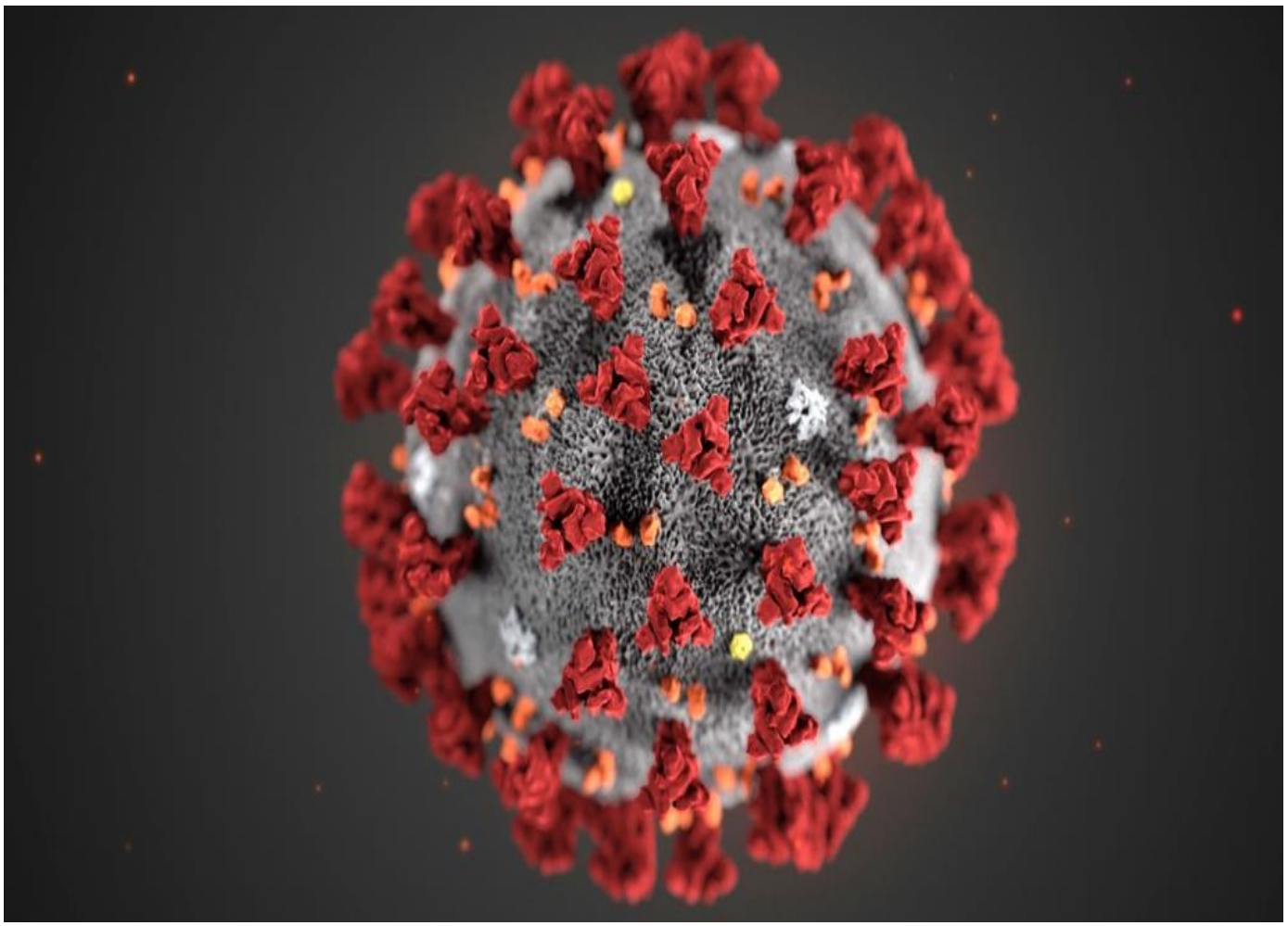
Report of Seminar 'International Update on COVID-19' held at THE TAMIL NADU DR M.G.R MEDICAL UNIVERSITY (TNMGRMU), Chennai on the 17th March 2020, Tuesday



Report prepared by the Department of Epidemiology, The Tamil Nadu Dr.MGR.Medical University under the guidance of Hon'ble Vice-Chancellor Dr. Sudha Seshayyan

Globally, as on 24th March 2020, more than 3,85,000 people have been affected, and more than 17,000 have died, as per Johns Hopkins University's Coronavirus Resource Center (accessed on 24th March @ 3 pm IST). In India, 585 people had been reported to have contracted COVID-19 and nineteen to have lost their lives to the illness, as of 24th March, 3 pm IST.

As the epidemic of COVID-19 is spreading all over the globe rapidly, a timely initiative to conduct a one day program on '**International Update on COVID-19'** by The Tamil Nadu Dr. M G R Medical University was proposed and executed by Dr. Sudha Seshayyan, Vice-Chancellor of the University. The objective was to provide a comprehensive and up-to-date assessment of the COVID-19 epidemic, the progress in the response to the epidemic, at global, regional and country levels in the context of global commitments and strategies, by bringing together international scientists working in the leading Universities and organizations across the globe under one roof and support the control of the pandemic. The program was jointly done in collaboration with INDIAN MEDICAL ASSOCIATION, Tamil Nadu State Branch and INDIAN MEDICAL ASSOCIATION Chennai South. The key topics for discussion included Current Global Situation, Virology of SARS COV-2, principles of testing, hospital preparedness, administrative preparedness, R & D response, Intricacies of Vaccine Development, etc.,

Four International scientists one each from Australia (University of New Castle), Switzerland (WHO), Delhi (CDC) and the United States (Emory Vaccine Centre) participated through videoconferencing. The event was conducted at the Silver Jubilee Auditorium of the Tamil Nadu Dr. M G R Medical University connecting the medical colleges located at Trichy, Madurai, Coimbatore, and Tirunelveli by videoconferencing. The program was also transmitted live through a webinar.

The Honorable Minister for Health & Family Welfare, Government of Tamil Nadu Minister and Pro-chancellor of the University Dr.C.Vijaya Baskar inaugurated the conference on 'International Update COVID-19' at 09.00 hours on 17th March 2020. After inaugurating the program, the Honb'le Health Minister also interacted with Dr. Vijayakumar Velu from Emory Vaccine Centre, Yerkes National Primate Research Center, Atlanta, USA, and Dr. Valan, Advisor to WHO working at the Country office for India located in New Delhi through video conference. He discussed on COVID-19 and explored the reasons for varying Case Fatality Rates of COVID-19 between countries.

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1. SARS-CoV-2/COVID-19: Current Global Situation and countermeasures

Vijayakumar Velu, Ph.D. (Emory Vaccine Center, Yerkes National Primate Center, Atlanta, Georgia, USA.

In the late December 2019, a number of pneumonia cases of unknown origins emerged in Wuhan, Hubei province of China. These cases reported being connected to the Hunan Seafood Wholesale Market that sells many live animals. On 3 January 2020, a novel member of enveloped RNA coronavirus was identified in samples of bronchoalveolar lavage fluid from a patient in Wuhan and subsequently confirmed as the cause of this disease by the Chinese Center for Disease Control and on 7 January 2020, the World Health Organization (WHO) named it as the 2019 novel coronavirus (i.e., 2019-nCoV). On 11 February 2020, WHO named the illness associated with 2019-nCoV as the 2019 coronavirus disease (COVID-19). The Chinese reacted very fast and released the sequence of the virus on 11th January 2020. The disease has rapidly started spreading to other parts of China during late January and in late February 2020 it started spreading outside china very rapidly and the total cases of infection reported per day exceed china. The disease has rapidly spread, internationally to other parts of the world and many countries across 6 continents by the first week of March 2020. The WHO on 12th March 2020 released the news that the COVID-19 as a pandemic and declared COVID-19 a public health emergency of international concern (PHEIC). Declaring a PHEIC is an urgent call, at the highest level, for the international community to launch a global coordinated effort to stop the outbreak, which requires strong public health response, high-level political commitment and sufficient funding. As of 22 March 2020, a total of 337,553 COVID-19 cases in the world and 14,654 deaths occurred. Despite the worldwide spread, the epidemiological and clinical patterns of the COVID-19 remain largely unclear. As of 22 March 2020, a total of 396 COVID-19 cases in India and 7 death was reported.

Coronaviruses are large, enveloped, positive-strand RNA viruses that can be divided into 4 genera: alpha, beta, delta, and gamma, of which alpha and beta CoVs are known to infect humans, which is called human coronaviruses (HCoVs). Four HCoVs (HCoV 229E, NL63, OC43, and HKU1) are endemic globally and account for 10% to 30% of upper respiratory tract infections in adults. Although HCoVs have long been regarded inconsequential pathogens due to their mild phenotypes in humans, in the early 21st century, two large-scale epidemics with alarming morbidity and mortality – *i.e.*, severe acute respiratory syndrome coronavirus (SARS- CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV), have changed that view. This SARS-CoV2 believed to be from BATS and has 25% distinct form the SARS 2002 outbreak virus, which represents anew clade emerged. It's a brand-new virus, the world does not have any vaccine or treatment to cure the virus. The transmission was reported to be human to human.

Clinical Prognosis and disease: Patients seem to have different conditions with asymptomatic to mild, moderate, severe, critical infection. **Asymptomatic infection:** without any clinical symptoms and signs and the chest imaging is normal, while the 2019-nCoV nucleic acid test is in a positive period. **Mild (40%):** symptoms of acute upper respiratory tract infection, including fever, fatigue, myalgia, cough, sore throat, runny nose, and sneezing. Physical examination shows the congestion of the pharynx and no auscultatory abnormalities. Some cases may have no fever or have only digestive symptoms such as nausea, vomiting, abdominal pain and diarrhea. **Moderate (40%):** with pneumonia, frequent fever and cough, mostly dry cough, followed by productive cough, some may have wheezing, but no obvious hypoxemia such as shortness of breath, and lungs can hear sputum or dry snoring and / or wet snoring. Some cases may have no clinical signs and symptoms, but chest CT shows lung lesions, which are subclinical. **Severe (15%):** Early respiratory symptoms such as fever and cough, may be accompanied by gastrointestinal symptoms such as diarrhea. The disease usually progresses around 1 week, and dyspnea occurs, with central cyanosis. Oxygen saturation is less than 92%, with other hypoxia manifestations. **Critical (5%):** Children may quickly progress to acute respiratory distress syndrome (ARDS) or respiratory failure, and may also have shock, encephalopathy, myocardial injury or heart failure, coagulation dysfunction, and acute kidney injury. This disease cause death rapidly in people with underlying conditions such as blood pressure, diabetes, lung disease and heart disease. Adults at all ages were sensitive to COVID-19 and there were no significant differences between the genders. Clinical manifestations of children's COVID-19 cases were less severe than those of adults. People with >60 years die with a case fatality rate of 14% currently. The cause of death is due to severe acute respiratory distress syndrome (ARDS).

Treatment: Since it's a brand-new virus, currently we don't have an effective treatment for this disease. However, now different parts of the world are testing anti-virals to treat patients. Remdesivir (nucleotide analogue) has been working in animal models both in vitro and in vivo, currently, this is tested in different parts of the world. Kaletra (lopinavir/ritonavir) protease inhibitors used in HIV treatment is working for some patients. Chloroquine a malaria drug seems to work in France with a combination of antibiotics (Azithromycin). Many countries are testing many antivirals to find a cure for COVID-19 disease currently.

Vaccine: Many countries are developing different types of vaccine for coronavirus. May be in a year time we may have a vaccine to be tested in people.

Source:

WHO Report on Coronavirus/COVID-19.

CDC report of Coronavirus/COVID-19. Chinese CDC.

NIH News on COVID-19, Pubmed- coronavirus, Google Search.

2. SARS-CoV-2/COVID-19: Administrative Preparedness

Professor Dr R Jayanthi, Dean, Madras Medical College, Chennai

Professor Dr R Jayanthi, Dean, Madras Medical College, Chennai delivered her lecture on Administrative Preparedness to face the development of this COVID-19 epidemic. She explained how the government has taken very quick response and initiative, including preparedness in government hospitals - case definitions, laboratory protocols, case transport guidelines, preventive measures, hospital and ambulance disinfection protocols and case management. Started with forming a team which included the Chiefs of the units of Internal Medicine, Nursing, Microbiology, Community Medicine and Administration Section and the team identified the challenges in facing the rapid spread of SARS-CoV2 infection and worked out on the essentials. Facilities were prepared for Isolation and IPC for health professionals in sanitizing their hands and other procedures to be followed in the isolation ward. She insisted on focus over respiratory and hand hygiene, surface cleaning with 1% hypochlorite solution or 5% lysol. She also insisted the importance of IEC materials in spreading awareness among the public in addition to the importance of nutritious diet.

3. SARS-CoV-2/COVID-19:Global Situation of COVID 19 and R&D Response

Dr Soumya Swaminathan, MD, Chief Scientist, WHO

Dr Soumya Swaminathan, MD, Chief Scientist, WHO connected to the seminar through video conference, presented “COVID-19: Global situation and R&D Response”. She made an in-depth discussion on the latest update on the COVID-19 cases all over the world – both confirmed and reported.

The current global situation of the spread of disease was as on 16th March 2020, which stated 165,065 confirmed cases since 31st December 2019 and 6472 deaths globally.

The situation in China and countries outside China in the last 24 hours was updated, which stated 12,281 cases from 85 countries and 736 new deaths and in China, 29 new cases were confirmed with 14 new deaths. Official government sources reporting on the spread of COVID-19 as on 16th March was explained as per the updates from all WHO regions. From WPRO, more than 10,000 cases and 119 deaths, from SEARO – 367 cases and 16 deaths were reported. EURO region reported with 54937 cases and 2330 deaths, among which Italy reported the highest of 24747 cases. EMRO region reported with 15361 cases and 740 deaths, PAHO with 2523 cases and 46 deaths and AFRO region with 153 cases and 3 deaths, being the lowest.

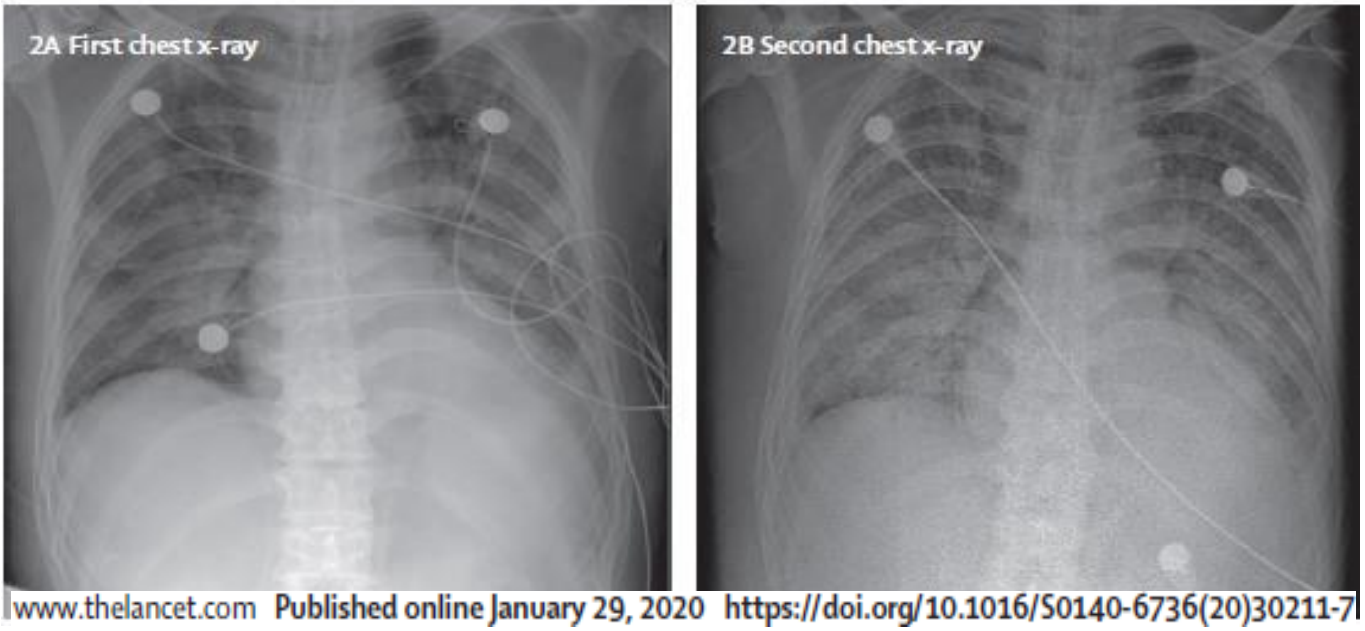
She then revealed about the WHO scientists meet up and the issues discussed in the meet which included the need for research road map with clearly defined priorities and governance framework. The components of a successful road map is essential to be defined to work on that protocol that would help to contain the spread was her statement. Later, she explained on the current research study being conducted on the treatments for COVID-19 in hospitalized patients which is aimed to estimate the effectiveness of antiviral treatments. The concept of randomisation, research design and procedures were explained and she concluded with the key roles of study governance.

She later answered few questions raised on the global scenario & spread of disease expected in the next few days and strategies to contain the spread, by the participants.

4. Hospital Preparedness –Infection Prevention and Control for COVID 19

Dr. A.S. Valan, Public Health specialist, CDC, India

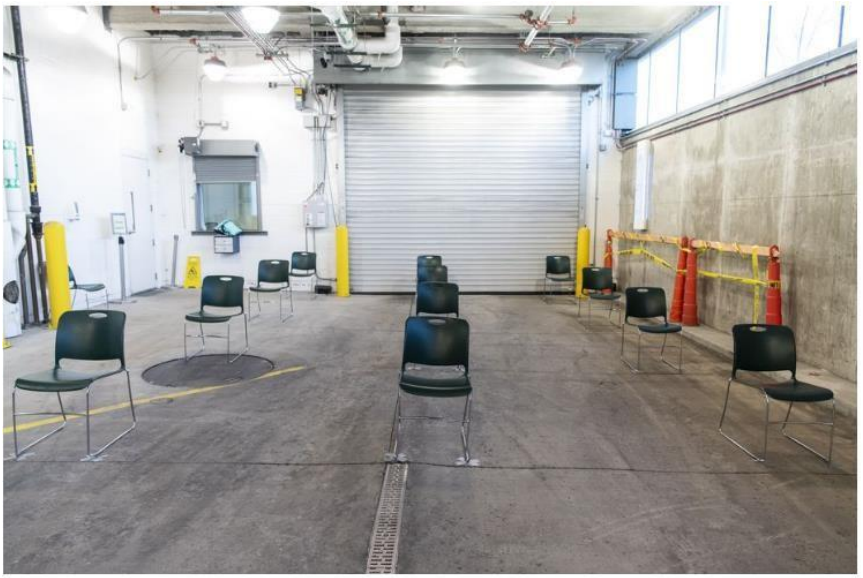
Dr.A.S. Valan who is a public health specialist, CDC, India highlighted that the virus spreads through close person to person contact thru droplets; symptoms of COVID19 may vary from fever, cough and shortness of breath with a complications of pneumonia, respiratory or Multi system organ failure.



Clinical Course of COVID 19 in Infected People will develop uncomplicated or mild illness (81%),14% develop severe disease that requires hospitalization and oxygen support,~ 5% require admission to an intensive care unit . Not all mild illness require admission in a health facility; **isolation to contain/mitigate virus transmission should be prioritized**

The next important key area was IPC properties which are **to Isolate, Identify and Inform and** to focus on Triage.

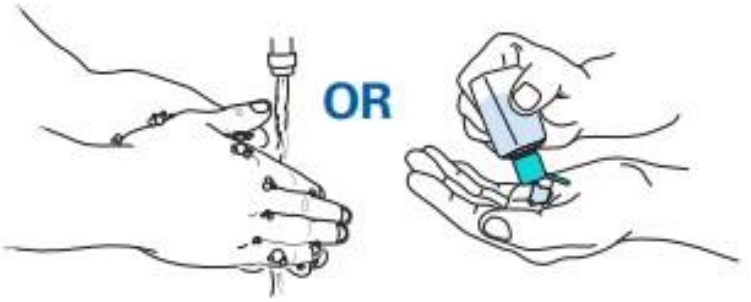
The patient has to be separated during triage (waiting areas, etc.) as much as possible

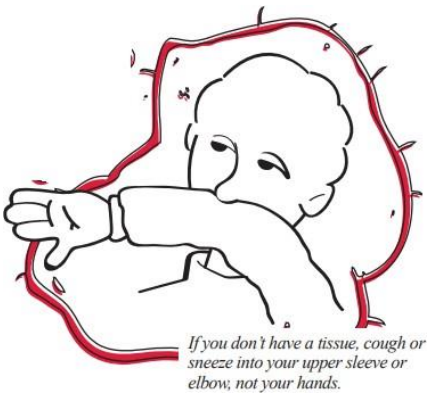


Chairs for patients to sit and wait to be tested, each chair is exactly 6 feet apart, at Rush University Medical Center's forward triage center for coronavirus placed in one of the hospitals ambulance bays, Tuesday, March 10, 2020. | Tyler LaRiviere/Sun-Times

He insisted the health care worker who is handling triage should adhere standard precaution by wearing gowns, gloves, face mask, and eye protection (goggles or face shield).

He also spoke about Standard precautions for all patient by following hand hygiene and Respiratory hygiene along with rational and correct use of PPE and also environmental cleaning and disinfections are very important in spread.





Key points for PPE use

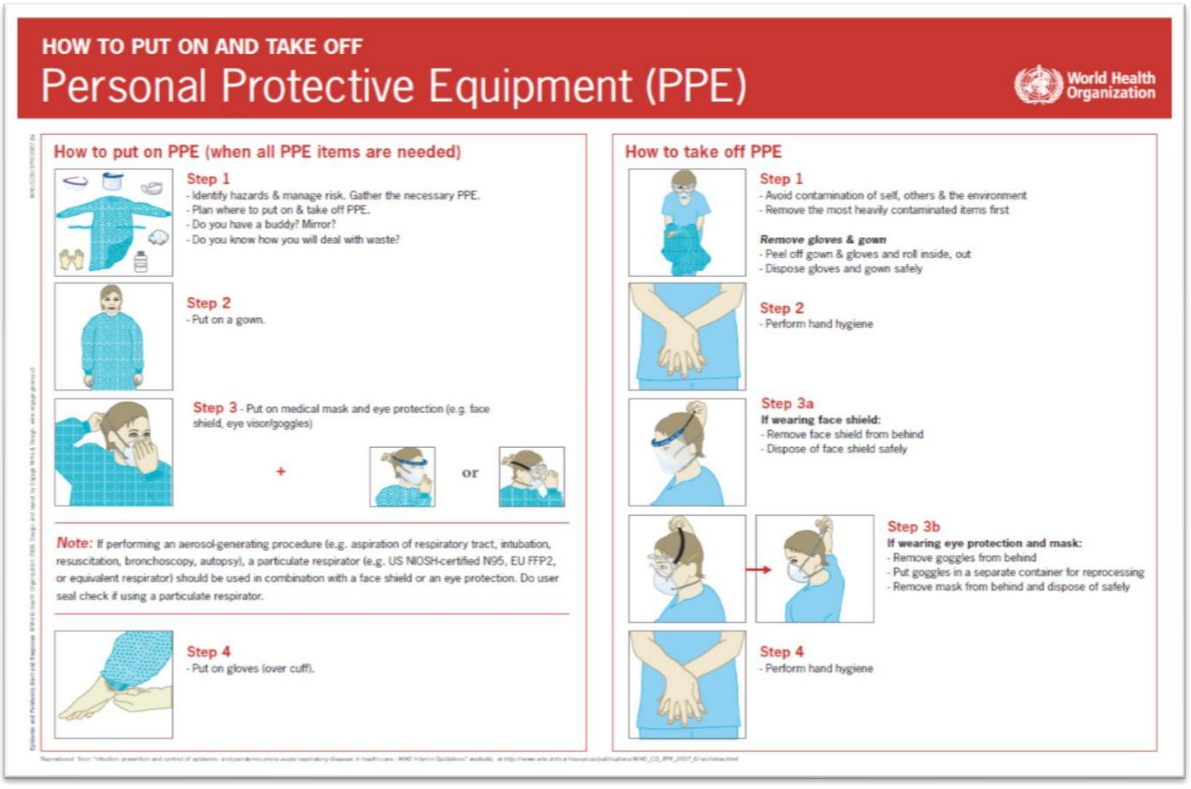
PPE relies on **consistent and correct use** by healthcare personnel

Trainings and practice for healthcare personnel in advance should be given

Risk of self-contamination is higher when removing PPE

Remove PPE slowly and carefully

Do not touch front of masks, respirators, or facial protection (likely most contaminated)



He also spoke about routine cleaning and disinfecting frequently touched and frequently contaminated surfaces like Light switches, bed rails, door handles, sinks, bathrooms should be done.

5. Virology of SARS COVID 2

Dr Hemalatha Varadhan, Deputy Director, Clinical Microbiology, NSW Health Pathology

Dr Hemalatha Varadhan, Deputy Director, Clinical Microbiology, NSW Health Pathology- Hunter shared her expertise under the topic of Virology of SARS-CoV-2.

I**ntroduction -** Most coronaviruses are typically referred to as common-cold viruses. The less-pathogenic variety include HCov-229E, HCoV-NL-63, HCoV-0C43 and HCoV-HKU1. The highly pathogenic group consists of SARS-CoV, SARS-CoV-2 and MERS-CoV.

Virology- SARS-CoV-2 is a beta coronavirus. Enveloped positive-sense single stranded RNA viruses, small genome- ~30kb. Consists of structural and non-structural proteins.

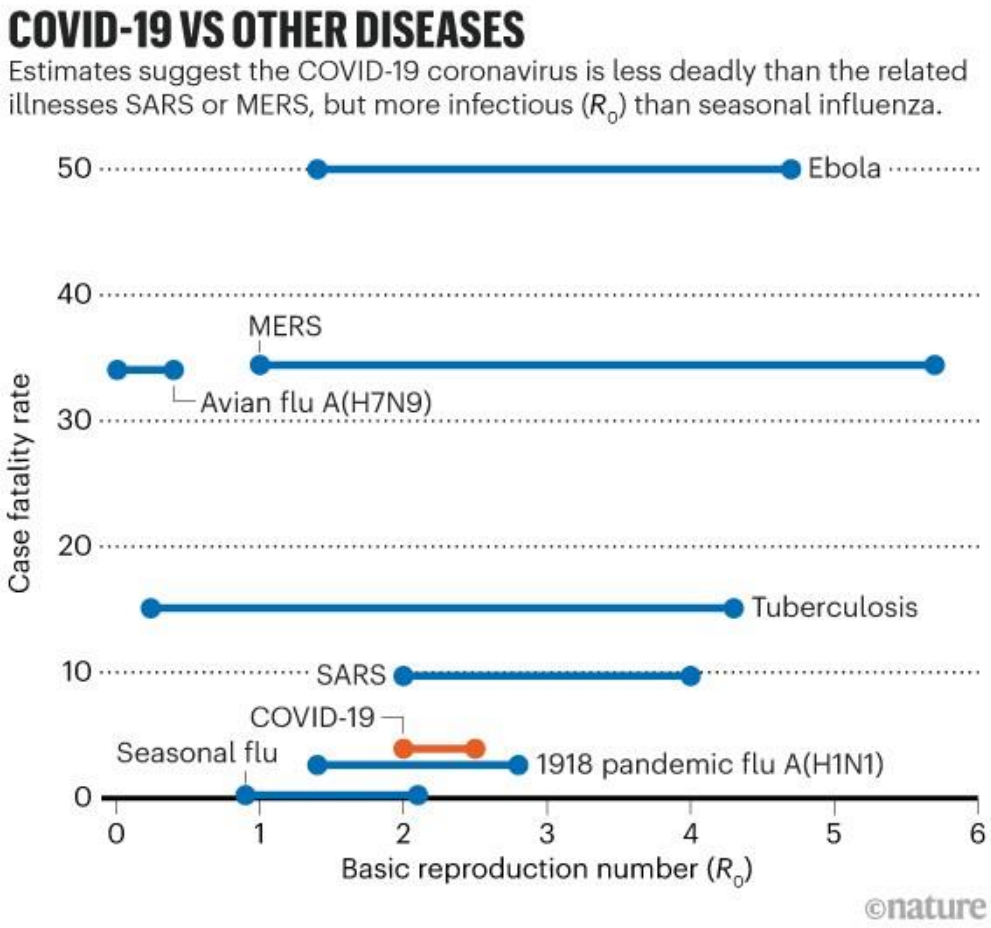
Binding- The structure of the receptor-binding gene region is very similar to that of the SARS coronavirus, and the virus has been shown to use the same receptor, the angiotensin-converting enzyme 2 (ACE2) for cell entry. The closest RNA sequence similarity is to two bat coronaviruses, and it appears likely that bats are the primary source.

Pathogenesis- The incubation period for COVID-19 is thought to be within 14 days following exposure, with most cases occurring approximately four to five days after exposure. A report by WHO-China joint mission that viral can be detected in the upper respiratory tract secretions 2-3 days prior to develop of symptom.

Clinical features- Mild to critical, mostly mild. Fever, fatigue and dry cough were most common symptoms in an earlier study in Wuhan published by Wang et al. GI symptoms uncommon but observed in few patients. Acute respiratory distress syndrome (ARDS) is a major complication in severe illness. In a study by Wu et in 201 patients, age greater than 65 years, diabetes mellitus, and hypertension were each associated with ARDS. Shedding can occur up to 2 weeks in severe cases. Virus can be detected in faeces in 30% at day 5 after symptom onset and persist up to 4-5 weeks in moderate cases.

Epidemiology- R_0= 2.5-3, Case-fatality rate- 2.4% varies with age group

Viral stability- Stable for 3 hrs, 4hrs, 24 hrs, 48hrs in aerosols. Copper, cardboard, steel and plastic respectively



Lab detection

Who to test- refer your local guidelines?

What to sample- lower respiratory tract specimens offer increased positivity rate than upper respiratory tract specimens. Swabs in viral transport medium or dry swab in saline are the optimal specimens.

How to test- Real time PCR for a range of targets- ORFs, RdRP gene, N, E and S genes. Commercial platforms are increasingly being deployed. High specificity and sensitivity. Serology is useful for serosurveys and when PCR is negative. Viral culture can be performed but available in limited centres.

Resources

- https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019- ncov
- https://hub.jhu.edu/novel-coronavirus-information/
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/872745/Infection_prevention_and_control_guidance_for_pandemic_coronavirus.pdf
- https://www.thelancet.com/coronavirus
- https://www.nejm.org/coronavirus
- https://www.cdc.gov/coronavirus/2019-ncov/index.html
- Critical care- https://emcrit.org/category/emcrit/
- Clinical guidelines- https://www.idsociety.org/public-health/COVID-19-Resource-Center/

6. COVID 19 Vaccine – Realm of Reality

Dr Dhinakar Raj, Director, Center for Animal Health Studies, Tamil Nadu Veterinary and Animal Sciences University, Chennai.

Intricacies of Vaccine Development

The topic of current status and strategies in vaccine development against SARC-CoV-2 was discussed under the guidance of **Dr Dhinakar Raj, Director, Center for Animal Health Studies,** Tamil Nadu Veterinary and Animal Sciences University, Chennai.

Corona viruses (CoVs) are enveloped positive-sense RNA viruses, characterized by club-like spikes that project from their surface (corona), an unusually large RNA genome and a unique replication strategy involving sub genomic RNAs. CoVs cause a variety of diseases in mammals and birds ranging from enteritis in cows and pigs and upper respiratory disease chickens to potentially lethal human respiratory infections. The ongoing disease pandemic is called, Corona virus infectious disease 99 (COVID 99) and the pathogen causing it, the SARS-CoV2 or novel CoV since it is similar to the SARS CoV but not the same. Hence the name novel CoV, as none of the humans has prior immunity to it.

The coronaviral genome encodes four major structural proteins, the spike (S), nucleocapsid (N), membrane (M) and the envelope (E) proteins. The ‘S’ protein is responsible for facilitating entry of CoV into the target cell. It is composed of a short intracellular tail, a transmembrane anchor, and a large ectodomain that consists of a receptor binding S1 subunit and a membrane-fusing S2 subunit.

SARS-CoV2 shared 79.5% sequence identity with SARS-CoV. Sequence analysis of the SARS-CoV-2 ‘S’ protein genome showed that it was only 75% identical with the SARS-CoV ‘S’ protein. The receptor binding motif (RBM) in the ‘S’ protein showed most of the amino acid residues essential for receptor binding were conserved between SARS-CoV and SARS-CoV-2. ACE-2 is the entry receptor for SARS-CoV-2. Protection against SARS-CoV2 has to be based on biosecurity, anti-virals and vaccines.

An ideal vaccine should have the following features:

- Safe and Potent
- No side effects
- Cheap
- Easy to administer
- Thermally stable
- Produce sterile immunity
- Broadly protective against all variants of pathogen
- Effective in all subjects
- Does not complicate diagnostic tools
- Immune correlates of protection
- Mass scale production (~7.8 billion people)

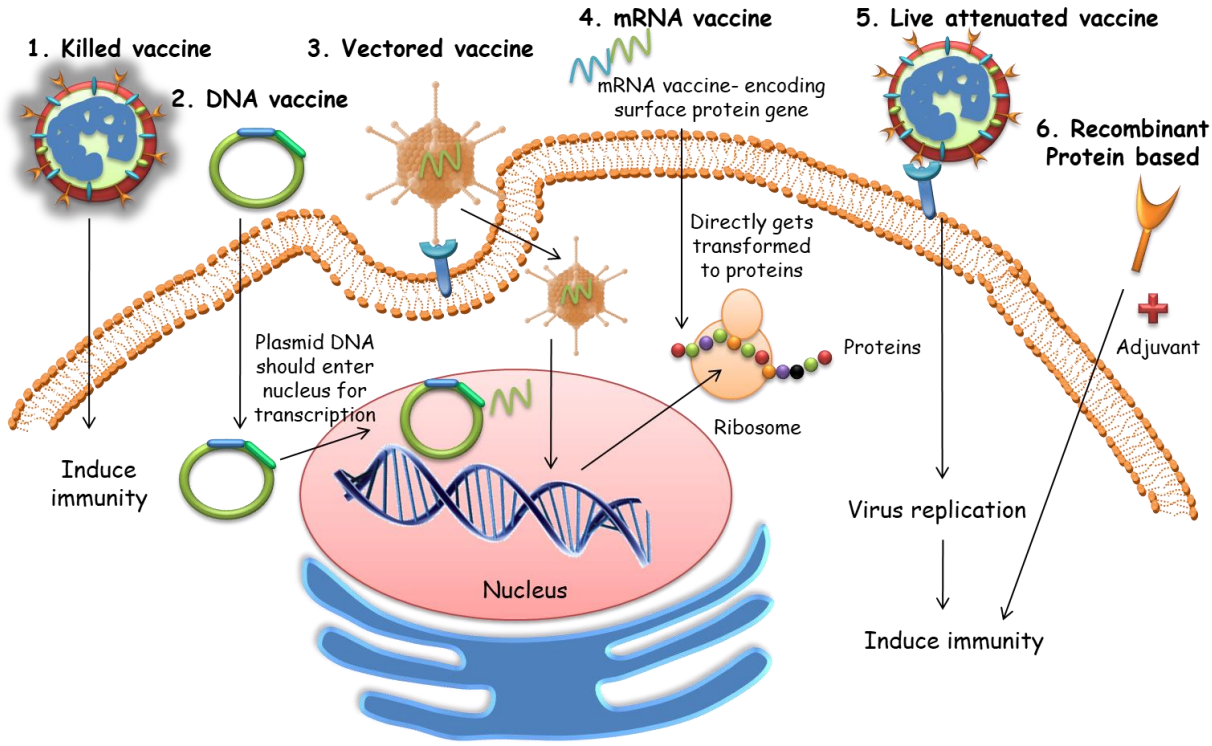
and many more….

In the case of SARS-CoV2, in addition to the vaccine being safe and potent, the scale of requirement (production) would be mind-boggling since the entire humanity has been affected. Further the correlates of protection are unknown, at this point of time. Additionally, the likely vaccine should provide sterile immunity i.e. protection not only against clinical disease but also against virus shedding.

Designing a CoV vaccine – Target antigens

- Target proteins – S, S2, S1 or RBD
- The S precursor protein of SARS-CoV-2 can be proteolytically cleaved into S1 (685 aa) and S2 (588 aa) subunits
- The S2 protein is well conserved among SARS-CoV-2 viruses - may boost the broad-spectrum antiviral effect
- S1 subunit consists of the RBD, which mediates virus entry through the host ACE2 receptor

Different approaches for development of COVID 19 vaccine and their pros and cons



S. No.	Type of Vaccine	Merits	Demerits
1	Inactivated virus vaccines	Easy to prepare, safe, elicit high-titer neutralizing antibodies	No cellular immunity, Needs booster vaccinations
2	Attenuated virus vaccines	Long time for development; induce both cellular and humoral immune responses	Reversion to virulence, recombination possible. empirical
3	Subunit vaccines	Similar to killed vaccines - Highly safe, consistent production, can induce high-titer antibodies	High cost of production, lower immunogenicity, require booster and adjuvants
4	Viral vector vaccines	Similar to attenuated vaccines - Induces high cellular and humoral immune responses	Possibly presence of pre-existing immunity
5	DNA vaccines	Easy to design and produce, long time to produce antibodies, induce cellular immunity	Possibility of genomic recombination
6	mRNA vaccines	Easier to design; high degree of adaptability; induce strong immune responses	Highly unstable

Other technologies such as Trimer Tag, Combined attenuation and Molecular Clamps are also being explored for SARS-CoV2 vaccine development.

COVID 19 vaccine- the way forward

- Within 17 years - 3 major CoV outbreaks encountered
- The race is on to develop a vaccine
- But time required for regulatory compliance to ensure that a vaccine is both safe and effective, means this won't happen overnight , may take 1-2 years
- Use of existing platforms / vaccines could reduce this time
- The novel vaccine platforms could be applicable for future outbreaks of other novel diseases.
- Introduction of innovative vaccine technologies that are radically different from traditional approaches would usher in a new era in the way we fight infectious diseases.

For further reading

- Roujian Lu et al. (2020) Genomic characterization and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding *The Lancet* 395, 565-574 DOI: (10.1016/S0140-6736(20)30251-8)
- Syed Faraz Ahmed et al. (2020) Preliminary identification of Potential Vaccine Targets for the COVID-19 Coronavirus (SARS-CoV-2) based on SARS-CoV Immunological Studies. Viruses, 12, 254; DOI: 10.3390/v12030254
- Shan Lu (2020) Timely development of vaccines against SARS-CoV-2, Emerging Microbes & Infections, 9:1, 542-544, DOI: 10.1080/22221751.2020.1737580
- Pang J, et al. (2020) Potential Rapid Diagnostics, Vaccine Therapeutics for 2019 Novel Coronavirus (2019-nCoV): A Systematic Review. *J. Clin. Med*. 9(3). DOI: 10.3390/jcm9030623.
- Menachery VD et al. (2018) Combination Attenuation Offers Strategy for Live Attenuated Coronavirus Vaccines. J Virol. 92(17). DOI: 10.1128/JVI.00710-18.
- Wang Ning et al. (2020) Subunit Vaccines Against Emerging Pathogenic Human Coronaviruses Front. Microbiol., DOI:10.3389/fmicb.2020.00298

7. Clinical Guidelines in Management

Professor Dr Raghunandhan, Director of Institute of Internal Medicine, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai,

Professor Dr Raghunandhan, Director of Institute of Internal Medicine, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai, in his lecture on 'Clinical Guidelines on Management of COVID-19' explained the various steps and procedures of early recognition of persons with suspected symptoms and immediate implementation of prevention & control measures. It included early supportive therapy and monitoring, collection of specimens for testing, prevention and management of various respiratory complications of COVID-19 including anti-nCoV options available. He also included some clarifications on guidelines of the Government of India in this issue. He delivered a clear picture on various stages of the disease and symptoms shown by the affected persons.

Corona infection has become a global problem and every country has to fight it out As far as clinical management is concerned we have to follow the WHO, GOVT OF INDIA guidelines and published data from reputed international journals.

Clinical management starts from the airport, seaport and national borders. All passengers should be screened for fever, cough and shortness of breadth. They should triaged as per guidelines. Next the patient may come to primary care doctor where he has to follow the personal protection protocols like wearing a mask, maintain one-meter distance etc. If the patient has symptoms he has to admitted and throat swap has to be taken and sample should to send to designated labs. All patients managed as outpatient should be advised on dos and don'ts for preventing corona infection. Home quarantine for 24 days is also advised. If they have foreign travel history or contact with corona positive patient. Any symptomatic medical care worker who provided treatment to suspected or confirmed case also should be admitted and testing must be

Once patient is admitted in isolation, ward the treating team should consists of a medical officer, nurse and hospital worker. They must wear PPE.Treatment is mainly symptomatic and supportive. Basic investigations can be done including x-ray, if needed CT chest. Regarding anti-viral drugs, follow the latest govt guidelines. If the patient is positive

continue the care in isolation ward. Provide him with good nutritious diet,counsel and make him to relax. Give him books for reading arrange for music etc. Establish communication between him and his relatives from the present data ,40 to 50 percent will have mild symptoms only and 30 to 40 percent will require o2 and minimal support. Rest may go for severe complications.

If the patient develop respiratory failure shift to ICU .Treat him as per guidelines.They may need ventilatory assistance.while intubating take utmost PPE precautions. Manage the co morbid illness also.If the patient is free of symptoms and x-ray shadow cleared, repeat throat swap twice within 24 hrs. and if both are negative patient can be discharged.He must be in home quarantine for 14 days.

The message is very simple.Prevention is better than cure.Practice hand washing.cough etiquette.social distancing ,avoid travel and report if any symptoms arise.Follow govt advice only. Together we fight and we win.

8. Principles of Testing and Who Needs to be Tested?

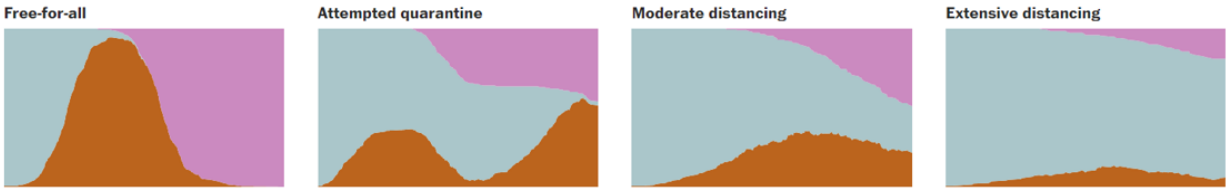
Dr. K. Kaveri, Deputy Director & Head of the Department of Virology, King's Institute of Preventive Medicine and Research, Guindy

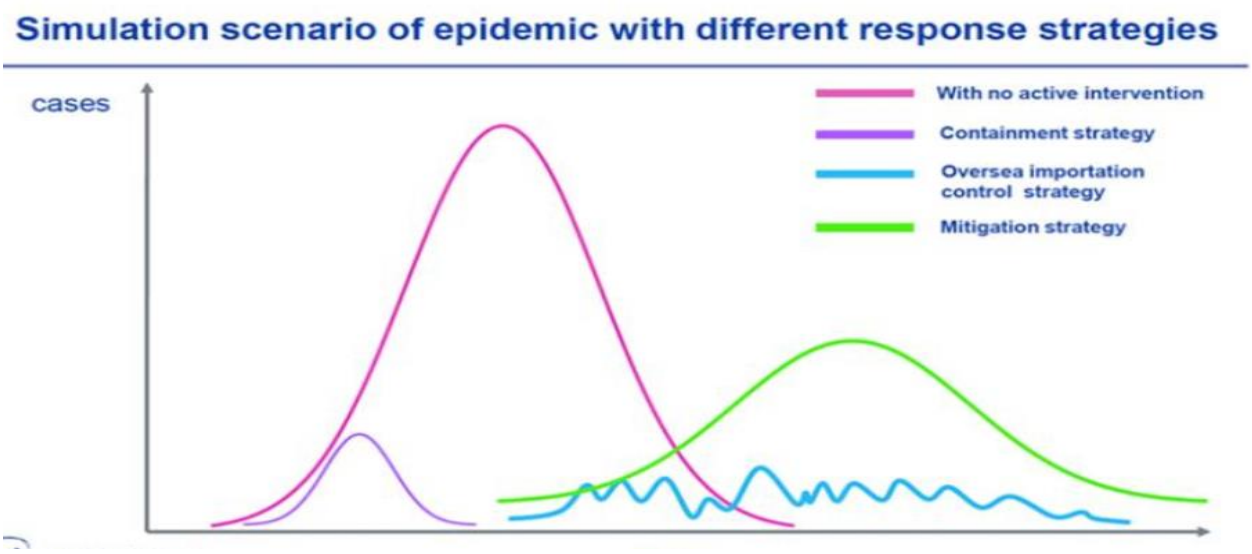
Dr.K.Kaveri, Deputy Director & Head of the Department of Virology, King's Institute of Preventive Medicine and Research, Guindy presented on the principles of testing and whom needs to be tested in COVID – 19. Initially she started with the genetic structure of the virus and the family to which it belongs to. Statements of who is considered as a case and a contact in this detection of COVID – 19 were described to the audience. A complete flow chart of the sample collection and testing criteria was projected to everyone. A complete process including the collection of samples, the areas from where it is collected, collection of blood samples, guidance for specimen collection were illustrated. Apart from the clinical side, the laboratory procedures of storing, transporting, checking for leakage, responsibilities of the sender and the receiver of the samples were described to the gatherings. The presentation on the later part covered topics like type of test needed to detect COVID -19. What are the first line screening test done, serological assays, laboratory protocols and confirmatory assays were projected to everyone. The presentation ended with explanation on how to avoid transmission, commonly used disinfectant and cough etiquette.

9. Summary Epidemiology

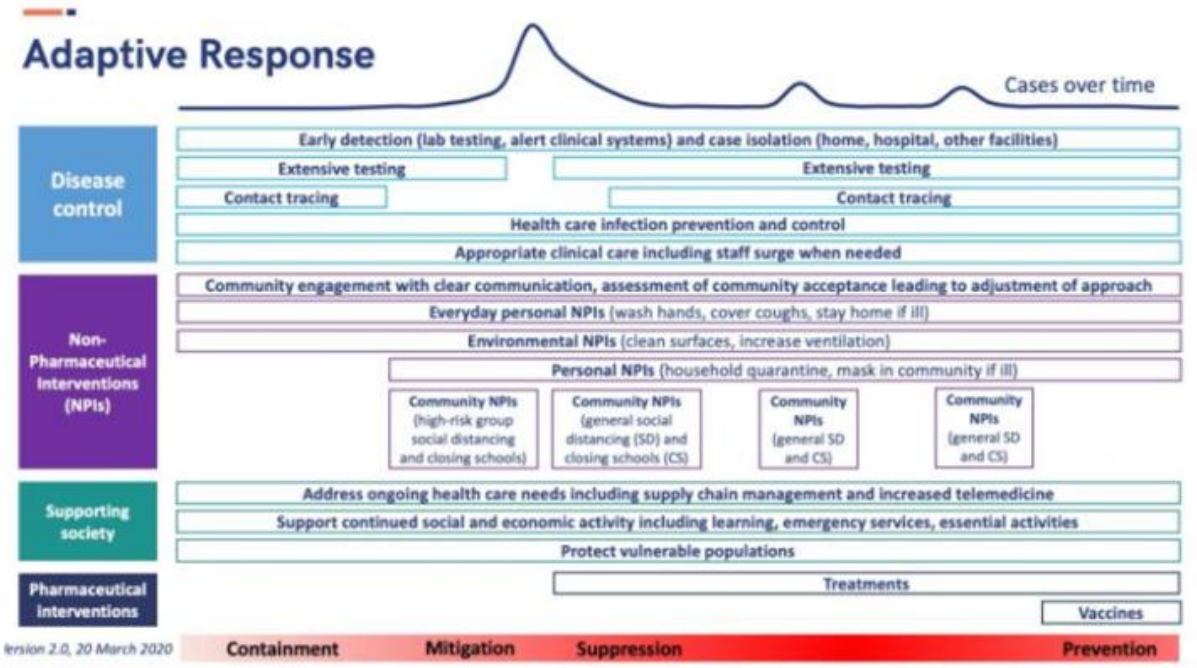
Dr G Srinivas, Professor, Department of Epidemiology, The Tamil Nadu Dr M G R Medical University

Dr G Srinivas, Professor, Department of Epidemiology, The Tamil Nadu Dr M G R Medical University quickly summarised on the Epidemiology of COVID-19. It included evidence from study reports of 44672 Chinese patients on the high infectivity, high pathogenicity, low fatality of the new virus, mild nature of illness mostly (80%) , and the risk factors for severity of the diseases (smoking, old age, comorbidity of hypertension, cardiac & lung disease). The data on the distribution of cases globally, India and reasons for high mortality in Italy was hypothesized. The Basic Reproductive Rate of an Infection (BRR) of an infection was defined as the number of cases one case generates on average over the course of its infectious period, in an otherwise uninfected population and was 2 to 3 for COVID 19. The SIR or Kermack McKendrick model was mentioned and the challenge of doubling of cases in few days leading to exponential curve was shown. The slope of red curve that represents number of sick people at 4 different scenarios (allowing free movement, quarantine, distancing modes) was illustrated as below:



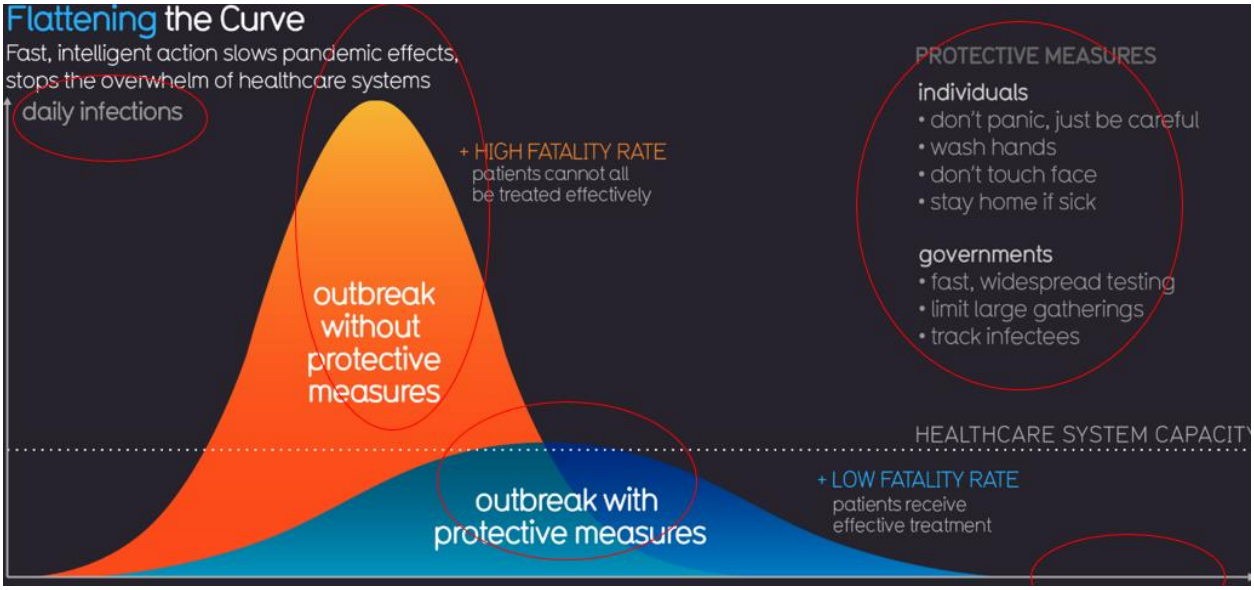


This, slowing of outbreak by social distancing (physical distancing), helps in flattening the curve. This is an important tactic to protect patients and health care workers from a surge that can overwhelm our hospitals, increase death rates and put health care workers' lives at risk.



This figure outlines response measures in COVID-19 containment and mitigation. Disease control activities to reduce spread and effectively treat those infected should be in place from the start of an outbreak. Contact tracing is critical in containment but is not used in areas with extensive spread in communities. Routine non-pharmaceutical interventions (NPIs) are also used early on as they are in a typical flu season, and include washing hands, covering coughs, staying home when ill, and making sure surfaces are cleaned. As COVID-19 becomes a pandemic, additional NPIs may be implemented, including additional personal measures such as staying home if a family member is sick, and community measures such as closing schools, mandatory telework and canceling mass gatherings. These measures will dampen the impact of the pandemic, reduce the size of the peak and thereby improve survival, and delay cases in the hope that pharmaceutical interventions such as antiviral treatments and vaccines will become available

He concluded that the probability of control decreases with long delays from symptom onset to isolation, fewer cases ascertained by contact tracing (To control the majority of outbreaks, for R_0 of 2·5 more than 70% of contacts had to be traced), and increasing transmission before symptoms. Hence to control the pandemic, Government should promote fast, widespread testing, limit large gatherings & track infectees while individuals should promote washing of hands, not touching their face,and stay home if sick .



References

https://www.washingtonpost.com/graphics/2020/world/corona-simulator/?itid=sf_

https://www.pharmaceutical-technology.com/special-focus/covid-19/coronavirus-covid-19-outbreak-latest-information-news-and-updates/

https://resolvetosavelives.org/prevent-epidemics

https://coronavirus.jhu.edu/

This program was attended by over 750 participants in person and many more online, the program ended on a productive note. The feedback of audience was positive and the program was a grand success in instilling the necessary scientific information from the best experts in the subjects to the medical fraternity.

Annexure 1: Programme Agenda

THE TAMILNADU DR M.G.R MEDICAL UNIVERSITY (TNMGRMU), Chennai
&
INDIAN MEDICAL ASSOCIATION TAMILNADU STATE BRANCH and
INDIAN MEDICAL ASSOCIATION CHENNAI SOUTH

International Update on "COVID19"

DATE:17.03.2020, Tuesday

TIME	TOPIC	SPEAKERS
8.00 am	Registration	
09.00 am to 09.30 am	Inauguration	Dr.C.Vijaya Baskar, Hon'ble Minister for Health & Family Welfare, Government of Tamil Nadu
09.30 am to 10.15 am	Current Global Situation & countermeasures	Dr .Vijayakumar Velu ** Emory Vaccine Center, Yerkes National Primate Research Cente, Atlanta
10.15 am to 10.45 am	Administrative Preparedness	Prof .R. Jayanthi,MD Dean, Madras Medical College(MMC) Chennai
10.45 am to 11.10 am	Clinical Guidelines in Management	Prof.S. Raghunanthan, Director, Institute of Internal Medicine, MMC, Chennai
11.10 am to 11.30am	Epidemiology & Data Gaps	Prof.G.Srinivas,MD Prof & HoD Department of Epidemiology,TNMGRMU
11.30 am to 11.50 am	'Virology of SARS-CoV-2'	Prof .Hemalatha Varadhan ** Senior Staff Specialist Microbiology | NSW Health Pathology, University of Newcastle , NSW, Australia
12 Noon to 12.45 pm	Global Situation of COVID 19 and R&D Response'	Dr. Soumya Swaminathan ** Chief Scientist, WHO, Geneva
12.45pm to 01.15 pm	Intricacies of Vaccine Development	Prof .G .Dhinakar Raj, Director, Centre for Animal Health Studies, TANUVAS, Chennai
1.15 pm to 01.45 pm	Principles of Testing and Who Needs to be Tested?	Prof. Kaveri Krishnasamy, Director i/c King Institute of Preventive Medicine, Chennai
02.00 pm	Lunch	

** *video conferencing*

Annexure 2: Program Invitation

The Tamilnadu Dr M G R Medical University

And

Indian Medical Association, Tamilnadu State Branch

Indian Medical Association, Chennai South

Cordially invite you to the

"INTERNATIONAL n-COVID '19 UPDATE"

On Tuesday, the 17th March 2020 at 0900 am at

The Silver Jubilee Auditorium

The Tamilnadu Dr MGR Medical University, Guindy, Chennai 32

Dr C Vijaya Baskar

Hon'ble Minister for Health and Family Welfare, Govt of Tamilnadu

Inaugurates

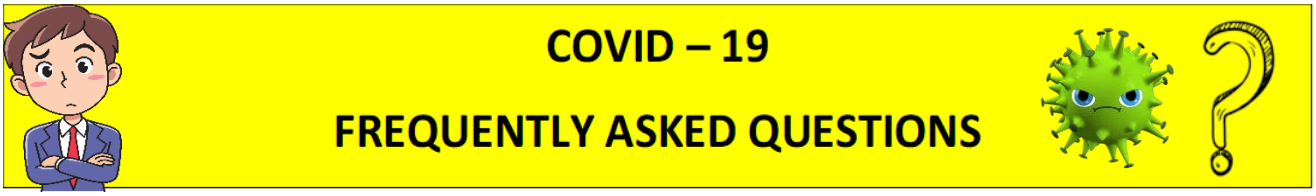
Dr C N Raja

President IMA Tamilnadu State Branch

Will be the Guest of Honour

Dr C N Raja President IMA TNSB	**Dr Sudha Seshayyan** Vice-Chancellor TNMGRMU	**Dr S Devaji Rao** President IMA Chennai South
Dr A K Ravikumar Secretary IMA TNSB	**Dr Aswath Narayanan** Registrar TNMGRMU	**Dr Santha Narayanan** Secretary IMA Chennai South

Annexure 3: Frequently Asked Questions (FAQs)



1. Who is at risk of developing severe illness?

Older persons and persons with pre-existing medical conditions (such as high blood pressure, heart disease, lung disease, cancer or diabetes) appear to develop serious illness more often than others.

2. Should I wear a mask to protect myself?

Only wear a mask if you are ill with COVID-19 symptoms (especially coughing) or looking after someone who may have COVID-19. If you are not ill or looking after someone who is ill then you are wasting a mask.

3 Can I catch COVID-19 from my pet?

While there has been one instance of a dog being infected in Hong Kong, to date, there is no evidence that a dog, cat or any pet can transmit COVID-19. COVID-19 is mainly spread through droplets produced when an infected person coughs, sneezes, or speaks. To protect yourself, clean your hands frequently and thoroughly.

4 Is it safe to receive a package from any area where COVID-19 has been reported?

Yes. The likelihood of an infected person contaminating commercial goods is low and the risk of catching the virus that causes COVID-19 from a package that has been moved, travelled, and exposed to different conditions and temperature is also low.

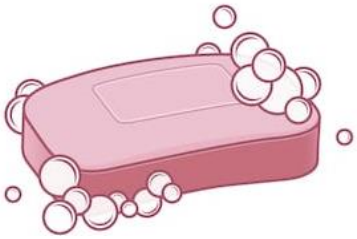
5 Can I catch coronavirus from my clothes?

Regular cleaning will prevent the spread of the disease, as the virus will live on the clothing for up to 3 days. The right amount of soap will properly clean and rinse from the clothing.

6 What is the risk of my child becoming sick with COVID – 19?

Based on available evidence, children do not appear to be at higher risk for COVID-19 than adults. While some children and infants have been sick with COVID-19, adults make up most of the known cases to date.

7 Should I use soap and water or a hand sanitizer to protect against COVID – 19?



Handwashing is one of the best ways to protect yourself and your family from getting sick. Wash your hands often with soap and water for at least 20 seconds, especially after blowing your nose, coughing, or sneezing; going to the bathroom; and before eating or preparing food. If soap and water are not readily available, use an alcohol-based hand sanitizer with at least 60% alcohol.

8 How should healthcare personnel protect themselves when evaluating a patient who may have COVID-19?

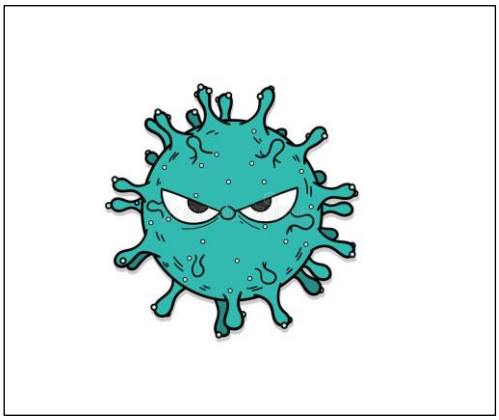
Although the transmission dynamics have yet to be determined, CDC currently recommends a cautious approach to persons under investigation (PUI) for COVID-19. Healthcare personnel evaluating PUI or providing care for patients with confirmed COVID-19 should use, Standard Transmission-based Precautions.

9 What cleaning products should I use to protect against COVID – 19?

Clean and disinfect frequently touched surfaces such as tables, doorknobs, light switches, countertops, handles, desks, phones, keyboards, toilets, faucets, and sinks. If surfaces are dirty, clean them using detergent or soap and water prior to disinfection.

Can a person test Negative and later test positive for COVID – 19?

Using the CDC-developed diagnostic test, a negative result means that the virus that causes COVID-19 was not found in the person's sample. In the early stages of infection, it is possible the virus will not be detected. For COVID-19, a negative test result for a sample collected while a person has symptoms likely means that the COVID-19 virus is not causing their current illness.



Annexure 4: Presentation Slides

International COVID-19- Update

SARS-CoV-2/COVID-19
Current Global Situation & Countermeasures

Vijayakumar Velu, Ph.D
Assistant Professor
Emory Vaccine Center
Yerkes National Primate Research Center
Emory University
Atlanta, Georgia- USA

Acknowledgements

Dr. C. Vijaya Baskar,
Hon'ble Minister of Health & Family Welfare, Tamil Nadu.

Dr. Sudha Seshayyan,
Vice Chancellor, TNMGRMU

Dr. Srinivas (Principal), Dr. Pushkala, Dr. Jasmine (TNMGRMU) and all members of the Organizing committee

Resources for this presentation:

- CDC – Coronavirus website link
- CROI 2020 –COVID-19
- Literature search on Coronavirus

EMORY VACCINE CENTER | EMORY UNIVERSITY
Where Science Meets Hope.

Emory Vaccine Center

Yerkes National Primate Center

Outline

- Brief history of SARS/SARSCoV-19, & China's response to COVID-19, what we learnt from them.
- Clinical Epidemiology and Transmission -What we learnt from the patients –Key questions
- Clinical profile of patients & clinical presentations flying under the radar (Key for identifying patients).
- Countermeasures (Development of Therapeutics and Vaccines)

2019 Novel Coronavirus (2019-nCoV/COVID-19/SARS-CoV-2)

Seven Human Coronavirus (HCoVs)

- Common HCoVs (lower pathogenicity)
  - HCoV-229E (alpha)
  - HCoV-NL63 (alpha)
  - HCoV-OC43 (beta)
  - HCoV-HKU1 (beta)

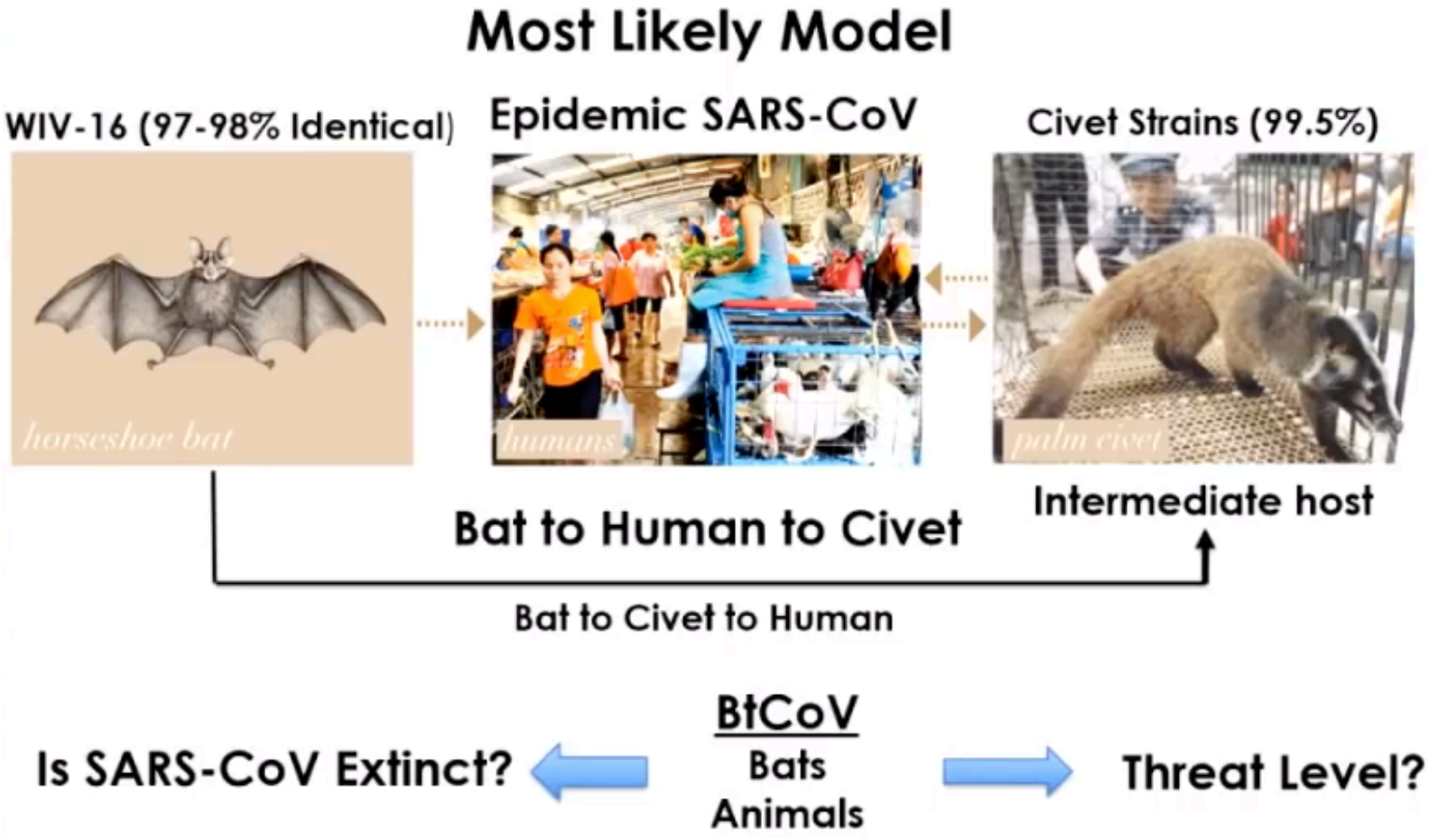
- Other HCoVs (higher pathogenicity)
  - SARS-CoV (beta) 2002
  - MERS-CoV (beta) 2012
  - SARS-CoV-2 (beta) 2019

The disease is called COVID-19 and the virus is called SARS-CoV2, which is more like SARS-COV than MERS-CoV.

Brief history of SARS

SARS-COV Emergence in 2002 in China

Cross Species Transmission



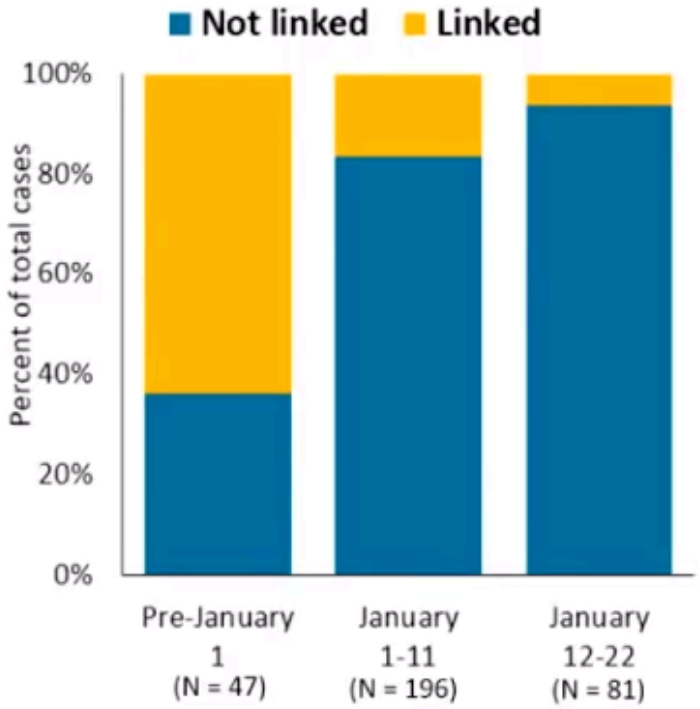
8096 cases, 774 deaths, 32 countries, Nov 1, 2002 to July 31st 2003

SARS-CoV2 (COVID-19)

- Believed to be from BATS
- 25% distinct from SARS
- ~About 6000 nucleotide different SARS
- Represents a new clade (very different) and indicative of a brand new virus
- Possibly through cross species transmission from animal reservoir to human

Linkage of Early COVID-19 Cases to Huanan Seafood Wholesale Market- Wuhan, China

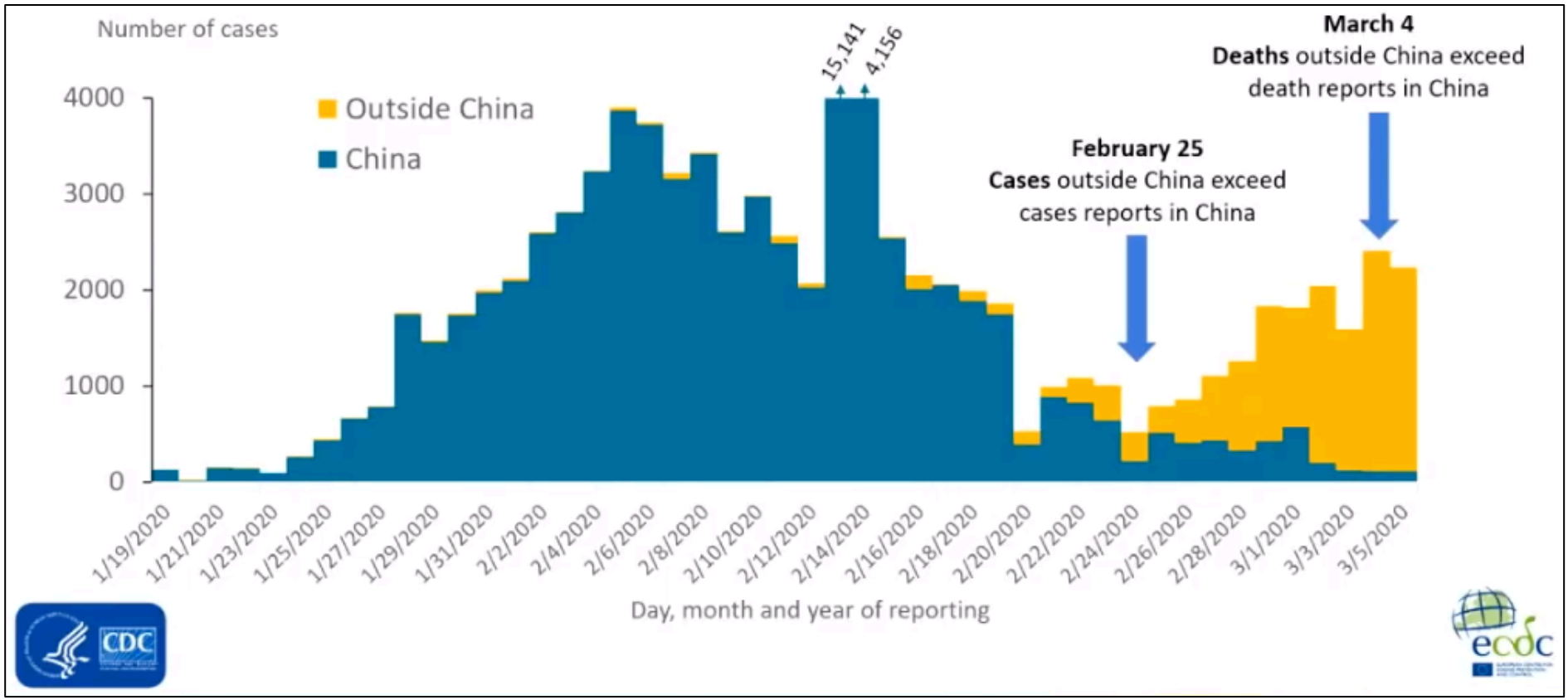
- >80,880 cases to date in China, >3,213 deaths



https://www.healthpolicy-watch.org/

At the end of January most of the cases were not linked to Wuhan –presumably from person to person contact suggesting rapid viral spread

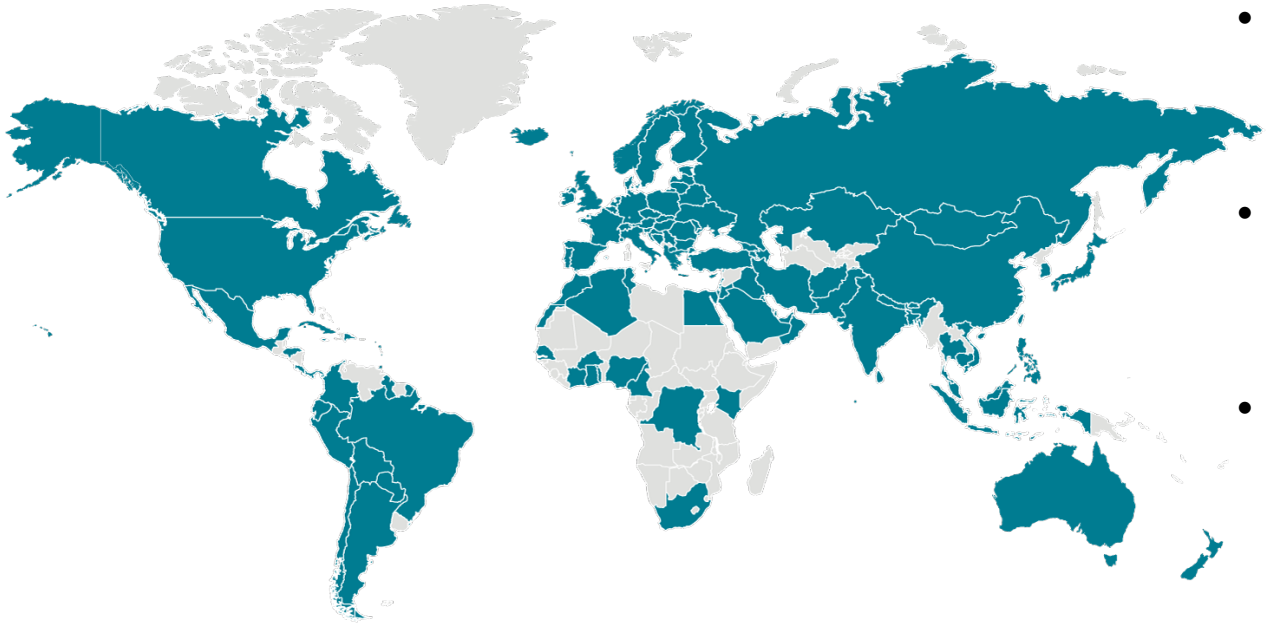
Distribution of COVID-19 cases in accordance with the applied cases definitions in the affected countries - as of March 2020



Suggesting a massive spread of the virus outside China

2019 Novel Coronavirus (SARS-CoV-2/COVID-19)-Pandemic

WHO announces Pandemic (March 12th 2020)



- >173,167 cases to date in the world, >6,664 deaths.
- Confirmed cases in 158 countries.
- With 129 date in India with 2 death reported

Confirmed cases in 158 countries, with 129 until today in India total of 6664 deaths globally and 2 in India

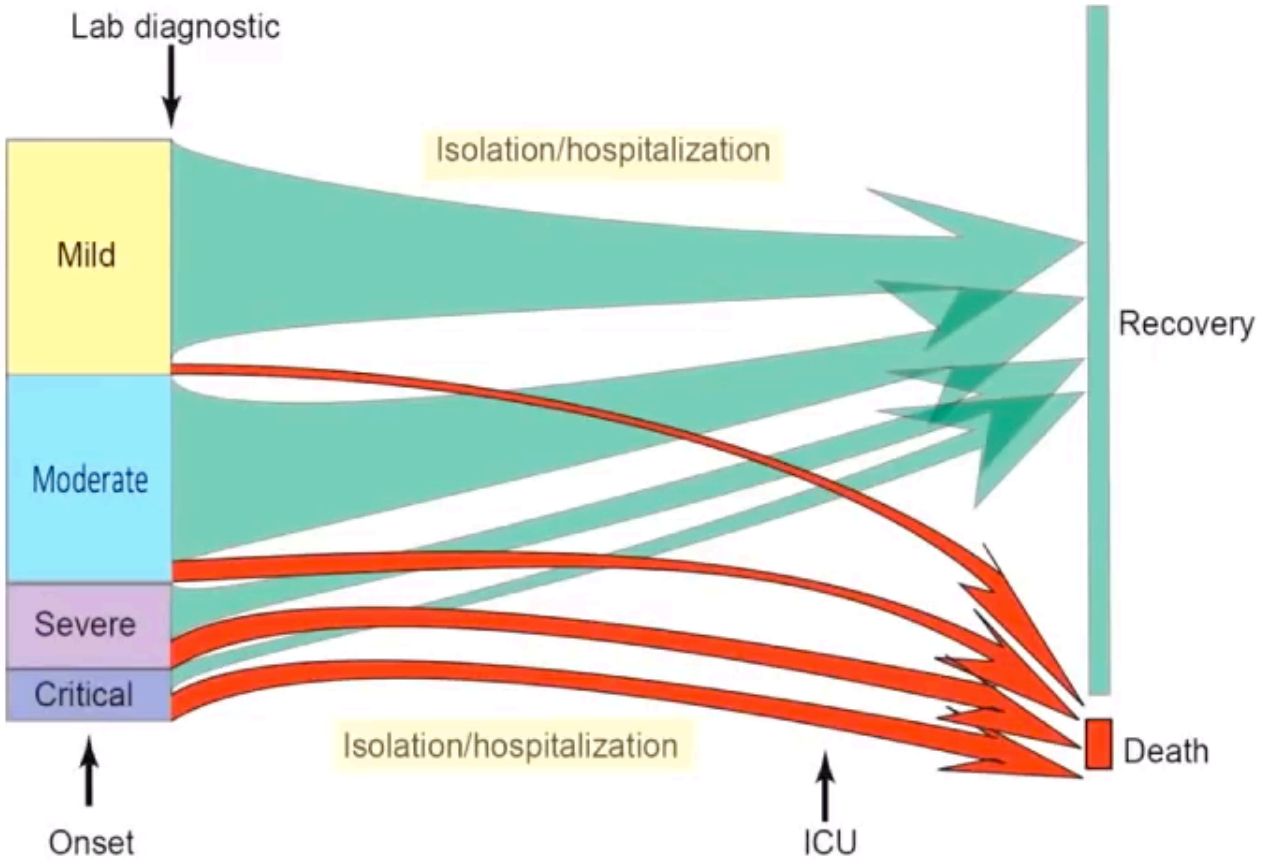
As of March 15th

China, Italy, and Iran -hit hard by this pandemic – as of March 15th 2020

Country, Other	Total Cases	New Cases	Total Deaths	New Deaths	Total Recovered	Active Cases	Serious, Critical	Tot Cases/ 1M pop
China	80,858	+14	3,213	+14	67,752	9,893	3,226	56.2
Italy	24,747	+3,590	1,809	+368	2,335	20,603	1,672	409.3
Iran	13,938	+1,209	724	+113	4,590	8,624		165.9
S. Korea	8,162	+76	75	+3	834	7,253	59	159.2
Spain	7,845	+1,454	292	+96	517	7,036	272	167.8
Germany	5,813	+1,214	11	+2	46	5,756	2	69.4
France	5,423	+924	127	+36	12	5,284	400	83.1
USA	3,714	+771	68	+11	73	3,573	10	11.2
Switzerland	2,217	+842	14	+1	4	2,199		256.2
UK	1,391	+251	35	+14	20	1,336	20	20.5
Norway	1,254	+145	3		1	1,250	27	231.3
Netherlands	1,135	+176	20	+8	2	1,113	45	66.2
Sweden	1,040	+79	3	+1	1	1,036	2	103.0

Clinical Epidemiology and Transmission

Clinical Prognosis & Recovery

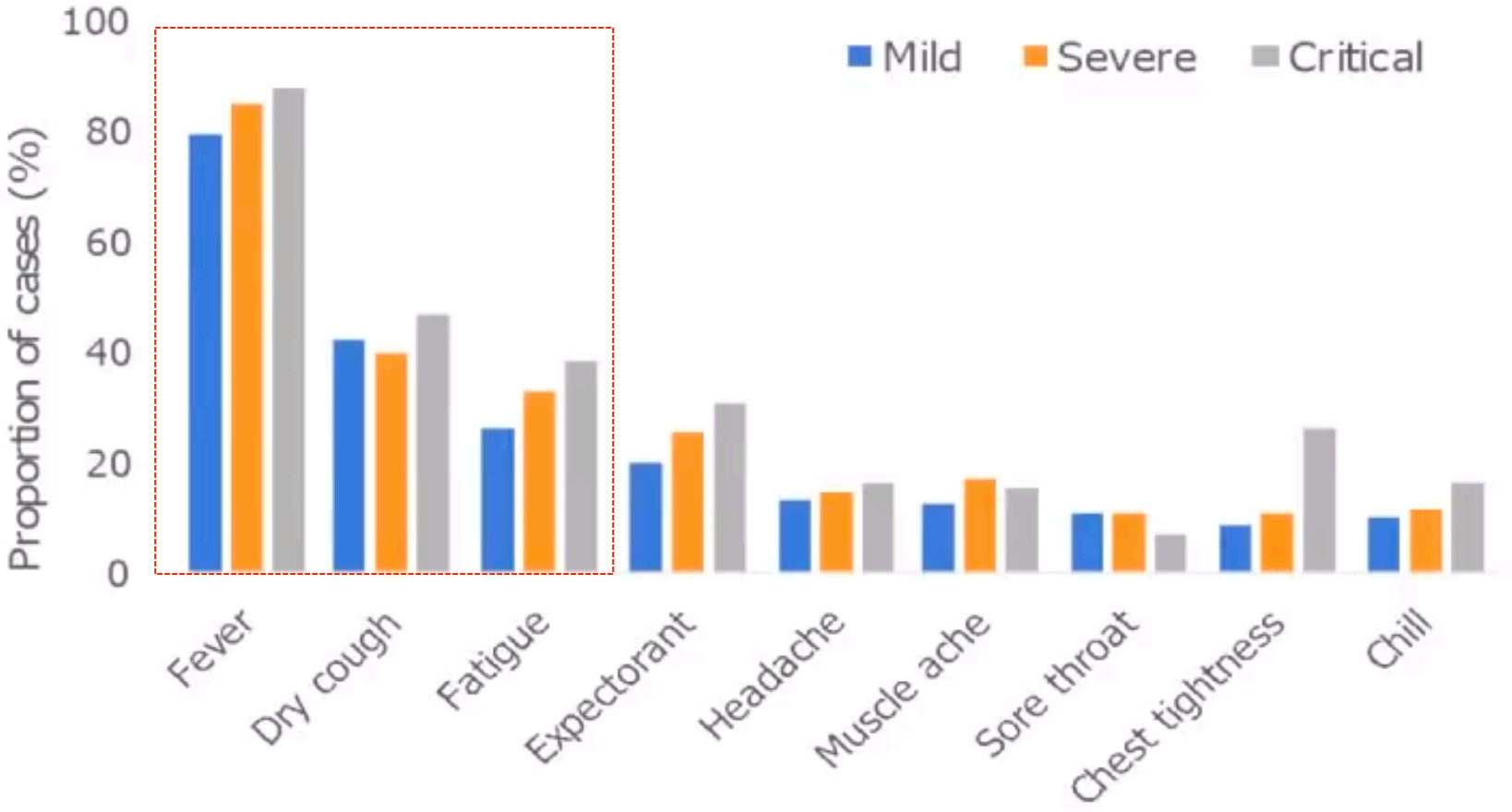


Aylward B et al, WHO-China Mission, 2020

Mild: 40% (without pneumonia), Moderate:40% (with pneumonia),
Severe (Oxygen supplement) 15%,
Critical (Septic shock) 5%

Common Symptoms of COVID-19

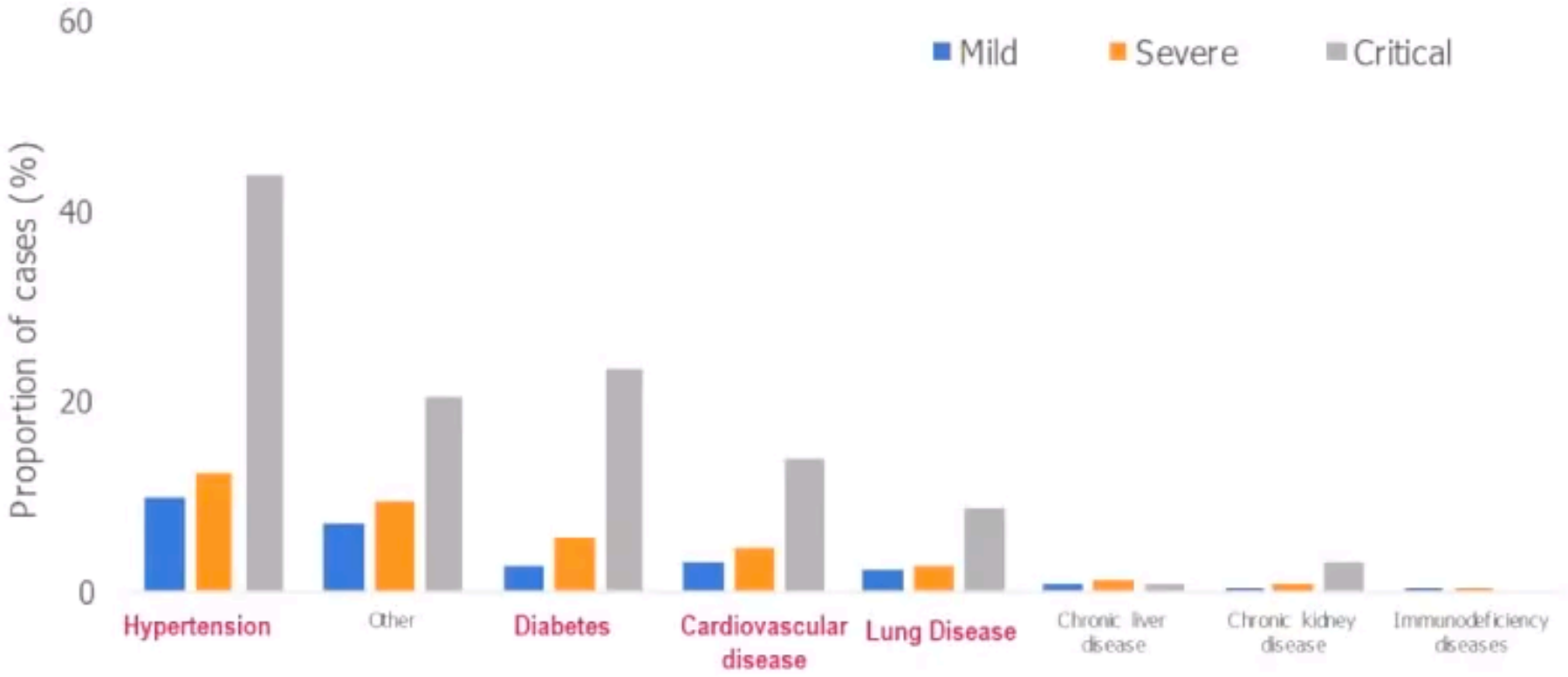
19230 confirmed cases



China CDC/NHC 2020

Underlying medical Conditions of COVID-19

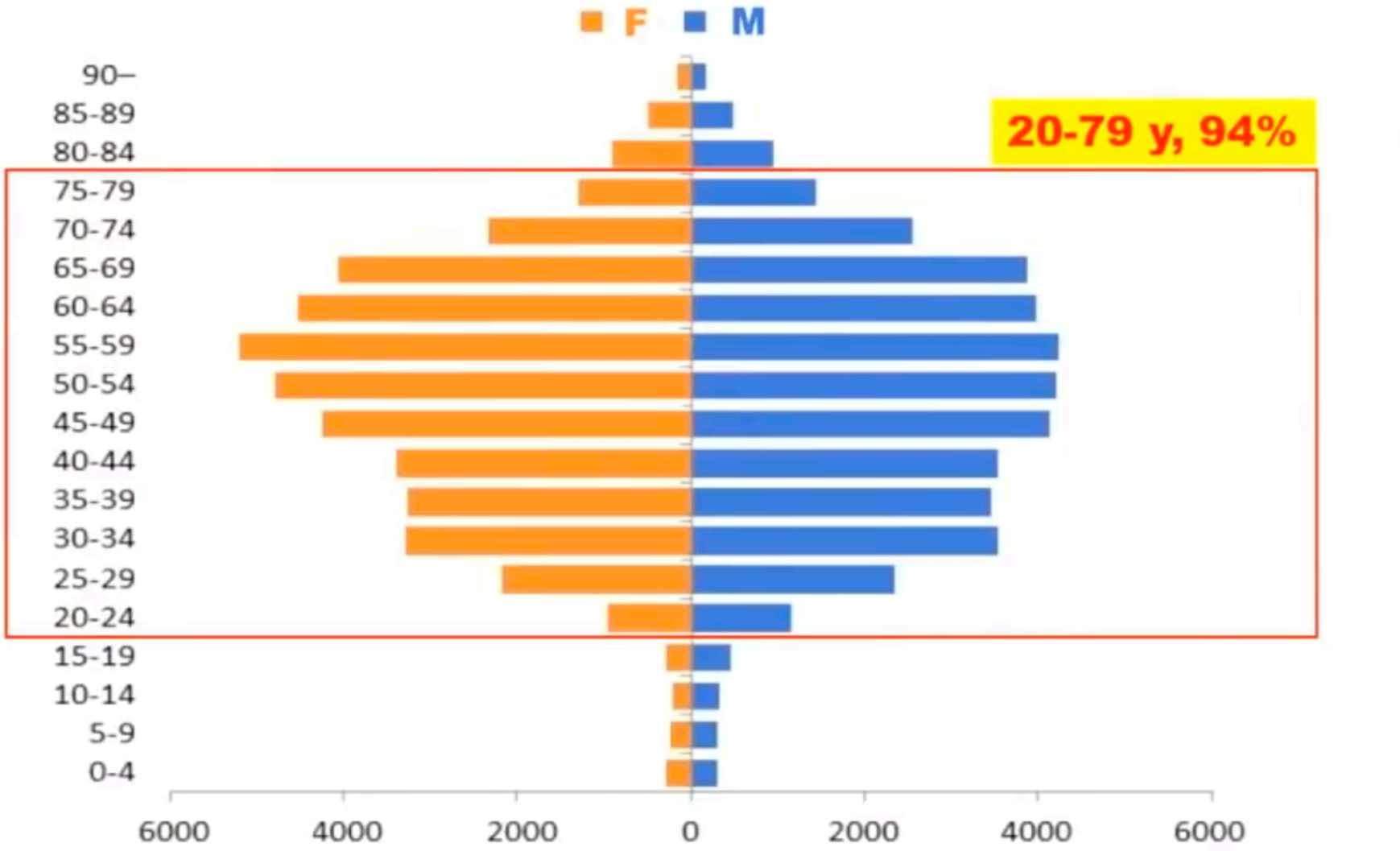
19230 confirmed cases



Patients with these conditions are vulnerable and may be become severe/critical easily

China CDC/NHC 2020

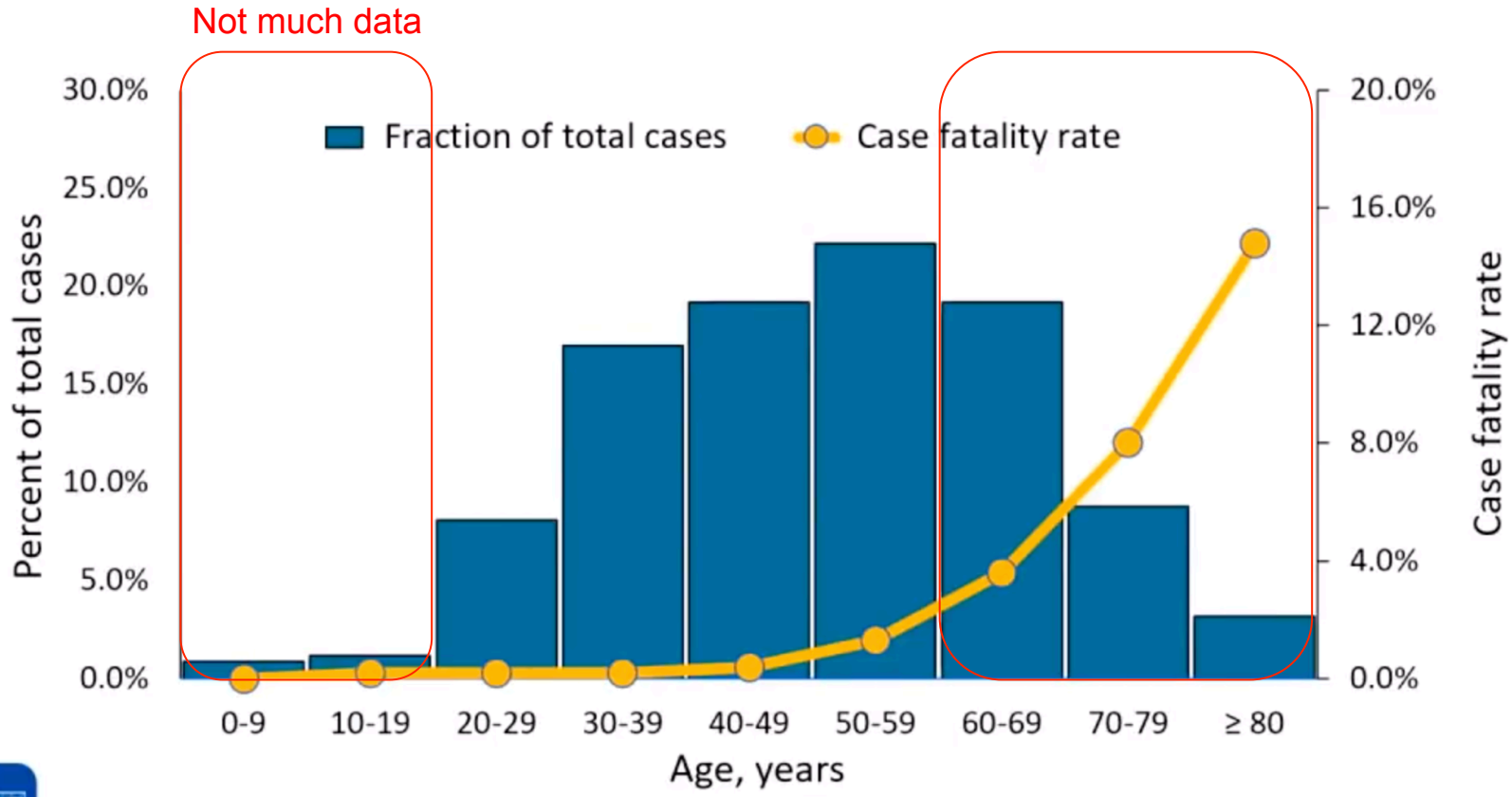
COVID-19 cases by Sex and Age



China CDC/NHC 2020

Age Distribution and Case Fatality Rate COVID-19

N= 44,672 confirmed cases –China as of 11th Feb 2020



adapted from Zhang 2020, China CDC Weekly Rep; 2(8):113-122.

Patients >60 years are at higher risk (likely less immune response and underlying issues)

What we learnt so far on COVID-19

Transmission
History
Virology

Transmission dynamics

- Majority of cases arise from close contacts of symptomatic;
  1-5% of 38,000 close contacts developed COVID-19
- Transmission is driven from family clusters (75-85% of clusters)
- 2^{O} household attack rates were- 10% early in the outbreak & fell to 3% with faster isolation
- Transmission in closed settings is happening but is not a major drivers in china (health facilities, nursing homes, prisons)
- Transmission in schools has not been observed-this may simply be because of the closure of schools during the outbreak

Natural history

- At **diagnosis**: ~80% are mild/moderate; 15% severe; 5% critical
- **Progression**: ~10-15% of mild/moderate cases become severe, & ~15-20% of severe become critical
- **Average Times:**
  - From exposure to symptom onset is 5-6 days
  - From symptom onset to recovery from mild cases is 2 weeks and for severe cases is 3-6 weeks
  - From symptom onset to death is 2-8 weeks
- Truly **asymptomatic** infection is unknown without serology, but appears to be rare using molecular testing (<1%)
  - an estimated 75% of asymptomatic cases at time of diagnosis soon progress to disease
- **Children:** Tend to have milder disease, but same risk of infection (could be silent carriers)

Virology

- Virus shedding is highest early in course of disease (vs. SARS shedding, which peaks at least 5 days after onset)
- Virus shedding can occur in the 24-48 hours prior to symptom onset.
- Virus can be isolated from stool but there is no epidemiologic evidence of fecal-oral transmission.
- Virus shedding usually continues for 7-12 days in mild/ moderate cases, and for >2 weeks in severe cases
- Patients who recover can be PCR positive after symptoms resolve.

COVID-19 in High-Risk Groups

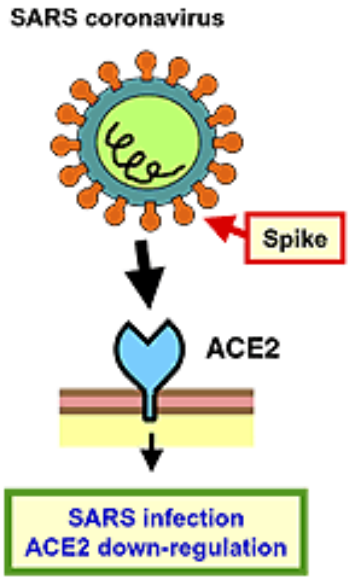
- **Comorbidity and advanced age increase risk for severe illness and death**
  - Cardiovascular disease, diabetes, chronic respiratory disease (5%)

- **Immunocompromised (medical, acquired) – no data at present**
  - For persons with HIV, risk likely greatest at low CD4 levels
  - For persons with Cancer

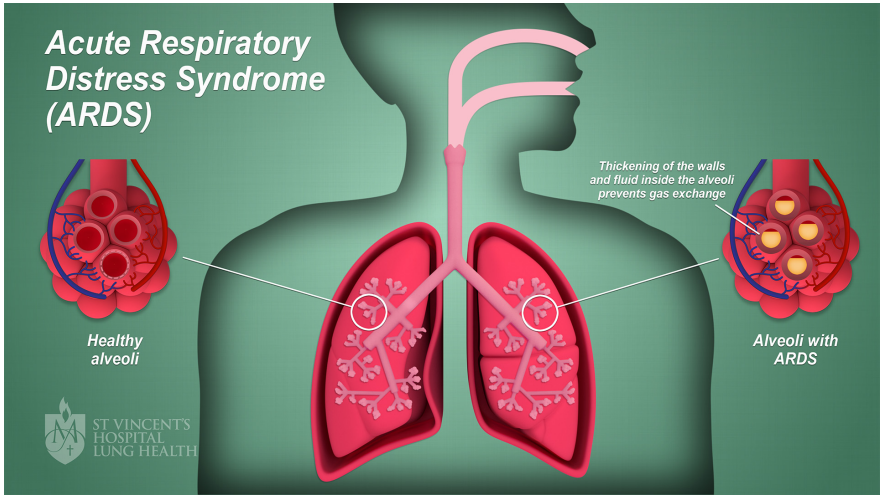
- **Pregnancy**
  - Current observational data only exist for women infected in the third trimester
  - Maternal morbidity similar to that of uninfected women without COVID-19.
  - No definitive evidence of infection transmitted perinatally

The Clinical Profile of SARS-CoV-2/COVID-19

Cause of death during SARS (ARDS)



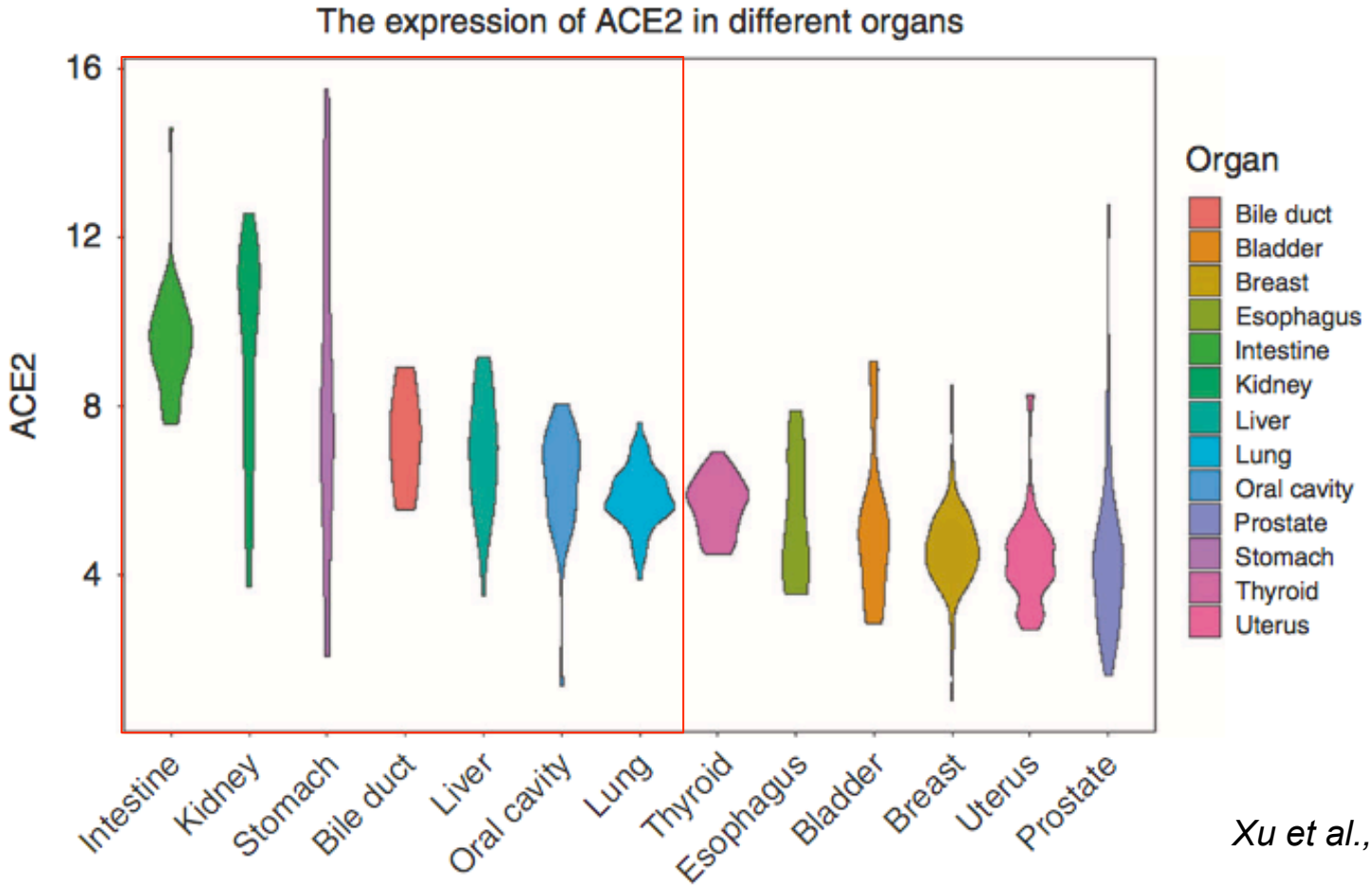
- Receptor- Angiotensis converting enzyme-2 (ACE2).
- Capillary lung blood vessels, lung epithelial layers express ACE2 in high levels
- The binding of SARS spike downregulates ACE2 expression and activates ACE-Angiotensin II (Ang II)-AT1 receptor (AT1R) which results in severe acute respiratory distress syndrome (ARDS) and lung failure.



ARDS (SARS, MERS and COVID-19):

- End stage lung disease
- 30% Mortality,
- 17% respiratory assistance
- 13% invasive ventilators
- ~2% of bacterial infection

Expression of Coronavirus receptor (ACE2) in different organs



Xu et al., IJOS 2020

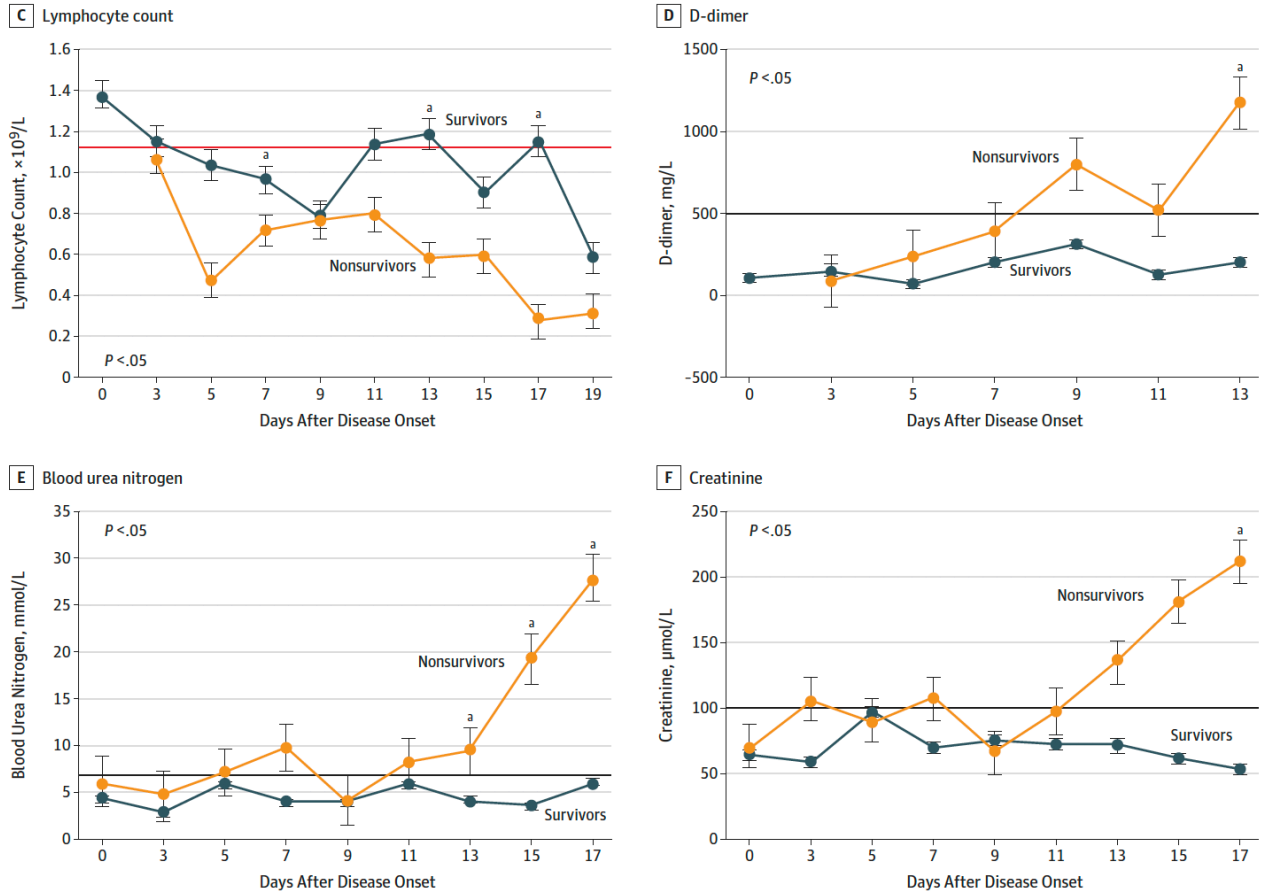
This suggest that many organs that express higher levels of these receptors could be affected

Characteristics of Patients with COVID-19 infected Pneumonia, China

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China

Dawei Wang, MD; Bo Hu, MD; Chang Hu, MD; Fangfang Zhu, MD; Xing Liu, MD; Jing Zhang, MD; Binbin Wang, MD; Hui Xiang, MD; Zhenshun Cheng, MD; Yong Xiong, MD; Yan Zhao, MD; Yirong Li, MD; Xinghuan Wang, MD; Zhiyong Peng, MD



Non-Survivors

Survivors

Suggesting immune activation could be a predictor of critical cases

As well as suggesting severe organ failures

Possibility of Fecal-Oral Transmission

nature medicine

BRIEF COMMUNICATION

https://doi.org/10.1038/s41591-020-0817-4

Check for updates

Characteristics of pediatric SARS-CoV-2 infection and potential evidence for persistent fecal viral shedding

Yi Xu[1,11], Xufang Li[1,11], Bing Zhu[2,11], Huiying Liang[3,4,11], Chunxiao Fang[1], Yu Gong[1], Qiaozhi Guo[5], Xin Sun[5], Danyang Zhao[5], Jun Shen[1], Huayan Zhang[1,4,6], Hongsheng Liu[7], Huimin Xia[3,4,8] ✉, Jinling Tang[3,4] ✉, Kang Zhang[8,9,10] ✉ and Sitang Gong[1,4] ✉

Children tested positive for rectal swabs are negative for nasal swab testing (very scary)

IJOS International Journal of ORAL SCIENCE

Article | Open Access | Published: 24 February 2020

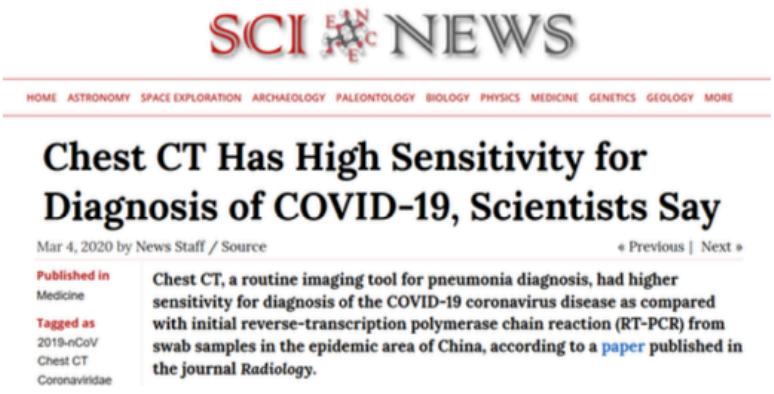
High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa

Hao Xu, Liang Zhong, Jiaxin Deng, Jiakuan Peng, Hongxia Dan, Xin Zeng, Taiwen Li ✉ & Qianming Chen

International Journal of Oral Science **12**, Article number: 8 (2020) | Cite this article

Other Possible Testing for COVID-19 identification

Chest CT has high sensitivity for Diagnosis of COVID-19 - Pneumonia



SCI NEWS

HOME ASTRONOMY SPACE EXPLORATION ARCHAEOLOGY PALEONTOLOGY BIOLOGY PHYSICS MEDICINE GENETICS GEOLOGY MORE

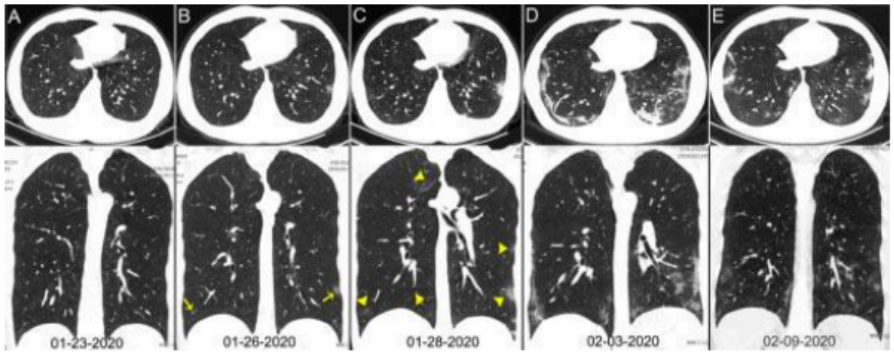
Chest CT Has High Sensitivity for Diagnosis of COVID-19, Scientists Say

Mar 4, 2020 by News Staff / Source « Previous | Next »

Published in Medicine

Tagged as 2019-nCoV Chest CT Coronaviridae

Chest CT, a routine imaging tool for pneumonia diagnosis, had higher sensitivity for diagnosis of the COVID-19 coronavirus disease as compared with initial reverse-transcription polymerase chain reaction (RT-PCR) from swab samples in the epidemic area of China, according to a paper published in the journal *Radiology*.



- PCR testing might have sensitivity issue at this point as 60-70%
- Patient may have pneumonia and CT abnormalities but be initially PCR negative
- Early course: Peripheral focal or multifocal ground-glass opacities affecting both lungs (up to 75% patients)
- With progression, paving and consolidating peaks at 9-13 days with slow clearing at 1 month

Chest CT may be considered as a primary tool for COVID-19 detection

Clinical presentations flying under the radar

- Cardiac presentation without respiratory symptoms, ACE2 responsible for healthy heart function

- Conjunctiva is an alleged route of exposure – it may cause ocular signs.

- Many abdominal discomfort has been recorded- Viral RNA is detected in stool and the ACE2 express in the gut lining, this may also cause fecal oral transmission (caution)-

- Viral RNA is detected in saliva, possible of saliva transmission, suggesting that digestive system is a likely route of infection in addition to respiratory, as well as the oral cavity

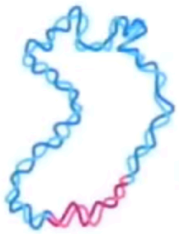
- Liver enzyme could be a predictor – 60% patients with SARS has liver impairment, markers pertaining to liver functions could be a predictor

The countermeasures for SARS-CoV-2/COVID-19

Vaccines and therapeutics

Vaccines Platform Technologies in Development of COVID-19

This is brand new virus, new immunity, new therapy and new vaccine



Genetic immunization (DNA and RNA vaccines)

NIAID/Moderna, CureVac/NIAID, Inovio/Beijing Advaccine

Recombinant protein

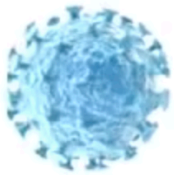
Baylor and collaborators

Viral vector (ex: adenovirus)

Johnson & Johnson, Jenner/NIAID

Nanoparticle (viral protein on particle)

Novavax



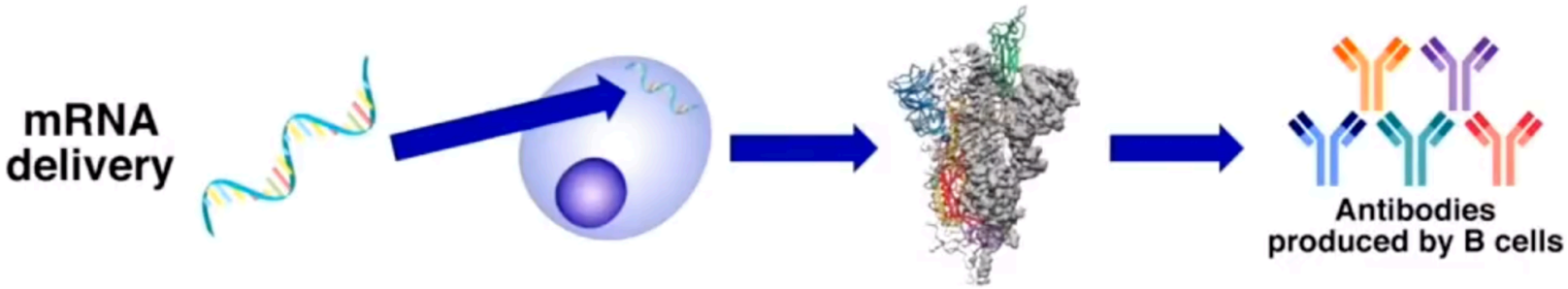
Live attenuated

Codagenix

Selected development programs

COVID-19 mRNA Vaccine Development (NIH) USA

- **NIAID Vaccine Research Center (VRC)** is collaborating with Moderna and the **Coalition for Epidemic Preparedness Innovations (CEPI)** on an mRNA vaccine candidate expressing the viral spike protein of COVID-19
- Production fast-tracked and GMP product for clinical trial shipped to trial site February 2020



Evidence of SARS antibodies that inhibits SARS-CoV-2 entry (ray of hope)

Article

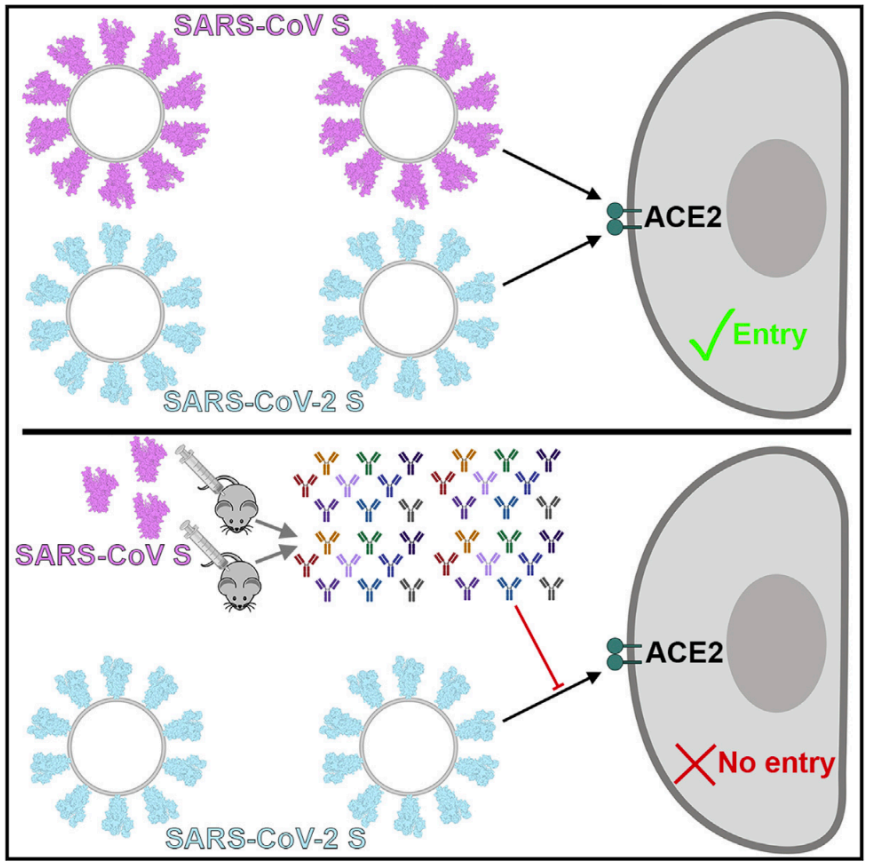
Cell

Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein

Alexandra C. Walls,[1,5] Young-Jun Park,[1,5] M. Alejandra Tortorici,[1,2] Abigail Wall,[3] Andrew T. McGuire,[3,4] and David Veesler[1,6,*]
[1]Department of Biochemistry, University of Washington, Seattle, WA 98195, USA
[2]Institute Pasteur & CNRS UMR 3569, Unité de Virologie Structurale, Paris 75015, France
[3]Vaccines and Infectious Diseases Division, Fred Hutchinson Cancer Research Center, Seattle, WA 98195, USA
[4]Department of Global Health, University of Washington, Seattle, WA 98195, USA
[5]These authors contributed equally
[6]Lead Contact
*Correspondence: dveesler@uw.edu
https://doi.org/10.1016/j.cell.2020.02.058

Highlights

- SARS-CoV-2 uses ACE2 to enter target cells
- SARS-CoV-2 and SARS-CoV bind with similar affinities to ACE2
- Structures of SARS-CoV-2 spike glycoprotein in two conformations
- SARS-CoV polyclonal antibodies inhibit SARS-CoV-2 spike-mediated entry into cells



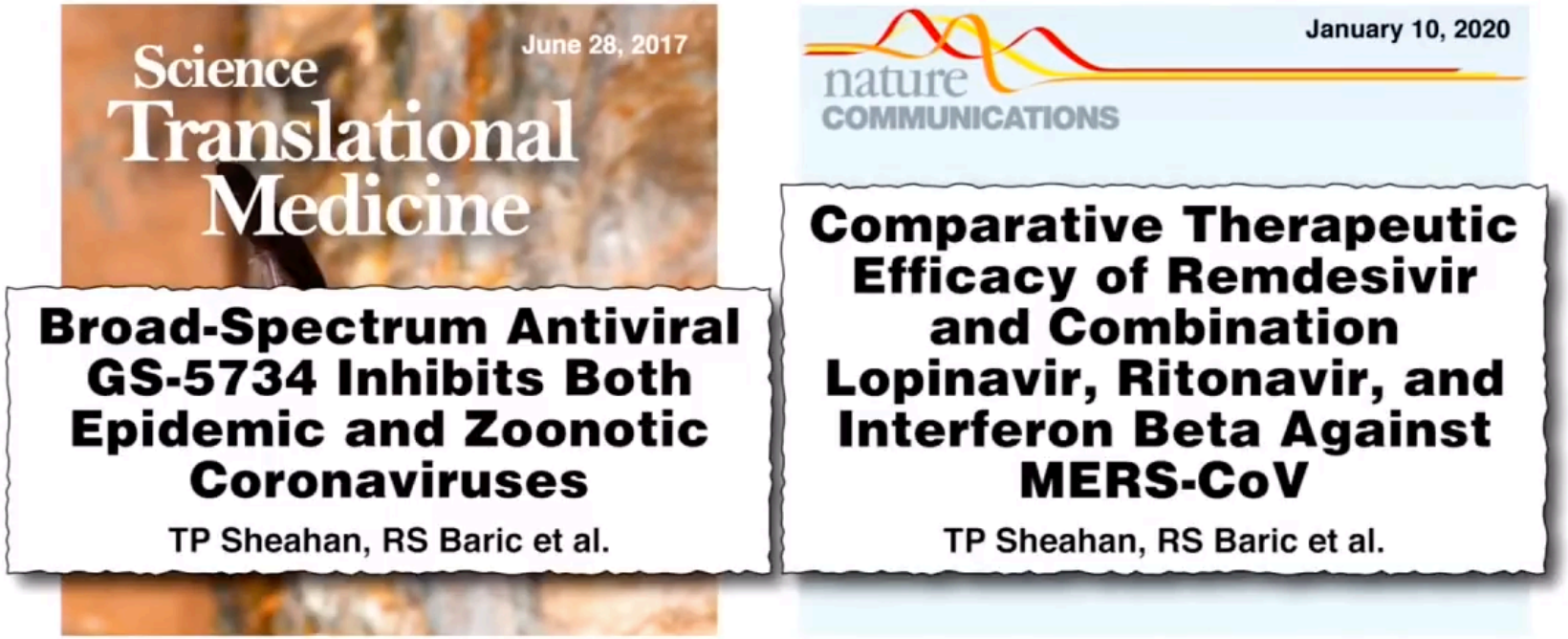
Plasma therapy from recovered patients is effective –Prof. Ian Lipkin from Columbia University (Fox news)

Therapeutics for COVID-19

- **Antivirals, monoclonal antibodies and other agents are being tested**
  - Remdesivir (nucleotide analogue), has shown promise against coronavirus in animal models (Gilead), currently tested in humans.
  - Kaletra (Lopinavir/ritonavir) (protease inhibitors) used in HIV infection
  - Chloroquine (Malaria drug)
  - Drug Screening and targeted drug design
  - Monoclonal antibodies being isolated and tested

Preclinical Evidence of Remdesivir's Potential for Treating Human Coronavirus infections

Ralph Braic's lab



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WORLD

Experimental Drug Helps Some Americans Ride Out Coronavirus, NIH Doctor Says

Antiviral drug remdesivir appeared to have an effect in American cruise passengers treated in Japan, although data are limited

CROI 2020

Update on newly discovered Coronavirus

	SARS CoV	MERS CoV	SARS CoV2
Virion Structure	Enveloped RNA Virus	Enveloped RNA Virus	Enveloped RNA Virus
Outbreak	2003-2004	2012-present	Dec2019-present
Initial isolation	**Guangdong, China**	**Saudi Arabia**	**Wuhan, China**
No. of Countries	**29**	**27**	**>148**
No. of cases (death)	**8,096 (9.6%)**	**2,494 (~34%)**	**155,840 (3.7%)**
Reservoir host	Bats (palm civet)	Bats, camels	Bats (likely zoonosis)
Incubation period	**2-7 days (range, 2-21)**	**2-7 days (range, 2-14)**	**2-14 days (mean 5-6)**
Super spreaders	**Yes**	**Yes**	**Yes (many examples)**
Asymptomatic/Mild Spread	**No**	**Rare**	**Yes/Yes**
Attach Rate	10.3 to 60%	4-20%	20-30% (early study)
Transmission	Droplet/Direct, Airborne/ Indirect?	Droplet/Direct, Airborne/ Indirect?	Droplet/Direct, Airborne/ Indirect/Fecal
Treatment (PEP)	Supportive (none)	Supportive (none)	Supportive (Drugs CU)
Infection Prevention	Airborne, Contact, face, Shield	Airborne, Contact, face Shield	Airborne, Contact, face Shield

Current major concern to this pandemic

CNN health Food Fitness Wellness Parenting Vital Signs • LIVE TV Edition

Infected people without symptoms might be driving the spread of coronavirus more than we realized

By Elizabeth Cohen, Senior Medical Correspondent

Updated 3:32 PM ET, Sat March 14, 2020

ScienceNews
INDEPENDENT JOURNALISM SINCE 1921

ALL TOPICS

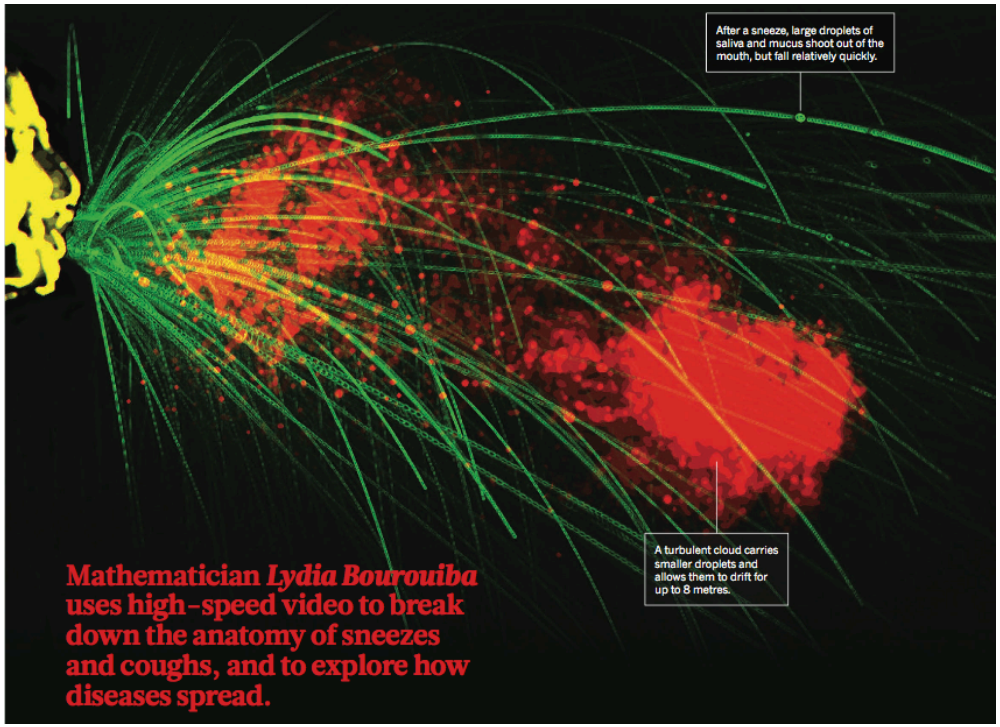
NEWS HEALTH & MEDICINE

Coronavirus is most contagious before and during the first week of symptoms

This suggest that caution should be taken care of asymptomatic people:
This could lead to rapid spread in the community (rapid testing is important)

“Super-Spreaders”

- Health experts believe “Super spreaders” could be an issue
  - more likely to infect others at high rates compared to typical infected person
- If super-spreaders exist- there is a general 80/20 rule
  - 20% infected individuals are responsible for 80% of transmissions



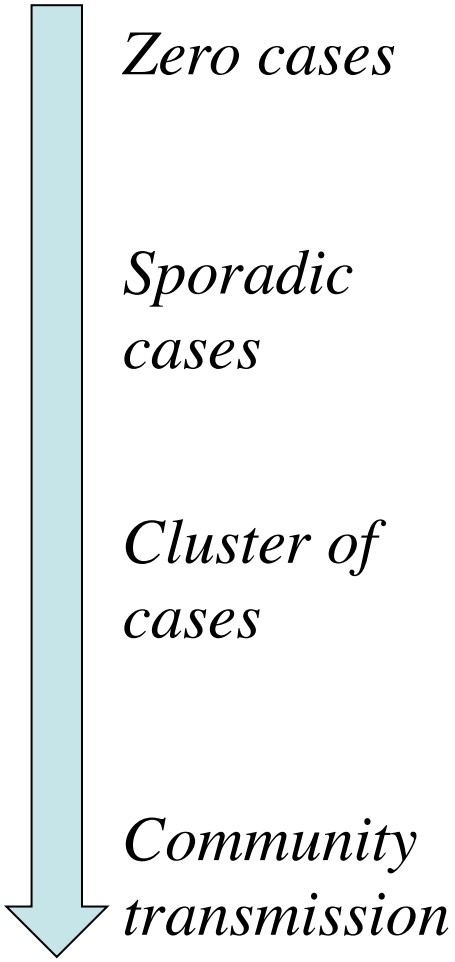
Known Coronavirus Cases in Mass. Up to 138; 104 Connected To Biogen Meeting

What we can do to manage this Pandemic

We have New virus, New immunity, New therapy and New vaccine
– so we should react differently

Fundamental Public Health Measures are Priority- Need of the hour

- **Universal population measures**
- **Case isolation and management**
- **Close contact quarantine**
- **Suspension of public gatherings**
- **Movements restrictions**



Preparedness and Response to COVID-19-Pandemic

- Intensify case finding and contact tracing
  Diagnostics, Serogical assays for seroservillance
- Isolate cases and quarantine contacts
- Characterize illness with various tests
- Prepare for mitigation with non-pharmaceutical interventions (NPI)

Containment

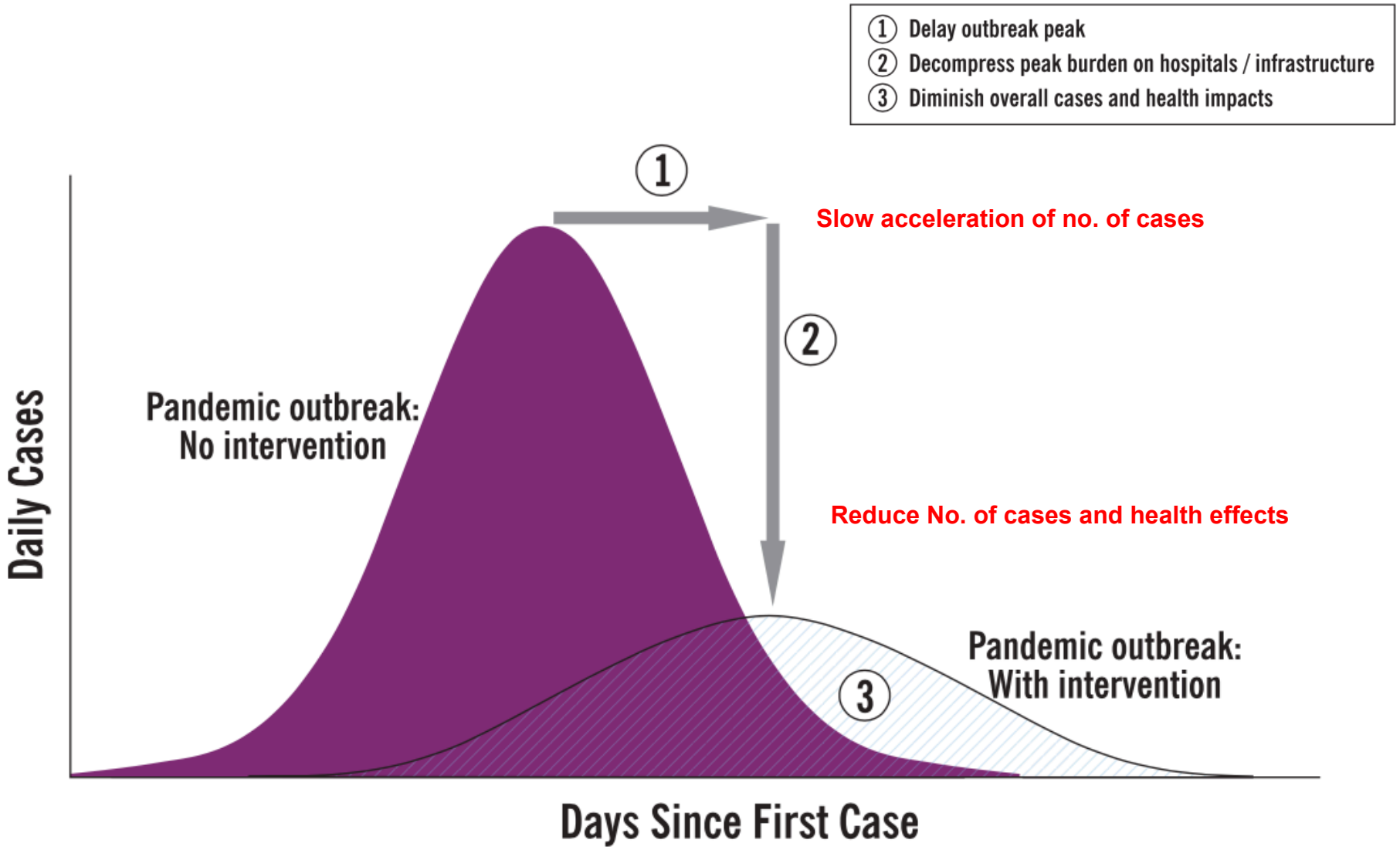
- Deploy Medical interventions (anti-virals & vaccines)
- Early institution of multilayered NPIs

Mitigation

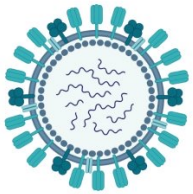
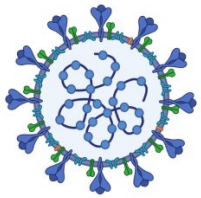
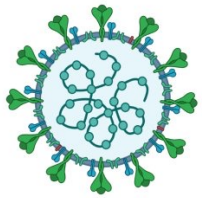
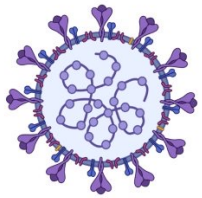
Recommendations for immunocomprimised

- Ensure ample medication supply (diabetes, hypertension, cardiovascular disease, HIV etc).
- Keep vaccinations up to date (influenza, bacterial pneumococcal.
- Establish plan for clinical care if isolated/quarantined. (Telemedicine, Physician online portal etc)
- Maintain social network but remotely

Strategy to manage COVID-19 Pandemic



Epidemiological Comparison of Respiratory Viral Infections

Disease	Flu	COVID-19	SARS	MERS
Disease Causing Pathogen	 Influenza virus	 SARS-CoV-2	 SARS-CoV	 MERS-CoV
R_0 Basic Reproductive Number	**1.3**	**2.0 - 2.5** *	**3**	**0.3 - 0.8**
CFR Case Fatality Rate	0.05 - 0.1%	~3.4% *	9.6 - 11%	34.4%
Incubation Time	1 - 4 days	4 - 14 days *	2 - 7 days	6 days
Hospitalization Rate	2%	~19% *	Most cases	Most cases
Community Attack Rate	10 - 20%	30 - 40% *	10 - 60%	4 - 13%
Annual Infected (global)	~ 1 billion	N/A (ongoing)	8098 (in 2003)	420
Annual Infected (US)	10 - 45 million	N/A (ongoing)	8 (in 2003)	2 (in 2014)
Annual Deaths (US)	10,000 - 61,000	N/A (ongoing)	None (since 2003)	None (since 2014)

* COVID-19 data as of March 2020.

COVI19 is 30X more deadly & 2X more contagious than Flu

Next steps to stop COVID-19 Pandemic

- Personal Hygiene, strict social norms, discouraging social gathering, Physical distance (since we low no of hospitals to treat COVID-19)
- Social distancing, Isolate cases and quarantine - have their contacts, document them and follow them for at least a month.
- Rapid testing is very important and should be available in many tertiary care hospitals around Tamil Nadu/India
- Characterize illness with virological and immunological testing – no one knows about the virus – its important to characterize them for more interventions
- Increase funding for researchers to identify anti-virals and vaccines

Don't panic and don't listen to false news &

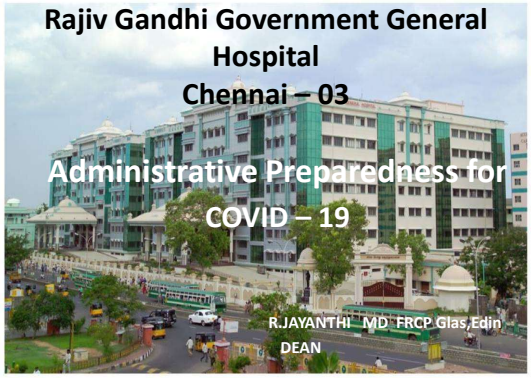
We should remain united in our response to this crisis

Thank you for your attention

Anyone with questions is welcome to contact me by email
vvelu@emory.edu

Rajiv Gandhi Government General Hospital
Chennai – 03

Administrative Preparedness for COVID – 19

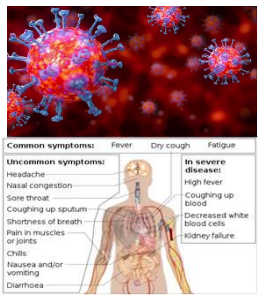


R.JAYANTHI MD FRCP Glas,Edin
DEAN

1

COVID - 19

- **COVID-19** Coronaviruses (CoV) are a large family of viruses that cause illness ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome and Severe Acute Respiratory Syndrome.
- Coronavirus disease (COVID-19) is a new strain that was discovered in 2019 and has not been previously identified in humans.



2

Case clusters and few deaths reported from China, 31st December mostly from Hubei Province

Other Countries Start reporting

- On 30th Jan WHO declared the out break a Public Health Emergency of International Concern (PHEIC)
- On 11th March WHO Director General Characterized COVID-19 as a pandemic


China 'shuts' 10 cities; 12 quarantined in India
26 Dead & 1,100 Affected Globally

3

COVID - 19 TEAM RGGGH

- Head of the Institution (Dean)
- Medical Superintendent
- Head Of Internal Medicine
- Head Of Nursing
- Head of Microbiology/ Infection control
- Community Medicine
- Administrative (RMO)

4

CHALLENGES IDENTIFIED

- Creation of Isolation Unit
  - Patient routing and placement
- Droplet precautions
- Stocking of PPEs and other consumables including hand sanitizers
- Sensitizing doctors, paramedics and public
- Creating awareness
- Case management OPD and IP
- Bio Medical Waste Management
- Mental & Physical Health among health personnel
- Handling Media

5

- **30 January -** India confirms its first case of coronavirus in a student who had returned from Wuhan University to Kerala
- **5 th March** – 45 Year Old tested positive for Coronavirus in RGGGH , making him the first person in Tamil Nadu to be reported of having the disease.

6

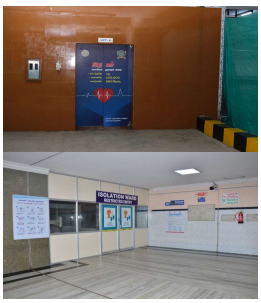
Patient routing and placement

- Ward 215 on the first floor of Tower 2 earmarked as isolation ward
- A dedicated pathway has been created to bring patients to the ward
- The ambulance transporting a patient will come into the basement of Tower 2, from where lift number 4 has been exclusively earmarked for use

7

Patient routing and placement

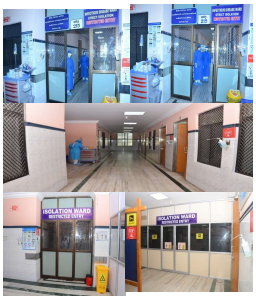
- The Patient will be taken directly from the basement to the isolation ward .
- Dedicated Lift
- An exclusive team of doctors, staff nurses and paramedical staff will work in the isolation ward. A stretcher bearer and lift operator have also been designated, They will also were N95 Masks



8

Isolation Units

- Based on WHO /CTC and GOI guidelines
- First 6 beds of isolation units (a 3 Tier)created on jan 20th with dedicated team including 18 staff nurses 20 workers and 10 doctors ,
- Later expanded to 12 beds and 20 beds



9

COVID- 19 Mock Drill

68 பேருக்கு கொரோனா வைரஸ்... முதல் பக்க தொடர்ச்சி

ராஜிவ் காந்தி மருத்துவமனையில் கொரோனா சிகிச்சைக்கு ஒத்திகை

10

Central Team Inspects RGGGH


Central team inspects State's arrangements to tackle disease

11

12

Droplet Precaution

13

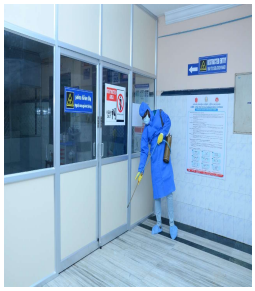
Stocking of consumables

- Personal Protection Equipments
- N95 Mask
- 3 layered Mask
- Hand Sanitizer
- IEC Activities

Personal Protective Equipment

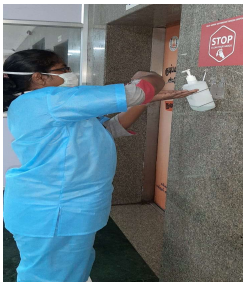
14

Infection Control



15

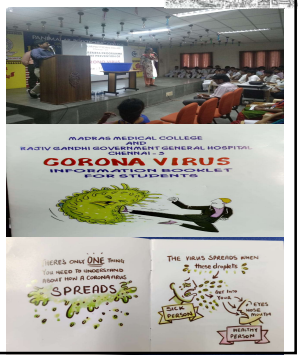
Indigenous Hand Sanitizer –A B



16

Sensitizing Medics & Public

- Training of doctors, nurses paramedics and workers
- About the disease and mode of transmission
- about the importance of universal precautions including droplet precautions
- donning and doffing of PPE
- hand hygiene

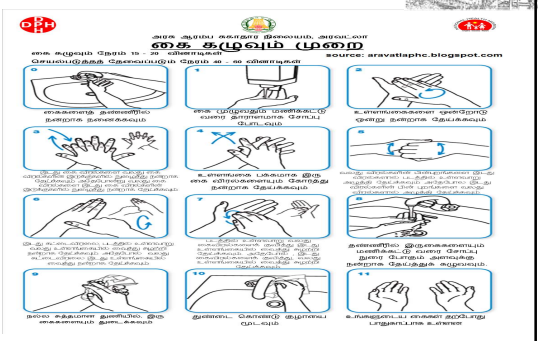


17

IEC

18

IEC



19

Case Management OPD & IP

OPD

IP

20

SPECIAL DIET

- Special care is taken to provide nutritious diet

Break fast-Idly, Onion chutney, samba wheat upuma, sambar, egg white and milk

Ginger and Lemon with skin hot water

Lunch- Chapatti, mint rice, veg porial, greens porial, rasam and roasted bengal gram dhall

Mid evening snack- Dal soup and channa

21

1st COVID -19 Patient @RGGGH

22

23

COVID-19: Global Situation and R&D Response

Soumya Swaminathan, MD
Chief Scientist, WHO

1

Current Situation (As of 16 Mar, 00H Geneva Time)

Updates from last 24 hours

Outside China:
- 12,281 new confirmed cases from 85 countries
- 7 countries/states/territories reported the 1st confirmed case: Congo (1), Seychelles (2), Rwanda (1), Saint Lucia (2), Suriname (1), Guatemala (1), Uruguay (4)
- 736 new deaths
- 4 countries reported the 1st death: Hungary (1), Sweden (2), Denmark (1), Sudan (1)

China:
- 29 new confirmed cases: 14 % (4) cases from Hubei
- Among new cases, 12 cases are imported
- 14 new deaths: Hubei(14)

Globally, between 31 Dec 2019 - 16 Mar 2020
- 165,065 confirmed cases
- 6,472 deaths

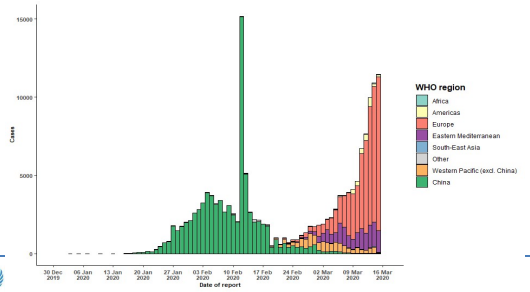
Outside China
- 83,988 cases from 150 countries/states/territories and 1 international conveyance (51 % of the total cases reported globally)
- 3,254 deaths
- Countries/states/territories with no new cases for >14 days: Nepal (51 days)

China
- 81,077 confirmed cases
- 3,032 severe cases
- 3,218 deaths

World Health Organization — HEALTH EMERGENCIES programme

2

Number of confirmed cases notified under IHR or from official government sources as of 16 Mar 00H

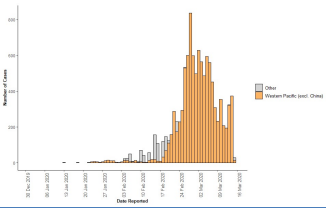


3

Key Updates from WPRO (excluding China)

Total 10,647 cases and 119 deaths reported to date from 12 countries/states/territories in WPRO excluding China

During past 24 hours:
- 326 new cases from 9 countries /states/territories: Australia (82), Republic of Korea (76), Philippines (76), Malaysia (41), Brunei Darussalam (15), International conveyance (Diamond Princess) (15), Singapore (14), Viet Nam (5), French Polynesia (2)
- 13 new deaths: Philippines (10), Republic of Korea (3)



World Health Organization — HEALTH EMERGENCIES programme

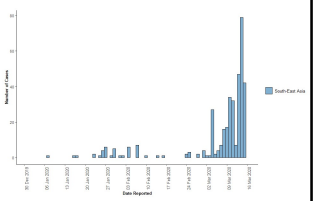
4

Key Updates from SEARO

Total 367 cases and 16 deaths reported to date from 8 countries/states/territories in SEARO

During past 24 hours:
- 119 new cases from 5 countries /states/territories : Indonesia (48), Thailand (39), India (23), Sri Lanka (5), Maldives (4)
- 9 new deaths: Thailand (9)

3 countries/states/territories have not reported any case: Democratic People's Republic of Korea, Myanmar, Timor-Leste



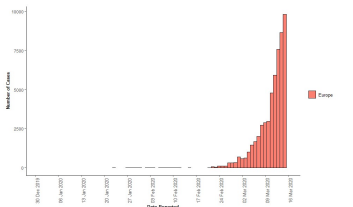
World Health Organization — HEALTH EMERGENCIES programme

5

Key Updates from EURO

Total 54937 cases and 2330 deaths reported to date from 57 countries/states/territories in EURO

During past 24 hours:
- 1.0198 new cases from 35 countries /states/territories
- 596 new deaths



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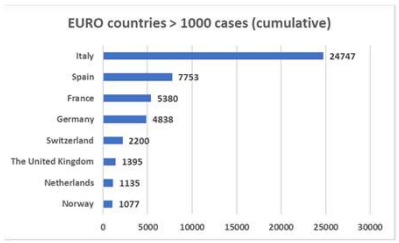
Most affected EURO countries



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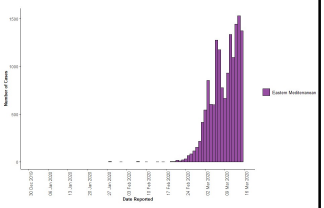
Key Updates from EMRO

Total 15361 cases and 740 deaths reported to date from 17 countries/states/territories in EMRO

During past 24 hours:

- **1381 new cases from 14 countries /states/territories :** Iran (Islamic Republic of) (1254), Iraq (31), Pakistan (24), Egypt (17), United Arab Emirates (13), Morocco (10), Kuwait (8), Lebanon (6), Afghanistan (6), Jordan (5), Bahrain (3), Oman (2), Tunisia (2)
- 117 new deaths: Iran (Islamic Republic of) (116), Sudan(1)

5 countries/states/territories have not reported any case: Djibouti, Libya, Somalia, Syrian Arab Republic, Yemen



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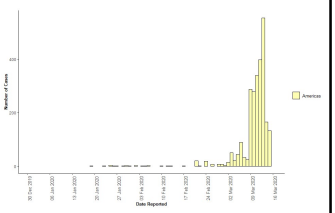
Key Updates from PAHO

Total 2523 cases and 46 deaths reported to date from 33 countries/states/territories in PAHO

During past 24 hours:

- **232 new cases from 15 countries /states/territories :** Canada (128), United States of America (36), Peru (15), Mexico (15), Venezuela (Bolivarian Republic of) (15), Martinique (5), Guadeloupe (3), Guyana (3), Curacao (1), Saint Barthelemy (2), Trinidad and Tobago (1), Costa Rica (4), French Guyana (1), Guatemala (1), Saint Lucia (2), Suriname (1), Uruguay (4)
- 0 new deaths



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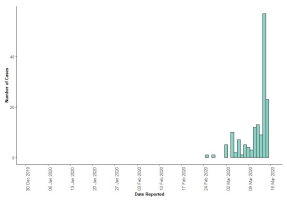
Key Updates from AFRO

Total 153 cases and 3 deaths reported to date from 24 countries/states/territories in AFRO

During past 24 hours:

- **25 new cases from 7 countries /states/territories :** Algeria (12), Senegal (5), Réunion (3), Ghana (1), **Congo (1), Rwanda (1), Seychelles (1)**
- 1 new deaths: Algeria (1)



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World scientists and researchers on COVID-19 met at WHO, 11- 12 Feb 2020

- To assess level of knowledge about COVID-19
- To agree on critical research questions
- To define ways to work together to accelerate and fund priority research

GLOPID-R Global Research Collaboration for Infectious Disease Preparedness

R&DBlueprint Powering research for epidemics EMERGENCIES

11

A research roadmap with clearly defined priorities and governance framework to accelerate research that can contribute to contain the spread of the epidemic

A To ensure that those affected are promptly diagnosed and receive optimal care; while integrating innovation fully within each research thematic area,

B To support research priorities in a way that leads to the development of global research platform(s) pre-prepared for the next disease X epidemic (an unexpected epidemic by a known or previously unknown pathogen); thus, allowing for accelerated research, R&D for diagnostics, therapeutics and vaccines and their timely access.

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An imperative for research to focus on actions that can save lives now.

1. Mobilize research on **rapid point of care diagnostics** for use at the community level
2. Immediately assess available data to learn what **standard of care approaches** from China and elsewhere are the most effective
3. Evaluate as fast as possible the **effect of adjunctive and supportive therapies**
4. Optimise use of **protective equipment and other infection prevention and control measures** in health care and community settings
5. Review all evidence available to **identify animal host(s), to prevent continued spill over and to better understand the virus transmissibility**, the severity of disease and who is more susceptible to infection
6. Accelerate the **evaluation of investigational therapeutics and vaccines** by using "Master Protocols
7. Maintain a **high degree of communication and interaction among funders** so that critical research is implemented
8. **Broadly and rapidly share** virus materials, clinical samples and data

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Key components for successful implementation of the Global Research Roadmap

- **A defined Global Research Roadmap** (with defined timelines and accountability)
- **National research plans at the core of research agenda**
- **Coordinated implementation of critical research** (using core generic protocols when possible)
- **Developers and manufacturers engaged** (on research and fair and equitable allocation decisions)
- **Funders aligned to support research priorities**
- **Harmonized plans for scale up manufacturing of products** (speed, access, cost)

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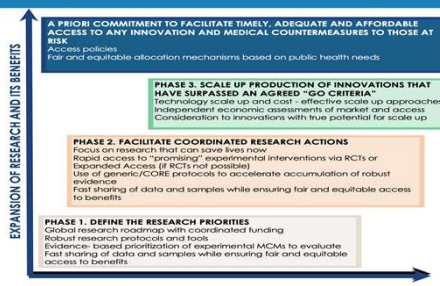
Scaling up research and innovation actions



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Solidarity core protocol

An international study of treatments for COVID-19 in hospitalized patients

The main objective of this study is to provide **reliable estimates of the effects of antiviral treatments on in-hospital mortality.**

The secondary objectives are to assess the effects of such antivirals on duration of hospital stay and, on receipt of ventilation or intensive care.

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Randomisation

Adults (age ≥18 years) recently hospitalised or already in hospital for COVID-19 who have given informed consent are randomly allocated between up to five treatments.

Patients will be randomly allocated between up to five study arms:

1 - the usual standard of care in each hospital.

2 - Remdesivir

3 - Lopinavir/Ritonavir

4 - Lopinavir/Ritonavir plus Interferon (β1b)

5 - Further anti-viral drugs or combinations may well emerge that require evaluation. Chloroquine is among those being considered.

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Simplicity of procedures

1. Start enrolment via study website - Global enrolment and randomisation center.
   Hospital, the ID of the randomising health staff
2. Obtain informed consent
3. Enter registration information
   Patient ID, age, sex
   Patient characteristics (diabetes, heart disease, chronic pulmonary disease, asthma, tuberculosis, HIV infection, current smoking)
   COVID severity at entry (shortness of breath, administration of oxygen, provision of ventilation and, if already imaged, any major radiological abnormality).
4. Proceed with randomisation
5. Initiate administration of drug allocated
6. At the end of hospitalization, enter information on 3 main patient outcomes (while in hospital)
   - Provision of ventilation or intensive care
   - Duration of hospital stay
   - Mortality

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Adaptive design

- Extra arms (additional treatments) may be added while the trial is in progress.
- Interim analyses will be monitored by a Global Data and Safety Monitoring Committee.
- In the light of these, and any other evidence they seek, the committee will advise if in their view, be discontinued

Add-on studies - Particular countries, or particular groups of hospitals, may want to collaborate in adding further measurements or observations, such as serial virology, serial blood gases or chemistry, serial lung imaging, or serial documentation of other aspects of disease status (e.g. through linkage to electronic healthcare records and routine medical databases).

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Numbers to be randomised

- No specific sample size is specified is this public health emergency core protocol.
- The larger the numbers enrolled the more accurate the results will be, but the numbers that can be entered will depend critically on how large the epidemic becomes.

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Key Roles and Study Governance

Interim and final trial analyses will be monitored by an independent Global Data and Safety Monitoring Committee.

The evidence on mortality must be strong enough and the range of uncertainty around the results must be narrow enough to affect national and global treatment strategies.
The Global Data Monitoring and Safety Committee will independently evaluate these analyses and, will inform the WHO policy-making committee if at any stage the results are sufficiently robust for general release and for affecting global recommendations.

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Research Roadmap

- https://www.who.int/blueprint/priority-diseases/key-action/novel-coronavirus/en/

Thank you

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Hospital Preparedness - Infection Prevention and Control for COVID-19

Dr A. S Valan
Public Health Specialist
CDC India Country office, New Delhi

COVID 19 CORONAVIRUS DISEASE

What you need to know about coronavirus disease 2019 (COVID-19)

How it spreads

- Investigations are ongoing to better understand spread
- Largely based on what is known from other coronaviruses
  - Presumed to occur primarily through close person-to-person contact
    - May occur when respiratory droplets are produced when an infected person coughs or sneezes
  - Possibly by touching a surface or object that has the virus on it and then touching the mouth, nose, or eyes

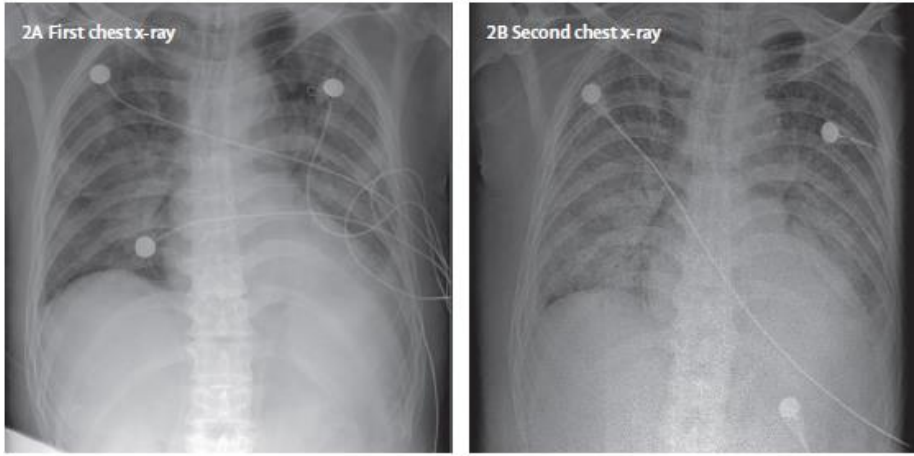
CDC

COVID 19 CORONAVIRUS DISEASE

What you need to know about coronavirus disease 2019 (COVID-19)

Symptoms and Complications

- Symptoms may include fever, cough, shortness of breath
- Wide range of illness severity has been reported (mild to severe)
- Complications may include pneumonia, respiratory failure, or multisystem organ failure



www.thelancet.com Published online January 29, 2020 https://doi.org/10.1016/S0140-6736(20)30211-7

CDC

Clinical Course of COVID 19 in Infected People

- Most people with COVID-19 develop uncomplicated or mild illness (81%)
- ~14% develop severe disease that requires hospitalization and oxygen support
- ~ 5% require admission to an intensive care unit
- Not all mild illness require admission in a health facility; **isolation to contain/mitigate virus transmission should be prioritized**

Team NCPERE. Vital surveillances: the epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) – China. China CDC Weekly. 2020;2(8):113-22.

Goal of IPC in Hospital Preparedness for COVID 19

- **Support maintenance of essential healthcare services by containing and preventing healthcare-associated COVID-19 transmission within healthcare facilities**

IPC priorities for COVID-19

- **IDENTIFY**
  - Early identification of suspected cases presenting for healthcare is critical
- **ISOLATE**
  - Prompt isolation of suspected cases to reduce opportunities for transmission in healthcare setting
- **INFORM**
  - Communication with public health response to initiate laboratory testing and coordinate patient placement

IPC priorities for COVID-19

- **IDENTIFY**
  - Early identification of suspected cases presenting for healthcare is critical

Focus on triage and isolation procedures

- **ISOLATE**
  - Prompt isolation of suspected cases to reduce opportunities for transmission in healthcare setting

- **INFORM**
  - Communication with public health response to initiate laboratory testing and coordinate patient disposition

Consider hotlines for patients to call ahead if they are seeking care for respiratory symptoms

Are You Considering Coming to the ER with Coronavirus (COVID-19) Symptoms?

STOP

PLEASE CALL FIRST

EMERGENCY Dial 911

Nursing Triage Line:
360-537-5100

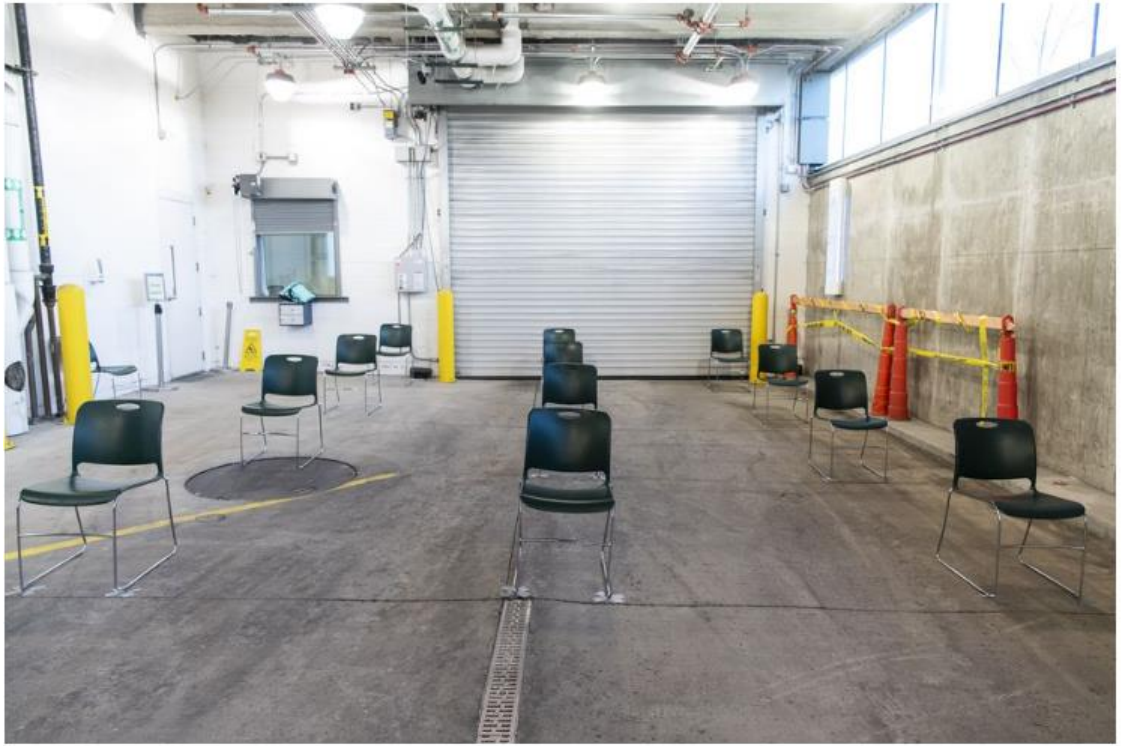
Emergency Room
360-537-4130

Identify suspect COVID-19 cases as soon as possible, ideally before they enter patient care areas

A woman leaves the a pre-triage medical tent in front of a hospital, in Cremona, Italy, last week.

MIGUEL MEDINA/AFP VIA GETTY IMAGES

Separate patients during triage (waiting areas, etc.) as much as possible



Chairs for patients to sit and wait to be tested, each chair is exactly 6 feet apart, at Rush University Medical Center's forward triage center for coronavirus placed in one of the hospitals ambulance bays, Tuesday, March 10, 2020. | Tyler LaRiviere/Sun-Times

Consider use of temporary structures for triage and isolation of suspect COVID-19 patients as transmission increases

DENNIS ODA /DODA@STARADVERTISER.COM

Tents were put up outside the Queen's Medical Center emergency entrance to evaluate and potentially test "walking well" patients for the novel coronavirus while keeping them separated from emergency room patients.

Preparing for triage

- Post clear signs at facility entrance to direct patients with respiratory symptoms to immediately proceed to triage or registration desk
- Ensure availability of face masks at registration desk
  - All patients with respiratory symptoms should put on a mask
  - If masks not available, provide tissues or request patient to cover their face with clothing during entire triage process, including waiting room
- Install physical barriers (e.g. glass/plastic screens) at registration desk to limit close contact between triage staff and patients

Sample visual alerts to post at facility entry

STOP!

If you are experiencing cold or flu symptoms like:

- **Fever**
- **Cough**
- **Shortness of breath**

REPORT immediately to the registration desk!

Protecting healthcare workers at triage

- All HCWs performing triage should always adhere to standard precaution
- All HCW should have convenient access to hand hygiene products
- HCWs conducting preliminary screening that does not require direct patient contact should maintain 1 m distance and does not require full PPE
  - These activities includes interviewing patients about symptoms and exposures and/or taking temperatures with non-contact infrared thermometer
- HCWs conducting physical examination of patients with respiratory symptoms should wear gowns, gloves, face mask, and eye protection (goggles or face shield)

Performing triage

- Patients presenting for care should be screened for signs and symptoms of respiratory infection and potential COVID-19 exposures at the triage station
- The questions asked during triage may vary depending on the COVID-19 epidemiological situation in the area
  - If there is no or little transmission in the community, then patients should be asked about recent travel history or contact with a patient with COVID-19
  - If there is widespread community transmission, questions about travel or contact with other COVID-19 patients are less relevant given the increased risk in the community
- Triage should be conducted adhering to local public health protocols

Sample triage of patients with suspected COVID-19 infection (no or limited community transmission)

Identify signs and symptoms of respiratory infection:
- Fever (>38°C)

-And-
- At least 1 sign or symptom of respiratory disease (e.g., cough or shortness of breath)

No → Continue with usual triage, assessment and care

Yes

Place facemask on patient

Identify Travel and Direct Exposure History:
- Has the patient traveled or resided in another country where COVID-19 is spreading during the 14 days prior to symptom onset?

- or -
- Has the patient had contact* with an individual with confirmed COVID-19 during the 14 days prior to symptom onset?

No → Continue with usual triage, assessment and care

Yes

Separate from the rest of the patients:
- Place the patient in a single-person room with the door closed or in other designated area
- Ensure healthcare personnel (HCP) caring for the patient adhere to Standard, Contact, and Droplet Precautions
- Only essential HCP with designated roles should enter the room and wear appropriate personal protective equipment

Inform
- Notify the hospital infection control committee and other appropriate staff

*A **contact** is a person who is involved in any of the following within 14 days after the onset of symptoms in the patient:
- providing direct care for patients with COVID-19 disease without using proper personal protective equipment;
- staying in the same close environment as a COVID-19 patient (including sharing a workplace, classroom or household or being at the same gathering);
- travelling in close proximity with (that is, having less than 1 m separation from) a COVID-19 patient in any kind of conveyance.

Isolation of suspect COVID-19 cases

- Patients who are identified as suspect COVID-19 cases through the triage process must be separated from other patients as soon as possible
  - Give the patient a face mask and ask them to put it on
    - If face masks are not available, have patient cover their mouth with clothing
  - Place the patient in a single-person room with the door closed
    - If single-person rooms are not available, designate a separate, well-ventilated area for these patients and ensure they maintain 1 m separation from each other
  - Only essential HCWs designated to care for suspect COVID-19 patients should enter the isolation area wearing appropriate PPE
  - Ensure that HCWs caring for patients in the isolation area adhere to standard, contact, and droplet precautions

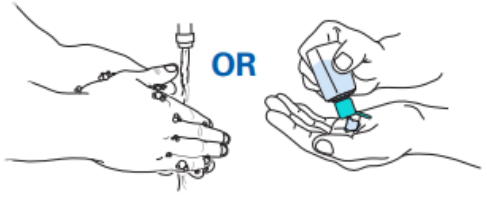
Isolation facility

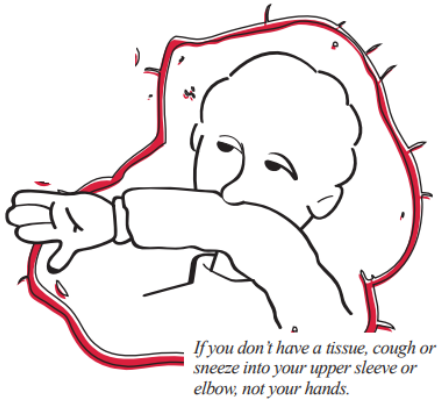
Rajiv Ghandhi Government General hospital in Chennai, Picture courtesy https://www.hindustantimes.com/india-news/isolation-wards-set-up-in-ncr-evacuees-awaited/story-obLXVkaJteu12hvw9JhefI.html

Additional IPC considerations

Standard precautions for all patient care

- Hand hygiene
- Respiratory hygiene
  - Ensure patients cover their nose and mouth with tissue or elbow when coughing or sneezing
  - Offer medical mask to patients with suspected COVID-19 while in waiting rooms/waiting hall
  - Perform hand hygiene after contact with respiratory secretions
- Rational and correct use of PPE
- Environmental cleaning and disinfection





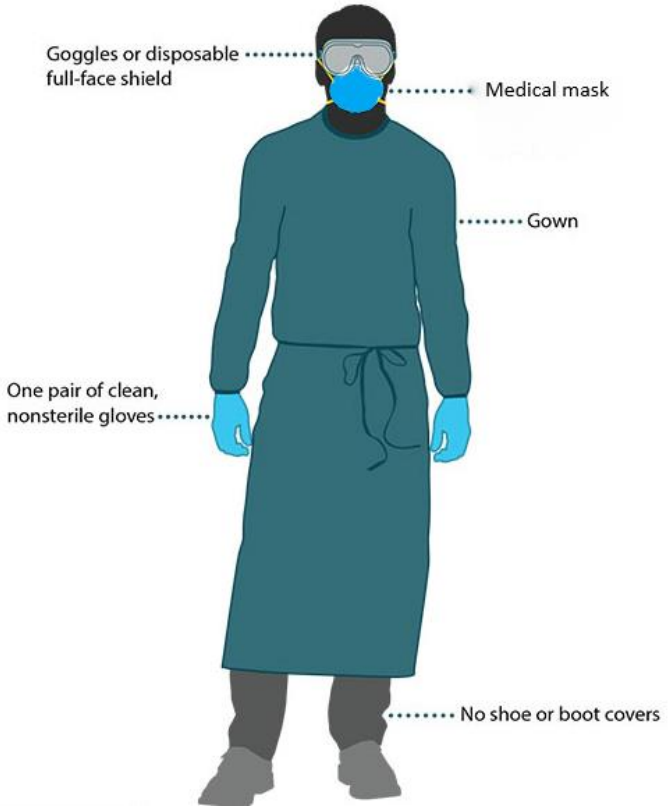
Transmission-based precautions for COVID-19

- Use adequately ventilated single rooms or ward rooms
- Wear PPE appropriate for contact and droplet precautions*
- Use disposable or dedicated patient care equipment (e.g., blood pressure cuffs, Stethoscopes)
- Avoid transporting COVID-19 patients out of room unless medically necessary
- Limit number of HCWs, family members, and visitors in contact with suspected or confirmed cases

*WHO recommendations

PPE for COVID-19*

- Gloves (non-sterile, examination)
- **Medical mask**
- Eye protection (goggles or face shield)
- Gown (long-sleeved, non-sterile)



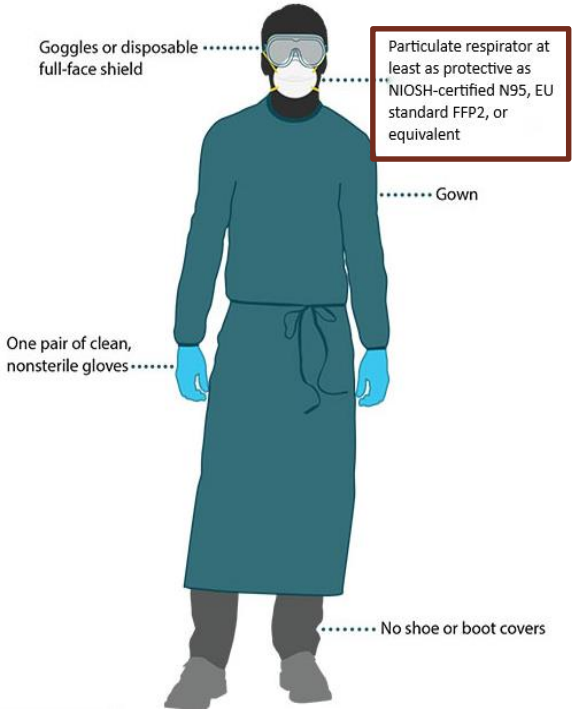
*Note: information on this slide is PPE as recommended by WHO

Aerosol-generating procedures (AGPs)

- AGPs associated with increased risk of transmission of other coronaviruses (SARS-CoV and MERS-CoV)

- Perform AGPs in adequately ventilated rooms
  - Negative pressure room (at least 12 air exchanges/hour) or natural ventilation (air flow at least 160 L/s per patient)

- Wear appropriate PPE
  - Gloves (non-sterile, examination)
  - **Particulate respirator**
  - Eye protection (goggles or face shield)
  - Gown (long-sleeved, non-sterile)



*Note: information on this slide is PPE as recommended by WHO

Key points for PPE use

- PPE relies on **consistent and correct use** by healthcare personnel
  - trainings and practice for healthcare personnel in advance

- **Risk of self-contamination** is higher when removing PPE
  - Remove PPE slowly and carefully
  - Do not touch front of masks, respirators, or facial protection (likely most contaminated)

- **Instructions** for putting on and removing PPE
  - https://www.cdc.gov/hai/pdfs/ppe/ppe-sequence.pdf

HOW TO PUT ON AND TAKE OFF

Personal Protective Equipment (PPE)

World Health Organization

How to put on PPE (when all PPE items are needed)

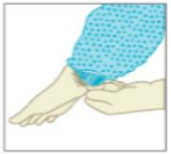
Step 1
- Identify hazards & manage risk. Gather the necessary PPE.
- Plan where to put on & take off PPE.
- Do you have a buddy? Mirror?
- Do you know how you will deal with waste?

Step 2
- Put on a gown.

Step 3 - Put on medical mask and eye protection (e.g. face shield, eye visor/goggles)

\+  or 

Note: If performing an aerosol-generating procedure (e.g. aspiration of respiratory tract, intubation, resuscitation, bronchoscopy, autopsy), a particulate respirator (e.g. US NIOSH-certified N95, EU FFP2, or equivalent respirator) should be used in combination with a face shield or an eye protection. Do user seal check if using a particulate respirator.



Step 4
- Put on gloves (over cuff).

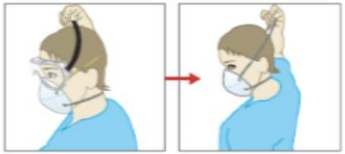
How to take off PPE

Step 1
- Avoid contamination of self, others & the environment
- Remove the most heavily contaminated items first

Remove gloves & gown
- Peel off gown & gloves and roll inside, out
- Dispose gloves and gown safely

Step 2
- Perform hand hygiene

Step 3a
If wearing face shield:
- Remove face shield from behind
- Dispose of face shield safely



Step 3b
If wearing eye protection and mask:
- Remove goggles from behind
- Put goggles in a separate container for reprocessing
- Remove mask from behind and dispose of safely

Step 4
- Perform hand hygiene

Environmental cleaning and disinfection

- Routine cleaning and disinfection procedures sufficient
- Focus cleaning on frequently touched and frequently contaminated surfaces
  - Light switches, bed rails, door handles, sinks, bathrooms
- Hospital-grade disinfectants effective
  - Products active against enveloped viruses

https://www.cdc.gov/hai/pdfs/resource-limited/environmental-cleaning-508.pdf

High-touch surfaces

Appendix C, Best Practices for Env. Cleaning in HCFs in Resource-Limited Settings, Appendix C

https://www.cdc.gov/hai/pdfs/resource-limited/environmental-cleaning-508.pdf

Appendix C - Example of high-touch surfaces in a specialized patient area

Strategies for Optimizing the PPE Supply

- **Conventional capacity**: measures consist of providing patient care without any change in daily contemporary practices. This set of measures, consisting of engineering, administrative, and PPE controls should be implemented in general IPC plans in healthcare settings
- **Contingency capacity**: measures may change daily contemporary practices but may not have any significant impact on the care delivered to the patient or the safety of the HCP. May be used temporarily when demands exceed resources.
- **Crisis capacity**: alternate strategies that are not commensurate with contemporary U.S. standards of care.

IPC Resources

- WHO IPC technical guidance for COVID-19
  - https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/infection-prevention-and-control
- WHO Q&A for health care workers
  - https://www.who.int/news-room/q-a-detail/q-a-on-infection-prevention-and-control-for-health-care-workers-caring-for-patients-with-suspected-or-confirmed-2019-ncov
- Best practices for environmental cleaning in HCFs in Resource-Limited Settings
  - https://www.cdc.gov/hai/pdfs/resource-limited/environmental-cleaning-508.pdf
- IPC trainings (not specific for COVID-19)
  - https://ipc.ghelearning.org/courses

Acknowledgement

- Dr Daniel VanderEnde, Medical Officer, CDC
- Paul Malpiedi, Epidemiologist, DHQP, CDC
- Dr Meghna Desai, Country Director, CDC India Country Office
- IMS Team COVID 19 response, CDC India Country Office

Thank you!

For more information, contact CDC Staff
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VIROLOGY OF SARS-COV-2

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2

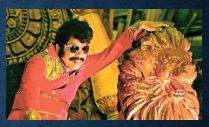
OUTLINE

- The family..
- Structure and implications
- Genomic composition
- Pathogenesis
- How is it different to SARS and MERS?
- What, when and how to test?

3

CORONAVIRUSES- 'COMMON-COLD' VIRUSES

- Common HCoV(Less pathogenic)
  - HCoV-229E
  - HCoV-NL63
  - HCoV-OC43
  - HCoV-HKU1



- Other HCoVs(highly pathogenic)
  - SARS-CoV
  - **SARS-CoV-2**
  - MERS-CoV

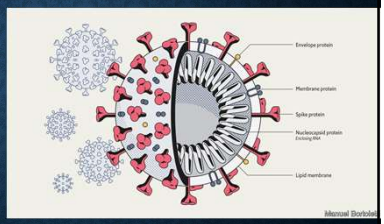
COVID-19 refers to the name of the disease caused by SARS-CoV-2

4

STRUCTURE

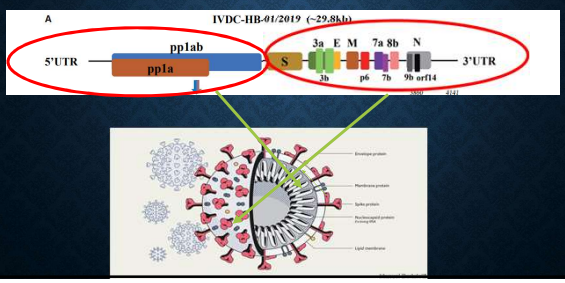
Coronaviruses are

- Enveloped
- Positive-sense
- Single stranded RNA viruses
- Genome- 30kb
- Structural and non-structural proteins



5

A CLOSER LOOK....



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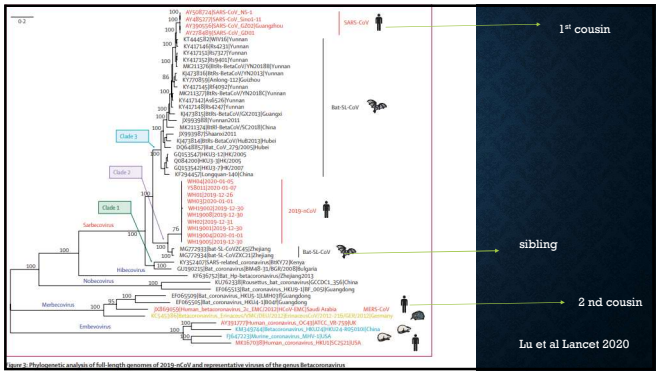
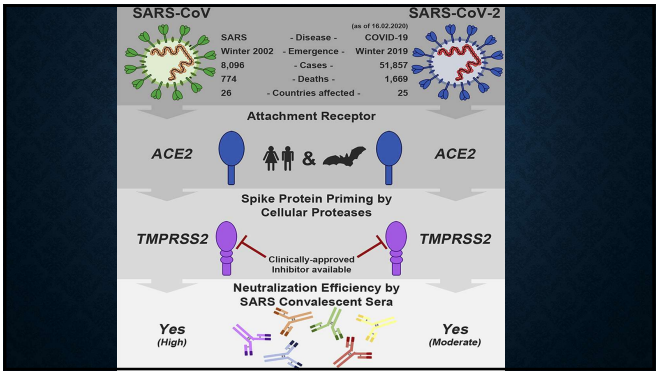
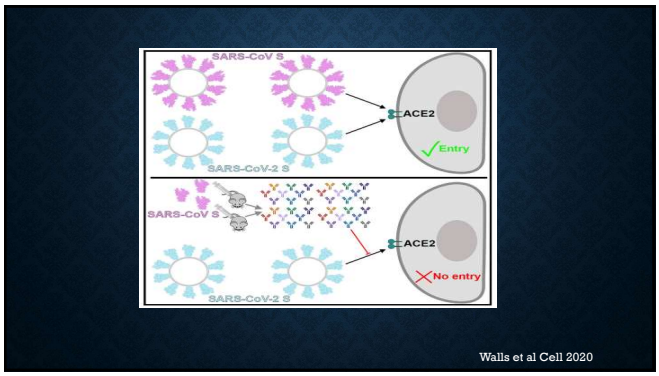

1st cousin
sibling
2 nd cousin
Lu et al Lancet 2020

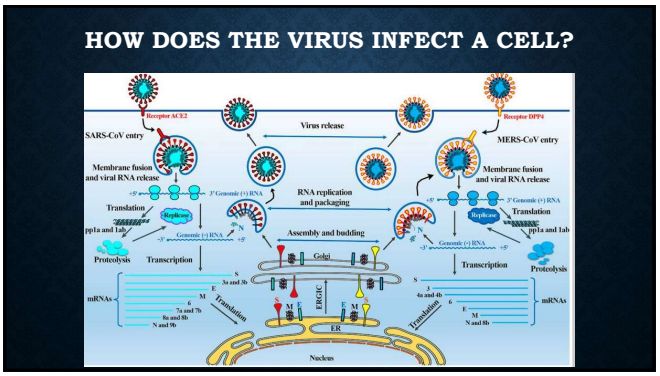
7


SARS-CoV
SARS-CoV-2
(as of 16.02.2020)
SARS
Winter 2002
8,096
774
26
- Disease -
- Emergence -
- Cases -
- Deaths -
- Countries affected -
COVID-19
Winter 2019
51,857
1,669
25
Attachment Receptor
ACE2
&
ACE2
Spike Protein Priming by Cellular Proteases
TMPRSS2
Clinically-approved Inhibitor available
TMPRSS2
Neutralization Efficiency by SARS Convalescent Sera
Yes
(High)
Yes
(Moderate)

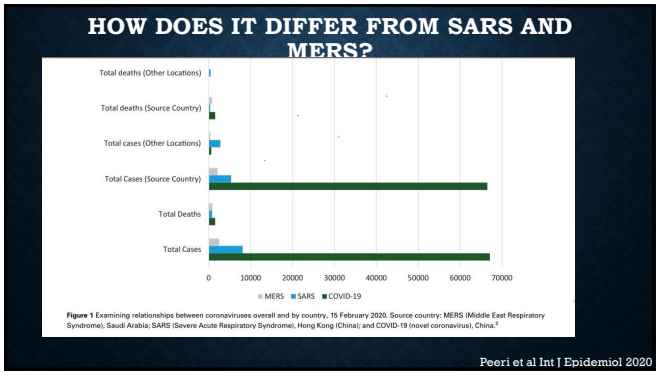
8


SARS-CoV S
ACE2
Entry
SARS-CoV-2 S
SARS-CoV S
ACE2
No entry
SARS-CoV-2 S
Walls et al Cell 2020

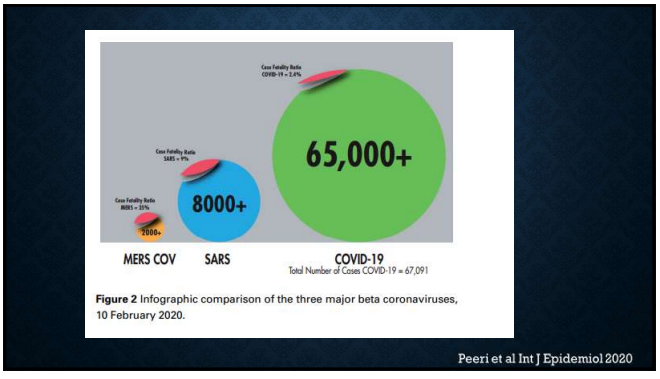
9


HOW DOES THE VIRUS INFECT A CELL?
Receptor ACE2
SARS-CoV entry
Virus release
Receptor DPP4
MERS-CoV entry
Membrane fusion and viral RNA release
RNA replication and packaging
Translation
Replicase
pp1a and 1ab
Genomic (+) RNA
Assembly and budding
Golgi
Transcription
Proteolysis
mRNAs
ERGIC
ER
Nucleus

10


HOW DOES IT DIFFER FROM SARS AND MERS?
Total deaths (Other Locations)
Total deaths (Source Country)
Total cases (Other Locations)
Total Cases (Source Country)
Total Deaths
Total Cases
0
10000
20000
30000
40000
50000
60000
70000
MERS
SARS
COVID-19
Figure 1 Examining relationships between coronaviruses overall and by country, 15 February 2020. Source country: MERS (Middle East Respiratory Syndrome), Saudi Arabia; SARS (Severe Acute Respiratory Syndrome), Hong Kong (China); and COVID-19 (novel coronavirus), China.
Peeri et al Int J Epidemiol 2020

11

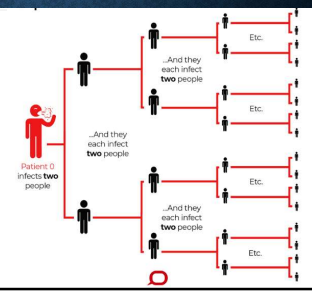

65,000+
8000+
3000+
MERS COV
SARS
COVID-19
Total Number of Cases COVID-19 = 67,091
Figure 2 Infographic comparison of the three major beta coronaviruses, 10 February 2020.
Peeri et al Int J Epidemiol 2020

12

HOW EFFECTIVE IS THE TRANSMISSION EXPLORING R_0

Virus	Case Fatality Rate (%)	R_0
2019-nCoV	3	1.4–5.5[a]
SARS-CoV	10	2–5
MERS-CoV	40	<1
Avian H7N9 (2013)	40	<1
H1N1 (2009)	0.03	1.2–1.6
H1N1 (1918)	3	1.4–3.8
Measles Virus	0.3	12–18
Rhinovirus	<0.01	6
Ebola Virus	70	1.5–2.5
HIV	80[b]	2–4
Small Pox Virus	17	5–7

[a] WHO: 1.4–2.5; S. Zhao et al.: 3.3–5.5; J. Read et al.: 3.6–4.0; M. Shen et al.: 4.5–4.9.



13

DETECTION OF VIRUS IN BODY FLUIDS

- Virus detected in upper respiratory specimens 1-2 days before onset of symptoms
- Shedding can occur up to 2 week in severe cases
- Detected in faeces in 30% at day 5 after symptom onset and persist up to 4-5 weeks in moderate cases

Does the extended detection translate to live virus shedding?

What is the role of faeco-oral transmission?

Alyward, WHO-China mission 2020

14

Lower respiratory specimens perform better than upper respiratory specimens

Table. Detection Results of Clinical Specimens by Real-Time Reverse Transcriptase–Polymerase Chain Reaction

Specimens and values	Bronchoalveolar lavage fluid (n = 15)	Fibrobronchoscope brush biopsy (n = 13)	Sputum (n = 104)	Nasal swabs (n = 8)	Pharyngeal swabs (n = 398)	Feces (n = 153)	Blood (n = 307)	Urine (n = 72)
Positive test result, No. (%)	14 (93)	6 (46)	75 (72)	5 (63)	126 (32)	44 (29)	3 (1)	0
Cycle threshold, mean (SD)	31.1 (3.0)	33.8 (3.9)	31.1 (5.2)	34.3 (8.6)	32.1 (4.2)	31.4 (5.1)	34.6 (0.7)	ND
Range	26.4-36.2	26.9-36.8	18.4-38.8	16.9-38.4	20.8-38.6	22.3-38.4	34.1-35.4	
95% CI	28.9-33.2	29.8-37.9	29.3-33.0	13.7-35.0	31.2-33.1	29.4-33.5	0.0-36.4	

Abbreviation: ND, no data.

Table Title:
Detection Results of Clinical Specimens by Real-Time Reverse Transcriptase–Polymerase Chain Reaction

JAMA 2020

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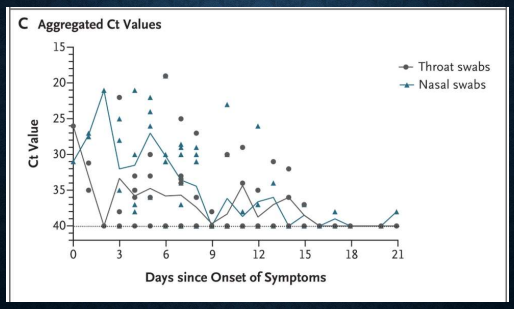
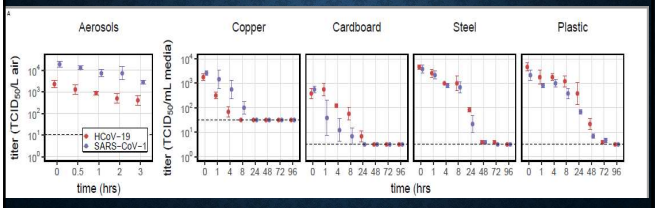


Zou et al NEJM 2020

16

VIRUS STAYS LONGER IN AEROSOLS AND OTHER SURFACES

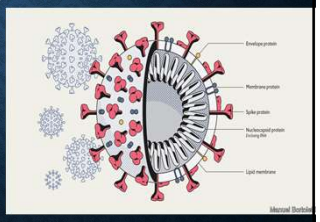


Van Doremelan et al medRxiv 2020

17

TESTING- ADHERE TO YOUR LOCAL TESTING CRITERIA

- Samples- Broncho-alveolar lavage, sputum, nasopharyngeal swabs and nasal swabs
- - Serum for storage and research only
- Tests
  - Test for common viruses/bacterial pathogens
  - PCR-SARS-CoV-2 specific
    - RT-PCR- RdRP gene, N, E, S genes
  - Atleast 2 targets should be positive .
  - Viral culture
  - Serology
- WHO-COVID-19-laboratory-2020.4-eng.pdf



18

19

COVID 19 vaccine – Realm of reality

Dr. G. Dhinakar Raj

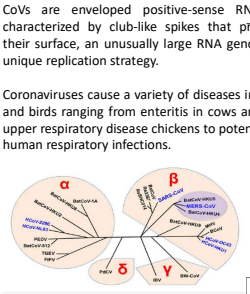
Director
Centre for Animal Health Studies
Tamil Nadu Veterinary and Animal Sciences University
Chennai 600 051

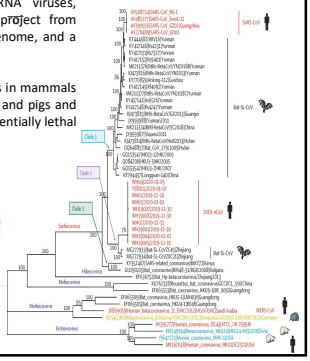
1

Corona virus classification

CoVs are enveloped positive-sense RNA viruses, characterized by club-like spikes that project from their surface, an unusually large RNA genome, and a unique replication strategy.

Coronaviruses cause a variety of diseases in mammals and birds ranging from enteritis in cows and pigs and upper respiratory disease chickens to potentially lethal human respiratory infections.

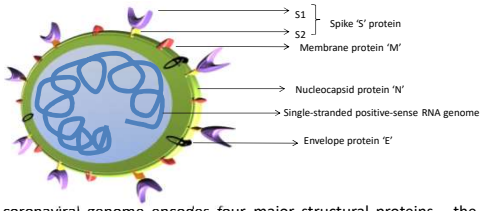




The Lancet 2020 395, 565-574DOI: (10.1016/S0140-6736(20)30251-8)

2

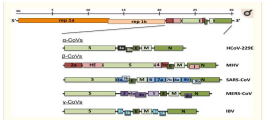
Structure of SARS-CoV2

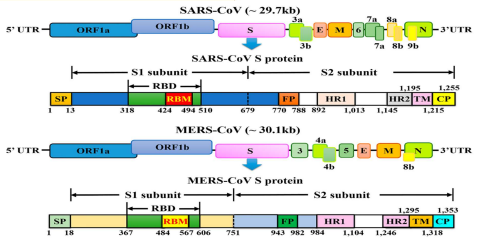


- The coronaviral genome encodes four major structural proteins - the spike (S) protein, nucleocapsid (N) protein, membrane (M) protein, and the envelope (E) protein.
- The S protein is responsible for facilitating entry of the CoV into the target cell. It is composed of a short intracellular tail, a transmembrane anchor, and a large ectodomain that consists of a receptor binding S1 subunit and a membrane-fusing S2 subunit.

3

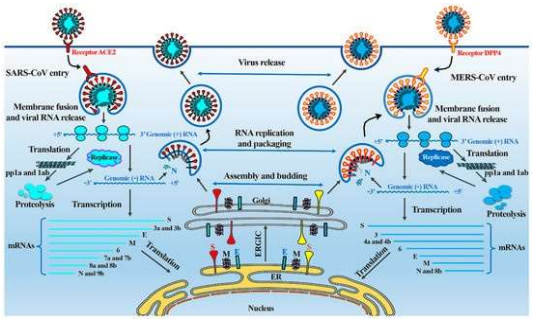
Corona virus genome organization





4

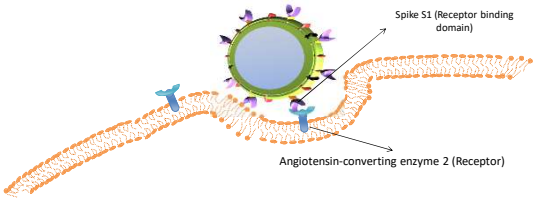
Corona virus replication cycle



Song *et al*., 2019

5

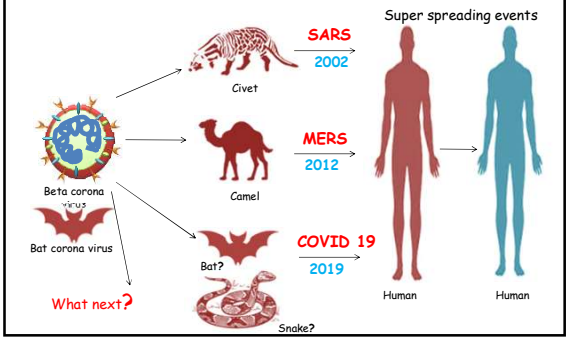
Receptor of SARS-CoV2



- SARS-CoV2 shared 79.5% sequence identity with SARS-CoV
- Sequence analysis of the SARS-CoV-2 S protein genome showed that it was only 75% identical with the SARS-CoV S protein
- The receptor binding motif (RBM) in the S protein showed most of the amino acid residues essential for receptor binding were conserved between SARS-CoV and SARS-CoV-2
- ACE-2 is an Entry Receptor for SARS-CoV-2

6

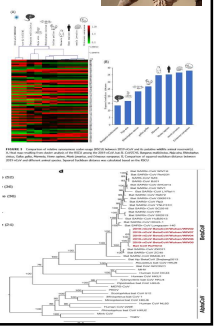
SARS, MERS and COVID 19…. What next?



7

Animal Source of SARS-CoV2 – Snakes, Bats, Pangolin….

- 2019-nCoV has most similar genetic information with bat coronovirus and has most similar **codon usage bias with snake** (Ji *et al.,* 2020).
- A whole-genome comparison found that the **pangolin and human viruses share 90.3% of their DNA.**
- SARS virus shared **99.8% of its genome with a civet coronavirus**, which is why civets were considered the source.



8

Corona viruses of veterinary importance

Genus	Virus	Host
Alphacoronavirus (Infects mammals)	Transmissible gastroenteritis virus	Porcine
	Porcine respiratory coronavirus	
	Porcine epidemic diarrhea virus	
	Feline enteric coronavirus	Feline
	Feline infectious peritonitis virus	
	Canine coronavirus	Canine
Betacoronavirus (Infects mammals)	Bovine coronavirus	Bovine
	Porcine hemagglutinating encephalomyelitis virus	Porcine
	Canine respiratory coronavirus	Canine
	Equine coronavirus	Equine
	Middle East respiratory syndrome (MERS) coronavirus	Camel
Gammacoronavirus	Avian infectious bronchitis virus	Chicken
Deltacoronavirus	Porcine deltacoronavirus	Porcine
	Wigeon coronavirus HKU20	Birds
	Munia coronavirus HKU13	

9

COVID 19 in animals

- **Tai Hang, Islands District, Hong Kong**

OIE COVID-19 (SARS-COV-2), Hong Kong (SAR - PRC)

Information received on 01/03/2020 from Dr Thomas Sit, Chief Veterinary Officer / Assistant Director (Inspection & Quarantine), Agriculture, Fisheries and Conservation Department, Hong Kong Special Administrative Region Government, Hong Kong , Hong Kong (SAR - PRC)

Summary

Report type	Immediate notification
Date of start of the event	26/02/2020
Date of confirmation of the event	26/02/2020
Report date	29/02/2020
Date submitted to OIE	01/03/2020
Reason for notification	Emerging disease
Morbidity	1 (scale 0 to 5)
Mortality	0 (scale 0 to 5)
Zoonotic impact	Zoonotic potential unknown at this time
Causal agent	SARS-CoV-2
Related reports	Immediate notification (28/02/2020) Follow-up report No. 1 (07/03/2020)

Diagnostic test results

OIE, Follow-up report No. 1 (07/03/2020)

Laboratory name and type	Species	Test	Test date	Result
Tai Lung Veterinary Laboratory (National laboratory)	Dogs	real-time reverse transcriptase/polymerase chain reaction (RRT-PCR)	28/02/2020	Positive
Tai Lung Veterinary Laboratory, Agriculture Fisheries and Conservation Department (National laboratory)	Dogs	real-time reverse transcriptase/polymerase chain reaction (RRT-PCR)	27/02/2020	Positive
School of Public Health, The University of Hong Kong (Regional Reference Laboratory)	Dogs	real-time reverse transcriptase/polymerase chain reaction (RRT-PCR)	27/02/2020	Positive

10

Vaccines against SARS

Organization Candidate	Country of Study	Trial Type; Study Design; Study Details	Outcome (Safety)	Outcome (Efficacy)	Reference
Sinovac Biotech Co. Ltd.; **Inactivacted SARS-CoV (ISCV)**	China (Beijing)	Phase I clinical trial; Randomised, double blind and placebo controlled; 2 doses of 16 SARS-CoV units (SU) or 32 SU ISCV or placebo control vaccine, intramuscular injection of vaccines in deltoid muscle, doses were 28 days apart.	No severe adverse reaction (grade 3) was reported.	Seroconversion reached 100% for both vaccine groups on day 42, persisted at 100% in the group receiving 16 SU but decreased to 91.1% for the group receiving 32 SU on day 56.	Lin *et al.*, 2007
NIH, National Institute of Allergy and Infectious Diseases, **VRC-SARS DNA015 00-VP**	United States (Maryland)	Phase I clinical trial; Open-label study; 3 doses of vaccine (4 mg/dose), intramuscular injection into lateral deltoid muscle via the Biojector 2000® Needle-Free Injection Management System™ on study days 0, 38 and 56	No severe adverse reaction (grade 3), 50% subjects reported at least one mild systemic symptom following vaccination.	SARS specific antibody was detected by ELISA in 8 of 10 (80%) of subjects at one or more time points.	Martin *et al.*, 2008

11

Vaccines against MERS

Organization; Candidate	Country of Study	Trial Type; Study Design; Study Details	Outcome (Safety)	Outcome (Efficacy)	Reference
GeneOne Life Science and Inovio Pharmaceuticals GLS-5300	United States (Maryland)	Phase I clinical trial; Open-label, single-arm, dose escalation study; 3 doses of 0·67 mg, 2 mg, or 6 mg GLS-5300; intramuscular 1 mL injection followed immediately by co-localised intramuscular electroporation with CELLECTRA®-5P	No vaccine-associated serious adverse events. 97% participants reported at least one solicited adverse event	Seroconversion measured by S1-ELISA occurred in 86% and 94% participants after 2 and 3 doses, respectively, and was maintained in 79% participants up to study end at week 60. Neutralising antibodies were detected in 50% participants at one or more time points during the study, but only 3% maintained neutralisation activity to end of study.	Modjarrad *et al.*, 2019

12

Vaccines against Animal Corona viruses

Animal	Disease	Vaccine name, Route	Type	Marketed by
Cat	Feline infectious peritonitis	FELOCELL FIP, intra nasal vaccine	Attenuated, temperature-sensitive (TS) strain of FIP virus	Zoetis, USA
Dog	Canine Corona virus gastroenteritis	Nobivac® Canine 1-DAPPv+Cv, subcutaneously or intramuscularly	Inactivated vaccine	Intervet/ Merck Animal Health, USA

13

Avian corona virus - Infectious Bronchitis

1931	First report of Infectious Bronchitis in USA
1950	Second serotype (Connecticut)
1960	First live vaccines developed
1970	Emergence of variant serotypes – some variants localised; some spread widely
1991	A variant IBV – 793 B or 4/91 first identified in UK – Now widely prevalent – no cross protection with existing vaccines – New vaccines prepared
1996	Another variant IBV – QX strain first identified in China – Now widely prevalent – New vaccines prepared
2020	IB still a major problem

14

Vaccines against IBV

S. No.	Vaccine name	Type	Strain	Marketed by
1	LIVE M48	Live	Mild Massachusetts Type	Hester, India
2	LIVE H120		Massachusetts Type H120	
3	CEVAC® MASS L		Massachusetts B48 strain	Ceva Santé Animale, France
4	NOBILIS® IB 4-91		Serotype 4-91	Intervet, Netherlands
5	NOBILIS® IB Primo QX		QX	
6	MILDVAC-Ma5™		Massachusetts type Ma5	Merck Animal Health, USA
7	MILDVAC™-MASS + CONN		Mild Massachusetts and Connecticut	
8	MILDVAC-GA-98®		Georgia type, GA98 strain	
9	MILDVAC™-MASS + ARK		Mild Massachusetts and Arkansas types	
10	SHOR-BRON®-D		Delaware Type	
11	INACTIVATED IB	Inactivated	Massachusetts Type	Hester, India
12	INACTIVATED IB (H52)		Massachusetts Type H52	
13	INACTIVATED IB+		Massachusetts & Arkansas Type	
14	GlobiVac® IBK		Massachusetts Type	Globion, India

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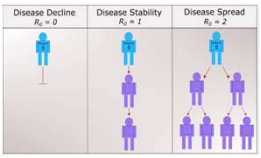
Basic Reproduction number - R_0

- The transmissibility of a virus is measured by the reproduction number
- R_0 is the average number of people who will catch a disease from one contagious person.
- It specifically applies to a population who were previously free of infection and not vaccinated.



- If R_0 is less than 1, each existing infection causes less than 1 new infection. In this case, the disease will decline and eventually disappear.
- If R_0 equals 1, the disease will stay alive, but there won't be an epidemic.
- If R_0 is greater than 1, cases could grow exponentially and cause an epidemic or even a pandemic.

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R_0 of SARS-CoV2

- Estimation of R_0 during the pre-epidemic stage can be constrained by data uncertainty and variability
- R_0 might also change according to climate or gatherings that put individuals in closer proximity.
- The estimated R_0 value for 2019-nCoV is getting reduced as case information accumulates.
- With control measures implemented, the effective reproduction number (R_e) has dropped to **2.08** (1.99–2.18) as of 22 Jan 2020

17

The Ideal Vaccine

- **Safe and Potent**
- No side effects in the population
- Cheap
- Easy to administer
- Thermally stable
- **Produce sterile immunity**
- Broadly protective against all variants of pathogen
- Effective in all subjects
- Transmit maternal protection to foetus
- Prevent carrier state
- Does not complicate diagnostic tools
- **Immune correlates of protection**
- **Mass scale production (~7.8 billion people)**

And many more….

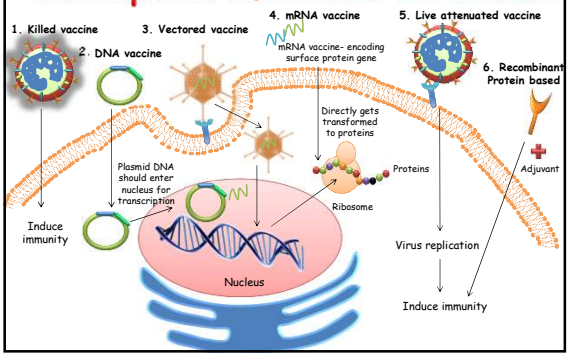
18

Designing a CoV vaccine – Target antigens

- Target proteins – S, S2, S1 or RBD
- The S precursor protein of SARS-CoV-2 can be proteolytically cleaved into S1 (685 aa) and S2 (588 aa) subunits
- The S2 protein is well conserved among SARS-CoV-2 viruses - may boost the broad-spectrum antiviral effect
- S1 subunit consists of the receptor-binding domain (RBD), which mediates virus entry through the host ACE2 receptor
- S protein, which induces neutralizing antibody responses and stimulates a protective cellular immunity against SARS-CoVs
- Administration of SARS-CoV RBD proteins can also induce highly potent neutralizing antibodies and long-term protective immunity
- Administration of vaccines by oral or aerosol routes will induce mucosal immune responses and are possible modes of SARS-CoV-2 vaccine immunization.

19

Different approaches for development of COVID 19 vaccine



20

Designing a CoV vaccine …

RNA-based vaccines

- Use of SARS-CoV-2 RNA
- Difficult to scale up
- Relatively expensive
- Potential for adjuvants to reduce the amount of RNA

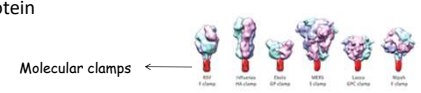
DNA-based technology

- More cheaper
- Difficult to scale up
- Not tested in elderly patients

21

Molecular Clamps

- Enveloped viruses- require fusion of viral and host cell membranes to enter and infect the host cell
- Viral fusion proteins -undergo structural rearrangements from a metastable 'pre-fusion' conformation to a highly stable 'post-fusion' conformation.
- Pre-fusion form of the viral fusion protein is more desirable- contain important epitopes cross-reactive and potently neutralizing antibodies
- Traditional recombinant expression of viral fusion proteins - result in premature triggering and shift to more stable post-fusion form.
- Molecular Clamp- polypeptide moiety - keeps protein in pre-fusion protein



22

Combination attenuation

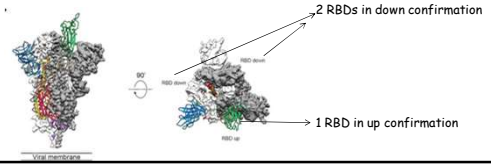
- **SARS- NSP16** mutant vaccine - evaluated in mice model- against heterologous challenge
- Virulence in the aged mice and potential for reversion- untenable approach
- **2'O methyltransferase** (MTase) mutation in NSP16 mutant - protection from heterologous virus challenge, efficacy in aged mice and no evidence for reversion
- **Combined mutation** approach mainly involving NSP16 is an effective method for future CoV vaccine

(Menachery *et al.*, 2018)

23

Trimer-Tag© technology

- COVID 19- bind to angiotensin-converting enzyme 2 (ACE2) to enter human cells
- S1 –RBD- bind to the peptidase domain (PD) of ACE2.
- ACE2 needs to dimerise to be active
- Resultant homodimer has two PDs, able to bind two COVID-19 **S protein trimers s**imultaneously.



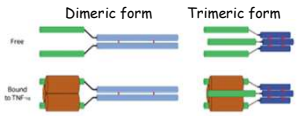
24

Trimer-Tag© technology

- Production of novel, **covalently-trimerized** fusion proteins
- Uses C-prodomains of **collagen proteins** - capable of efficient self-trimerization.

Advantages

- **Naturally Secreted Trimer** (C-Propeptide of Collagen)
- Disulfide Bond-Linked
- Turn Any Secreted Protein into Covalently Linked Trimer



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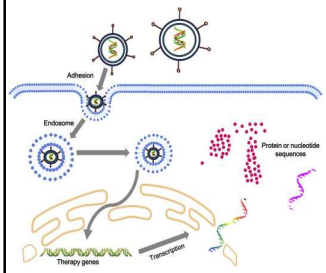
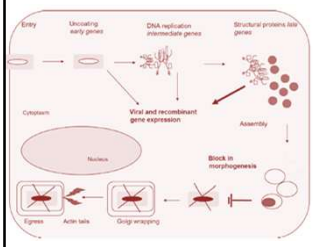
Adenovirus vector technology



- Absence of viral replication genes
- The first generation vectors are deficient in the **E1 and E3 regions**.
- The second generation vectors are deficient in **E2 and E4**
- High-capacity - AdVs are beneficial because they lack the viral elements that can cause an immune response in the host.

26

Modified Vacciniavirus Ankara as vaccine platform

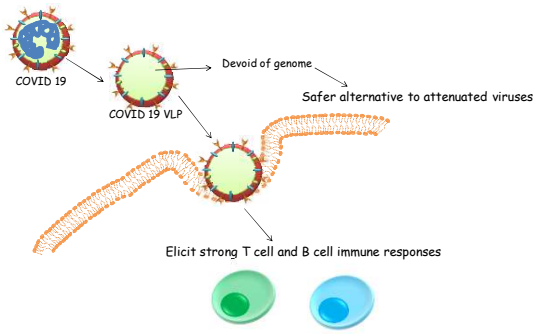


- MVA does not productively replicate in most mammalian cells - can efficiently enter any cell and start its cascade-like life cycle resulting in unimpaired expression of **viral early and intermediate genes, synthesis of viral genomic DNA**, and the abundant expression of viral late genes.
- Thus, foreign and MVA proteins are efficiently produced and the **block of the MVA life cycle occurs at the step of virion assembly** resulting in assembly of immature virus particles that are not released from the infected cell.

(Volz and Sutter, 2017)

27

VLP based vaccines



28

SARS-CoV2 vaccine platforms

Vaccine strategy	Advantages	Disadvantages
Inactivated virus vaccines	Easy to prepare; safety; high-titer neutralizing antibodies	Potential inappropriate for highly immunosuppressed individuals
Attenuated virus vaccines	Rapid development; induce high immune responses	Phenotypic or genotypic reversion possible; can still cause some disease
Subunit vaccines	High safety; consistent production; can induce cellular and humoral immune responses; high-titer neutralizing antibodies	High cost; lower immunogenicity; require repeated doses and adjuvants
Viral vector vaccines	Safety; induces high cellular and humoral immune responses	Possibly present pre-existing immunity
DNA vaccines	Easier to design; high safety; high-titer neutralizing antibodies	Lower immune responses in humans; repeated doses may cause toxicity
mRNA vaccines	Easier to design; high degree of adaptability; induce strong immune responses	Highly unstable under physiological conditions

Shang *et al.*, 2020

29

COVID 19 vaccine- ongoing studies

(Pang et al., 2020)

S. No.	Technology	Company	Estimated Timeline	Stage/Funding
1	Messenger RNA vaccine	Moderna Therapeutics—US National Institute of Allergy and Infectious Diseases	3 months to early stage (phase 1) clinical trial in US (earliest); much longer for full testing and regulatory approval	Preclinical Awaiting preclinical tests and phase 1 study by NIAID, Funding by CEPI.
2	INO-4800-DNA based vaccine (DNA synthesized in lab, does not require actual virus sample)	Inovio Pharmaceuticals	Human testing in the next few months	Preclinical Funding by Coalition for Epidemic Preparedness Innovations (CEPI)
3	Nanoparticle vaccine	Novavax	3 months	Preclinical

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S. No.	Technology	Company	Estimated Timeline	Stage/Funding
4	Rapid Response Technology, 'Molecular clamp' vaccine platform (gene added to viral proteins, misleads body to generate antibodies)	University of Queensland	6 months	Preclinical Funding by Coalition for Epidemic Preparedness Innovations (CEPI)
5	Anti-coronavirus monoclonal antibodies. Additionally, using "whole-genome CRISPR based screening capabilities to identify the host receptor for Wuhan coronavirus"	Vir Biotechnology	Not available	Preclinical
6	Not available Inactivated virus vaccine (postulated, not verified)	Chinese Centre for Disease Control and Prevention (CDC)	At least 1 month for development, 2-3 years before availability for use	Preclinical; virus successfully isolated, currently selecting Strain
7	mRNA technology	Shanghai East Hospital (Tongji University)—Stermirna Therapeutics	<40 days for manufacture of vaccine samples	Preclinical

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S. No.	Technology	Company	Estimated Timeline	Stage/Funding
8	Adenovirus—vectored technology used for Ebola vaccine (and Zika and HIV vaccine candidates)	Johnson & Johnson	1 year to market	Preclinical
9	Modified nasal spray influenza vaccine (with surface antigen of coronavirus) prevents both influenza and corona virus	University of Hong Kong	Months for animal testing, At least 1 year for clinical trials on humans	Preclinical; vaccine developed
10	Modified Vaccina Ankara—Virus Like Particles (MVA-VLP) vaccine platform	GeoVax—BravoVax	Not available	Preclinical
11	Highly purified recombinant 2019-nCoV S protein subunit-trimer vaccine (S-Trimer), produced using Trimer-Tag® technology	Clover Biopharmaceuticals	Not available	Preclinical

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S. No.	Technology	Company	Estimated Timeline	Stage/Funding
12	mRNA technology	CureVac	Not available	Preclinical
13	Not available	University of Saskatchewan (VIDO-InterVac)	Target for animal testing in 6-8 weeks, human trials in at least a year	Preclinical

33

Glycoprotein analysis between SARS, MERS & COVID 19

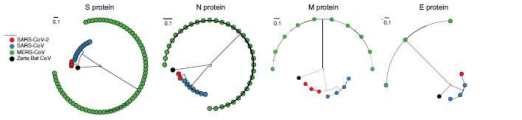
viruses MDPI

Article

Preliminary Identification of Potential Vaccine Targets for the COVID-19 Coronavirus (SARS-CoV-2) Based on SARS-CoV Immunological Studies

Percentage sequence identity with SARS-CoV-2

	S protein	N protein	M protein	E protein
SARS-CoV	76.0%	90.6%	90.1%	94.7%
MERS-CoV	29.4%	45.9%	39.2%	34.1%



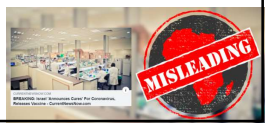
- B cell and T cell epitopes of SARS and COVID 19 screened, spike (S) and nucleocapsid (N) proteins map identically was identified.
- No mutation was observed in these **120 identified epitopes.**
- These epitopes can be used for development of vaccine (Ahmed et al., 2020)

34

IB vaccine for COVID 19 ?

Israeli scientists 'close' to developing Covid-19 vaccine, but no announcement or release yet

- There is no clear claim that IB vaccine under development in Israel – can be used for COVID 19
- COVID 19 & IBV – belong to beta and gamma coronavirus respectively
- Phylogenetic analysis- S1 gene- IBV and COVID 19 – different cluster
- Similarly - receptor for COVID 19 is ACE 2 while IBV is sialic acid



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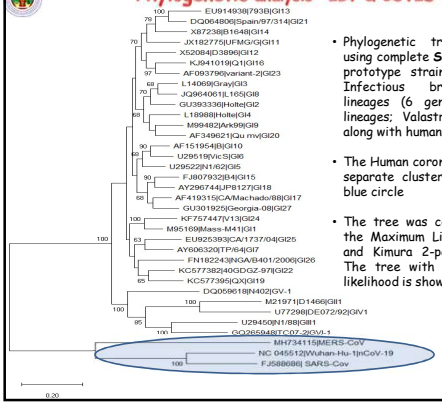
Phylogenetic analysis- IBV & COVID 19



- Phylogenetic tree constructed using complete **S1 gene** of all the prototype strains of worldwide Infectious bronchitis virus lineages (6 genotypes and 32 lineages; Valastro et al., 2016) along with human coronaviruses .
- The Human coronaviruses forms a separate cluster indicated by a blue circle
- The tree was constructed using the Maximum Likelihood method and Kimura 2-parameter model. The tree with the highest log likelihood is shown.

36

Challenges in vaccine development

- Vaccine development is still far from being a perfect science
- HIV vaccine - HVTN702 discontinued recently - big gap between science and vaccine after almost four decades' effort
- Traditional vaccine technologies are empirical and need improvement
- Political or commercial barriers
- Funding for production at an unprecedented scale, the pricing and supply chain and the coordinated administration of such a vaccine

37

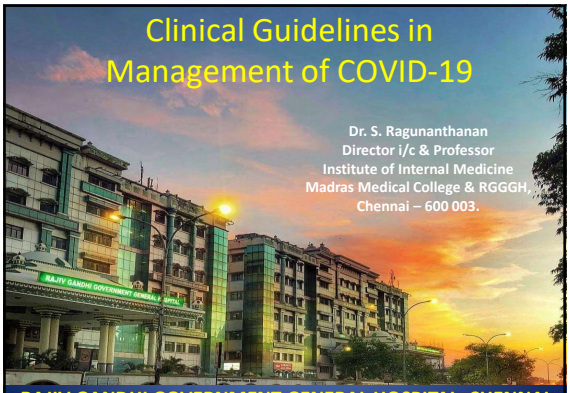
COVID 19 vaccine- the way forward

- Within 17 years- 3 major CoV outbreaks
- **The race is on to develop a vaccine**
- But time required for regulatory compliance to ensure that a vaccine is both safe and effective, means this won't happen overnight
- Use of existing platforms could reduce this time
- The **novel types of vaccines being investigated could serve us well for future outbreaks of other novel diseases.**
- Introduction of innovative vaccine technologies that are radically different from traditional approaches, **ushering in a new era in the way we fight infectious disease.**

38

Clinical Guidelines in Management of COVID-19

Dr. S. Ragunanthanan
Director i/c & Professor
Institute of Internal Medicine
Madras Medical College & RGGGH,
Chennai – 600 003.



RAJIV GANDHI GOVERNMENT GENERAL HOSPITAL, CHENNAI

1

Outline of my talk

1. Triage: recognize and sort patients with SARI
2. Immediate implementation of appropriate infection prevention and control (IPC) measures
3. Early supportive therapy and monitoring
4. Collection of specimens for laboratory diagnosis
5. Management of hypoxemic respiratory failure and acute respiratory distress syndrome (ARDS)
6. Management of septic shock
7. Prevention of complications
8. Anti-nCoV treatments

2

Triage: early recognition of patients with SARI associated with COVID-19 infection

- **Triage:** Recognize and sort all patients with SARI at first point of contact with health care system (such as the emergency department). Consider COVID-19 as a possible etiology of SARI under certain conditions. Triage patients and start emergency treatments based on disease severity.

3

Guidelines from Ministry of Health & Family Welfare, Government of India

- SOP for Categorization of Passengers for COVID 19 coming from China, Democratic Republic of Korea, France, Germany, Spain, Italy, Iran for Airport Screening
- **Categorisation for passengers coming from at Health Counters**
- **Categorise the passengers into A, B, C**

4

Category A (High Risk)

A passenger with
- Fever,
- Cough,
- Shortness of breath with a
- History of travel to or
- Residence in a country/area or territory

reporting local transmission of COVID-19 disease during the 14 days prior to Symptom onset **OR**

A patient with any acute respiratory illness **AND**

Having been in contact with a COVID19 case in the last 14 days prior to onset of symptoms;

- **Action:** - Segregated from other passengers and sent for Isolation

5

Category B (Moderate Risk)

- A asymptomatic passenger coming from China, Democratic Republic of Korea, France Germany, Spain, Italy, Iran and are elderly (above 60 years), Hypertensive, Diabetic, Asthmatic
- **Action:** - To be shifted by State Government to a dedicated quarantine facility and monitored daily by State Government for next 14 days. In case, they develop symptoms, they should be isolated.

6

Category C (Low Risk)

- A asymptomatic passenger coming from any COVID 19 affected country including passengers coming from China, Democratic Republic of Korea, France Germany, Spain, Italy, Iran.
- **Action:** - Kept under Home Quarantine and will be monitored by IDSP network for 14 days, if they develop Fever/ Cough/ Difficulty in breathing within 14 days after return from any COVID 19 affected countries should immediately call at National helpline (011-23978046) for further management.

7

Triage in Out Patient

- Give the patient a three layer mask
- Maintain one metre distance
- Detailed history including travel history, transit destinations, date of arrival, onset of symptoms, comorbid illness, travel after arrival, whether he / she had symptoms before the start of travel.
- Clinical examination
- Basic investigation if necessary
- Symptomatic treatment
- Counseling – hand wash, cough hygiene, quarantine and
- Call if any symptoms develop.

8

Definitions of patients with SARI, suspected of 2019-nCoV infection*

- An ARI with history of fever or measured temperature ≥38 C° and cough; onset within the last ~10 days; and requiring hospitalization. However, the absence of fever does NOT exclude viral infection.

9

Surveillance case definitions for 2019-nCoV*

A. Patients with severe acute respiratory infection (fever, cough, and requiring admission to hospital), AND with no other etiology that fully explains the clinical presentation AND at least one of the following:

• A history of travel to or residence in the city of Wuhan, Hubei Province, China in the 14 days prior to symptom onset,

or

• Patient is a health care worker who has been working in an environment where severe acute respiratory infections of unknown etiology are being cared for.

10

Surveillance case definitions for 2019-nCoV*

B. Patients with any acute respiratory illness AND at least one of the following:

• Close contact with a confirmed or probable case of 2019-nCoV in the 14 days prior to illness onset,

or

• Visiting or working in a live animal market in Wuhan, Hubei Province, China in the 14 days prior to symptom onset,

or

• Worked or attended a health care facility in the 14 days prior to onset of symptoms where patients with hospital-associated 2019-nCov infections have been reported.

11

Clinical syndromes associated with 2019-nCoV infection

Uncomplicated illness:

- Patients with uncomplicated upper respiratory tract viral infection, may have non-specific symptoms such as
  - ✓ Fever
  - ✓ Cough
  - ✓ Sore throat
  - ✓ Nasal congestion
  - ✓ Malaise
  - ✓ Headache
  - ✓ Muscle pain or
  - ✓ Malaise.
- The elderly and immuno-suppressed may present with atypical symptoms.
- These patients do not have any signs of dehydration, sepsis or shortness of breath.

12

Clinical syndromes associated with 2019-nCoV infection

- **Mild pneumonia:** Patient with pneumonia and no signs of severe pneumonia.
- **Severe pneumonia:** Adolescent or adult: fever or suspected respiratory infection, plus one of respiratory rate >30 breaths/min, severe respiratory distress, or SpO2 <90% on room air.

13

Clinical syndromes associated with 2019-nCoV infection

Acute Respiratory Distress Syndrome:

- Onset: new or worsening respiratory symptoms within one week of known clinical insult.
- Chest imaging (radiograph, CT scan, or lung ultrasound): bilateral opacities, not fully explained by effusions, lobar or lung collapse, or nodules.
- Origin of oedema: respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (e.g. echocardiography) to exclude hydrostatic cause of oedema if no risk factor present.

14

Clinical syndromes associated with 2019-nCoV infection

Sepsis:

- **Adults:** life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection, with organ dysfunction*.
- Signs of organ dysfunction include:
  - ✓ Altered mental status,
  - ✓ Difficult or fast breathing,
  - ✓ Low oxygen saturation,
  - ✓ Reduced urine output,
  - ✓ Fast heart rate,
  - ✓ Weak pulse,
  - ✓ Cold extremities or low blood pressure,
  - ✓ Skin mottling, or laboratory evidence of coagulopathy,
  - ✓ Thrombocytopenia,
  - ✓ Acidosis,
  - ✓ High lactate or hyperbilirubinemia.

15

Clinical syndromes associated with 2019-nCoV infection

Septic shock:

- **Adults:** persisting hypotension despite volume resuscitation, requiring vasopressors to maintain MAP ≥65 mmHg and serum lactate level >2 mmol/L.

16

Immediate implementation of appropriate IPC measures in the Isolation Ward

Apply droplet precautions:

- Droplet precautions prevent large droplet transmission of respiratory viruses.
- Use a medical mask if working within 1-2 metres of the patient.
- Place patients in single rooms, or group together those with the same etiological diagnosis.
- If an etiological diagnosis is not possible, group patients with similar clinical diagnosis and based on epidemiological risk factors, with a spatial separation.

Contd..

17

Immediate implementation of appropriate IPC measures in the Isolation Ward

Apply droplet precautions:

- If an etiological diagnosis is not possible, group patients with similar clinical diagnosis and based on epidemiological risk factors, with a spatial separation.
- When providing care in close contact with a patient with respiratory symptoms (e.g. coughing or sneezing), use eye protection (face-mask or goggles), because sprays of secretions may occur.
- Limit patient movement within the institution and ensure that patients wear medical masks when outside their rooms.

Contd..

18

Immediate implementation of appropriate IPC measures in the Isolation Ward

Apply droplet precautions:

- Droplet and contact precautions prevent direct or indirect transmission from contact with contaminated surfaces or equipment (i.e. contact with contaminated oxygen tubing/interfaces).
- Use PPE (medical mask, eye protection, gloves and gown) when entering room and remove PPE when leaving.
- If possible, use either disposable or dedicated equipment (e.g. stethoscopes, blood pressure cuffs and thermometers).

19

Immediate implementation of appropriate IPC measures in the Isolation Ward

Apply contact precautions:

- If equipment needs to be shared among patients, clean and disinfect between each patient use.
- Ensure that health care workers refrain from touching their eyes, nose, and mouth with potentially contaminated gloved or ungloved hands.
- Avoid contaminating environmental surfaces that are not directly related to patient care (e.g. door handles and light switches).
- Ensure adequate room ventilation.
- Avoid movement of patients or transport. Perform hand hygiene.

20

Immediate implementation of appropriate IPC measures

Apply airborne precautions when performing an aerosol generating procedure:

- Ensure that healthcare workers performing aerosol-generating procedures
  - open suctioning of respiratory tract,
  - intubation,
  - bronchoscopy,
  - cardiopulmonary resuscitation
- Use PPE, including gloves, long-sleeved gowns, eye protection, and fit-tested particulate respirators (N95 or equivalent, or higher level of protection). (The scheduled fit test should not be confused with user seal check before each use.)

21

Immediate implementation of appropriate IPC measures

Apply airborne precautions when performing an aerosol generating procedure:

- Whenever possible, use adequately ventilated single rooms when performing aerosol-generating procedures, meaning negative pressure rooms with minimum of 12 air changes per hour or at least 160 litres/second/patient in facilities with natural ventilation.
- Avoid the presence of unnecessary individuals in the room.
- Care for the patient in the same type of room after mechanical ventilation commences.

22

Early supportive therapy and monitoring

- Give supplemental oxygen therapy **immediately to patients with SARI and respiratory distress, hypoxaemia, or shock.**
- **Use conservative fluid management in patients with SARI when there is no evidence of shock.**
- **Give empiric antimicrobials to treat all likely pathogens causing SARI. Give antimicrobials within one hour of initial patient assessment for patients with sepsis.**

23

Early supportive therapy and monitoring

- **Do not routinely give systemic corticosteroids for treatment of viral pneumonia or ARDS outside of clinical trials unless they are indicated for another reason**
- **Closely monitor patients with SARI for signs of clinical deterioration, such as rapidly progressive respiratory failure and sepsis, and apply supportive care interventions immediately.**
- **Understand the patient's co-morbid condition(s) to tailor the management of critical illness and appreciate the prognosis. Communicate early with patient and family.**

24

Collection of specimens for laboratory diagnosis

- Collect blood cultures for bacteria that cause pneumonia and sepsis, ideally before antimicrobial therapy. DO NOT delay antimicrobial therapy to collect blood cultures.
- Collect specimens from BOTH the upper respiratory tract (URT; nasopharyngeal and oropharyngeal) AND lower respiratory tract (LRT; expectorated sputum, endotracheal aspirate, or bronchoalveolar lavage) for 2019-nCoV testing by RT-PCR.
- Clinicians may elect to collect only LRT samples when these are readily available (for example, in mechanically ventilated patients).

25

Management of hypoxemic respiratory failure and ARDS

- Recognize severe hypoxemic respiratory failure when a patient with respiratory distress is failing standard oxygen therapy.
- High-flow nasal oxygen (HFNO) or non-invasive ventilation (NIV) should only be used in selected patients with hypoxemic respiratory failure.
- The risk of treatment failure is high in patients with MERS treated with NIV, and patients treated with either HFNO or NIV should be closely monitored for clinical deterioration.
- Endotracheal intubation should be performed by a trained and experienced provider using airborne precautions

26

Management of hypoxemic respiratory failure and ARDS

- Implement mechanical ventilation using lower tidal volumes (4–8 ml/kg predicted body weight, PBW) and lower inspiratory pressures (plateau pressure <30 cmH2O).
- In patients with severe ARDS, prone ventilation for >12 hours per day is recommended.
- Use a conservative fluid management strategy for ARDS patients without tissue hypoperfusion.
- In patients with moderate or severe ARDS, higher PEEP instead of lower PEEP is suggested.

27

Management of hypoxemic respiratory failure and ARDS

- In patients with moderate-severe ARDS (PaO2/FiO2 <150), neuromuscular blockade by continuous infusion should not be routinely used.
- In settings with access to expertise in extracorporeal life support (ECLS), consider referral of patients with refractory hypoxemia despite lung protective ventilation.
- Avoid disconnecting the patient from the ventilator, which results in loss of PEEP and atelectasis.
- Use in-line catheters for airway suctioning and clamp endotracheal tube when disconnection is required (for example, transfer to a transport ventilator).

28

Prevention of complications

Reduce days of invasive mechanical ventilation

- Use weaning protocols that include daily assessment for readiness to breathe spontaneously
- Minimize continuous or intermittent sedation, targeting specific titration endpoints (light sedation unless contraindicated) or with daily interruption of continuous sedative infusions

Reduce incidence of ventilator-associated pneumonia

- Oral intubation is preferable to nasal intubation in adolescents and adults
- Keep patient in semi-recumbent position (head of bed elevation 30-45º)
- Use a closed suctioning system; periodically drain and discard condensate in tubing
- Use a new ventilator circuit for each patient; once patient is ventilated, change circuit if it is soiled or damaged but not routinely
- Change heat moisture exchanger when it malfunctions, when soiled, or every 5–7 days

29

Prevention of complications

Reduce incidence of venous thrombo embolism

- Use pharmacological prophylaxis (low molecular-weight heparin [preferred if available] or heparin 5000 units subcutaneously twice daily) in adolescents and adults without contraindications. For those with contraindications, use mechanical prophylaxis (intermittent pneumatic compression devices).

Reduce incidence of catheter-related bloodstream infection

- Use a checklist with completion verified by a real-time observer as reminder of each step needed for sterile insertion and as a daily reminder to remove catheter if no longer needed

30

Prevention of complications

Reduce incidence of pressure ulcers
- Turn patient every two hours

Reduce incidence of stress ulcers and gastrointestinal bleeding
- Give early enteral nutrition (within 24–48 hours of admission)
- Administer histamine-2 receptor blockers or proton-pump inhibitors in patients with risk factors for GI bleeding. Risk factors for gastrointestinal bleeding include mechanical ventilation for ≥48 hours, coagulopathy, renal replacement therapy, liver disease, multiple comorbidities, and higher organ failure score

Reduce incidence of ICU-related weakness
- Actively mobilize the patient early in the course of illness when safe to do so

31

Specific anti-Novel-CoV treatments and clinical research

- There is no current evidence from RCTs to recommend any specific anti-nCoV treatment.
- Clinical characterization protocols are available, at the WHO 2019 nCoV website: https://www.who.int/emergencies/diseases/novel-coronavirus-2019. WHO has established Global 2019-nCoV Clinical Data Platform, for member countries to contribute. Contact EDCARN@who.int for additional questions.

32

Medication tried so far

- Tab. Remdesivir
- Tab. Lopinavir / Ritonavir
- Tab. Baricitinib – Janus Kinase Inhibitor
- Tab. Nelfinavir – Protease Inhibitor – 2BD
- Tab. Fapilavir
- Tab. Tamilflu
- Inj. IV IG
- Inj. Methylpredisolone

33

Lopinavir / Ritonavir combination therapy among symptomatic COVID-19

- 200 mg/50mg – 2 tablets every 12 hours for 14 days or for 7 days after becoming asymptomatic whichever is earlier.
- Side effects:
  - Acute pancreatitis
  - Elevation of ALT
  - Anaphylaxis

34

Thank You

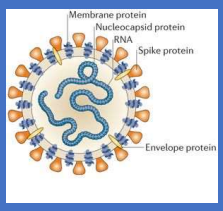
35

Principles of Testing
&
Who needs to be tested for COVID-19

1

SARS CoV-2

Morphology



Family: Coronaviridae
Genera: Betacoronavirus

- There are seven coronaviruses known to cause disease in humans
- Four of them are human coronaviruses, (229E, NL63, HKU1 and OC43) the rest three are zoonotic in origin, meaning they are acquired from animals
- When humans come in close contact with infected animals, they get the infection
- Recent novel coronavirus named COVID-19 was identified in Dec 2019 after clusters of patients with pneumonia of unknown cause were linked to a seafood and wet animal market in Wuhan, China
- It is closely related to coronavirus that circulates in bats
- Person-to-person spread occurs mainly via droplets spread in the air during coughing and sneezing

2

Case definitions – Laboratory confirmed case

- A person with **laboratory confirmation** of COVID-19 infection, irrespective of clinical signs and symptoms.

3

Case definitions – Suspect case

- A patient with **acute respiratory illness** {fever & at least one sign/symptom of respiratory disease (e.g., cough, shortness of breath)}, **AND** a **history of travel** to or residence in a country/area or territory reporting local transmission of COVID-19 disease during the 14 days prior to symptom onset;

OR

- A patient/Health care worker with **any acute respiratory illness AND** having been in ***contact*** **with a confirmed** COVID-19 case in the last 14 days prior to onset of symptoms;

OR

- A patient with **severe acute respiratory infection** {fever and at least one sign/symptom of respiratory disease (e.g., cough, shortness breath)} **AND requiring hospitalization AND** with **no other etiology** that fully explains the clinical presentation;

4

Definition of Contact

A contact is a person that is involved in any of the following:

- Providing direct care without proper personal protective equipment (PPE) for COVID-19 patients
- **Staying in the same** close environment of a COVID-19 patient (including **workplace, classroom, household, gatherings**).
- Traveling together in **close proximity** (1 m) with a **symptomatic person** who later tested **positive** for COVID-19.

5

Types of contacts

High Risk

- Touched body fluids of the patient (Respiratory tract secretions, blood, vomit, saliva, urine, faeces)
- Had direct physical contact with the body of the patient including physical examination without PPE.
- Touched or cleaned the linens, clothes, or dishes of the patient.
- Lives in the same household as the patient.
- Anyone in close proximity (within 3 ft) of the confirmed case without precautions.
- Passenger in close proximity (within 3 ft) of a conveyance with a symptomatic person who later tested positive for COVID-19 for more than 6 hours.

Low Risk

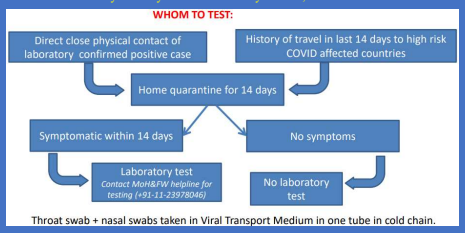
- Shared the same space (Same class for school/worked in same room/similar and not having a high risk exposure to confirmed or suspect case of COVID-19).
- Travelled in same environment (bus/train/flight/any mode of transit) but not having a high-risk exposure.

6

Identification of case for sample collection

COVID-19 Testing Criteria

Issued by Ministry of Health & Family Welfare, Govt of India



Throat swab + nasal swabs taken in Viral Transport Medium in one tube in cold chain.

- There is currently no community transmission of COVID19.
- Disease is primarily reported in individuals with travel history to the affected countries or close contacts of positive cases.
- Therefore all individuals need not be tested

7

Samples to be collected

- Essential samples:
  - Throat swab (oropharyngeal swab).
  - Nasal swab (Nasopharyngeal swab)
- Other preferred samples:
  - Bronchoalveolar lavage
  - Tracheal aspirate — Wide mouth sterile plastic containers
  - Sputum
- In lab confirmed patients:
  - Blood
  - Stool and urine - Wide mouth sterile plastic containers

8

PERSONAL PROTECTIVE EQUIPMENT

Table 1. Recommended type of personal protective equipment (PPE) to be used in the context of COVID-19 disease, according to the setting, personnel and type of activity*

Setting	Target personnel or patients	Activity	Type of PPE or procedure
Healthcare facilities			
Inpatient facilities			
Patient room	Healthcare workers	Providing direct care to COVID-19 patients.	Medical mask Gown Gloves Eye protection (goggles or face shield).
		Aerosol-generating procedures performed on COVID-19 patients.	Respirator N95 or FFP2 standard, or equivalent. Gown Gloves Eye protection Apron
	Cleaners	Entering the room of COVID-19 patients.	Medical mask Gown Heavy duty gloves Eye protection (if risk of splash from organic material or chemicals). Boots or closed work shoes
	Visitors[b]	Entering the room of a COVID-19 patient	Medical mask Gown Gloves
Other areas of patient transit (e.g., wards, corridors).	All staff, including healthcare workers.	Any activity that does not involve contact with COVID-19 patients.	No PPE required

WHO interim guidance document for Rational use of personal protective equipment for coronavirus disease 2019 (COVID-19)

9

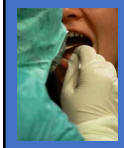
Collection of OP and NP swabs

- Optimal timing:

- Within 3 days of symptom onset and no later than 7 days.
- Preferably prior to initiation of antimicrobial chemoprophylaxis or therapy.

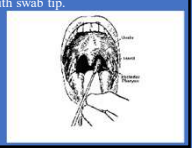
10

Collection of Oropharyngeal swab



Materials:
- Sterile Dacron/Nylon flocked swab
- Viral Transport Medium (3 ml sterile VTM)

Procedure:
- Hold the tongue out of the way with a tongue depressor.
- Use a sweeping motion to swab posterior pharyngeal wall and tonsillar pillars
- Have the subject say "aahh" to elevate the uvula.
- Avoid swabbing soft palate and do not touch the tongue with swab tip.
- Put the swab in VTM



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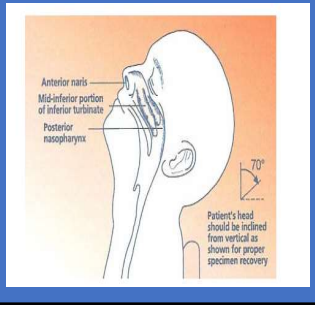
Collection of Nasopharyngeal swabs

- Materials
  - Sterile Dacron/Nylon flocked swab
  - Viral Transport Medium (3 ml sterile VTM)
- Procedure
  - Tilt patient's head back 70 degrees
  - Insert swab into nostril (Swab should reach depth to distance from nostrils to outer opening of the ear
  - Leave swab in place in place for several seconds to absorb secretions
  - Slowly remove swab while rotating it
  - Place tip of swab into VTM and snap/cut off the applicator stick



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Blood collection from positive cases

- Blood sample collection from all positive cases
- Plasma sample collection in EDTA vials
- Resin separator tubes for serum sample collection

13

Guidance for Specimen Collection

- Consider all specimens as POTENTIALLY HAZARDOUS / INFECTIOUS.
- Handle all specimens with gloves in a secure manner.
- Place each specimen into a separate container labeled with the patient's name and identification number, the collection site, the date of collection and the time of the collection.
- Do not contaminate the outside of the specimen container.
- Do not handle laboratory requisition forms with gloves.
- A BSL2 containment level is required to handle suspected samples.

14

Storage of Specimen

- Keep refrigerated (2-8 °C) if it is to be processed (or sent to a reference laboratory) within 48 hours.
- Keep frozen (-10 to -20 °C) if it is to be processed after the first 48 hours or within 7 days.
- Keep frozen (-70 °C) if it is to be processed after a week. The sample can be preserved for extended periods.

15

Classification of Infectious Substances

- Category A: An infectious substance which is transported in a form that, when exposure to it occurs, is capable of causing permanent disability, life-threatening or fatal disease in otherwise healthy humans or animals.
  - UN 2814 for Infectious substances which cause disease in humans or both in humans and animals.
  - UN 2900 for Infectious substances which cause disease only in animals

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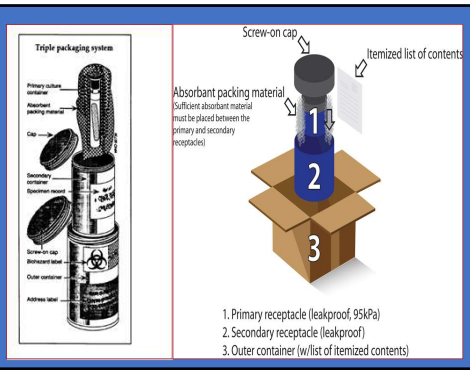
Classification of Infectious Substances

- **Category B:** ***An infectious substance which does not meet the criteria for inclusion in Category A.***
  - **Infectious substances in Category B shall be assigned to UN 3373**

SARS-CoV-2 virus infectious/potentially infectious material falls under category B

17



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Transport Precautions

- Adequate cushioning materials inside the box to absorb shocks during transport
- Do not stick the request form on the specimen
- Specimen request forms should be put into a separate plastic bag
- The outer container, secondary containers and specimen racks for transport should be thoroughly cleansed and disinfected periodically (i.e. at least daily) and when contaminated.

19

Labeling of Package

- Sender's, name, address and telephone number
- Whom to contact in case of emergency with telephone number
- Receiver's name, address and telephone number
- Proper shipping name (e.g. "BIOLOGICAL SUBSTANCE, CATEGORY B")
- UN number e.g. 3373
- Temperature storage requirements
- Quantity of dry ice inside the container
- Arrow mark to indicate upright direction

20

Responsibility of Sender

- Make advance arrangements with the carrier and recipient
- Prepare necessary documentation, including permits, dispatch and shipping documents
- Notify the receiver in advance of transportation arrangements and expected date of delivery of shipment

Sequel Courier & World Courier

21

Responsibility of Receiver

- Acknowledge receipt of specimen
- Verify the integrity of packaging
- Box to be opened by personnel wearing adequate PPE in BSL cabinet
- Check the specimens with the data sent
- Apply acceptance and rejection criteria

22

Types of Tests

- No validated serological tests
- Only molecular diagnosis
  - PCR based test aims at detection of the virus.
- Real time PCR platform is required.

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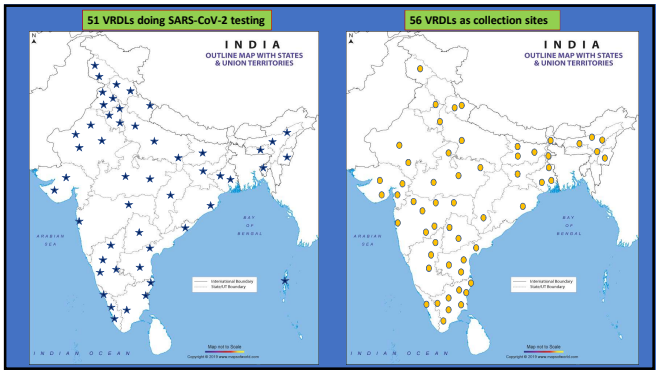

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Tests for SARS-CoV-2

- No validated serological tests are available.
- Only Molecular tests available.
- Laboratory protocols designed on the basis of WHO guidance and sequences available in GISAID.
- First line screening assay: E gene.
- Confirmatory assays: RdRp and ORF 1b.
- SoPs and testing protocol shared with all testing laboratories.

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Viral Transmission

General Principles

- Healthcare environment contains a diverse population of microorganisms, but only few are significant pathogens
- Contaminated surfaces with microbes can serve as reservoirs of potential pathogens
- Contaminated surfaces not directly associated with transmission but is mostly via hand contact with the surface
- Hand hygiene is important to minimize the impact of this transfer

Air borne infection
Aerosol < 5um
Droplet > 5um

Aerosol is responsible for 20% spread
Droplets for 80 % spread

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Contd…

- COVID-19 virus can potentially survive in the environment for several hours/days
- Premises and areas potentially contaminated with the virus to be cleaned before their re-use

Remove the majority of bio burden, and Disinfect equipment and surfaces

- **Virus can survive on porous surface for up to 12 to 24 hours if the temperature of the environment is conducive**
- **Virus can survive up to 24- 48 hours on non porous metallic surfaces**

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Commonly used disinfectants

- Lysol (50% cresol and 50% liquid soap)

Hospitals/ clinic / ambulances - 5% lysol
In public places 2.5% Lysol
1% household and clean places

Sodium hypochlorite 1%

In spills 5%
Freshly prepared sodium hypochlorite is preferred

28

Spill management

- Worker assigned to clean the spill should wear gloves and other personal protective equipment
- Most of the organic matter of the spill to be removed with absorbent material
- Surface to be cleaned to remove residual organic matter
- Use disinfectant: hypochlorite
  - 1% for small spills
  - 5% for large spills

29

Respiratory hygiene/Cough etiquette

- All persons with signs and symptoms of a respiratory infection (regardless of presumed cause) must follow respiratory hygiene/cough etiquette
  - Cover the nose/mouth when coughing or sneezing
  - Use tissues to contain respiratory secretions
  - Dispose of tissues in the nearest waste receptacle after use
  - Perform hand hygiene after contact with respiratory secretions and contaminated objects/materials

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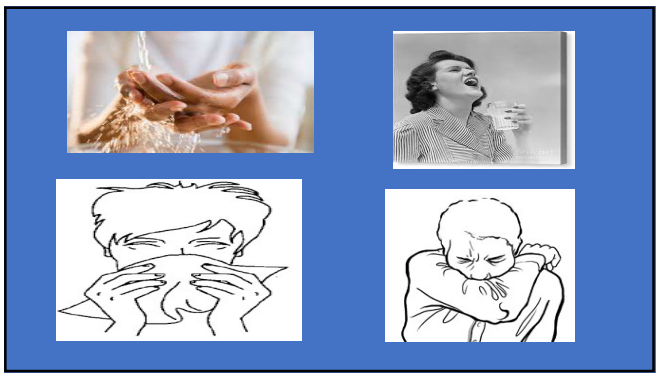

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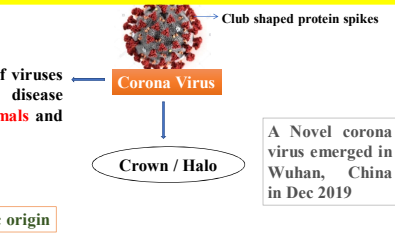
COVID 19 Epidemiology

Dr. G. Srinivas, MD
Department of Epidemiology
The Tamil Nadu Dr.MGR Medical University

1

The virus is new & highly contagious- long incubation period

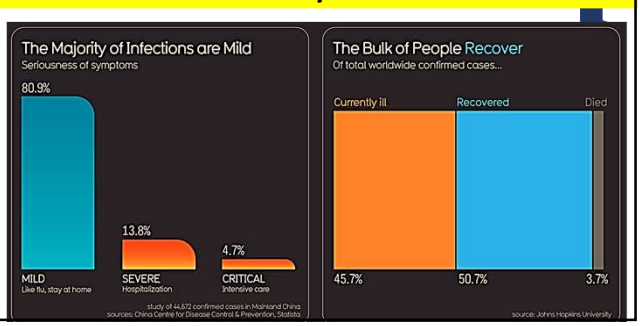


Virus : Severe Acute Respiratory Syndrome Coronavirus 2 - (SARS-CoV-2)

Disease: Coronavirus Disease - (COVID-19).....

2

Natural History of COVID 19



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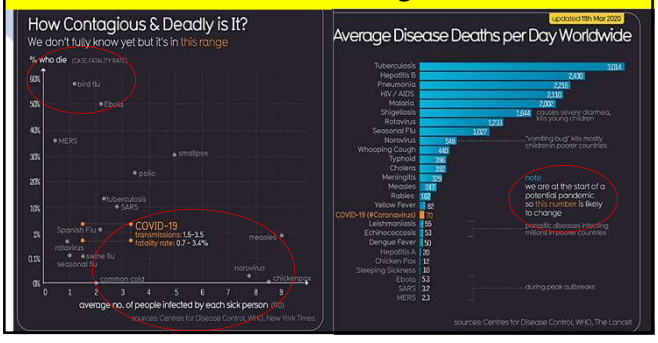
How Contagious is the Virus?

- Microbes can be highly contagious like measles to others if they are not immune.
- They can also be not very contagious, like rabies, which rarely spreads from one person to another.
- Sometimes organisms spread to just a few people, particularly close contacts such as family caregivers, and then stop.

4

Transmission & Killing Power ?



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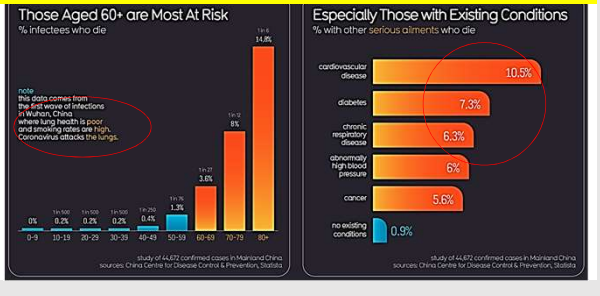
Risk Factors...



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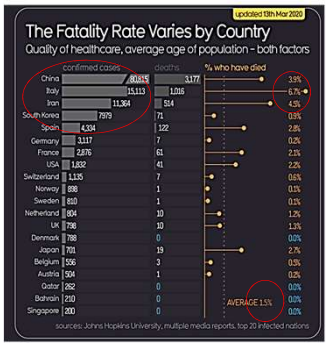
COVID 19 Burden

Top three countries:
- *China*
- *Italy*
- *Iran*



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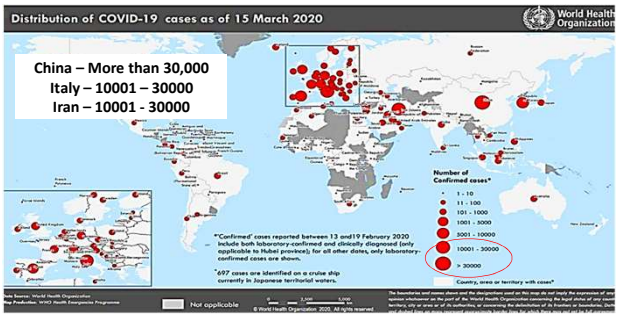

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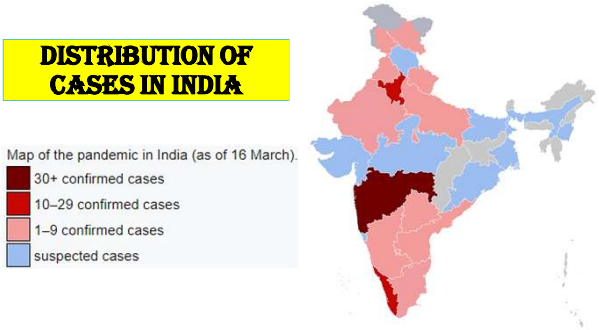
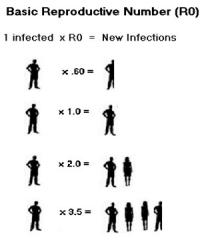
DISTRIBUTION OF CASES IN INDIA



9

Basic Reproductive Rate of an Infection
(& SIR or Kermack McKendrick model)

- BRR of an infection can be thought of as the number of cases one case generates on average over the course of its infectious period, in an otherwise uninfected population.
- Helps to determine whether or not an infectious disease can spread through a population.
- First modern application in epidemiology was by George MacDonald in 1952, who constructed population models of the spread of Malaria.



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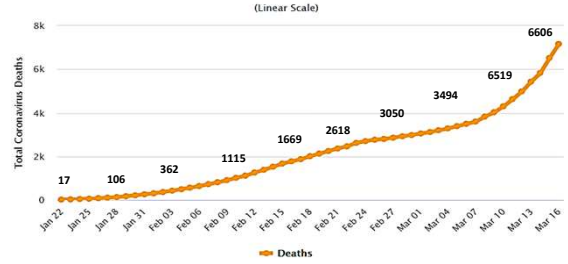
Exponential curve



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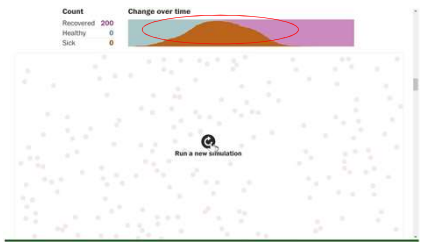
No Social Distancing (Free-for-all)



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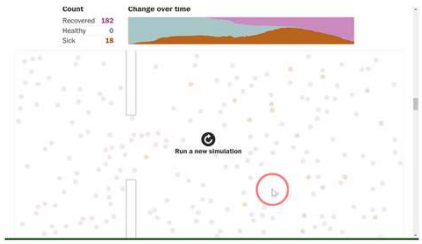
Attempted Quarantine



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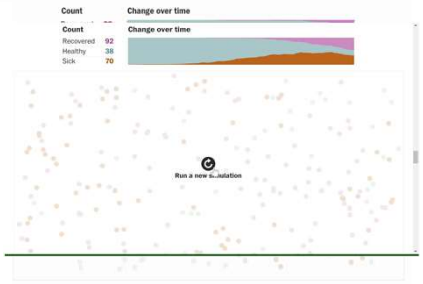
Moderate Social Distancing



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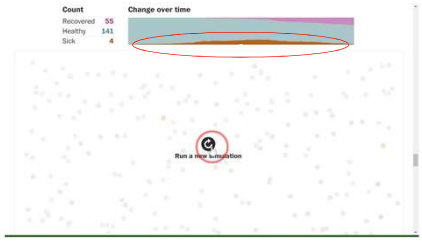
Extensive Social Distancing



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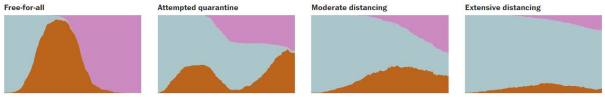

16

Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts

Joel Hellewell, PhD, Sam Abbott, PhD, Amy Gimma, MSc, Nikos I Bosse, BSc, Christopher I Jarvis, PhD, Timothy W Russell, PhD, James D Munday, MSc, Adam J Kucharski, PhD, Prof W John Edmunds, PhD Fiona Sun, Stefan Flasche, Billy J Quilty, Nicholas Davies, Yang Liu, Samuel Clifford, Petra Klepac, Mark Jit, Charlie Diamond, Hamish Gibbs, Kevin van Zandvoort, Sebastian Funk, PhD, Rosalind M Eggo, PhD Joel Hellewell, PhD, Sam Abbott, PhD, Amy Gimma, MSc, Nikos I Bosse, BSc, Christopher I Jarvis, PhD, Timothy W Russell, PhD, James D Munday, MSc, Adam J Kucharski, PhD, Prof W John Edmunds, PhD Fiona Sun, Stefan Flasche, Billy J Quilty, Nicholas Davies, Yang Liu, Samuel Clifford, Petra Klepac, Mark Jit, Charlie Diamond, Hamish Gibbs, Kevin van Zandvoort, Sebastian Funk, PhD, Rosalind M Eggo, PhD

The Lancet Global Health

DOI: 10.1016/S2214-109X(20)30074-7

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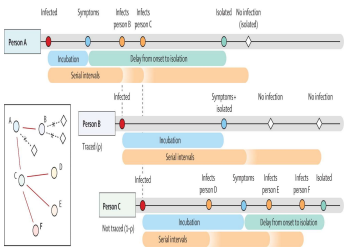

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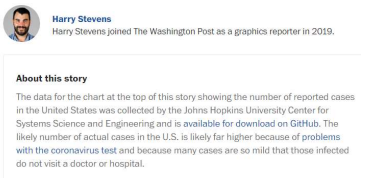
Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts

- outbreaks starting with five initial cases, an R_0 of 1·5, and 0% transmission before symptom onset could be controlled even with low contact tracing probability;
- however, the probability of controlling an outbreak decreased with the number of initial cases, when R_0 was 2·5
- To control the majority of outbreaks, for R_0 of 2·5 more than 70% of contacts had to be traced
- In most scenarios, highly effective contact tracing and case isolation is enough to control a new outbreak of COVID-19 within 3 months.
- The probability of control decreases with long delays from symptom onset to isolation, fewer cases ascertained by contact tracing, and increasing transmission before symptoms.

19



Harry Stevens
Harry Stevens joined The Washington Post as a graphics reporter in 2019.

About this story

The data for the chart at the top of this story showing the number of reported cases in the United States was collected by the Johns Hopkins University Center for Systems Science and Engineering and is available for download on GitHub. The likely number of actual cases in the U.S. is likely far higher because of problems with the coronavirus test and because many cases are so mild that those infected do not visit a doctor or hospital.

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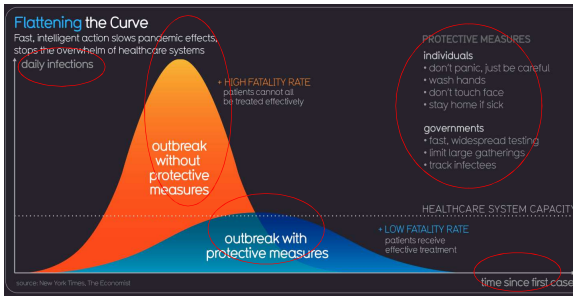

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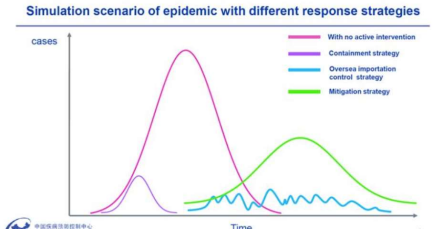

Tom Frieden · 2nd
President & CEO Resolve to Save Lives | Sr Fellow Global Health CFR | Physician, public health | Focused on saving lives

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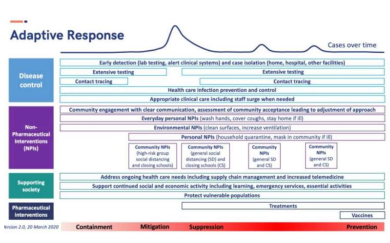

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Thank you

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