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COVID-19 IS RIGOROUS

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Abstract: *Coronavirus is single RNA virus . Innovative coronavirus (nCoV) spill out out event, with its epicenter in Wuhan, People's Republic of China, has appear as a public healthiness disaster of international concern. In this article are mainly discuss in structure of corona virus then classification life cycle, pathogenesis ,sign and symptom, transmission, death rate .In this article are mainly focus life cycle and transmission . Coronavirus disease 2019 (COVID-19) is an communicable disease caused by rigorous acute respiratory disorder coronavirus 2 (SARS-CoV-2). The foremost coronavirus of human origin, B814, was described in 1965 and since that time only 31 additional strains have been improved. Ten of these were originally improved in human sprouting tracheal organ cultures only, and the remains in monolayer cell cultures*

Keywords: *Structure, life-cycle , Classification, Pathogenesis, Transmission.*

I INTRODUCTION

Human coronaviruses were primary exposed in the behind 1960s. The initial ones exposed were an communicable bronchitis disease in chickens and two in human being patients with the common wintry (later named human coronavirus 229E and human coronavirus OC43). Other members of this family have since been recognized as well as SARS-Cove in 2003, HCoV NL63 in 2004, HKU1 in 2005, MERS-CoV in 2012 and SARS-CoV-2 previously known as 2019-nCoV) in 2019. The majority of these have drawn in severe respiratory area infections in excess of the previous not many decades, the globe has seen the survival of new viruses that posed grave intimidation to worldwide strength. In behind December 2019, more than a few patients in Wuhan, China in progress exposure symptoms that similar to pneumonia. A new virus was well-known and originally called the 2019 original coronavirus (2019-nCoV). The World Health Organization (WHO) ultimately distorted the name of the disease to rigorous sensitive respiratory disease coronavirus 2 (SARS-CoV-2) . The disease it causes has been named coronavirus disease 2019 (COVID-19). The SARS-CoV is a positive-stranded RNA virus that derives from the Coronaviridae family. Extra viruses from the identical family contain the rigorous sensitive respiratory disease coronavirus (SARS-CoV), which seems in 2002, and Middle East respiratory syndrome coronavirus (MERS-CoV), which was

described in 2012. Since the virus is dispersal worldwide, on March 11, 2020, the WHO authoritatively reported the COVID-19 eruption as a pandemic. Coronavirus (2019-nCoV) or the rigorous sensitive respiratory syndrome coronavirus 2 (SARS-CoV-2) as it is currently called, is quickly dispersion from its starting point in Wuhan town of Hubei Province of China to the respite of the globe. Till 05/03/2020 about 96,000 belongings of coronavirus disease 2019 (COVID-19) and 3300 deaths have been described. India has described 29 cases turn over date. Providentially so far-off children have been rarelypretrntious with no deaths. But the prospect path of this virus is nameless. This editorial gives a bird's eye vision regarding this new virus. Seeing as acquaintance with reference to this virus is quickly sprouting, readers are urged to inform themselves frequently.

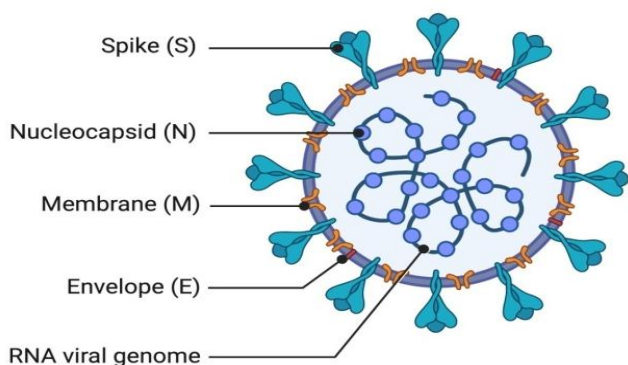
II HISTORY AND ORIGINE

Primary case of coronavirus was informed as wintry in 1960. Ac-cording to the Canadian study 2001, in the region of 500 patients were recognized as Flu-like symptoms. 17-18 belongings of them were established as unhygienic with coronavirus twist by polymerase chain reaction. Corona was treated as straightforward non incurable virus turn over 2002. In 2003, a range of anecdote available with the proofs of dispersal the corona to a lot of countries such as United States America, Hong Kong, Singapore, Thailand, Vietnam and in

Taiwan. Numerous case of rigorous acute respiratory syndrome give rise by corona and their extremely further 1000 patient was reported in 2003. This was the black year for microbiologist. When microbiologist was in progress sharp to grasp these issue. Behind a profound work out they finish and grasp the pathogenesis of disease and exposed as coronavirus. But turn over total 8096 patient was established as unhygienic with coronavirus. So in 2004, World health organization and centers for disease manage and avoidance affirmed as “state emergency”. An additional cram statement of Hong Kong was established 50 patient of severe acute respiratory syndrome while 30 of them were definite as corona virus grimy. In 2012, Saudi Arabian intelligence were accessible several infected patient and deaths.COVID-19 was initial acknowledged and remote from pneumonia rights belongs to Wuhan, china.

Microbiology-Coronavirus is sphere-shaped or pleomorphic, solitary stranded, covered RNA and enveloped with guild shaped glycoprotein. Coronaviruses are four sub types such as alpha, beta, gamma and delta coronavirus. Each of sub type coronaviruses has a lot of serotypes. A number of of them were distress human of other exaggerated animals such as pigs, birds, cats, mice and dogs.

III STRUCTURE- Coronavirus Structure



Coronaviruses are bulky, roughly spherical, particles with rounded exterior projections. The middling width of the virus particles is approximately 125 nm (.125 μm). The width of the cover is 85 nm and the spikes are 20 nm lengthy The cover of the virus in electron micrographs appears as a discrete brace of electron-dense shells (grenades that are moderately dense to the electron beam used to examine the virus particle).

The virus cover consists of a lipid bilayer, in which the membrane (M), envelope (E) and spear (S) structural proteinare anchored. The coronavirus exterior spikes are Homotrimers of the S protein, which is poised of an S1 and S2 subunit. The homotrimeric S protein is a class I fusion

protein which mediates the receptor binding and membrane fusion flanked by the virus and host cell. The S1 subunit forms the head of the spike and has the receptor obligatoryarea(RBD).

PROTEINS [18]	FUNCTION	
SPIKE (S) PROTEIN	Type I glycoprotein	1. Gives virus its corona- or crown-like morphology under the electron microscope. 2. Mediates attachment, fusion and its entry of the virus to the host cell
NUCLEOCAPSID (N) PROTEIN		Primarily to bind to the CoV RNA genome.
MEMBRANE(M) PROTEIN (MOST ABUNDANT)	Short N-terminal ectodomain and a cytoplasmic tail	Defines the shape of the viral envelope.
ENVELOPE (E) PROTEIN (SMALLEST)	Hydrophobic protein short ectodomain, a transmembrane domain and a cytoplasmic tail (63).	Expression inside the infected cell during replication
HEMAGGLUTININ ESTERASE (HE) (28)	An additional membrane protein in some group II	Unknown

IV CLASSIFICATION

Based on Groups

Genus *Coronavirus*

Group 1

- I. Canine coronavirus (CCoV)
- II. Feline coronavirus (FeCoV)
- III. Human coronavirus 229E (HCoV-229E)
- IV. Porcine epidemic diarrhea virus (PEDV)
- V. Transmissible gastroenteritis virus (TGEV)
- VI. Human Coronavirus NL63 (HCoV-NL63)

Group 2:

- I. Bovine coronavirus (BCoV)
- II. Canine respiratory coronavirus (CRCoV) - Common in SE Asia and Micronesia
- III. Human coronavirus OC43 (HCoV-OC43)
- IV. Mouse hepatitis virus (MHV)
- V. Porcine hem agglutinating encephalomyelitis virus (HEV)
- VI. Rat coronavirus (RCV): HCoV-HKU1

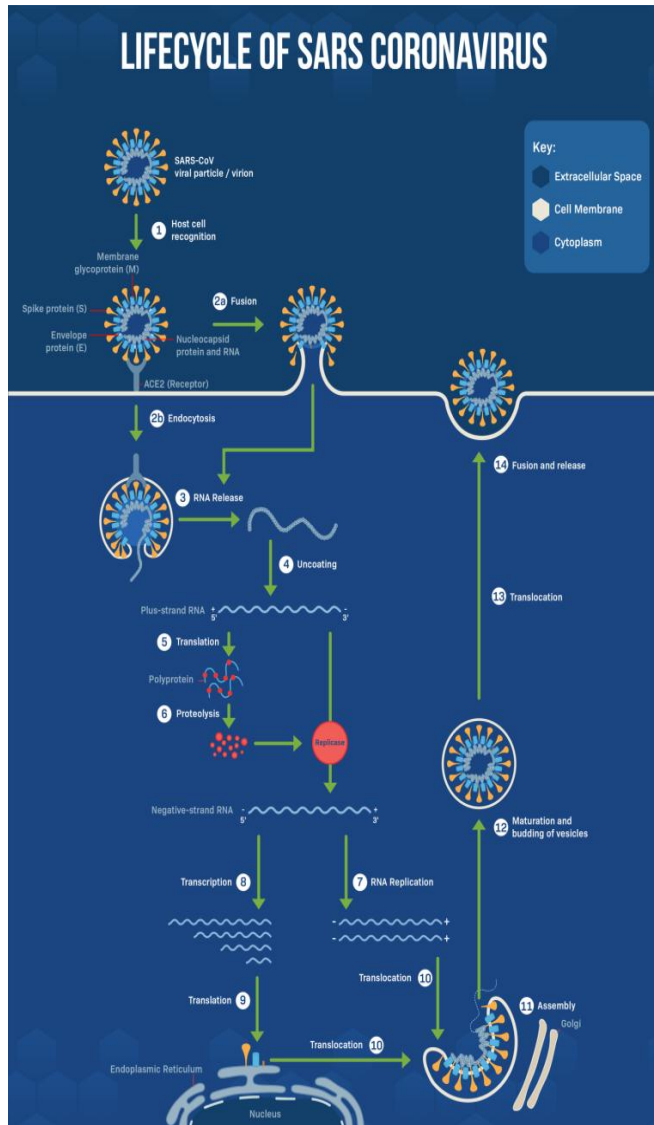
Group 3 :

- I. Infectious bronchitis virus (IBV)
- II. Turkey coronavirus (Bluecomb disease virus)
- III. Goose coronavirus
- IV. Duck coronavirus

Human Coronaviruses :

- I. HCoV-229E
- II. HCoV-OC43
- III. SARS-CoV

- IV. NL63/NL/New Haven coronavirus
- V. HKU1-CoV
- VI. Novel Coronavirus 2012 (HCoV-EMC)
- VII. SARS-CoV-2
- VIII. MERSCoV



Step 1-

- I. In the case of SARS-CoV, this receptor is angiotensin-converting enzyme 2 (ACE2).
- II. ACE2 is a usual cellular protein that happens to be worn by the virus to enlarge access to the cell.
- III. It has been confirmed that the new coronavirus SARS-CoV-2 also binds to ACE-2 and structurally resembles SARS-CoV.
- IV. Previously, the binding linking the spike protein and the receptor is inclusive, the virion enters the cell during one of two processes.

Step 2

Step 2a: covering blend from exclusive of where viral and cellular membranes blend and the RNA genome of the virus gets entrance to the cytoplasm.

Step 2b: In this step consist two parts

Endocytosis where the receptor-sprung virus is enveloped by the cell membrane and enters to the cytoplasm within a vesicle.

- I. subsequent either route of cell entry, the viral RNA genome is unconfined into the cytoplasm

Step 3

Which is followed by uncoating of the RNA

Step 4

Previously in the host cytoplasm, a replication gene on the RNA strand is translated into two replicase polyproteins

Step 5-

I. Translation is the creation of proteins from RNA, and a polyprotein is a large protein that can be cleaved into minor proteins.

II. The polyproteins are additionally processed by viral proteinases (enzymes that split down proteins) to give up entity replicase proteins

Step 6.

These replication reconcile the invention of full-distance end to end negative-strand RNA, which afterward serves as a template for positive-strand virion genomic RNA

Step 7.

- I. In dissimilarity to plus-strand RNA, negative-strand RNA is corresponding to the mRNA and cannot be translated unswervingly.
- II. It desires to be transformed to plus-strand RNA by RNA polymerase first.
- III. The full-length negative-strand RNA is transcribed to construct shorter mRNAs

Step 8.

These shorter mRNAs code for the structural proteins (e.g., S, E, M, and N) and nonstructural ornament proteins, including the viral proteinases, during translation

Step 9.

The newly formed plus-strand viral genomic RNA as well as nonstructural and structural proteins are translocated

Step 10-

- I. To assembly site at a transitional sector connecting the endoplasmic reticulum (ER) and the Golgi body.
- II. The Golgi body and the ER are both organelles occupied in protein synthesis, post-translational alteration of proteins, protein wrapping into membrane-bound vesicles, and protein convey. Here the new virions collect

Step 11

Create growing, and bud off from the Golgi membranes as vesicles

Step 12

These vesicles are translocate to the host cell covering

Step 13

Wherever they combine with the host cell membrane and are unconfined into extracellular freedom

Step 14

This let loose process does not break the host cell and is called non-lytic exocytosis.

V PATHOGENESIS:

1-The rigorous symptoms of COVID-19 are related with an escalating statistics and rate of wounded especially in the epidemic section of China. On January 22, 2020, the China National Health Commission described the facts of the primary 17 deaths and on January 25, 2020 the death cases amplified to 56 deaths . The proportion of death in the middle of the reported 2684 cases of COVID-19 was about 2.84% as of Jan 25, 2020 and the middle age of the deaths was 75 (range 48–89) years .

2-Patients tainted with COVID-19 showed higher leukocyte numbers, uncharacteristic respiratory result and amplified levels of plasma pro-inflammatory cytokines.

3- One of the COVID-19 case information showed a patient at 5 days of fever existing with a cough, uncouth breathing sounds of both lungs, and a body heat of 39.0 °C. The patient's sputum showed positive factual-time polymerase chain reaction consequences that definite COVID-19 infection.

4-The laboratory studies showed leucopenia with leukocyte counts of 2.91×10^9 cells/L of which 70.0% were neutrophils. In addition, a rate of 16.16 mg/L of blood C-reactive protein was noted which is above the normal range (0–10 mg/L). High erythrocyte sedimentation rate and D-dimer were also observed .

5- The major pathogenesis of COVID-19 illness as a respiratory system targeting virus was rigorous pneumonia, RNAemia, mutual with the occurrence of ground-glass opacities, and acute cardiac damage.

6-Considerablyelevated blood levels of cytokines and chemokines were eminent in patients with COVID-19 infection that built-in IL1-β, IL1RA, IL7, IL8, IL9, IL10, vital FGF2, GCSF, GMCSF, IFNγ, IP10, MCP1, MIP1α, MIP1β, PDGFB, TNFα, and VEGFA.

7-Some of the rigorous gear that were admitted to the severe care unit showed high levels of pro-inflammatory cytokines including IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1α, and TNFα that are logical to support disease rigorousness. Rigorousness.

Transmission:

1-Since the primary cases of the COVID-19 disease were related to straight revelation to the Huanan Seafood Wholesale Market of Wuhan, the animal-to-human communication was reputed as the most important mechanism. Nonetheless, ensuing cases were not connected with this revelation mechanism. Therefore, it was accomplished that the virus could also be transmitted

from human-to-human, and indicative people are the mainly recurrent source of COVID-19 extend. Because of the prospect of communication previous to symptoms, and thus persons who stay behind asymptomatic might send out the virus, remoteness is the preeminent mode to enclose this epidemic.

2-As with further respiratory pathogens, take in flu and rhinovirus, the communication is whispered to arise from first to last respiratory droplets (particles >5-10 μm in width) from coughing and sneezing. Aerosol spread is also potential in case of extended revelation to prominent aerosol secure contact among persons is obligatory. Of note, pre- and asymptomatic persons may well supply to up 80% of COVID-19 spread The extend in fact, is mainly inadequate to kindred, healthcare professionals, and further close associates (6 feet, 1.8 meters).

3-Regarding the extent of infectivity on matter and surfaces, a revise showed that SARS-CoV-2 can be establish on synthetic for up to 2-3 days, stainless steel for up to 2-3 concentrations in congested places.

4-Examination of facts connected to the extent of SARS-CoV-2 in China seems to point out that days, cardboard for up to 1 day, copper for up to 4 hours. Furthermore, it seems that contagion is superior in rigorous mind units (ICUs) than universal wards and SARS-Cov-2 can be establish on floors, CPU mice, waste cans, and sickbed handrails in addition to in air up to 4 meters from patients.

5-Based on information from the primary belongings in Wuhan and investigations conducted by the China CDC and local CDCs, the incubation time might be normally inside 3 to 7 days (middle 5.1 days, alike to SARS) and up to 2 weeks as the greatest time as of illness to symptoms was 12.5 days (95% CI, 9.2 to 18). This facts also showed that this new epidemic doubled in relation teach seven days, while the indispensable replication number (R0 - R naught) is 2.2.

6-In other words, on middling, every patient transmits the illness to an extra2.2 persons. Of note, estimations of the R0 of the SARS-CoV epidemic in 2002-2003 were around 3.

7- It should be emphasized that this in order to the consequence of the primary information. Thus, advance studies are needed to appreciate the mechanisms of spreading, the incubation times and the medical line, and the time of infection

VI SIGN AND SYMPTOM-

Most common symptoms:

- I. fever
- II dry cough
- III.tiredness

IV. Less common symptoms:

V. ches and pains

VI. sore throat

VII. diarrhoea

VIII. Conjunctivitis

IX. headache

X. loss of taste or smell

XI. a rash on skin, or discolorations of fingers or toes

XII. Serious symptoms:

XIII. Difficulty breathing or shortness of breath

XIV. Chest pain or pressure

XV. Loss of speech or movement

Prevention the spread of COVID-19:

- I. Clean your hands often. Use soap and water, or an alcohol-based hand rub.
- II. Maintain a safe distance from anyone who is coughing or sneezing.
- III. Don't touch your eyes, nose or mouth.
- IV. Cover your nose and mouth with your bent elbow or a tissue when you cough or sneeze.
- V. Stay home if you feel unwell.
- VI. If you have a fever, cough and difficulty breathing, seek medical attention. Call in advance.
- VII. Follow the directions of your local health authority

PREVENTION CORONAVIRUS



WASH YOUR HANDS
Wash them often, with water and lots of soap. Wash at least 20 seconds.



SNEEZING/ COUGHING ETIQUETTE
Cover your mouth when you cough or sneeze, with a tissue or the inside of your elbow



EYES, NOSE, MOUTH
Hands touch many surfaces and can pick up viruses. Avoid touching your eyes, nose or mouth. The virus can enter your body and can make you sick.



IF YOU'RE SICK
if you have a flu-like illness, inform the people around you. If your illness isn't mild, seek medical care.



Treatment-

1. There is no exact antiviral cure not compulsory for COVID-19, and no vaccine is at present obtainable. The cure

is indicative, and oxygen cure represents the primary stair for addressing respiratory injury.

2. Non-invasive (NIV) and invasive mechanical ventilation (IMV) perhaps necessary in cases of respiratory failure refractory to oxygen therapy.

3. Once more, exhaustive care is desired to contract with intricated forms of the illness. In relation to ARDS cure, accumulating familiarity on the pathophysiology of lung injure, have steadily induced clinicians to assessment strategies for commerce with respiratory failure.

4. As Gattinoni et al. recommended, COVID-19-induced ARDS (CARDS) is not a "Typical" ARDS. This feature of the disease is of essential significance and has almost certainly negatively exaggerated the curative move toward in the early on stages of the pandemic.

5. Certainly, regardless at commencement of the pandemic, early on IMV was postulated as the enhanced approach for addressing CARDS, in COVID-19 pneumonia the distinctive ARDS respiratory mechanics featuring abridged lung conformity (i.e., capability to draw out and enlarge lungs) cannot be originate. On the divergent in CARDS, good pulmonary obedience can be established.

6. As a outcome and in disparity, to what was at first alleged NIV can have a key role in CARDS cure .

A-O2 Fast Challenge

In a patient with a SpO2 < 93-94% (< 88-90% if COPD) or a respiratory rate > 28-30 / min, or dyspnea, the administration of oxygen by a 40% Venturi cover must be performed. After a 5 to 10 minutes reconsideration, if the medical and influential image has enhanced the patient continues the cure and undergoes a reassessment surrounded by 6 hours. In case of failure enhancement or new aggravation the patient undergoes a non-invasive treatment, if not contraindicated.

B-HFNO and non-invasive ventilation

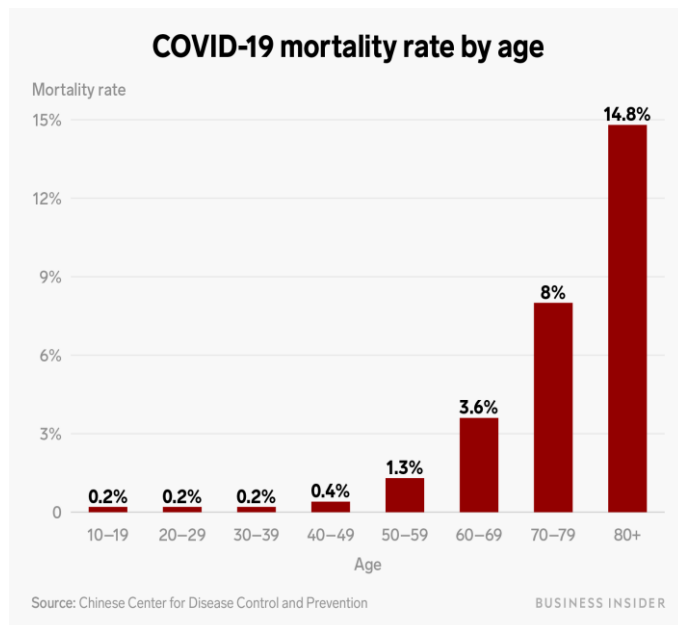
In considers to HFNO or NIV, the experts' section, points out that these approaches performed by systems with good interface appropriate do not form prevalent dispersal of exhaled air, and their use can be measured at low risk of airborne spread.

C-OTHER THEREPY-

- i. Chloroquine (500 mg every 12 hours), and hydroxychloroquine (200 mg every 12 hours) were anticipated as immune modulatory treatment. Of note, in a non-randomized trial, Gautret et al.
- ii. hydroxychloroquine was appreciably related with viral freight lessening awaiting viral desertion and this consequence was enhanced by the macrolides azithromycin. In vitro and in vivo studies, certainly, have

shown that macrolides may moderate soreness and amend the immune system.

- iii. In fastidious, these drugs may encourage the down guideline of the union molecules of the cell surface, tumbling the invention of pro-inflammatory cytokines, stimulating phagocytosis by alveolar macrophages, and inhibiting the commencement and recruitment of neutrophils. However, additional studies are desirable for recommending the use of azithromycin, unaccompanied or related with other drugs such as hydroxychloroquine, outside of any bacterial overlaps.
- iv. Again, awareness should be paid with the attendant use of hydroxychloroquine with azithromycin as the alliance can bring about a superior hazard of QT hiatus continuation and cardiac arrhythmias. Chloroquine can also persuade QT persistence



V. Particularly, the research showed that patients ages 10 to 19 had the similar possibility of disappearing from COVID-19 as patients in their 20s and 30s, but the illness appeared to be a great deal additional deadly in people ages 50 and over. About 80 percent of COVID-19 cases are mild, the investigate showed, and specialists suppose lots of gentle belongings haven't been reported since a number of people aren't departing to the doctor or hospitals for cure.

VII CONCLUSION:

Close to prospect route of COVID-19 has extend almost all above the globe except for few, therefore its opportune analysis is necessary for quarantine and incorporated interventions to manage the eruption Seeing as there is no effectual treatment or vaccine, the most excellent events now are to manage the source of illness, untimely analysis coverage, segregation kind treatments, and appropriate

publishing epidemic in sequence to stay away from redundant fright. For persons, good personal cleanliness, modified coverairing, and avoiding teeming spaces will assist to avert CoVs illness.

REFERENCE-

1. Sexton NR., et al. “Homology-Based Identification of a Mutation in the Coronavirus RNA-Dependent RNA Polymerase That Confers Resistance to Multiple Mutagens”. *Journal of Virology*90.16 (2016): 7415-7428.8.
2. Kahn Jeffrey and McIntosh Kenneth. “History and recent advances in coronavirus discovery”. *Pediatric Infectious Disease Journal* 24.11 (2005): s223-s227
3. Centers for Disease Control and Prevention: coronavirus disease 2019 (COVID-19) - situation summary. (2020). Accessed: March 11, 2020: <https://www.cdc.gov/coronavirus/2019-ncov/summary.html>.
4. Centers for Disease Control and Prevention: human coronavirus types. (2020). Accessed: March 11, 2020:
5. Wang Chen, Horby Peter W, Hayden Frederick G, Gao George F. A novel coronavirus outbreak of global health concern. *The Lancet*. 2020;395(10223):470–473. doi: 10.1016/S0140-6736(20)30185-9. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
6. Conavirus Outbreak. Available at: <https://www.worldometers.info/coronavirus/>. Accessed 23 Feb 2020.History and origin-Centers for Disease Control and Prevention (CDC). Update: Outbreak of severe acute respiratory syndrome--worldwide, 2003. *MMWR Morb Mortal Wkly Rep*. 2003;52(12):241–6.2.
7. World Health Organization. Coronavirus never before seen in humans is the cause of SARS– update 31. Geneva: The Organi-zation; 2003.3.
8. World Health Organization. Summary of probable SARS cases with onset of illness from 1 November 2002 to 31 July 2003. Available at http://www.who.int/csr/sars/country/table2004_04_21/en/index.html. Accessed 14 feb 2020.4.
9. Peiris JS, Lai ST, Poon LL, Guan Y, Yam LY, Lim W, et al. Coronavi-rus as a possible cause of severe acute respiratory syndrome. *Lancet*. 2003;361:1319–25. [CrossRef]
10. World Health Organization. WHO Statement Regarding Clus-ter of Pneumonia Cases in Wuhan, China Geneva 2020 [up-dated 9 January 2020 and 14 January 2020]. Available from:<https://www.who.int/china/news/detail/09-01-2020-who-statement-regarding-cluster-of-pneumoniacases-in-wuhan-china>
11. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China,

2019. 24 January 2020. *New England Journal of Medicine*. [CrossRef]
12. Mailles A, Blanckaert K, Chaud P, van der Werf S, Lina B, Caro V, et al. First cases of Middle East respiratory syndrome Corona-virus (MERS-CoV) infections in France, investigations and implications for the prevention of human-to-human trans-mission, *Euro Surveill*. 2013;18:20502
13. Buchholz U, Müller MA, Nitsche A, Sanewski A, Wevering N, Bauer-Balci T, et al. Contact investigation of a case of human novel coronavirus infection treated in a German hospital, October-November 2012. *Euro Surveill*. 2013;18:20406
14. Saif LJ. Animal coronaviruses: what can they teach us about the severe acute respiratory syndrome? *Rev Sci Tech*. 2004;23:643–60. [CrossRef]
15. Gwaltney JM Jr. Virology and immunology of the common cold. *Rhinology*. 1985;23:265
16. Tyrrell DAJ, Myint SH. Chapter 60: Coronaviruses. In Barson S, editor. *Medical microbiology*. 4th edition. Galveston: University of Texas Medical Branch at Galveston; 1996.
17. Goldsmith CS, Tatti KM, Ksiazek TG, Rollin PE, Comer JA, Lee WW, et al. (February 2004). "Ultrastructural characterization of SARS coronavirus". *Emerging Infectious Diseases*. 10 (2): 320–26. doi:10.3201/eid1002.030913. PMC 3322934. PMID 15030705. Virions acquired an envelope by budding into the cisternae and formed mostly spherical, sometimes pleomorphic, particles that averaged 78 nm in diameter (Figure 1A).
18. Neuman BW, Adair BD, Yoshioka C, Quispe JD, Orca G, Kuhn P, et al. (August 2006). "Supramolecular architecture of severe acute respiratory syndrome coronavirus revealed by electron cryomicroscopy". *Journal of Virology*. 80 (16): 7918–28. doi:10.1128/JVI.00645-06. PMC 1563832. PMID 16873249. Particle diameters ranged from 50 to 150 nm, excluding the spikes, with mean particle diameters of 82 to 94 nm; Also See Figure 1 for double shell.
19. Fehr AR, Perlman S (2015). "Coronaviruses: an overview of their replication and pathogenesis". In Maier HJ, Bickerton E, Britton P (eds.). *Coronaviruses*. *Methods in Molecular Biology*. 1282. Springer. pp. 1–23. doi:10.1007/978-1-4939-2438-7_1. ISBN 978-1-4939-2438-7. PMC 4369385. PMID 25720466. See section: Virion Structure.
20. Lai MM, Cavanagh D (1997). "The molecular biology of coronaviruses". *Advances in Virus Research*. 48: 1–100. doi:10.1016/S0065-3527(08)60286-9. ISBN 9780120398485. PMC 7130985. PMID 9233431.
21. Woo PC, Lau SK, Chu CM; et al. (2005). "Characterization and complete genome sequence of a novel coronavirus, coronavirus HKU1, from patients with pneumonia". *J Virol*. 79: 884–895. doi:10.1128/JVI.79.2.884-895.2005.
22. Vabret A, Dina J, Gouarin S; et al. (2006). "Detection of the new human coronavirus HKU1: a report of 6 cases". *Clin Infect Dis*. 42: 634–639. doi:10.1086/500136.
23. "Coronavirus - MicrobeWiki". Retrieved 2012-12-28.
24. Denison MR. Coronavirus research: keys to diagnosis, treatment, and prevention of SARS. In: Institute of Medicine (US) Forum on Microbial Threats; Knobler S, Mahmoud A, Lemon S, et al., editors. *Learning from SARS: Preparing for the Next Disease Outbreak: Workshop Summary*. Washington (DC): National Academies Press (US); 2004.
25. Fehr, A. R., & Perlman, S. 2015. Coronaviruses: an overview of their replication and pathogenesis. *Methods in molecular biology* 1282, 1–23.
26. Du, L., He, Y., Zhou, Y. et al. The spike protein of SARS-CoV — a target for vaccine and therapeutic development. *Nat Rev Microbiol* 7, 226–236 (2009)
27. Sinosh, S., Basavaraj, C.S., Swathi, P., Toplar, K.S., Sneha, S.V. 2019. Recent Aspects on the Pathogenesis Mechanism, Animal Models and Novel Therapeutic Interventions for Middle East Respiratory Syndrome Coronavirus Infections. *Frontiers in Microbiology* 10:569
28. Siu, Y. L., Teoh, K. T., Lo, J., Chan, C. M., Kien, F., Escriou, N., Tsao, S. W., Nicholls, J. M., Altmeyer, R., Peiris, J. S., Bruzzone, R., & Nal, B. 2008. The M, E, and N structural proteins of the severe acute respiratory syndrome coronavirus are required for efficient assembly, trafficking, and release of virus-like particles. *Journal of virology* 82(22), 11318–11330
29. Wang, H., Yang, P., Liu, K. et al. 2008. SARS coronavirus entry into host cells through a novel clathrin- and caveolae-independent endocytic pathway. *Cell Research* 18, 290–30
30. Weiss, Susan R., Navas-Martin, Sonia. 2005. Coronavirus Pathogenesis and the Emerging Pathogen Severe Acute Respiratory Syndrome Coronavirus. *Microbiology and Molecular Biology Reviews* 69 (4) 635-664
31. D. Wrapp et al., *Science* 10.1126/science.abb2507 (2020). Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation.
32. Zhong, Yanxin & Tan, Yong & Liu, Ding. 2012. Recent Progress in Studies of Arterivirus- and Coronavirus-Host Interactions. *Viruses*. 4. 980-1010
33. Wang, J. Tang, F. Wei Updated understanding of the outbreak of 2019 novel coronavirus (2019-nCoV) in Wuhan,

- China. *J. Med. Virol.*, 92 (4) (2020), pp. 441-447, 10.1002/jmv.25689
34. J. Lei, J. Li, X. Li, X. Qi. CT imaging of the 2019 novel coronavirus (2019-nCoV) pneumonia. *Radiology* (2020), p. 200236, 10.1148/radiol.2020200236
35. C. Huang, Y. Wang, X. Li, L. Ren, J. Zhao, Y. Hu, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*, 395 (10223) (2020), pp. 497-506, 10.1016/S0140-6736(20)30183-5
36. Guo ZD, Wang ZY, Zhang SF, Li X, Li L, Li C, Cui Y, Fu RB, Dong YZ, Chi XY, Zhang MY, Liu K, Cao C, Liu B, Zhang K, Gao YW, Lu B, Chen W. Aerosol and Surface Distribution of Severe Acute Respiratory Syndrome Coronavirus 2 in Hospital Wards, Wuhan, China, 2020. *Emerging Infect. Dis.* 2020 Apr 10;26(7) [PubMed]
37. Lauer SA, Grantz KH, Bi Q, Jones FK, Zheng Q, Meredith HR, Azman AS, Reich NG, Lessler J. The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application. *Ann. Intern. Med.* 2020 May 05;172(9):577-582. [PMC free article] [PubMed]
38. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, Ren R, Leung KSM, Lau EHY, Wong JY, Xing X, Xiang N, Wu Y, Li C, Chen Q, Li D, Liu T, Zhao J, Liu M, Tu W, Chen C, Jin L, Yang R, Wang Q, Zhou S, Wang R, Liu H, Luo Y, Liu Y, Shao G, Li H, Tao Z, Yang Y, Deng Z, Liu B, Ma Z, Zhang Y, Shi G, Lam TTY, Wu JT, Gao GF, Cowling BJ, Yang B, Leung GM, Feng Z. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. *N. Engl. J. Med.* 2020 Mar 26;382(13):1199-1207. [PMC free article] [PubMed]
39. Bauch CT, Lloyd-Smith JO, Coffee MP, Galvani AP. Dynamically modeling SARS and other newly emerging respiratory illnesses: past, present, and future. *Epidemiology*. 2005 Nov;16(6):791-801. [PubMed]
40. <https://www.google.com/search?client=firefox-b-d&bih=545&biw=1138&hl=en-GB&sxsrf=41>. <https://www.msf.org/msf-update-2019-ncov-coronavirus-outbreak?component=image-277349>
42. Gattinoni L, Coppola S, Cressoni M, Busana M, Rossi S, Chiumello D. COVID-19 Does Not Lead to a "Typical" Acute Respiratory Distress Syndrome. *Am. J. Respir. Crit. Care Med.* 2020 May 15;201(10):1299-1300. [PMC free article] [PubMed]
43. Hui DS, Chow BK, Lo T, Tsang OTY, Ko FW, Ng SS, Gin T, Chan MTV. Exhaled air dispersion during high-flow nasal cannula therapy versus CPAP via different masks. *Eur. Respir. J.* 2019 Apr;53(4) [PubMed]
44. Gautret P, Lagier JC, Parola P, Hoang VT, Meddeb L, Mailhe M, Doudier B, Courjon J, Giordanengo V, Vieira VE, Dupont HT, Honoré S, Colson P, Chabrière E, La Scola B, Rolain JM, Brouqui P, Raoult D. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *Int. J. Antimicrob. Agents.* 2020 Mar 20;:105949. [PMC free article] [PubMed]
45. Zarogoulidis P, Papanas N, Kioumis I, Chatzaki E, Maltezos E, Zarogoulidis K. Macrolides: from in vitro anti-inflammatory and immunomodulatory properties to clinical practice in respiratory diseases. *Eur. J. Clin. Pharmacol.* 2012 May;68(5):479-503. [PubMed]
46. <https://www.sciencealert.com/covid-19-s-death-rate-is-higher-than-thought-but-it-should-drop>