makers”.

Implementing policies without a scientific basis could lead to catastrophic consequences particularly in light of attempts to re-open the economy of many countries.

Personal Note: I do accept the dire warning at the end of the paper which, in my experience is very unusual in a PNAS paper and of course the journal is high quality. I feel that the problem in many countries (probably not in China) are commercial companies offering masks of varying quality. We know that poorly fitting masks leak virus for example. However, I feel that this properly reviewed paper is an important contribution. In this rather thorough paper, the authors looked at the efficiency of humidity, indoor and outdoor, use of masks and the effects of temperature in virus survival. In an enclosed environment virus bearing aerosols accumulated, whereas in the open air the virus aerosols were easily diluted. They rather criticise WHO and CDC for ignoring aerosol transmission whilst concentrating on preventing contact transmission from surfaces.

My own conclusion for this paper is that we have still not learnt the important lessons from the Spanish Influenza in 1918. These were that non-pharmaceutical interventions as described here had to be implemented quickly and simultaneously. It was not successful in many USA cities to try one method (e.g. masks) and then add another (e.g. hand wash) later. I would have liked to have seen a paragraph comparing the quality and material composition of the masks used in these three countries.

Could changing pollen levels across the year explain the seasonal effect of respiratory virus?

We considered last week in our international SOS expert review the benefits (speed) and drawbacks (no peer review) of publication in MedRxiv. However, the authors are important as well.

The [authors in this paper](#) include a microbiologist from Viroscience in Rotterdam, whilst the senior author, Martin Hoogreen, is from the Technical Science Department of the Open University. Their theory is that pollen plays a part as an immune stimulant and appears to lower the R_0 of flu-like viruses. They tested the theory over four years in

Holland, with a population of 17 million, by analysing the flu-like incidence per 100,000 population and weekly pollen counts and meteorological data.

They found a highly significant inverse association for pollen and flu-like illness. This correlation was highest when pollen thresholds of 610 total pollen grains m^3 per week, 120 allergen pollen grains m^3 per week and a solar radiation threshold of 510 J/cm^2 are passed.

Their rather dramatic conclusion is that COVID-19 may revive in the Netherlands after week 33, the start being preceded by the relative absence of pollen. Other studies have failed to show that ambient temperature is a prediction of flu outbreaks. Association of humidity is also inconsistent. Neither high UV nor high temperatures correlate with COVID-19 infections.

This hypothesis is that aerosol pollens deactivate aerosol viruses before they can infect a new host. The prevalence of allergic disease in the Netherlands is 52% and thus "the allergenic path provides a plausible explanation for an inhibitory effect of pollen on flu-like epidemics.

What could happen in the next 'flu' season?

It is quite possible that COVID-19, like other respiratory viruses, RSV, common cold, influenza, meta pneumovirus and Coronavirus EC43 could 'settle down' as an epidemic virus occurring seasonally. It is also quite possible for COVID-19 to spread at the same time as the annual influenza and even produce co-infections.

This is why there is a growing campaign to persuade more people to be vaccinated with influenza vaccines. There will be enough vaccine for example, in the EU and not just those over the age of 60 years or those in the 'at risk' group, more or less the same as for COVID-19. It is also possible that vaccination with live influenza vaccine may give some cross protection.

Virus interference is known in the laboratory and is more likely a result from intense competition for cells in which to grow. Another factor could be stimulation of interferon by one virus which then influence both viruses. Alternatively, COVID-19 could "interfere" with influenza. There is some evidence of the latter. We are talking about a seasonal flu which typically kills 290,000 - 650,000 people each year globally and so these factors are very important in clinical practice. There is some evidence that the influenza 2019/20 epidemic has already been shortened by COVID-19 (Flu Net data of global surveillance).

Personally, I would like to see a rapid diagnostic test that will identify flu and COVID-19. Of course, with influenza we can vaccinate, and we have antiviral drugs of two classes against the neuraminidase and also the influenza RNA replication complex.

Just as important will be the effect of social distancing, masks and hand hygiene. So, an unanticipated collateral benefit of our prevention of COVID-19 could be a destruction of influenza, common cold and even diarrheal and vomiting viruses like norovirus!

A “Directed” Research programme like the MRC AIDS disease programme of the 1980’s for Covid-19?

Tim Daffoir in the University of Birmingham is suggesting that governments coordinate a research programme. The UK Medical Research Council (MRC) had such an initiative in the 1980’s for the AIDS epidemic. This makes sense. He notes that the situation at present encourages researchers to “self-assemble” and views this as inadequate for a national crisis. A COVID-19 directed programme would set up a leadership council to coordinate research including social scientists and those working in “academic” institutions and pharmaceutical groups. It may be anathema to some politicians, but the UK is facing a disaster with over 60,000 deaths and perhaps 100,000 very seriously ill survivors of an undirected programme.

Could wild animals and/or pets spread Coronavirus?

Members of the family of coronavirus infect both birds and mammals in their natural habitat. Humans are infected from “spill-over virus” which can then establish itself as a “human coronavirus”. Common cold coronaviruses were first isolated from humans 60 years ago. But could COVID-19, which almost certainly emerged from a fruit bat, move “backwards” from humans to pets like ferrets or mink. In London, for example, at least 10,000 people keep a pet ferret! The SARS virus, for example, infected animals in 2005. The interface between humans and animals needs greater examination and study.

Obviously, this is cautious and particularly dangerous work for laboratories and needs Category IV laboratories where the scientists wear complete protective outfits and have piped air individually. But so far fear of pet dogs and cats being infected have not been fulfilled! Or at least very rarely, and the opposite, from pets to humans is extremely rare!

Early stage development of an experimental messenger RNA vaccine for COVID-19

If I had launched a team of virologists on the development of a COVID-19 vaccine I would have gone the traditional route: grow the virus in Vero cells in the laboratory, harvest after 5 days, scientifically purify with chromatography and then kill the virus with formaldehyde. This is the well tried and tested route used for influenza and polio vaccine production.

However, Moderna, a US company, has embarked on a molecular biology pathway. The scientists have isolated viral messenger RNA from the spike (S) protein of COVID-19. This mRNA is basically the vaccine. In theory, the S protein will be presented to the immune system as if it was the virus itself and should stimulate both T and B cell immune responses.

This is a “Platform Technology” which can be used for a range of viruses, This, is Phase 1 trials and first in manmade vaccine safety studies. In theory, mRNA’s from several viruses could be combined in the future. Experimental vaccines are under development for RSV, influenza (H7N9), zika and chikungunya.

Now the Company has finalised a Phase 3 protocol and has support from BARDA for 30,000 participants enrolled in the USA in conjunction with NIAID. The primary endpoint will be prevention of symptomatic disease, and secondary endpoints will be prevention of severe disease and hospitalisation and prevention of infection. The trial will begin in July. These are noble and important goals.

In theory this production technology could be used to produce up to 1 billion doses per year. Meanwhile even in the real world the results are somewhat impressive! This also illustrates how state assistance can be used to assist private companies in commercial ventures. Knowing the nucleotide sequence of the virus RNA, Moderna synthesized mRNA and prepared a clinical batch by 20 February. The first volunteer at the National Institute of Allergy and Infectious Disease (NIAID) was dosed on 16 March. The Phase IV trial starts in July.

Unfortunately, there are still plenty of people being infected in the USA, however, this may allow the results of real-life protection studies to come within 2-3 months; these studies are harder to run if there is no or little disease in the population.

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