A Review of The Progress of COVID-19 Vaccine Development

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Abstract- ***A coronavirus disease pandemic (COVID-19) is still a global problem with not sufficient evidence of a declining pattern caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It is generally accepted that normal life is impeded by securing a reliable vaccine strategy. Many countries have accelerated the process of clinical trials to create effective treatment with COVID-19. More than 200 candidate vaccines have been started for SARS-CoV-2 testing. This review attempts to provide an overview of the currently emerging COVID-19 vaccine types, address the theoretical and practical challenges of vaccines for COVID-19 and discuss possible strategies to help vaccine design succeed. The first move was to take out papers using the initial keyword "pandemics, vaccines and vaccine types". A total of 63,538 results (including 1,200 journals; 16,875 books; and 12,871 web pages), with the initial keyword, searched for in the Scopus database. Further improvements were searched on keywords such as "pandemic and vaccine types" (711 newspapers and 5,053 webpages). This review attempts to overview the historical and important basic information about the pandemics viz. history, virological characteristics, structure, origin and physio-chemical properties. The second phase includes the vaccination types and strategies in depth. It includes the diagnosis, virology and pathogenesis of SARS-CoV-2 and SARS-COV-2/COVID-19 vaccines. The development, planning strategies, types, cost and current scenarios of COVID-19 vaccines are depicted in detail.***

I. INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has a place in a family of coronaviruses, which is a family known as zoonotic infections, and which sorts betacoronavir and is closely associated with two other infections, including severe acute respiratory syndrome Coronavirus (SARS-CoV) and the Middle East respiratory syndrome coronavirus (MERS-CoV). It should be cover in an icosahedral shell of protein. The surface has different club-shaped spikes; the electron microscopy (EM) reveals a sun-faced crown. The surrounding virus contains a lipid bilayer in which auxiliary proteins are protected for layer (M), envelope (E) and spike (S). Both coronaviruses are Used as receptors of cellular passage by angiotensin converting protein. In any event, the propensity of SARSCoV-2 to join these receptors is far higher, and it has strong infectivity (1). The various variants of the coronavirus disease 2019 (COVID-19) virus circulate around the world:

The United Kingdom (UK) has reported the B.1.1.7 strain with a large number of mutations in the fall of 2020. This version is simpler and quicker to spread than other variants. Experts in the UK stated in January 2021 that the risk of this variant was higher than the other variant viruses, but more studies are needed to confirm it. In several countries around the world, it has since been identified. This version was first observed in the United States in late December 2020. Another edition named B.1.351 appeared in South Africa separately from B.1.1.7. B.1.351 shares

certain mutations with B.1.1.7 originally detected in early October 2020 (2). At the end of January 2021, cases arising from this variant were registered in the USA. A P.1 variant, first observed in Brazilian travellers who had routine check-ups checked on an airport in Japan in early January, was established in Brazil. This modification includes a variety of other mutations, which can impact the ability of antibodies to be recognised. In the USA, at the end of January 2021, this variant was first observed (3).

II. NEED FOR CORONAVIRUS VACCINE

The active sedation against infection or the subsequent infection was severely examined and no operators were moved further. There have been several medications, primarily hydro-xychloroquine and resuscitation advocated as frenetic steps to tackle COVID-19 on the basis of a vast number of preparatory, contradictory and ambiguous studies. These and other medicines can save lives but do not shut their doors to regularity in the expressed turmoil of the pandemic. It brings us, as it was, to a particular option of a successful and stable antibody, which must be rendered as long as all nations and communities influenced by the widespread at fair prices may conceive and accessible (1). Vaccination may build an insensitivity of the crowd inside a society that can decrease the disease incidence, minimise square transmission and reduce the social and financial impact of the disease. Except for a widespread vaccine scope, an auxiliary contamination wave can be prevented, and frequent endemic disease revolutions can be regulated. Finally, the disease could be murdered, as it was in many other illnesses with a higher potential to cause pandemics such as smallpox, poliomyelitis, etc. than COVID-19 (2)

III. HISTORY OF VACCINES FOR CORONAVIRUSES

A single-stranded po fictively receptive RNA genome is encircled by coronaviruses, which have an expansive (30+kb), helical nucleocapsid (N) and an exterior surface consisting of a protein grid M, a protein E or S proteins (3 The S protein, usually trimeric, includes the space for the receptor retention (RBD) that can officially be converted into the angiotensin over the protein 2 (ACE2) and into the cell (Figure 1). S protein has been shown to elicit a neutralising counteracting agent in SARS-CoV, all of the essential proteins, and maybe a main vaccine antigen target (4). The progression of coronavirus immunisations has been verified with issues. In the animal models that mimic human disease, coronavirus antibodies were immunogenic and it mostly ineffective in preventing infection securing. There is fear; however, that inoculation might not be practicable for long-lived insusceptibility, as with a typical corona viral illness, and reinfection may be conceivable. Improvement of illness linked to immunisation in several cases. Former usage of certain animal models of corona viral antibodies (SARS-CoV and MERS-CoV) posed protection issues with Th2, and immunopathology interfered. Two days after the SARS-CoV challenge was not found in the lungs of threatened non-vaccinated mice, mice vaccinated with two inactivated whole infection antibodies, recombinant DNA spicy protein immunisations or viral molecule vaccines produced a lung pathology counting eosinophilic

IV. VIROLOGICAL CHARACTERISTICS OF SARS-CoV-2

The causative pathogen of COVID-19 is SARS-CoV-2, with the coronaries family as its place. Near after other β-CoVs, the ~3-kb genome-estimated SARS-CoV-2 vision comprises a nucleocapsid of genomic RNA and the nucleocapsid phosphorylated (N) protein (8). Nucleocapsids are inserted in bilayers of phospholipids and enclosed in the two separate kinds of spiking proteins: spoken glycoprotein-trimmers demonstrate in both CoVs. The S protein plays an important function in receptor authority and it's the gateway to the determination of tropism and transmitting capability (Figure 2). On the side of the viral envelope, the lattice protein (M) is located within the viral envelope. Genome analysis showed that SARS-CoV-2 comprises 5 and 3 terminal groupings with a quality structure 5 -free screen perusing (ORF).Particles of the infection are 60-100 nm long and spherical or oval (9). It may be inactivated or warmed at 56 °C for 30 minutes by light and touches much of the disinfectants (i.e. ether, 75% ethanol, per acetic, chlorine and chloroform) (10). Collection of evidence indicates that SARS-CoV-2 is comparable to the human cell receptor SARS-CoV-2 (ACE2),

whereas the pivotal dipeptidyl peptidase-4 pivotal MERS-CoV is similar to the cell-section. Collection of the data ACE2 can be a kind of film I protein, mostly linked to cardiovascular infections, communicated within lungs, hearts, kidneys and digestion tracts. Later analysis of the cryogenic electron microscope structure of the SARS-CoV-2 S protein showed that ACE2 is approximately 10 to 20 times more official than SARS-CoV.

V. STRUCTURE AND ORIGIN OF CORONAVIRUS

Coronavirus is a packaged infection, and RNA belongs to the Coronaries family, the Coronaries family, and organise Noroviruses, with one stranded, non-segmented and positive sensory infections. The coronavirus genome estimate is approximately 26-32 kb and is the major recognised RNA infection genome. Its dimensions vary from a gap of 60 nm to 140 nm through club estimates of the spike (Figure 1). Beneath the lens, the spike appears like a coronavirus (12). Helically symmetrically, coronavirus has nucleocapsid, which is unusual in positive sensory RNA infections. The subfamily, which is phylogic, comprises of four genera: alpha-CoV, beta coronavirus (β-CoV), gamma-CoV and delta coronavirus (μ-CoV). This is a genetic part of the Coronavirus. α-CoV and β-CoV normally causes human air problems, whereas μ-CoV and μ-CoV deflect mammals.

VI. TRANSMISSION

In December 2019 in Wuhan, Hubei Province, China, a novel β-coronavirus was to start. The third plague of the twenty-first century, now exceeding SARS and MERS, in China. Right now, an immense amount of pneumonia patients who were subjected to fish ads were detailed, which may be a centre for many live creature organisms. The entire COVID-19 genome groups were dumped into an open database in 10 January 2020 and noticed that there is a certain similarity to SARS. The International Scientific Categorisation Committee for Infections 2019-nCoV was renamed as SARS-CoV-2. The inherited COVID-19 arrangement reveals about 80% similarity to the Serco and 50% proximity to the MERS-CoV (14). A detailed analysis of phylogenetic has shown that the COVID-19 belongs to the family of beta-coronavirus. The receptor authorship is the key stage in viral disease after cell fusion. It is known that the interactions between

VII. SYMPTOMS AND DIAGNOSIS

Fever, hacking and exhaustion are typical side effects of this infection. A few patients may have defining signs such as throbbing, nasal blockage, sputum generation, haemoptysis, nose running, a sore jaw, loose bowels, lymphedema and dyspnoea. Following hatching, the signs turn up for around 5.2 days (16). The duration from coronavirus disease starting to death differs between 6 and 41 days, with an intermediate of 14 days. Patient vulnerability and age depend on the time of infection. In patients >70 years of age, the duration of diseases is shorter than those below 70 years of age. Chest CT philtres shown as pneumonia, intensive reflex sympathetic dystrophy (RSD), extreme renal injury, heart hurt and, indeed, passing can occur in serious cases clinical characteristics shown as Chest CT philtres. Numerous ground glass turbulence observed in a few patients in the sub pleural location of the lungs, which triggered both localised and healthy reactions leading to inflammation cobras SARS-CoV-2 Qualitative assay for use on the cobras 6800/8800 Systems Roche Molecular Systems, Inc.Primerdesign Ltd COVID-19 genesis Real-Time PCR assay Primer design Layabout Real-time SARSCoV-2 Abbott Molecular Inc. PerkinElmer® SARS-CoV-2 Real-time RT-PCR Assay PerkinElmer Inc. Real-time fluorescent RT-PCR kit for detecting 2019-nCoV BGI Europe A/Detection Kit for 2019 Novel Coronavirus (2019-nCoV) RNA (PCR-Fluorescence Probing) Da An Gene Co., Ltd. Of Sun Yassin University Real Star SARS-CoV-2 RT-PCR kit 1.0 Altoona Diagnostics Pathos Detect MY LAB Allele 2019-nCoV assay See gene nCoV Real-Time Detection kit SD BiosensorTRUPCR SARS-CoV-2RT-qPCR kit version 2 KILPEST (BLACKBIO) Quantiles CoVs detection KIT Veer 2.0 Howell Lifesciences Pt. Ltd. Taman 2019-nCoV Control Kit v1 ABI (Applied bio systems)BIO COVID ID/ COVID-19 qualitative PCR detection Kit version 2 Bio genomics (India)qSARS-CoV-2 IgG/IgM Rapid Test Cellex, Inc. Quest SARS-CoV-2 rate-PCR Quest Diagnostics Infectious Disease, Inc. Overwhelm COVID-19 Test Home

Collection Kit Eyelevel, Inc.COVID-19 RT-PCR Test Laboratory Corporation of America (LabCorp)Panther Fusion SARS-CoV-2 Assay Logic, Inc. Towpaths COVID-19 Combo Kit Thermos Fisher Scientific, Inc.

VIII. CLINICAL FEATURES AND SUSCEPTIBILITY

Persons of any age level would not be allowed to utilise COVID-19. Indications during the normal flu (Flu), include fever, hack, an ailment of the mouth, migraine, tiredness, myalgia, smell and taste misfortune and dyspnoea. In asymptomatic or mellow infections up to 80 % of the cases have (21). Simple co-morbidities in a few patients may help to exacerbate the illness, influenza, intensive respiratory diseases (ARDS) and multigrain fractures, and in a long-term, fatal at the end of the primary

IX. PHYSICOCHEMICAL PROPERTIES

SARS-CoV-2 can be practical on surfaces like the sodium hypochlorite, hydrogen peroxide, dialyze ether, 75% ethanol, chlorine etc. on surfaces of plastic and stainless steel up to 72 h under positive environment conditions but is prone to the most typical disinfectant compounds. The cleanser has also been seen to work as the lipid bilayer of the bacteria breaks down promptly. Moreover, UV inactivating or warming at 60 °C for 30 min can be achieved for SARS-CoV-2 (22)

X. DIAGNOSIS AND PATHOGENESIS OF SARS-CoV-2

The quick and accurate conclusion of COVID-19 is critical for managing the outbreaks in populations and centres of healing (23). The ideal demonstration research for CoVs was carried out with developments such as polymerase chain response (PCR), reverse-transcription polymerase chains (RT-PCR), Real-Time RT-PCR (rate-PCR), invert translation isothermal loop controlled change (RT-Light). PCR testing has been performed to date on the leading edge of SARS-CoV-2. As the gold standard used to identify the disease source, PCR prevails that the requisite preliminary steps will normally be generated easily until the virus system is established (Figure 4). Prior to the identification of the virus long time earlier, WHO initiated and disseminated in January 2020, the key quantitative RT-PCR steps to classify SARS-CoV-2. This evaluation convention was complex, costly and is basically ideal for broad centralised demonstrative testing facilities. All of this is taken into consideration. With regard to the demonstrative standards currently identified by the China National Wellness Board, the standardised COVID-19 evaluation has matured nasopharyngeal and oropharyngeal swab studies. Three new RT-PCR experiments were added, with slightly fewer in vitro discovery maximum, based on the polymerase of RNA (Drip)/helicase (Hel), nucleocapsid and SARS-CoV-2 spike qualities (Rider). In conjunction with the one-step RT-PCR framework, the SARS-Cove E consistency discovery is popular. The PCR E-Quality was fine for SARS-CoV-2 disease diagnosis, while the Drape Convention was accepted as positive

XI. DIAGNOSTIC TESTING FOR COVID-19

Strictly speaking, a new FDA-licensed COVID-19 procedure has already been developed using Abbott ID. Presently, this diagnostic process will be delivered, all in order to try to draw a verdict in reasonably five minutes. As SARS-CoV-2 efficiency results can result in untrue negative effects, counteracting agent discovery may be accompanied in particular by enhancing the screening of asymptomatic individuals. Clinically, in any event with unfavourable RT-PCR findings, the assessment of the disorder COVID-19 should be carried out with ordinary chest computerised Tomography (CT) properties for those who are late suffering from headache, weariness, sore throat, hacking, or dyspnoea due to introduction. Most instances showing the two-sided transmitting of sketchy shadows and dark glass, often with a ring shape, and a lunge conveyance, reveal comparable characteristics on the CT images (24).

XII. PATHOGENESIS OF SARS-COV-2

For SARS-CoV-2 transmissions, an effective viral Replication in the mucosal epithet of the upper respiratory tract is required to occur and promotes proliferation of the lower respiratory tube and gastrointestinal mucinous membranes, triggering mother vermeil. Exceptionally, few pathogens are under surveillance at this stage and remain

asymptomatic. Moreover, a variety of patients may be impacted by non-respiratory side effects (i.e. extreme cardiac and liver injury, deception of the kidney, runs). Since ACE2 is extensively distributed through the nasal mucosa, bronchus, lunge, cardiovascular and kidney, and so on, SARS-CoV-2 is defenceless in various human organs. In particular, S protein plays a key role in evaluating the cell tropism and consequently, the transmission of SARS-CoV-2 interspecies as it has the effect of infection in a cellular receptor. The spike protein would catalyse the viral combination handle, enabling the viral genome to reach the cytoplasm, after the receptor's official location. The division of S into subunits, regarded as planning, is a prerequisite for this technique (Figure 3). Hoffmann et al.'s study has unmasked the usage of the ACE2 receptor for transient and the TMPRSS2 serine protease for S protein preparation by SarS-CoV-2. TMPRSS2 supported inhibitors for therapeutic usage will then position the entrance to offer an alternative to simple therapy. The fact that S will easily be able to get unused protease cleavage premises, as well as the fact that multiple proteases can conduct the same role, indicates that this disorder will effectively be modified to replicate in a few cell species (26). The SARS-CoV-2 and SARS-CoV-CoV CoV (RBD), which had been detailed beforehand as incapable of transacting with S protein, includes apparent antigens errors between SARS-CoV-2 and SARS-CoV, were all murine monoclonal Antikeros (mob's) and polyclonal antibodies (pub's). The main neurotic study of severe COVID-19, based on neurotic analysis discoveries, indicates that cellular fibromyxoid exudates induced diffuse alveolar harm on both sides of the lung (27). The right lung revealed a fascinating arrangement of the hyaline and lung shedding and ARDS recommendation. In comparison, pneumonic oedema and the hyaline layer arrangement tended to clean away lung tissue, which indicates early ARDS. Lymphocytes have overwhelmed, in both lungs, interstitial Mononuclear Explosive Infiltrate. Another thought about how the passage of COVID-19 disease may often contribute to severe kidney damage and proteinuria.

XIII. CRUCIAL SARS-CoV-2 TARGETS FOR NOVEL

- DRUG DEVELOPMENT

The schematic of SARS-CoV-2's virology as well as the broad-reaching possible danger tools provide the foundation for care and expectation in particular. In the statistic, there is a general interpretation of immediate deadlines for sedate revelation. 6.-6. Inside the virus-cell receptor transaction, the part of the surface auxiliary S is of particular intrigue for antiviral development. S1 subunit mob's and S2-focused inhibitors are likely to have in vitro or in vivo capacities for anti-SARS-CoV-2. As ACE2 is essential to use for SARS-CoV-2 receptors, mob's or atoms that depend on their receptors are viable in deciding pathogenesis against SARS-CoV-2 medicines, as long as they do not provide inspiration to immunologic effects on the animal models (29). The test was subsequently performed at a protein binding site COVID-19 S to the cell-surface receptor. The effects of their observations showed a more desirable position between the official S-protein districts III and IV and GRP78. The most tractive drive for the official GRP78 is locale IV, which can be used to schedule preventive action against this infection (30). It was noticed that, notwithstanding the fact that protease inhibitors which have a combined Prime S antiviral activity, several inhibitors are important because S may use a variety of proteases in the preparation of this product. If they develop, prospective care applicants will be operators focused primarily on the well-preserved S2 subunit. The expansive polyproteins 1a (pp1a) and pp1ab encoded by the ORF1a / b are subjected to two viral proteases, papain like protease (PL professional) and cleavage 3C protease (M master), for a non-substantive protein produced by viral translation and replication (Figure. 3) (31). (SARSCoV-2)

- SARS-CoV-2/COVID-19 VACCINES

Creating and scaling up mass immunisation production in a global context rapidly and broadly is difficult because, in comparison to a typical decade of successive planning in the process of preclinical trials, phases of clinical trials, arranged generation and dispersion, multiple practices need to be well organised and conducted at once. These problems contribute to a build-up of savings and a lifting of monetary opportunities. Delayed immunisation will lead to the episodes of amassing death and dreariness, as defined by the 2013/14 Western African Ebola flag that killed more than 11,000 people at the expense of over $53 B. Appallingly, the antibody was advanced

and was then proved feasible in Ebola protection which could have related to episode management (35). Tragically, the 2003 SARS plague has just ended a phase of progression of antibodies. It is frustrating that at that time, subsidising organisations moved shops that were dedicated to advance immunisations, disturbed suppliers and re-established other immunisation programs. The 2017 merger of pesticide readiness creative initiatives (CEPI) was planned to resolve previous disappointments in an effort to build smoother reactions to irresistible infection hazards in order to ensure the progression of immunisation and the early reaction of scourges (36). Different characteristics of phases of invention one technique was used for solving street squares in order to further advance immunisation (37). Immunisations approved for individuals typically include live constriction infections (for example, measles, mumps, rubella), protein or polysaccharide conjugated subunits (protein: a cellular pertussis; hepatitis B; pneumococcus, meningococcal), polysaccharide conjugated with viruses. A collection of unused technological platforms was developed in the last decade, combining anticorrosive (DNA and RNA) nuclear antibodies and viral vectors as well as recombinant patient

XIV. DEVELOPING COVID-19 VACCINES

- Stages of Vaccine Development

Every modern vaccine is conducted following a strict Investigate and Advancement convention that has to be taken rapidly and recently completed and has been approved (Figure 3). The rules on improving anticuerpos are more restrictive than the rules on drug creation, which are relevant in clinical evaluation, are provided by administrative specialists directly WHO, US Sedate & Diet Organisations, the European Solutions Organisation and national specialists from various countries (38). This should be apparent because antimicrobials are used globally, have tremendous demographic potential and are distributed to stable communities, including infants, elderly and pregnant moms.

- A Race against Time

Due to certain truths, almost antibody progress is dazzling. Immunisation from exploratory agreements to exhibiting can be a long task that typically requires 5 to 10 y. For COVID-19, the usage of innovative technologies to establish candidate antibody (preclinical arrangements) and swift permission by regulatory institutions for clinical trials has greatly compressed this time. This period of immunisation. It took 42 d from community monitoring of the infection to form an unexploited immunisation period (mRNA-1273) at the cGMP office of Modern Inc. (the American biotech corporation located in Cambridge, Massachusetts). It would have taken typically more than two long stages to produce such a vaccine without stage invitation

- Success Rate

The moment that requires to be considered is the pace of development of immunisation from authorisation for clinical studies to authorise. In the years 2000-2010 period, the rate was consistently < 10%. One of the 37 antibodies developed for Ebola, as one was approved depending on viability and protection within the step II research, is a 2015 study that indicates only 20 % of therapeutic immunisation tests vary from stage I to licence. In the immunising scene of COVID-19 examiners introduced untapped, nuclear corrosive technology-based vaccines. Such advancement in immunisation against irresistible diseases is no scientific procedure, and specialists recognise the effective rate of an approved urgent immunisation of 5% (39).

- Costs

It must be considered, too, that progression to immunisation will entail a high risk. Apart from a rivalry between other large suppliers of antibodies, it has been considered to be worth more than1 M USD to establish a single untreated immunisation against an irresistible infection. The Figure 1 includes deserted antibodies in readiness for improvement. A few institutional and non-governmental organisations here have upheld the teaching of sufficient stores in the light of the human tragedy and worldwide extinction. Coalition for Scourge Preparation Advances (CEPI) will be an organisation that takes the donations of free investigative projects to build antibodies to evolving unstoppable pathogens through transparent, private, cogitative and respectful organisations in society. The US Government decided to offer 483 M USD to Modern Inc. to produce the vaccine COVID-19.61 The Canadian Government started the CAD 1.3 B in

improving immunisation financing to investigate the advancement and improve it is now using in its 2022.62 stage technology - a Game changer breakthrough. Conventional biotechnology techniques have been used to generate the nominee antibodies throughout the year. As it took between 2 and 5 y for a model ant corps to be developed and some vaccinations were prohibited. The accessibility of bleeding-edge investigations into offices was essential for the enticing expert to be included, which could be conceived of as it was in just a few testing facilities worldwide.

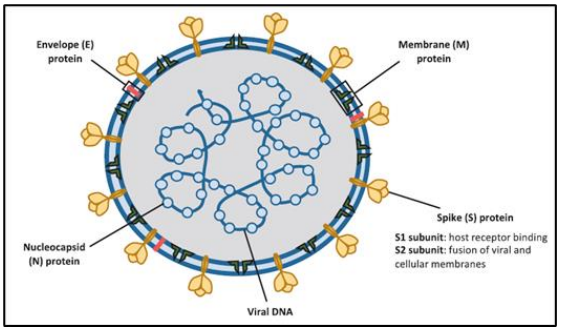

Figure 1. Schematic of the structure of SARS-CoV-2

Rehashed dosages and adjuvants to boost insensitivity. In such vaccines, ADE has been detailed and to prevent this, the arrangement of epitopes on the antigen surface should be controlled during inactivation. Poliomyelitis (IPV), HAV, rabies, etc., are illustrations of such ant corps. The new anticorrosive made available by cutting-edge advances are the nucleic corrosive antibodies. Incorporations of DNA that encode a pathogen into plasmid DNA are the foundation for DNA immunisation. RNA antibodies use SARS-CoV-2 lipid-coated mRNA that transmits Spike protein. The proteins are displayed from CD + 8 T cells BY MHC course I and activating a solid T cell response. These antiporters are healthy, simple to produce by stage advancement, and are likely to improve immunisations for the future. No nucleic acid vaccines are presently licenced in clinical practice. Recombinant vector infection vaccines are developed by the invention of recombinant DNA. The DNA is integrated into the cells and then filtered (42). In the process of the vaccine, the vector duplicates and alongside, the embedded DNA is communicated and generated, which produces a robust T cell and B cell-resilient reaction. It often involves the usage of DNA as microbes or infection vector. Microscopic species like E can be vectors. Coli, Adenovirus or poxvirus diseases. Coli. Standard vector anti-corps examples are HBV, HPV, Hiba and Meningococcal. Antibodies consisting of antigenic decontaminated peptides from pathogens such as SARSCoV-2 Spike Protein are healthy to use. Such antigen is expressed directly at the MCH Lecture II and does not routinely induce a significant cytotoxic T cell reaction. These vaccines need revived dose and tolerance adjuvants. Virus-like particles are composed of inherited tissue free purge infection particles. These vaccinations are healthy and immunogenic, which are difficult to produce in any event

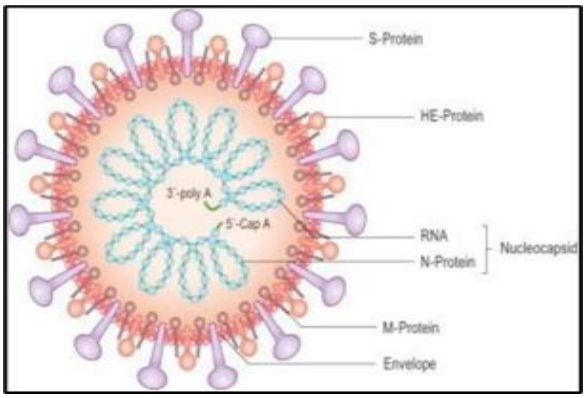

Figure 3. Skeleton of coronavirus; inside and outside

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