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STUDY OF CORONAVIRUS PREVENTION, INFECTION AND TREATMENT

Neha*, Hemraj Vashist and Shivani Dogra

L.R. Institute of Pharmacy, Vill. Jabli Kyar, P/O Oachghat, Sultanpur Road, Distt. Solan (H.P).

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***Corresponding Author**
Neha
L.R. Institute of Pharmacy, Vill. Jabli Kyar, P/O Oachghat, Sultanpur Road, Distt. Solan (H.P.)

ABSTRACT

Human corona virus is a pandemic diseases which is also known as novel corona virus. Human pathogenic coronavirus genome is polycistronic, covered and having single strand. SARS-CoV-2 belong to the order of nidovirales, with in the subfamily of coronaviridae, under the family of coronavirinae, and belongs to the beta coronavirus genus. Novel corona virus genome indicates that the coronavirus further is divided into two types, L type (70%) and S type (30%). They both play significant role in the current outbreak. More than five coronavirus infect the human host and cause respiratory disease. Between them the type of beta corona virus (SARS and MERS) are severe infection which are zoonotic and extremely threatening corona viruses leads to worldwide eruption. Coronaviruses have a distinct stratification. We have observed in the past 15 years that the appearance extremely threatening HCoV: are type of beta corona virus. Repetition is controlled through variety of multitude influences, persuades radical changes in anatomy and myology. Complete statistics is provided in this review.

KEYWORD: Sars, Human Coronavirus, Coronavirinae, Epidemiology, Replication Cycle, Pathogenesis.

INTRODUCTION

Corona viruses are the animal and human pathogens which will cause destructive infections which is transmitted from animals to humans. Human corona virus comprises of single strand, polycistronic, and covered genome. Corona virus genome (~26- 32 kilo bases) are the most important RNA genomes.[1] Corona viruses, a family of viruses with within the Nidovirus superfamily, were divided into three groups (1, 2, and 3) primordially supported

antigenic reactivity, later confirmed by genome sequencing. It is divided into three genus that is alpha, beta, gamma and respective groups 1, 2, 3. Novel corona virus belongs under the order of nidovirales, with in the subfamily of coronaviridae, under the family of coronavirinae.[2] Covid-19 belongs to the beta CoVs category.[8] Corona viruses cause ailments in a very style of domestic and wild animals likewise as in humans. Perhaps the foremost well studied corona virus is that the beta corona virus, murine corona virus (MuCoV), mouse hepatitis virus (commonly said as MHV). Most corona virus infections cause the respiratory illness. Beta corona virus unwavering the potential for further significant human disease to result from corona virus infections.[2] Corona viruses (CoVs) are an oversized family of viruses that cause ailment starting from the cold to more severe diseases like Middle East Respiratory Syndrome (MERS- CoV) and Severe Acute Respiratory Syndrome (SARS-CoV). A unique coronavirus (nCoV) may be a new strain that has not been antecedently identified in humans. Novel corona virus spread from civet cats to individuals. Thoroughly research originate that the severe acute deficiency syndrome was zoonotic infection.[3]

2019-nCoV as pandemic

The Novel pathogenic corona virus also known as 2019-nCoV is newly developed strain which is originated from the china in the province of Wuhan in the region of Hubei. In China the first case appeared in December. World Health Organization declared the novel corona virus as outbreak on 30th January 2020. The WHO gave the virus name to 2019-nCoV in which “n” is stand for new, “CoV” is stand for corona virus and 2019 stands for the year in which COVID-19 is first recognized. International Committee on Taxonomy of Viruses gave the new name for Covid-19 on 11th February 2020 as SARS-CoV-2 which means severe acute respiratory syndrome corona virus-2 which is type of beta corona virus. On 11th march 2020 World Health Organization announce the Covid-19 as deadly disease. The virus keep mutated itself consequences that it shows minimum two different strain. Novel corona virus genome indicates that the coronavirus further is divided into two types, L type (70%) and S type (30%). They both play significant role in the current outbreak. More than five coronaviruses infect the human host and cause respiratory disease. Between them the type of beta corona virus (SARS and MERS) are severe infection which are transmitted from animals to humans and extremely threatening corona viruses leads to worldwide eruption.[24] Coronaviruses have a distinct stratification. Due to crown-likes spikes on their surface hence it is named as corona virus. Alpha, Beta, Gamma, and Delta genus are the four main groups

in which it is further divided. In the mid-1960s the human corona virus was recognized first. The seven type of corona viruses has impact on individuals are classified below:

Types of corona virus

1. Alpha genus- 229E corona virus, NL63 corona virus
2. Beta genus- OC43, HKU1, SARS, MERS, SARS-CoV-2.[4]

Corona virus diversity

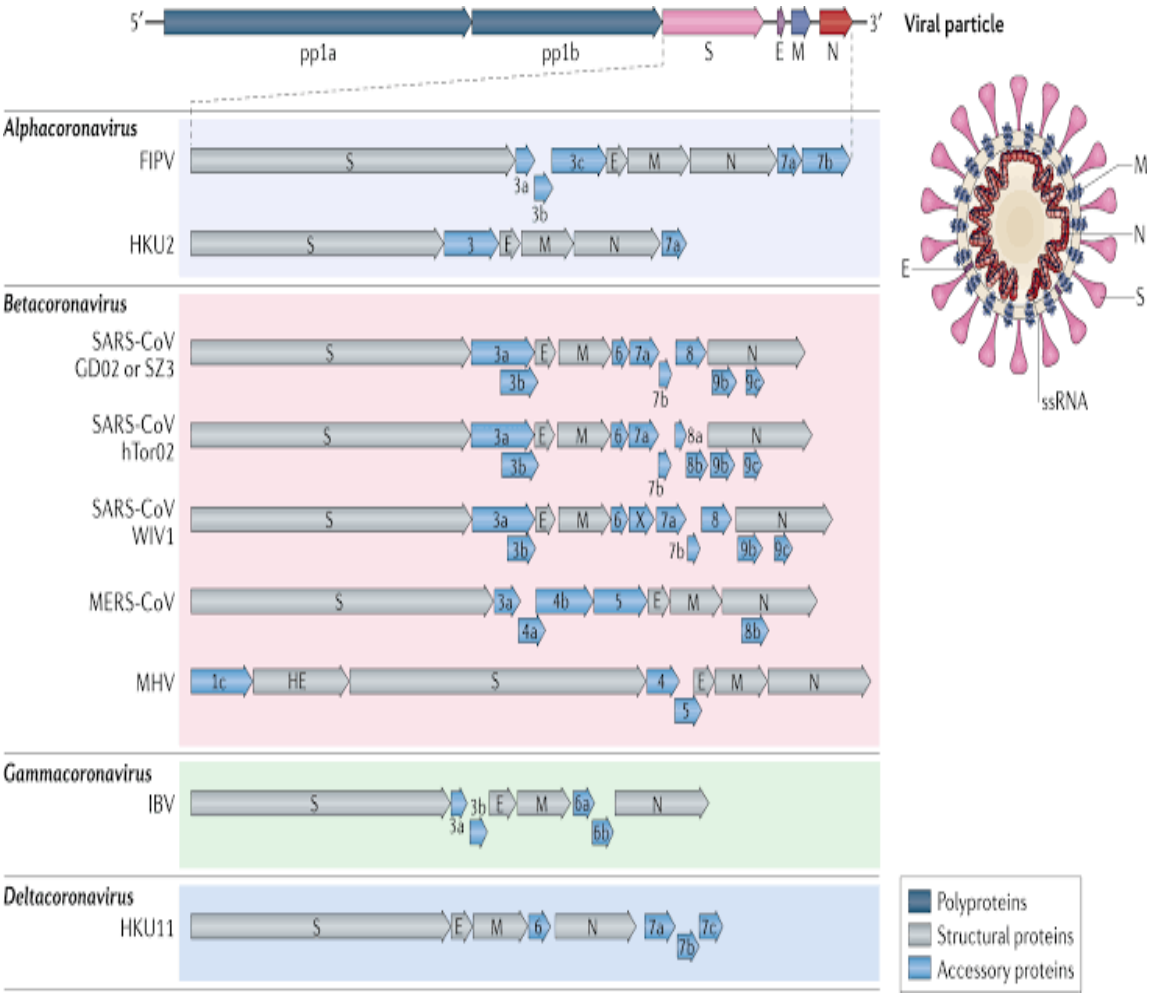


Figure 1: Genomes, and Proteins of the various cov.[3]

The novel strain of corona virus genome has covered, round shaped molecule ranges in caliber from 100–160 nm. They comprise of a polycistronic, positive and (ss RNA) genomes, of 30-32kb. In size. Corona viruses are assembled in the way that at 5'end structural proteins and at 3'end spikes, membranes, nucleocapsid, proteins, and HE are encoded. Additionally to the alleles that coding fundamental proteins, are auxiliary alleles that are particular and expendable for pathogen duplication.[3]

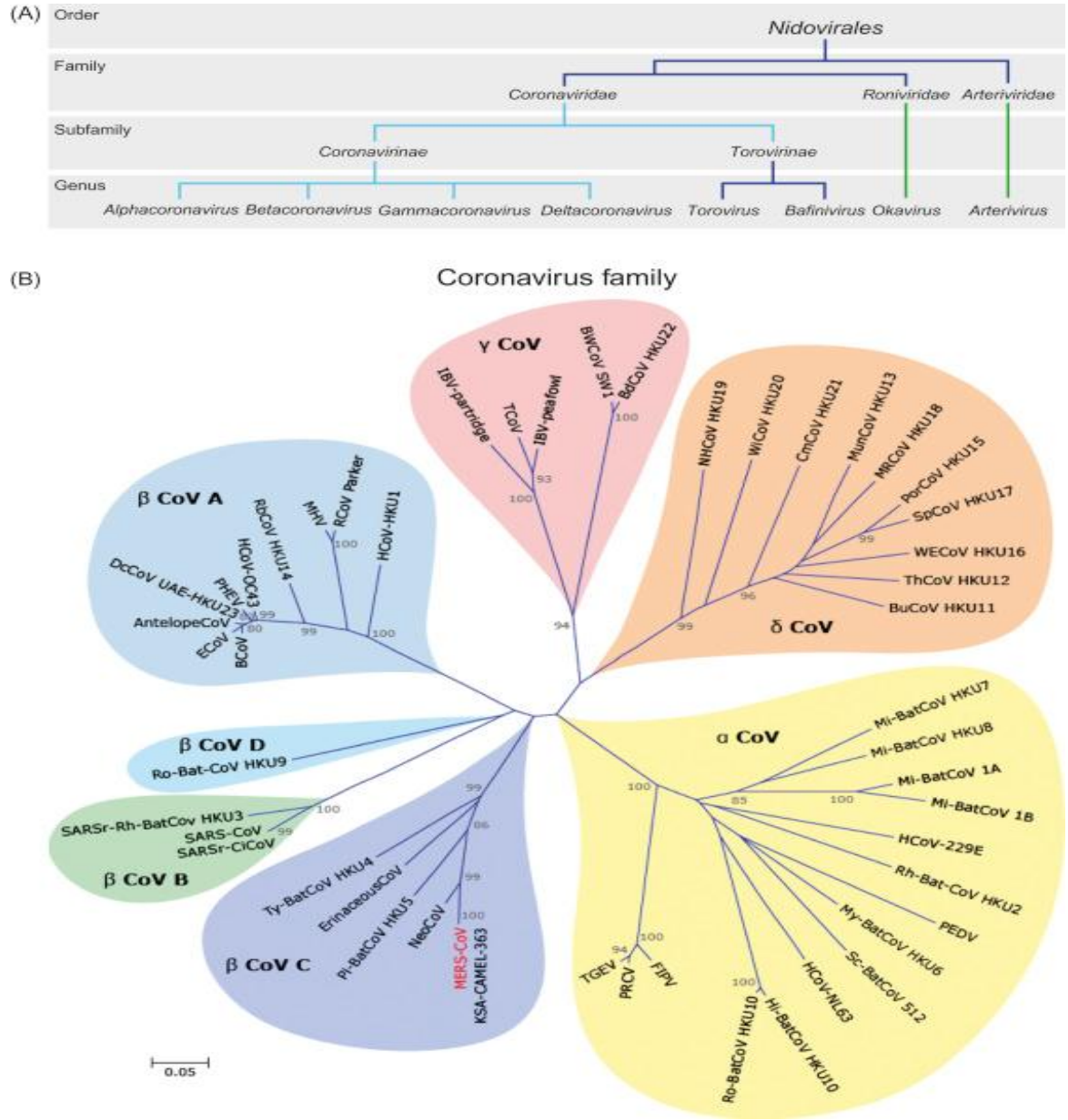


Figure 2: present taxonomy of coronaviridae.

Phylogenetic diagram of fifty coronaviruses with inadequate nucleotide. Neighbor-joining technique has used to create diagram.[31]

Genome and virion

Corona viruses are covered, polycistronic, single stranded of RNA genomes, of 30-32kb. All corona viruses are assembled in the way that at 5'end structural proteins and at 3'end spikes, membranes, nucleocapsid, proteins, and HE are encoded. Viral envelope has comprises of RNA genome along with the complex of nucleocapsid proteins. 5`end of the genome encodes the replicase gene, and having two open leading frames that is orf1a, and orf1b including 20kb of the genome. The replicase has translated PP1a and 1ab, with PP1ab manifested by a

translational frame shift encoded near the end of orf1a. These large molecules composed of one or more long chains of amino acids are be different in function among the coronavirus group and between MHV and SARS CoV as well as different in number, and sequence.[2]

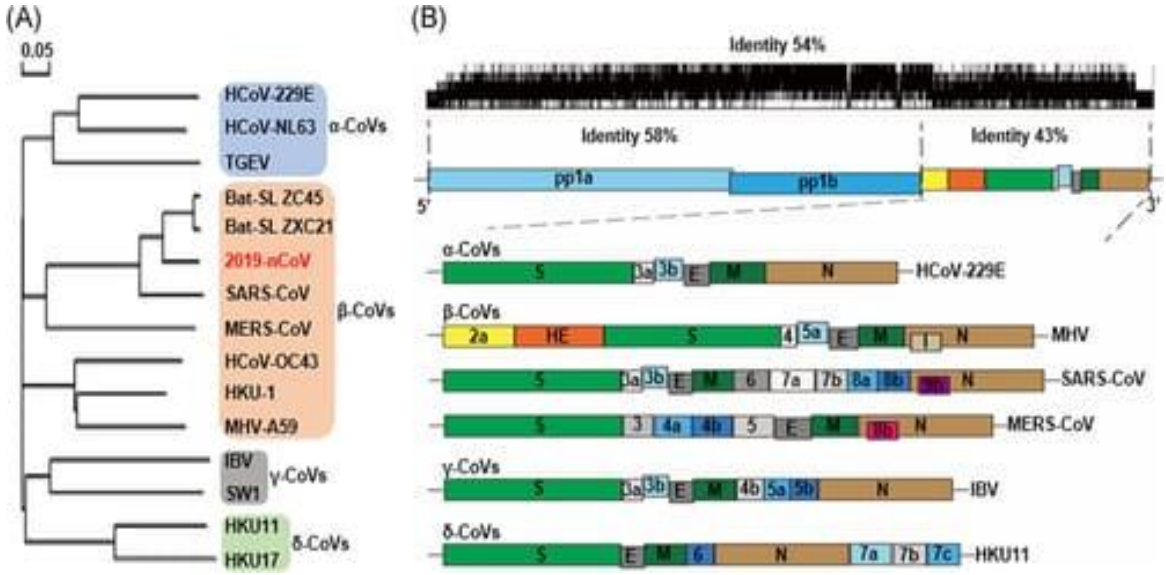


Figure 3: Phylogenetic diagram of demonstrative corona virus.

Diagram showing composition of coronavirus Genome PP1a and 1ab, with PP1ab manifested by a translational frame shift encoded near the end of orf1a.[7]

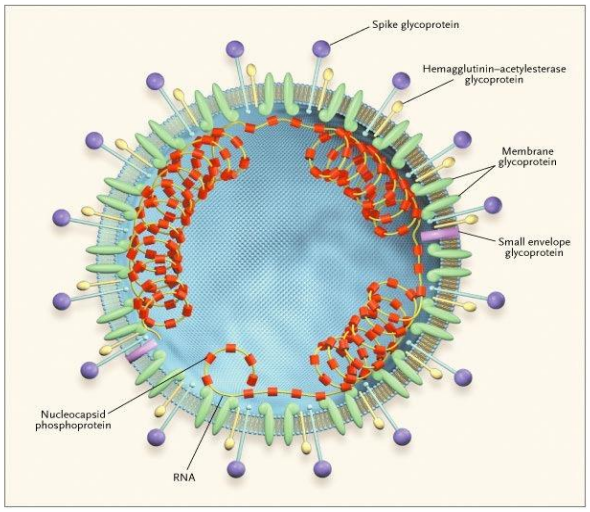


Fig. 4: Sars associated corona virus.[9]

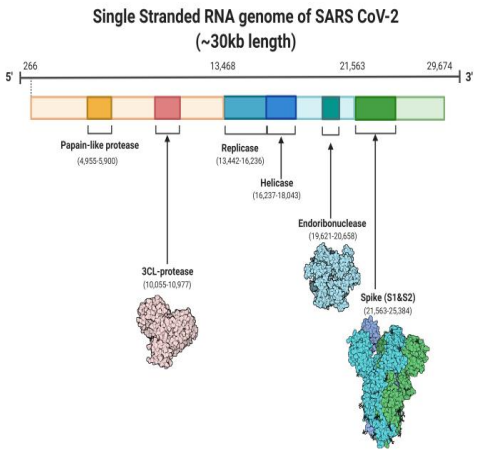


Fig. 5: Rna genome.[13]

Pathogenesis of novel corona virus

In the province of China Imprescriptible symptoms of threatening pathogenic corona virus are associated with high rate of fatalities. The confirmed case of SARS-Cov-2 patients was 5 on Dec. 29, 2019 and 571 cases on Jan. 22, 2020 and in which death cases in China as on 29th

Dec. is 1, the number of patients increased day by day and the death toll no. increased up to 56 as on Jan. 25 2020.[14]

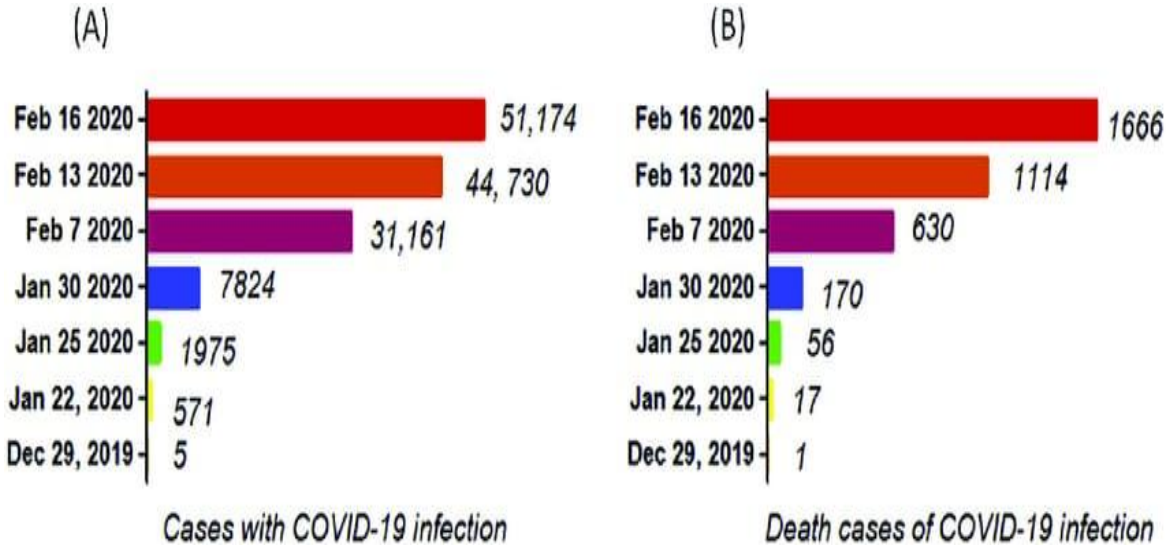


Fig. 6: Chronological existence of 2019-nCoV Infections and Death cases in china.

There have been 51,174 confirmed covid-19 cases on February 16, 2020 and death toll number is more than 1666.[15]

Patients who is suspected to Covid-19, report shows highly increased numbers of leukocytes and plasma pro-inflammatory cytokines, with shortness of breath, pyrexia, coughing, chest pain, weight loss etc. The positive real-time polymerase chain reaction test confirmed the COVID-19infection.[14]

Corona virus entry and replication

- The first step in the replication that the virus has to enter into the host cell.
- Spikes glycoproteins of novel strain human corona virus SARS-CoV-2 binds to the ACE-2 (angiotensin-converting enzyme 2) cellular receptor,[23]
- Novel strain corona virus direct enter into the cells through integument
- After that there is amalgamation in between the plasma integument and pathogens.
- A censorious hydrolysis of peptide bonds of proteins division happened at site S20.
- The RNA genome of the virus is liberate in the cytoplasm when it is reached into the cell and translated into two Pp. and structural proteins, after that genome of virus commences to reproduce.

- Amalgamation of nucleocapsid protein and RNA genome formulate nucleocapsid. Glycoproteins are introduced into the Golgi and endoplasmic reticulum
- The Viral particles mature in the endoplasmic reticulum-Golgi intermediate compartment. At the end the vesicles which contain virus particles combine with the plasma integument to liberate the virus.[16]

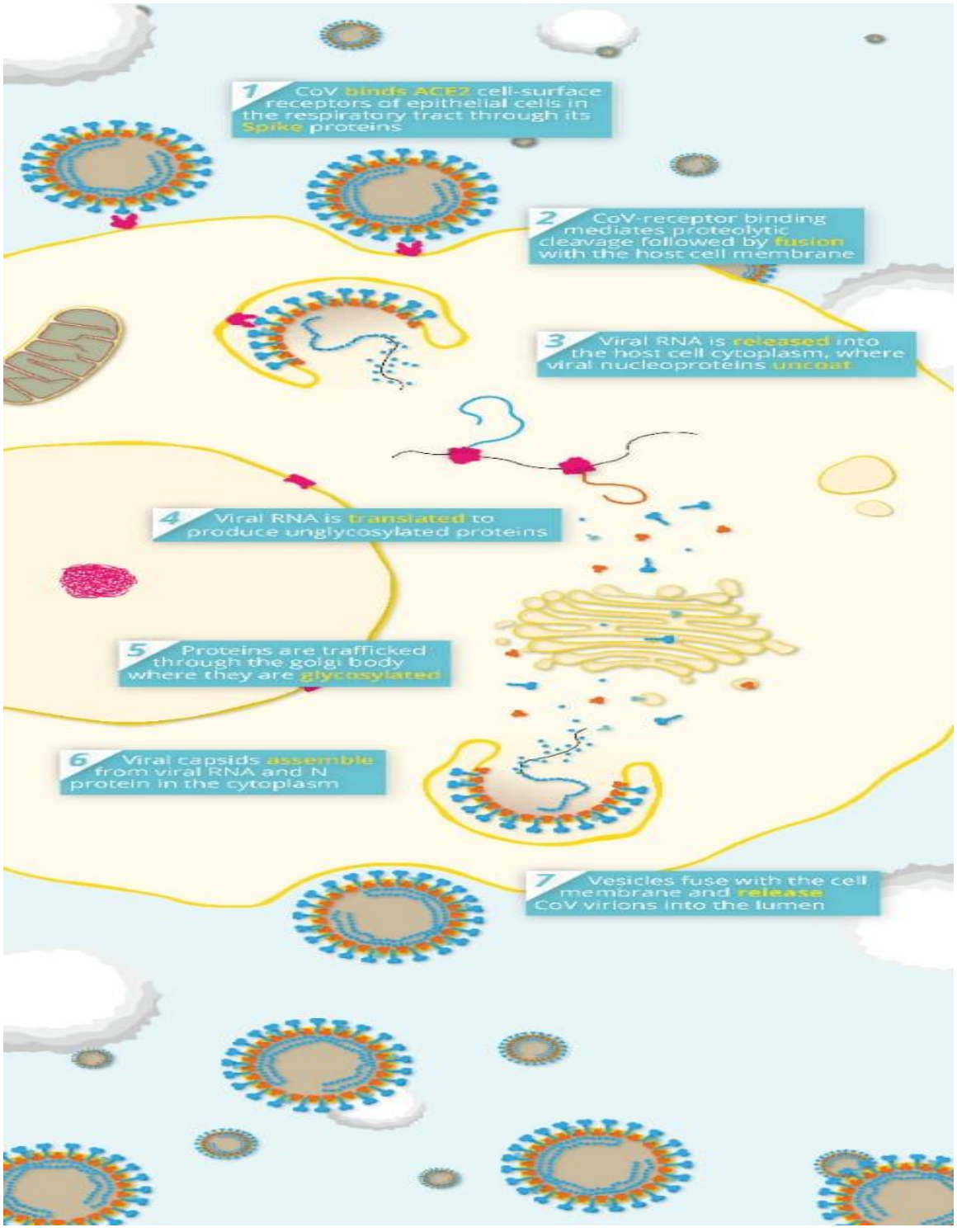


Figure 7: Replication cycle.[17]

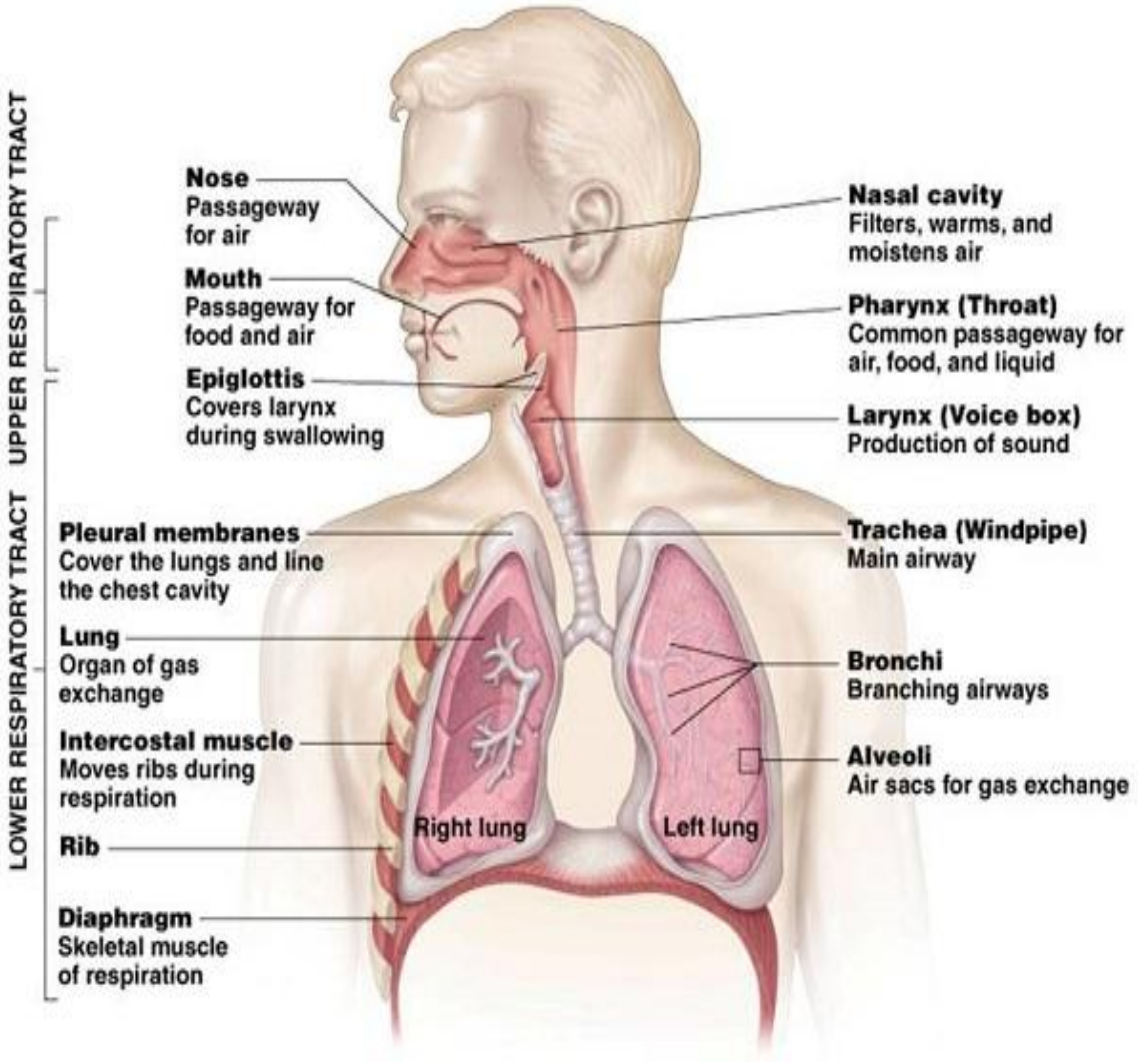


Figure 8: Structure and Function of the respiratory system.[20]

Functions of nonstructural proteins

There is total 16 nonstructural proteins which plays significant role in the replication and are known for their accurate function in replication of CoVs. They both have different functions. Some of the functions of nonstructural proteins are unknown while others are well established. M protein, S proteins, E protein, and N protein are important for coronavirus infection. Due to presence of S proteins it gets attached to the host receptor and E proteins has a crucial part in virus release, M protein binds with the nucleocapsid and N protein bind to RNA genome.

Table 1: The 16 nonstructural Proteins and ITS functions.

Nsps	Functions
nsp1	Cellular mRNA degradation, inhibiting IFN signaling
nsp2	Unknown
nsp3	PLP, polypeptides cleaving, blocking host innate immune response, promoting cytokine expression
nsp4	DMV formation
nsp5	3CLpro,Mpro, polypeptides cleaving, inhibiting IFN signaling
nsp6	Restricting autophagosome expansion, DMV formation
nsp7	Cofactor with nsp8 and nsp12
nsp8	Cofactor with nsp7 and nsp12, primase
nsp9	Dimerization and RNA binding
nsp10	Scaffold protein for nsp14 and nsp16
nsp11	Unknown
nsp12	Primer dependent RdRp
nsp13	RNA helicase, 5′ triphosphatase
nsp14	Exoribonuclease, N7-MTase
nsp15	Endoribonuclease, evasion of dsRNA sensors
nsp16	2′-O-MTase; avoiding MDA5 recognition, negatively regulating innate immunity

Abbreviations: 3CLpro (chymotrypsin-like protease); DMV (double membrane vesicle); (dsRNA) double-stranded RNA; (IFN) interferon; (mRNA) messenger RNA; (Mpro) main protease.[7]

Table 2: List of important pathogenic coronavirus.

Virus	Genus	Host	Symptoms
Human CoV-229E	Alpha	Human	Minor respiratory tract infections
Human CoV-NL63	Alpha	Human	Mild respiratory tract infections
PRCV/ISU-1	Alpha	Pig	Respiratory tract infections
TGEV/PUR46-MAD	Alpha	Pig	Diarrhea
Human CoV-HKU1	Beta	Human	Pneumonia
Human CoV-OC43	Beta	Human	Respiratory tract infections
SARS-CoV	Beta	Human	Severe acute respiratory syndrome
MERS-CoV	Beta	Human	Severe acute respiratory syndrome
Beluga whale	Gamma	Whale	Pulmonary disease, and terminal acute liver
IBV	Gamma	Chicken	severe respiratory syndrome
Bulbul HKU11	Delta	Bulbul	Respiratory disease
Coronavirus HKU17	Delta	Sparrow	Respiratory disease

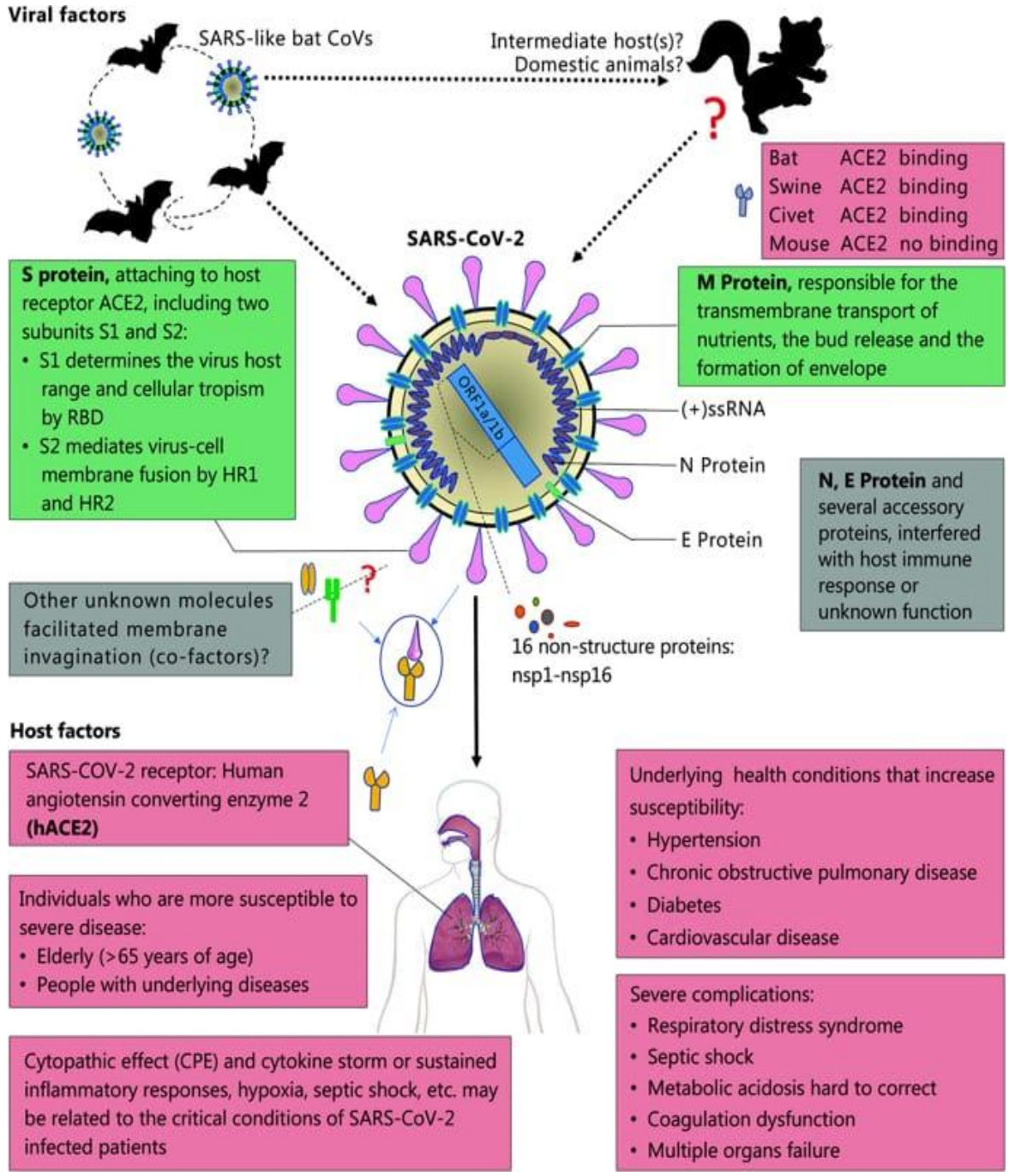


Figure 9: Viral and Host factors impact on pathological process of covid-19.[11]

Nurture time for SARS-CoV-2 as of 3-15 days.

1. Senior people.
2. Individual shaving medical conditions like lung disease, cerebrovascular disease, and renal disease, hypertension, liver diseases, cancer, and heart failure.
3. Pregnant women.

Epidemiology

Sometimes HCoV are discovered seasonally like in winter for instance human corona virus NL63, OC43 are endemic human corona virus but sometimes it appeared infrequently all over the year. Middle East Respiratory Syndrome, Severe Acute Respiratory Syndrome corona virus, Severe Acute Respiratory Syndrome coronavirus -2 (novel strain) is pandemic human corona virus. 2019-nCov Pandemic originated from the Wuhan in the region of Hubei is a zoonotic infection transferred from animals to humans.[12] Covid -19 is type of beta corona virus. Dispensation of corona virus in different mammalian species is unidentified.[18]

The Signs and Symptoms

There is the various signs or symptoms which are associated with the Covid-19. These are given below:

- Pyrexia
- Languor
- salivation
- Pharyngitis
- Empties
- weight loss

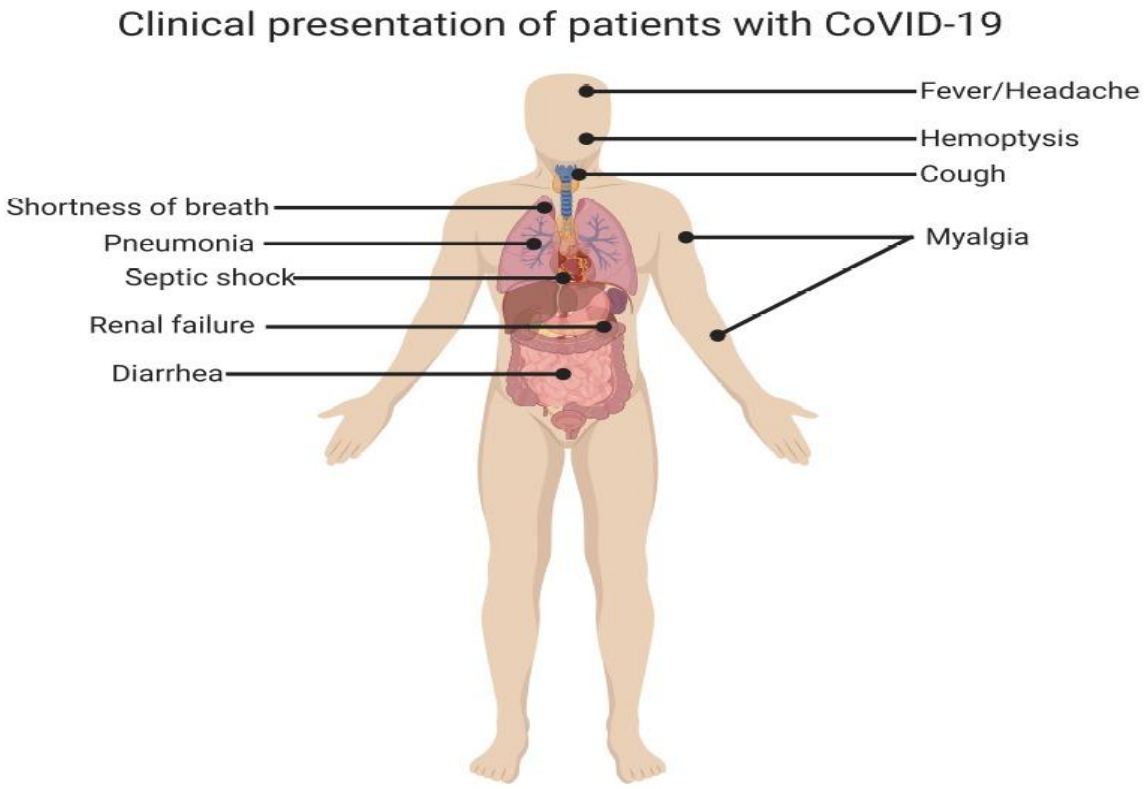


Figure 10: Clinical presentation of covid-19 patient.[21]

Table 3: World health organization on 11th feb. 2020.[31]

Country	Region	Deaths	Cases
Thailand	Asia	0	33
South Korea	Asia	0	28
Japan	Asia	0	26
China	Asia	1.017	42.708
Singapore	Asia	1	45
Hong Kong	Asia	0	42
Malaysia	Asia	0	18
Vietnam	Australia	0	15
Australia	Australia	0	15
Germany	Europe	0	16
France	Europe	0	11
United State	North America	0	13
United kingdom	Europe	0	8
Macao	Asia	0	10
United Arab Emirates	Asia	0	8

Laboratory diagnosis: Specimen Collection

For the diagnosis of corona virus nasopharyngeal swab and oropharyngeal (OP) swab, sputum, stool, urine, blood specimens are collected but NP and OP swaps are mostly used to diagnosis corona virus infection and stool ,urine are less used in the diagnosis. Because nasopharyngeal swab and oropharyngeal (OP) swab are easy to collect that's why it is used mostly in the diagnosis purpose. Bronchoscopy might be extremely difficult because it is too challenging and require well expert staff. Serum is another source for recognition of SARSCoV-2.

Respiratory specimens

A. Bronchial tube

Broncho alveolar lavage: collect 1-2ml of BAL into slobber collection cup which is impervious, and aseptic in nature.

Sputum

Firstly you should rinse the person's mouth. After that sputum should be collected in impervious, aseptic, and in the slobber collection cup or germ free water less ampule.

B. Upper tract

Collection of swabs

Nasopharyngeal and oropharyngeal swabs are mostly collected to diagnose presence of virus. Nasopharyngeal swab is collected from the nostril and oropharyngeal swab from the throat.

Don't use calcium alginate swab because as they will hold the substances which deactivate a no. of the viruses. *Nasopharyngeal swab:* Insert a swab into nostril, placed it over there for a while to absorb the secretions. Gradually take away the swab.

Oropharyngeal swab: Insert a swab into pharynx. Placed it over there for a while to absorb the secretions. Gradually take away the swab and accumulate 1-2 mL into a sterile, impervious germ-free water less ampule.

Second step in the diagnosis: Storage

Second step is to accumulate them in the cold conditions at 2-8°C for 3 days. Store them at -70°C or below.

If there is any delay in the process.

Safety from exposure to infectious agent's contemplations

If severe symptoms of infection are shown by the patients then it required carefully handling of sample, should be apply under the two situations until the sample is noninfectious by lysis or other manner. The seclusion of the virus shouldn't be consistently achieved Cell culture during this condition.

Cell Culture

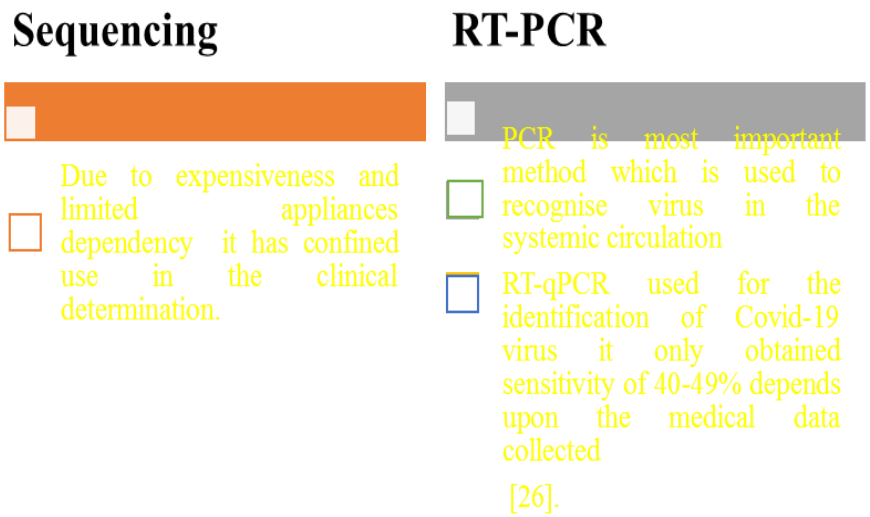
Separation of HCoV in cell culture isn't regularly performed because of the dearth of economical antisera. For pathogen separation is precarious to achieve or maintenance the occurrence of vaccines and therapeutic agents.

Rapid antigen tests

Rapid antigen tests will give satisfactory results with in short time but they undergo from poor sensitivity. It is an initial, fast, and modest technique used for identifying nucleocapsid protein. Antibodies are used which are effectively against to the novel strain of pathogenic corona virus. Sona Nanotech developed prompt-response, test to screen COVID-19 patients.[18]

Figure 11: Sona nanotech device.

Molecular Method



Biochemistry

Higher amount of procalciton is directly associate with higher infection although interferon-gamma is one of the most important factor which play significant role in the inhibition of synthesis of procalciton. Higher the calcitonin value may cause severe respiratory infection. During viral infection the concentration gets increased and cause severe superinfection. Further studies required.[18]

CT SCAN

Fig. 12: Normal lungs.[26]

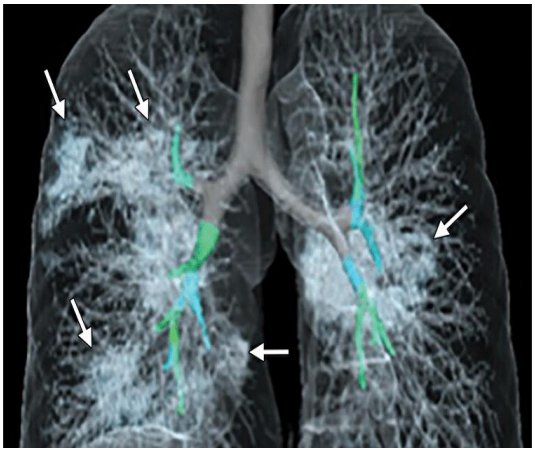


Fig. 13: Covid-19 infected lunges.[25]

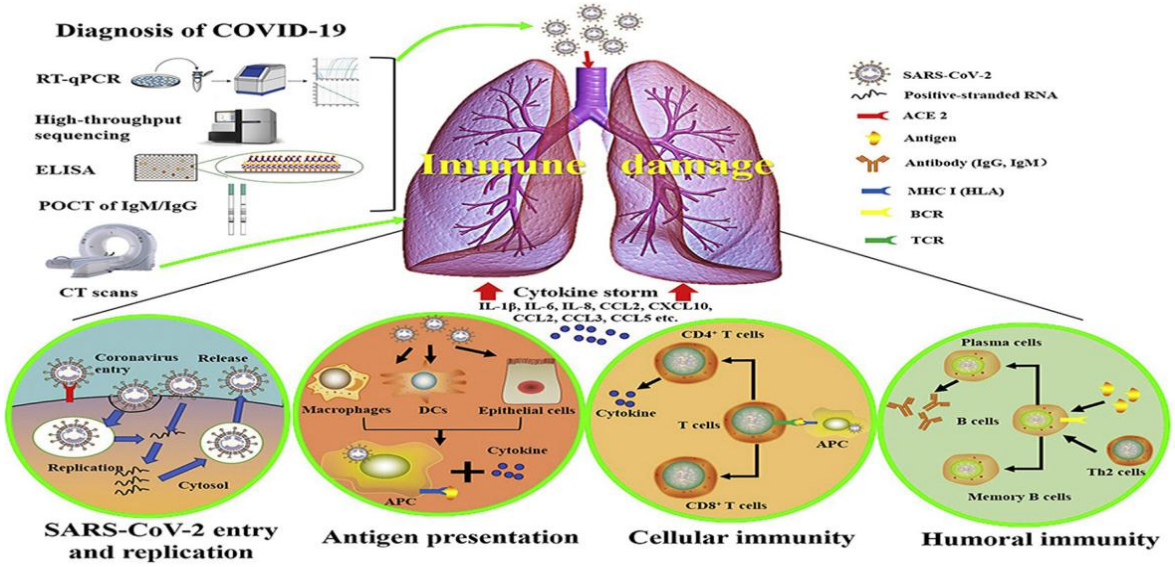


Fig. 14: Diagosis of covid-19 through RT-qPCR, high-throughput sequencing, elisa, & poct of IgM/IgG and CT scans.[23]

How ≥60% ethanol or water & soap can kill COVID-19?

Washing hands with water and soap that removes oils from our hands that can harbor microbes. Soap froth inhibited the lipid in the virus shell and lift the virus from surfaces and this is then washed off by water.

Alcohol is well-known to be capable to kill most germs.

Alcohol attacks and abolishes the envelope protein that surrounds coronaviruses. This protein is significant for a virus's existence and multiplication.[16]

Figure 15: How long is coronavirus detectable on surfaces?

Table 4: Cleaning options for different settings. S: suggested, O: optional.

	Healthcare setting	Non-healthcare setting	General settings
Surfaces	• Neutral detergent AND • Virucidal disinfectant OR • 0.05% sodium hypochlorite OR • 70% ethanol **[S]**	• Neutral detergent AND • Virucidal disinfectant OR • 0.05% sodium hypochlorite OR • 70% ethanol **[S]**	• Neutral detergent **[S]**
Toilets	• Virucidal disinfectant OR • 0.1% sodium hypochlorite **[S]**	• Virucidal disinfectant OR • 0.1% sodium hypochlorite **[S]**	• Virucidal disinfectant OR • 0.1% Sodium hypochlorite **[O]**
Textiles	• Hot-water cycle (90°C) AND • regular laundry detergent • alternative: lower temperature cycle + bleach or other laundry products **[S]**	• Hot-water cycle (90°C) AND • regular laundry detergent • alternative: lower temperature cycle + bleach or other laundry products **[S]**	n/a

Cleaning equipment	• Single-use disposable OR
	• Non-disposable disinfected with:
	  • Virucidal disinfectant OR
	  • 0.1% sodium hypochlorite
	[S]
		• Single-use disposable OR
		• Non-disposable disinfected with:
		  • Virucidal disinfectant OR
		  • 0.1% sodium hypochlorite
		[O]
			• Single-use disposable OR
			• Non-disposable cleaned at the end of cleaning session
			[S]

PPE for cleaning staff	• Surgical mask • Disposable long-sleeved water-resistant gown • Gloves • FFP2 or 3 when cleaning facilities where AGP have been performed **[S]**	• Surgical mask • Uniform and plastic apron • Gloves **[S]**	• Uniform • Gloves **[S]**
Waste management	• Infectious clinical waste category B (UN3291) **[S]**	• In a separate bag in the unsorted garbage **[S]**	• Unsorted garbage **[S]**

Treatment: Various treatment which are used for Covid-19 are given below:

Medical management medicines

For the safety and efficiency of patients there is no medication and vaccine entirely verified. But some of the vaccines and antibiotics are in the clinical trials so they can be used for treatment of Covid-19, eradicate the pathogens or to cure the patients.

Application of antibacterial drugs or glucocorticoid

The consequences exposed amalgamation comprising umifenovir can expressively truncate the undesirable effect and there is no benefits when consuming the mentioned potential medications. We should cautiously express the dosage schedule meticulously to observer efficiency or to evade side effects.

Convalescent plasma therapy

Convalescent plasma therapy can be tried to treat the victims have prompt, severe and perilous ailment development. Therapy operates a certain virus particular antibodies are used to treat the individuals that are suspected from the covid-19. This therapy include usage of plasma which contain antibodies and that antibodies have highly protected in nature or they fight against the virus present in blood or help body to obtain active immunity or get rid of from this ailment by eradicate pathogens. This technique is an emphatic treatment which has been efficaciously utilized H1N1 influenza. Various principles can be followed by the convalescent plasma therapy the first principle that the course of disease doesn't exceed more than 21days.

Improvements in immunization

Meanwhile booster expansion progression includes events for instance scientist are doing medical investigation, animal experiments, isolation of strains and also doing vitro experiments. The whole process is time consuming so its takes time for looking up things. The Ministry of Science and Technology has prepared national key elements to convey combined study, organized practical ways, for improvement in immunization.

Improvement of medical investigation used for management

The medicines in medical trials generally contain out dated Chinese medicine (TCM) interventions (including 64 items), and antiviral drugs (having 40 items), then immunotherapy drugs and various other drugs are used for the treatment of SARS-CoV-2, like hydroxychloroquine, favipiravir and medical investigation of remdesivir, which has maximum therapeutic effect against COVID-19.

Precautions: To control spread of virus people who have suspicion to covid-19 and initial symptoms which are appeared to patients they should be quarantine or separated. Individuals who had public connection they must be monitored with the help of medical teams.

Pharmacy activities

Pharmacy progressions and services: safeguarding protection and steadiness of service Due to the SARS-CoV-2 or pandemic, they are not declare usual initial time in the absence of squad. Novel working time must interconnected to community.

Patient service: Through distribution of medicines, connection with patients must reduce. Patients shouldn't go in the pharmacy and druggists are recommended to utilize suitable distinct defensive equipment, where it is desired in command to evade attention of individuals.

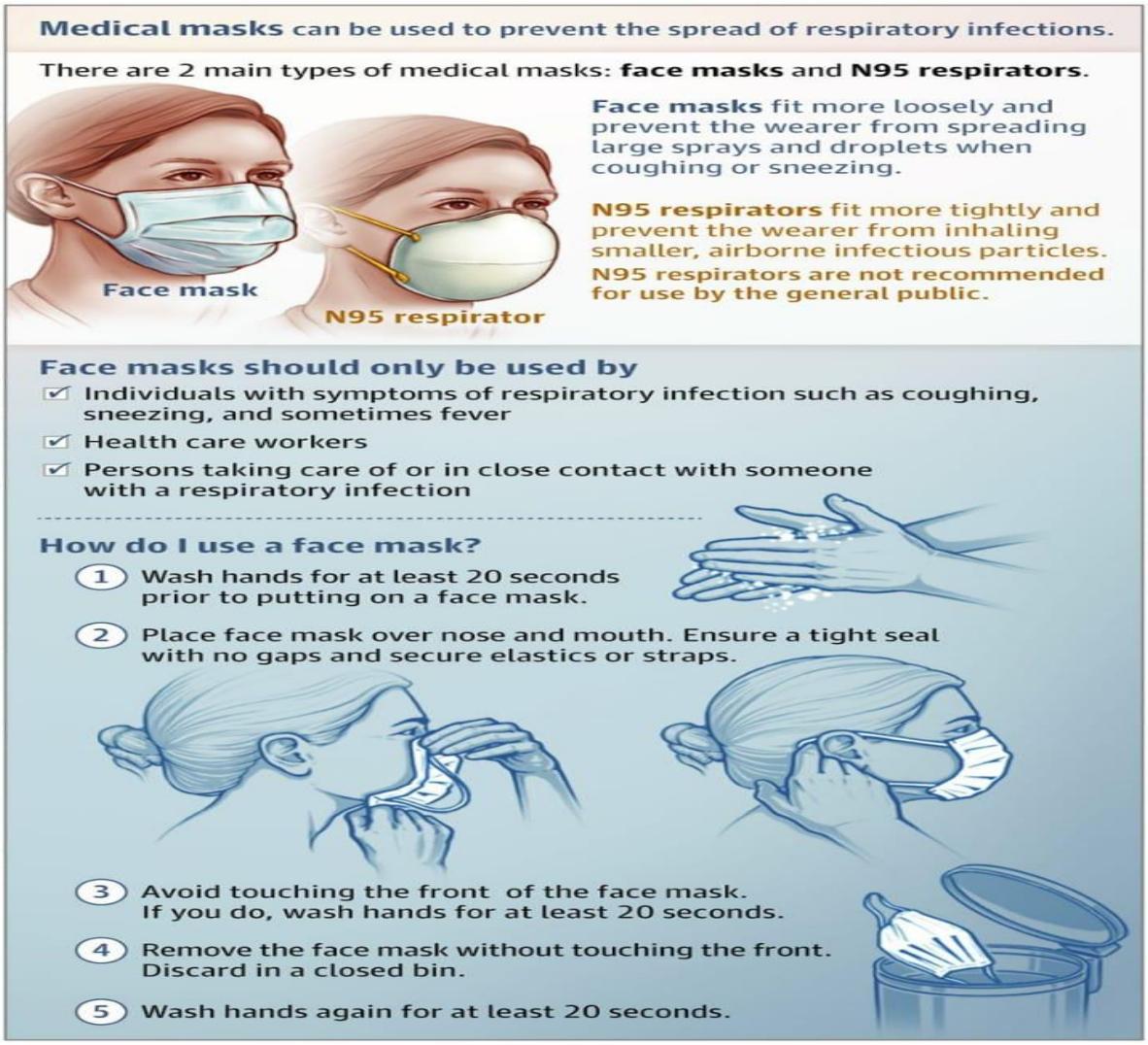


Figure 16: Types of medical mask.

Respirational protections

- Before entry into the patient room, wear respirational masks.
- Non reusable respirators must be abolish.
- Do hand sanitation after removal of respirator.

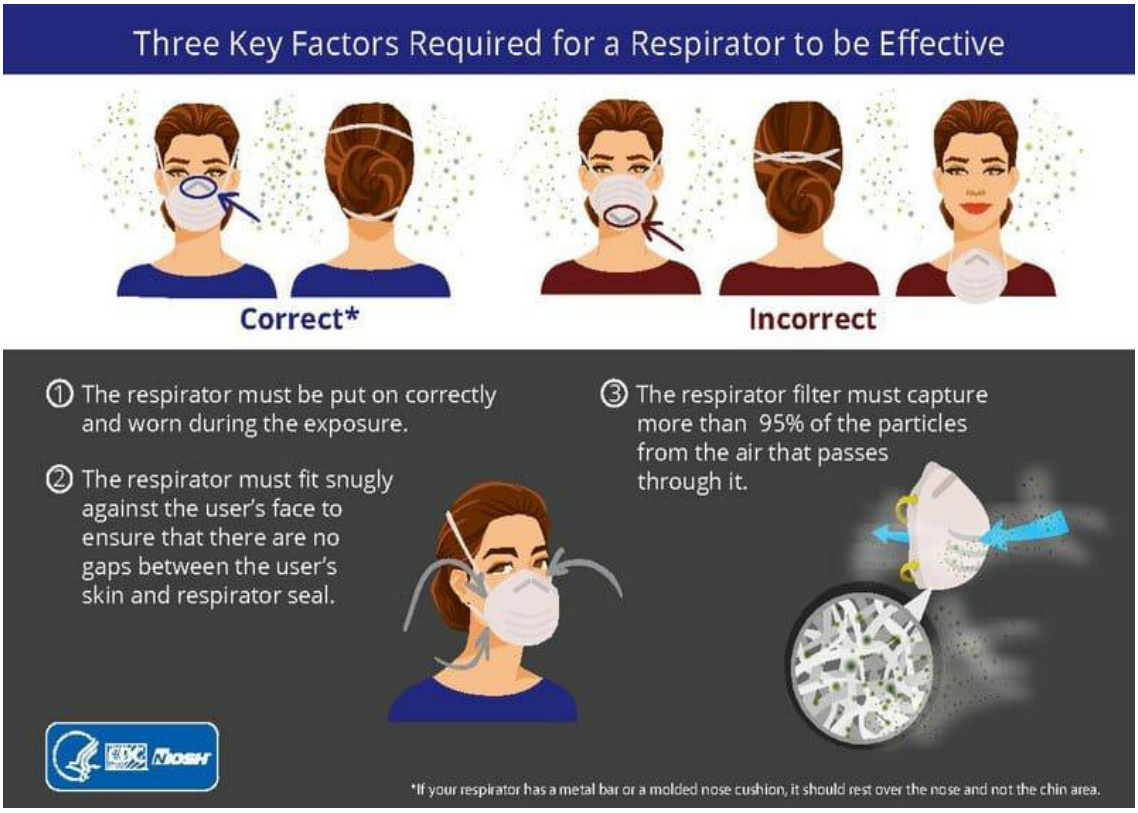


Fig. 17: Key factors required for respirator to be effective.

Endorsement used for casualty care

The steps we have to take for septicity inhibition or to minimize, the ordinary defenses must realistic in all medical management services, counting ambulatory maintenance. The numerous steps must be embrace • Initial cognizance; • Importance of sanitation, respirational asepsis, respirational indications about the usage of masks; • prioritization, maintenance for indicative victim; • There must be distinct waiting area when the indicative patients are required to wait Educate each person about the initial recognition of signs, and precautions must be taken.[24]

CONCLUSION

COVID-19 is a pandemic disease as reported by WHO on 11th March, 2020 which is spreading with unpredictable speed of transmission in early 2020 and marked its name as headlines all over the world. There is no specific vaccine available for the disease. United

States is the most affected country. For some people it's not initially cause any symptoms. Handwashing is the key to get rid from this virus, others are social distancing, self-quarantine, using sanitizer, avoid crowdie place, stay at least 2 meters away from people, good hygiene to prevent virus transmission. The study underlines the preventive measure of corona virus infection. Also the study in torch different ways of identification and treatment of Covid-19 infection.

CONSENT FOR PUBLICATION

Not Applicable.

CONFLICTS OF INTEREST

Do not have any Conflicts of Interest.

ACKNOWLEDGEMENTS

Declared none.

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