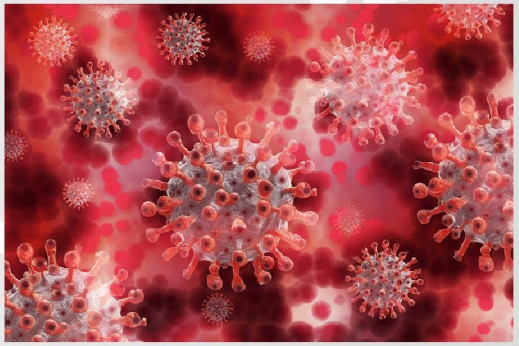


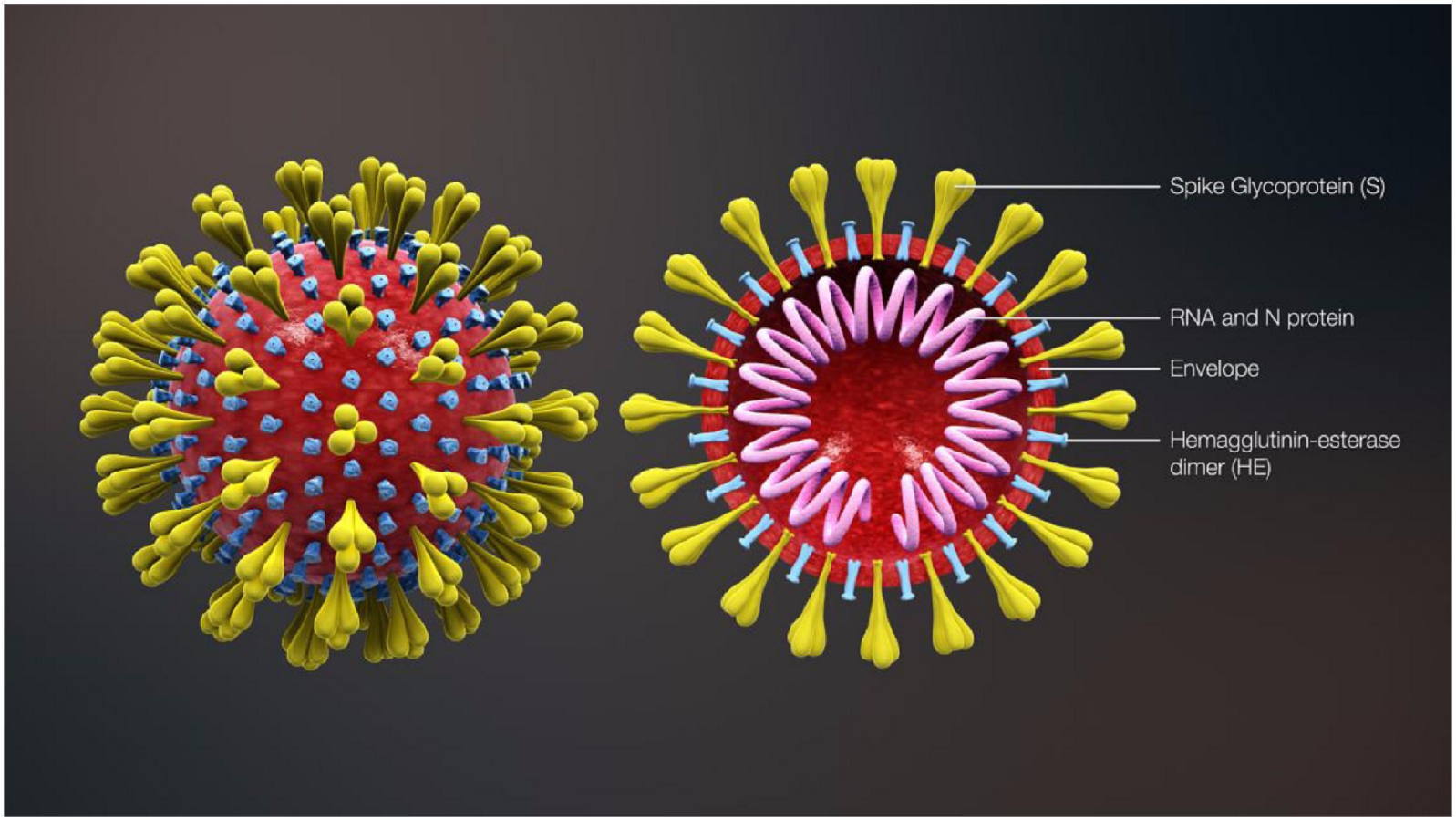
SARS-COV-2 VACCINES

JCVI secretariat

SARS-COV-2

- Coronaviruses (CoVs) comprise of a large family of single-stranded RNA viruses
- Can infect animals and also humans, causing respiratory, gastrointestinal, hepatic, and neurologic diseases
- CoVs are further divided into four genera: alpha-coronavirus, beta-coronavirus, gamma-coronavirus and delta-coronavirus
- SARS-CoV-2 is a beta coronavirus of lineage B
- SARS-CoV-2 encodes a surface glycoprotein (spike), which binds to the host-cell receptor and mediates viral entry
- In SARS-CoV-2 a single region of the spike protein called the receptor-binding domain (RBD) mediates the interaction with the host-cell receptor
- The host receptor for SARS-CoV-2 is angiotensin-converting enzyme 2 (ACE2)

Letko, Marzi, and Munster (2020) Functional assessment of cell entry and receptor usage for SARS-CoV-2 and other lineage B betacoronaviruses Nat Microbiol. 2020 Feb 24 : 1–8. https://doi.org/10.1038/s41564-020-0688-y


Spike Glycoprotein (S)
RNA and N protein
Envelope
Hemagglutinin-esterase dimer (HE)

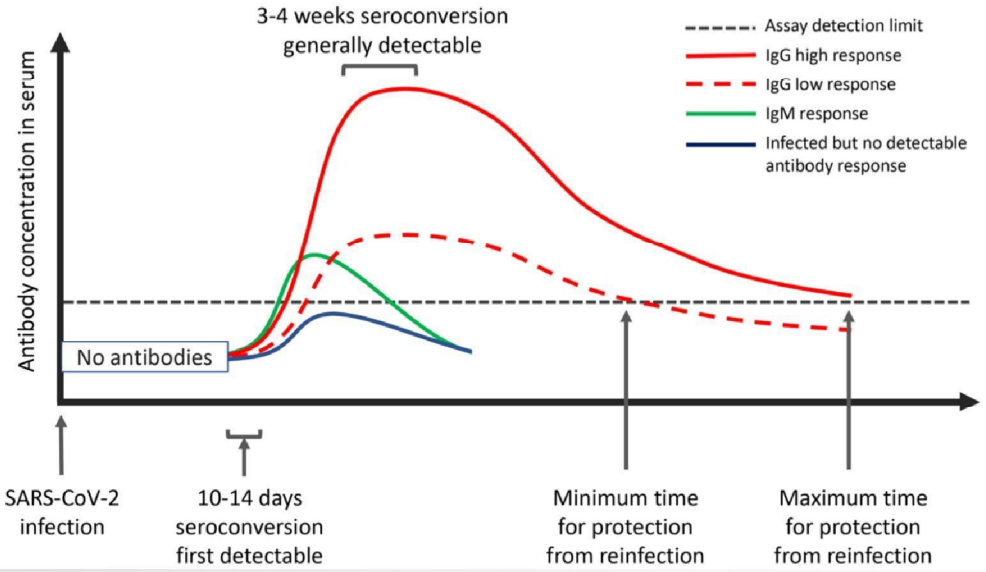
ANTIBODY RESPONSE TO INFECTION

- The timing, magnitude and longevity of humoral immunity is not well understood for SARS-CoV-2
- There is currently a lack of knowledge about 'protective levels' of antibody, and the duration of any protection to SARS-CoV-2
- Many ELISA assays are based on the spike protein (or a subunit of it), or a nucleocapsid protein
- Evidence available indicates that most people infected with SARS- CoV-2 display an IgG antibody response between 10 and 14 days after infection.
- It is also important to understand about functional antibodies as assessed by neutralisation assays
- There is some evidence which indicates a reasonable correlation between some spike protein based ELISA assays and neutralisation assays
- In some mild cases, detection of antibodies requires a long time after symptoms, and in a small number of cases, antibodies are not detected at all
- Longitudinal analyses report detection of IgG and/or IgM up to 1-2 months post illness onset

Kellam and Barclay 2020 - The dynamics of humoral immune responses following SARS-CoV-2 infection and the potential for reinfection
https://doi.org/10.1099/jgv.0.001439

ANTIBODY RESPONSE TO INFECTION

Kellam and Barclay, *Journal of General Virology* 2020



Developer	Platform	Type of candidate vaccine	Target protein	Trial phase	Same platform for non-CoV
University of Oxford/ Astra Zeneca	Non- Replicating Viral Vector	Chimp Adenovirus - non replicating	Spike	Phase 3	MERS, influenza, TB, Chikungunya, Zika, MenB, plague
CanSino Biological Inc./Beijing Institute of Biotechnology	Non- Replicating Viral Vector	Adenovirus Type 5 - non replicating	Spike	Phase 2	Ebola
Moderna/NIAID	RNA	mRNA	Spike	Phase 2	multiple candidates
Imperial College London	RNA	saRNA	Spike	Pre-Clinical	EBOV; LASV, MARV, Inf
Wuhan Institute of Biological/Sinopharm	Inactivated	Inactivated	Inactivated virus	Phase 1/2	
Beijing Institute of Biological Products/ Sinopharm	Inactivated	Inactivated	Inactivated virus	Phase 1/2	
Sinovac	Inactivated	Inactivated + alum	Inactivated virus	Phase 1/2	SARS
Novovax	Protein Subunit	Glycoprotein nanoparticle with Matrix M adjuvant	Spike	Phase 1/2	
BioNTech/ Fosun Pharma/Pfizer	RNA	mRNA	Spike/RBD	Phase 1/2	
Institute of Medical Biology, Chinese Academy of Medical Sciences	Inactivated	Inactivated	Inactivated virus	Phase 1	
Inovio Pharmaceuticals	DNA	DNA plasmid vaccine	Spike	Phase 1	multiple candidates
Shenzhen Geno-Immune Medical Institute	Recombinant Protein	Pathogen-specific aAPC	Minigenes and immune modulatory genes	Phase 1	
Shenzhen Geno-Immune Medical Institute	Non-Replicating Viral Vector	Lentiviral-SMENP-DC	SMENP minigene and immune modulatory genes	Phase 1/2	

TIMELINES

Oxford has started Phase 3 trials with ~10,000 participants

A number of vaccines are moving towards Phase 2 and 3 trials, including Moderna, Pfizer and CanSino

Oxford/AZ have estimated that 30m doses of vaccine could be available in the UK by September 2020

Other developers have stated some vaccine could be available late 2020 or early 2021, with ranges of 10m to 1b doses of vaccine available in 2021

UK Government is supporting vaccine development and manufacturing

PHE has begun planning for delivery of a vaccination programme

EARLY RESULTS

- Oxford/AZ vaccine pre-clinical results indicated immunisation with two different doses (3 or 6 µg) provided partial or complete protection in macaques against SARS-CoV-2 challenge, respectively.
- No antibody-dependent enhancement of infection was seen.
- Oxford Phase 1 results are anticipated in the next two weeks
- Moderna announced on 18 May that mRNA-1273 (spike protein) elicited neutralizing antibody titre levels in all eight initial participants across the 25 µg and 100 µg dose cohorts, reaching or exceeding neutralizing antibody titres generally seen in convalescent sera
- Cansino published results from their phase one trial which indicated that ELISA antibodies and neutralising antibodies increased significantly at day 14, and peaked 28 days post-vaccination. Specific T-cell response peaked at day 14 post-vaccination.

QUESTIONS TO ANSWER

- Vaccine study questions
  - Vaccine safety, immunogenicity and efficacy in:
    - older adults
    - those with underlying conditions
    - children
  - Concomitant administration with influenza vaccines used in the UK (aTIV, QIV, QIVc and TIV-HD)
  - Evidence from studies in similar vaccine technologies regarding safety, immunogenicity, efficacy and concomitant administration