COVID-19 Variants, Vaccine and Booster

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Background

Severe acute respiratory symptom corona virus 2 (SARS-CoV-2) mutated at a regular frequency throughout corona virus infectious disease 2019 (COVID-19) pandemic. Significant mutations in spike protein (S protein) and elsewhere enabled emergence of variants of concern (VOC) that include Alpha, Beta, Gamma, Delta and recent Omicron variant.

Three major vaccine platforms/ technologies such as 1) mRNA, 2) viral vector and 3) protein were utilized to develop the currently available and administered vaccines world-wide. All these vaccines aimed to develop S protein-specific immune response to prevent binding of SARS-CoV2 S protein to angiotensin convertase enzyme 2 (ACE2) receptor in human thus conferring immune protection against infection.

These vaccines are remarkably safe and effective against original SARS-CoV2 infection, although immune protection waned over time. Also, mutations in S protein led to immune escape by VOC, increased transmission, higher viral load with severe infection and death primarily in unvaccinated and in certain vaccinated individuals.

This presentation will examine various COVID-19 vaccine formulations, immune responses, real-world vaccine efficacy, protection against VOC, and recommendation for booster.

Purpose

The purpose is to provide an overview of COVID-19 VOC, various vaccine formulations, immune protection and requirements for a booster dose. Clinical data on 1) vaccine-induced immune protection; 2) waning of immune protection against the emerging variants such as Delta and Omicron, and 3) recommendation for a booster dose to enhance immune protection.

Methods

COVID-19 related keyword search and review of primary and tertiary literatures available in medRxiv, bioRxiv, PubMed, CDC, NIH and NIAID databases were utilized. The search specifically focused on COVID-19 vaccine clinical trial and real-world vaccine effectiveness (VE) data, emergence of VOC, waning of immune-protection, and recommendation for a booster dose.

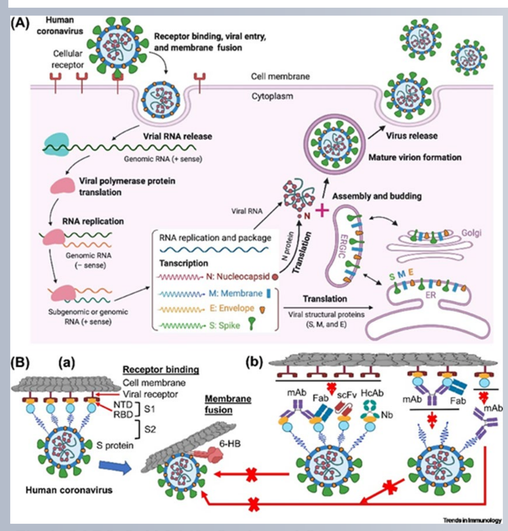

Fig 1. SARS-CoV-2 Life Cycle and Structure Important for Vaccine and Drug Development.

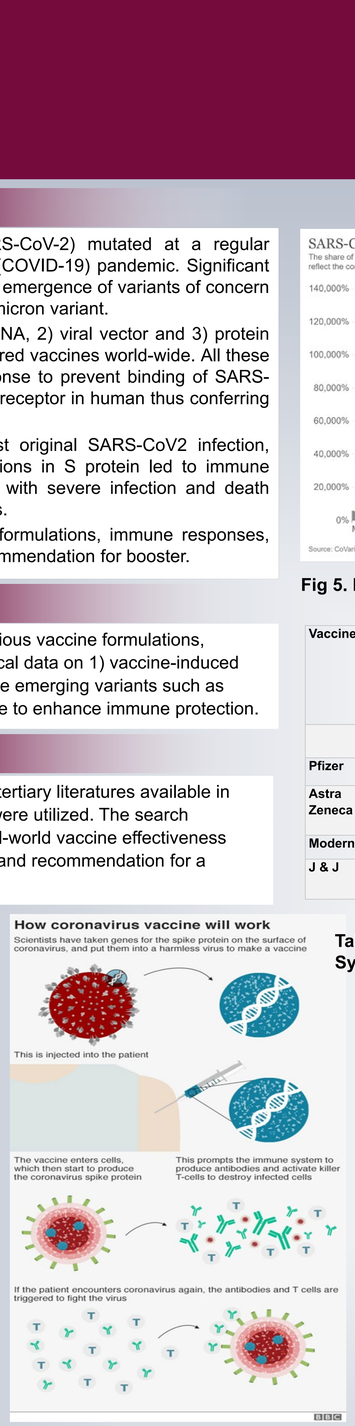

Fig 2. Proposed Mechanisms of Vaccine-induced Immune Response.

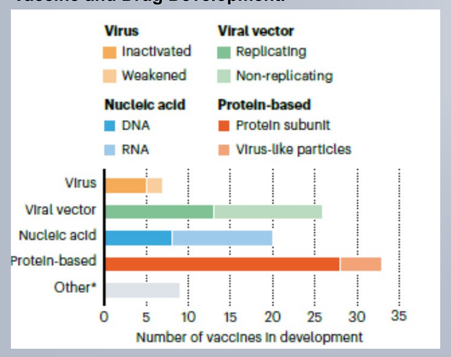

Fig 3. COVID-19 Vaccine Platforms.

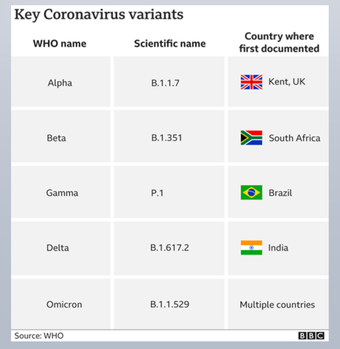

Fig 4. Corona Virus Variants.

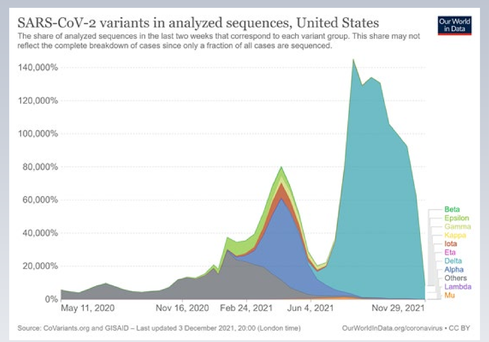

Fig 5. Frequency of COVID-19 Variants in USA

Vaccine	% efficacy against variants (symptomatic disease)					% efficacy against variants (hospitalization)				
	Original virus	Alpha	Beta	Gamma	Delta	Original virus	Alpha	Beta	Gamma	Delta
Pfizer	95	90-94	72-89	77-84	88	100	97	97-100	97-100	96
Astra Zeneca	76	70	48-50	48-50	76-71	100	90	82	82	87
Moderna	86-94	92	77	77	72-76					96
J & J	67-72		52-64	66-68	67-71	86		82	85	96

Table 1. The Efficacy (%) of COVID-19 Vaccines Against Variants in Fighting Symptomatic Disease & Hospitalization

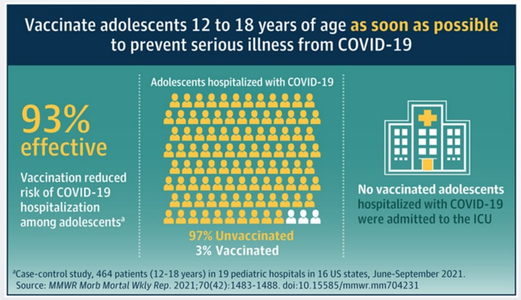

Fig 7. Pfizer Vaccine Is Highly Protective Against Hospitalization Among Adolescents Against Delta Variant.

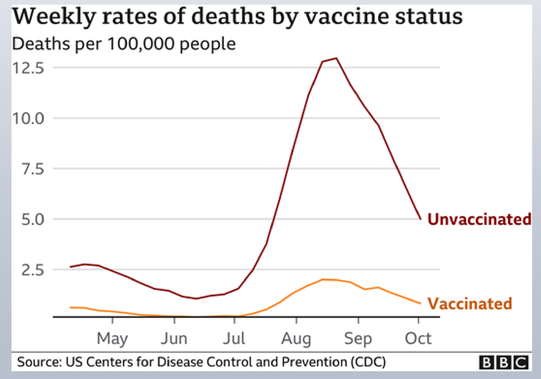

Fig 8. Vaccination Protected Americans Against Original COVID-19 and Variants.

Results

Safety and Efficacy of COVID-19 Vaccines

- COVID-19 vaccines are safe with minimum adverse reactions in adults and adolescents.
- These vaccines also generated T cell responses which is important in clearing the virus.
- Pfizer Vaccine was well-tolerated and generated protective antibody response in pregnant and lactating women
- Pfizer and Moderna vaccines conferred >90% protection against original infection.
- Real-world data demonstrate strong and durable immunity against symptomatic disease caused by original virus (70-95% protection), and against Delta variant, 70-88% protection.
- Vaccine protection against hospitalization due to original virus or Delta infection was high, 90-100%.
- Although vaccination generated robust, durable and neutralizing Ab response, yet immune protection waned ~4-6 months after vaccination.
- Waning immunity combined with low vaccination led to generation of many VOCs including Omicron (BA.1).
- Vaccine effectiveness (VE) against COVID-19 associated emergency care was higher after the 3rd dose (booster) than after 2nd dose.
- VE against Omicron-associated emergency/urgent care and hospitalization was 87% and 91% respectively for first 2 months that declined to 66% and 78% respectively ≥4 month after the booster dose.
- VE was higher protecting against hospitalization and emergency care need for both Delta and Omicron.
- SIREN study in health workers in UK with high vaccination (>95%) showed higher rates of reinfection with Omicron and Omicron subvariant BA.2 as determined by PCR positivity.
- The risk of hospitalization does not appear to be higher following a BA.2 infection than BA.1 infection.
- Clinical data also indicate that hospitalization and death in unvaccinated person (44x times higher) was significantly higher than vaccinated person.
- Overall, COVID-19 vaccines are protective against the emerging VOC in varying degrees.

COVID-19 Vaccine Formulations, Schedules & Protection

- ***mRNA-based vaccines:*** S-protein mRNA in lipid nanoparticle formulation
  - Moderna, 2 shots 28d apart, 94% protection Pfizer-BioNTech: 2 shots 21d apart, ~95% protection
- ***Viral vector-based: genetically engineered adenovirus with 'S protein' DNA***
  - AstraZeneca, 2 shots 28d apart, ~70 (60-90%) efficacy; Johnson & Johnson (J & J) 1 shot, 85% protection against severe infection; Sputnik V: 2-dose 28d apart, 95% efficacy
- ***Killed virus vaccine***
  - Covaxin, Bharat Biotech, 2 doses 14d apart, ~80% effective against infection
- ***S Protein-based vaccine***
  - Novavax (S protein with Matrix-M adjuvant), 2 doses 21d apart, 100% efficacy against severe disease
- ***DNA vaccine***
  - Inovio, phase III clinical trial, broad, cross-reactive neutralizing Ab and T cell responses, against VOC (alpha, beta, gamma and, delta).

Conclusion

- Effective, safe and well-tolerated COVID-19 vaccines have been developed and administered.
- The vaccine technology platform ranged from lipid nanoparticle-mRNA, adenoviral vector-mediated, adjuvanted protein vaccine and killed virus vaccine.
- Vaccine formulations targeted 'S' protein, ligand for ACE2 receptor and critically important for blocking the infection.
- Significant mutations in spike protein enabled emergence of variants of concern (VOC) such as Alpha, Beta, Gamma, Delta and recent Omicron variant.
- Vaccines induced robust and protective immune responses in wide age group and ethnicity.
- Vaccination triggered both B and T cell responses with memory function necessary for long-term protection against original strain and the emerging variants.
- Vaccines conferred significant protection against both asymptomatic, and severe infection, thus preventing hospitalization and death.
- Vaccine-induced immune protection waned around 6 month after vaccination requiring booster dose for continued protection particularly against Omicron variant and subvariant BA.2
- Overall, vaccine protection remain significantly high against the original strain and the variants of concern.
- Adequate vaccination, boosting along with antiviral drug, monoclonal antibody treatment, and other preventative measures would help us getting over with pandemic of our life-time!

Reference

Vaccine efficacy against different SARS-CoV-2 Variants. K. Boyle. Tech Networks.
https://www.technologynetworks.com/tn/articles/vaccine-efficacy-against-different-sars-cov-2-variants
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