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Review Article

A basic insight into COVID-19 vaccines: an overview

Sarfaraz Alam Khan[1]*, Nazeem Ishrat Siddiqui[2]

[1]Department of Pharmacology, Chhindwara Institute of Medical Sciences, Chhindwara, Madhya Pradesh, India
[2]Department of Physiology, Government Medical College, Khandwa, Madhya Pradesh, India

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***Correspondence:**
Dr. Sarfaraz Alam Khan,
Email: emailsarfaraz74@gmail.com

ABSTRACT

Atypical serious respiratory illnesses were reported in December 2019 from Wuhan, a city of China, which later spread to other places rapidly and became a global pandemic. Soon it was discovered to be caused by a novel corona virus, named as the severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) and the disease caused by it as corona virus disease-19 (COVID-19). Since COVID-19 is a new viral disease, world is still struggling to find out a permanent remedy to overcome this serious health problem. Developing safe and effective vaccine against SARS-CoV-2 has become the only way forward to tackle it. Various vaccines have been developed and are approved for mass vaccination on emergency basis. Both classical and next generation vaccine platforms are being used to develop COVID-19 vaccine. It seems interesting to have a look on the various types of vaccines and get an insight into them so that we can get familiarize with the COVID-19 vaccination.

Keywords: COVID-19, COVID-19 vaccine, SARS-CoV-19

INTRODUCTION

COVID-19, a global pandemic, which is caused by the zoonotic virus called as serious acute respiratory syndrome corona virus 2 (SARS-CoV-2). It was first reported in Wuhan, China in December 2019.[1-3] It has caused serious respiratory disease and significant mortality throughout the world.[4]

Strict compliance to COVID appropriate behaviour has played very important role in containing the spread of infection. Despite that Infections are being spread across the world and posing serious challenges to existing health care services and society at large. Further, there is no definitive treatment for the COVID-19 so far. In the emerging scenario developing safe and effective vaccine against SARS-CoV-2 has become the only way forward to tackle this serious health problem.

Vaccine development has been going on war footing since the time epidemic started. Various vaccines have been introduced in the market on emergency basis after regulatory approval and many more are under development. Both classical and next generation platforms have been used in developing COVID-19 vaccine. It seems imperative to have a look on the various types of vaccines and get a pathophysiological insight into them so that we can get familiarize with the COVID-19 vaccination.

In this review, we discuss in brief the biology and pathophysiology of SARS-CoV-2. We also discuss the various types of vaccines being developed for COVID-19 vaccination which are listed by World Health Organization (WHO) and are available for mass vaccination.

SARS-COV-2 BIOLOGY AND PATHOPHYSIOLOGY

Human SARS-CoV-2 comes from family corona viridae and the superfamily orthocoronavirinae.[5] SARS-CoV-2 is a single stranded RNA virus. It has 79% genetic similarity with SARS-Co V and about 50% similarity with MERS

CoV (middle east respiratory syndrome coronavirus). Phytogenetic analysis has shown its close similarity (88%) with corona viruses occurring in bats.[6] The genetic elements of SARS-CoV-2 include proteins, lipids, polysaccharides and nucleic acids. The whole cell antigens are employed for developing killed and live attenuated vaccines.[7] Major structural proteins of SARS-CoV-2 are spike protein (S), nucleocapsid protein (N), membrane glycoprotein (M) and envelop protein (E) (Figure 1).[8,9]

The spike protein is a surface fusion glycoprotein which is involved in mediating virus entry inside the human cells through angiotensin converting enzyme-2 (ACE-2) receptor.[10] The S protein consists of two subunit S1 and S2. The S1 subnit has two domains which include C-terminal domain (CTD) and N-terminal domain (NTD). This is receptor binding domain (RBD). The S2 subunit is involved in facilitating fusion of virus and host cell (Figure 1).[9]

After entering the host cell, virus replicates and passes to the lower respiratory tract leading to severe pneumonia. The gateway to host cell entry (magnified view) is via angiotensin converting enzyme 2 (ACE 2) interactions with cleavage of spike in the perfusion state by proteases TMPRSS-2/furin.[11,12] Life cycle of virus and potential immune response is depicted in Figure 2.[13]

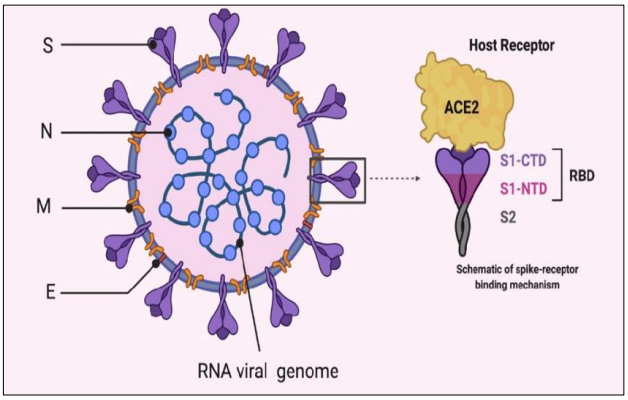

Figure 1: Structure of SARS-CoV-2 and spike protein.[9]

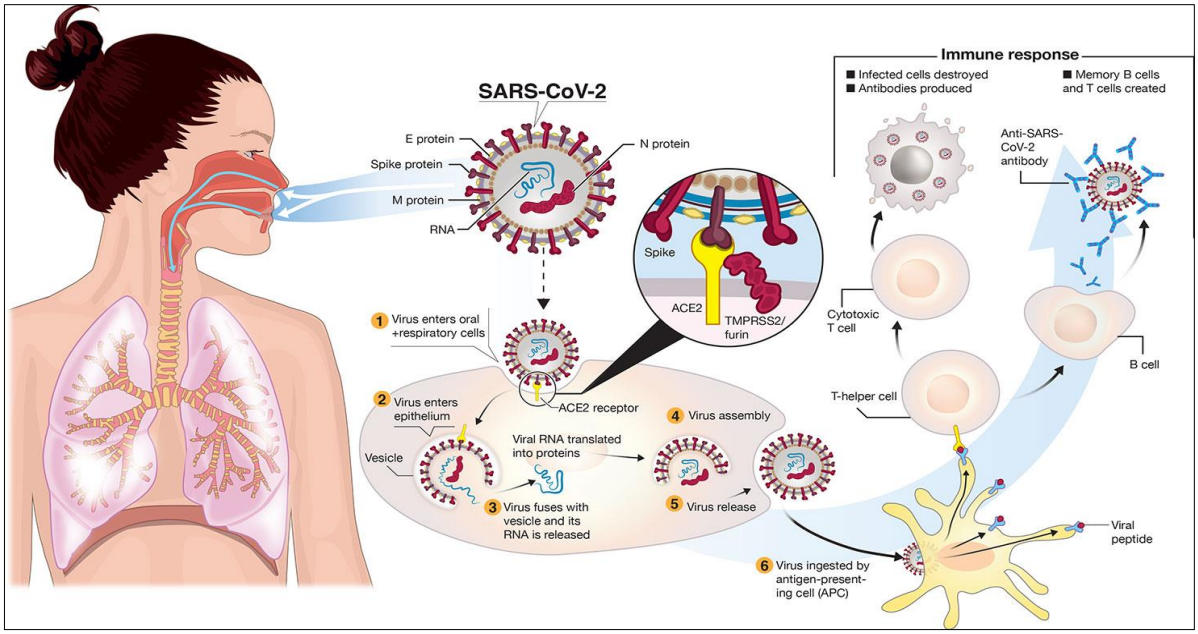

Figure 2: Transmission and life-cycle of SARS-CoV-2 causing COVID-19.[13]

Nucleocapsid protein (N) has multiple functions like it is involved in packaging of viral genome, formation of the viral capsid, virus budding, RNA replication and mRNA transcription.[14] The membrane protein (M) is a transmembrane glycoprotein with three domains. It is involved in virus assembly and also enhances the viral proliferation by inhibiting production of cox-2 and activation of nuclear factor kappa B (NFkB).[15,16]

The envelop protein (E) is a small membrane protein with ion channel activity.[17] It is involved in viral assembly, virion release and viral pathogenesis.[18]

COVID-19 VACCINES

Vaccine efficacy and safety is of paramount importance while developing a vaccine especially for mass vaccination. It is reported that vaccine efficacy should be at least 70% to prevent an epidemic and 80% to terminate an epidemic.[19]

COVID-19 vaccine is developed on classic vaccine platform and next generation vaccine platform. Classic (conventional) is based on vaccines already licensed and used in humans and include virus based and protein based vaccines. Virus based vaccines contain live attenuated

virus or inactivated virus. In live attenuated vaccine, virus has no virulence but induce mild type of infection. In inactivated vaccine, virus is unable to replicate and is rendered non contagious. However, it requires adjuvant to properly stimulate immune system. Protein based vaccine contains a virus purified protein, a recombinant protein or virus like particle (VLP). It also requires adjuvants to stimulate the immune system.[20-23]

The next generation vaccines are developed solely on the sequence of the antigenic viral proteins rather than actual viral particle. These types of vaccines include viral vector vaccine, nucleic acid-based vaccine and antigenic presenting cell vaccine (Figure 3).[22,24]

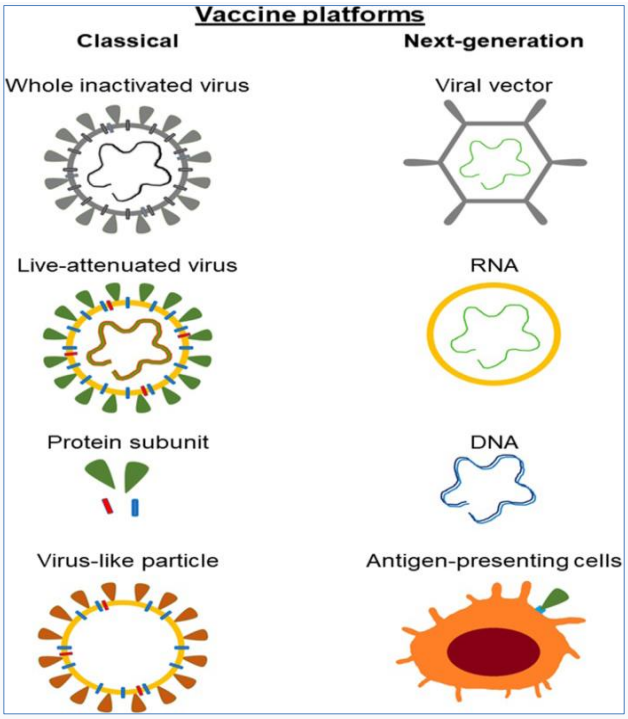

Figure 3: Classical and next generation vaccine platforms used in development against SARS-CoV-2.[24]

Live attenuated vaccine

It is a classical viral vaccination strategy and contains multiple antigenic components.[7] It induces strong immunogenicity and stimulate Toll like receptors. Live vaccines provide long term protection like small pox, polio and measles. It has a well-established developmental process but requires handling of live virus.[25] Live vaccine has potential risk of serious infection in immuncompromised persons. At present a live attenuated vaccine that express spike protein of SARS-CoV-2 is under clinical stages of development by Meissa vaccines, Inc.[26]

Inactivated vaccine

It also belongs to classical strategy for viral vaccination. It contains multiple antigenic components and potentially induces diverse immunogenic responses. It is less reactogenic as compared to live vaccine and produces a weaker immune response.[7] Inactivated vaccine requires multiple inoculations and strong adjuvants to be effective. Developmental process is well established but requires handling of live virus.[27] Inactivated vaccines approved for vaccination is produced by Sinopharma/Beijing Institiute of Biological Products, Sinovac Life Sciences and Bharat Biotech (covaxin).[28]

Subunit vaccine

It is prepared from one or more antigens with strong immunogenicity. It is relatively easy to manufacture but requires effective adjuvants to elicit strong immune response. Subunit vaccine is considered to be safer than inactivated vaccine.[7] Subunit vaccines approved employing S protein as antigens include Covovax by Serum Institute of India and Nuvoxovid by Novavax. Subunit vaccines using RBD domain of S protein as antigen are Corbevax by Biological E and recombinant SARS CoV-25-RBD by West Vac Biopharma.[28]

Virus like particle vaccine (VLP)

VLP vaccines contain various viral structural proteins which mimic viruses but do not contain viral genome. Therefore, they are non-infectious and very safe.[29] The plant cells are very good platform for oral delivery of vaccines.[30] The genes for viral proteins are mostly introduced into host plant using pathogenic bacteria Agrobacterium. The genes of interest get incorporated into nuclear or chloroplast genome. This leads to production of very large amount of virus like particles in the plant host. Plant based vaccines developed for avian influenza and influenza-A have been found to be safe and effective.[31] A candidate VLP plant-based vaccine for COVID-19 is under development by Medicago.[28]

Viral vector-based vaccines

These are live recombinant viruses which deliver vaccine genes or antigens to the target host tissues. The viral vector imitates infection by virus and may induce stronger cellular response.[27] The adenoviral vectored vaccines include recombinant ChAdOx1 encoding spike protein by Astra Zeneca/Oxford/Serum Institute of India (Covishield), adenovirus type 26 (Ad 26) vectored vaccine encoding spike protein by Jansen–Cilag International and human adenovirus vectored based COVID-19 vaccine (Sputnik) by Russian Direct Investment Fund.[28]

mRNA vaccine

mRNA vaccine works by introducing a piece of mRNA that corresponds to a viral protein such as spike protein. Immune system recognizes that as foreign protein and produce antibody against it providing protection against future infection. There is no risk of infection with mRNA vaccine.[32] mRNA vaccine for COVID-19 by Moderna

Biotechnology and Pfizer/BioNTech has been approved for vaccination.[28]

Nucleic acid/DNA vaccine

DNA vaccines consists of plasmid DNA encoding one or more antigens. They need to enter the nucleus for synthesis of antigenic proteins. Then immune system produces antibodies against antigens.[33] These vaccines eliminate the need for using live viruses. They can be freezed for long term storage.[27] First DNA vaccine for COVID-19 developed by Zydus Cadila (ZyCoV-D) has been approved by DCGI, India recently.[34]

A general comparison of some of the approved or WHO listed vaccines with reference to type, doses and storage is shown in Figure 4.[35]

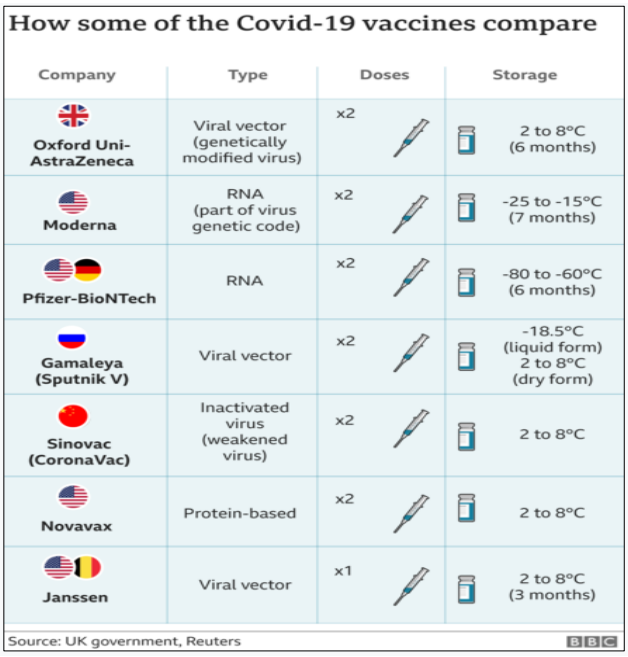

Figure 4: A general comparison of some commonly used COVID-19 vaccine.[35]

Limitations

This review has included only those vaccines which have been approved by regulatory bodies and is on the WHO list. However, this review will give readers a basic insight into COVID-19 vaccines which are available for mass vaccination.

CONCLUSION

COVID-19 epidemic has caused tremendous loss to the human resources in the last 2 to 21/2 years. Despite our best efforts no effective cure is available till date. The only way to control this global pandemic is to develop safe and effective vaccine. COVID-19 vaccination has led to containment of infection in many parts of the world including India. Various types of vaccines developed and approved under emergency use or under development include live vaccine, killed vaccine, VLP based vaccine, vector-based vaccine, mRNA vaccine and DNA vaccine. Over all safety and efficacy of approved vaccines have been found to be satisfactory so far but long-term safety data needs to be seen.

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