Evidence Update on COVID-19
V7 - Virus biology and serology

SARS-CoV2

- Single stranded RNA virus of 80-220nm diameter
- Consists of:
  - RNA genome wrapped up in nucleoprotein, surrounded by
  - Viral envelope which
  - Contains matrix proteins and spike proteins which are anchored to the envelope
- Contains 5 essential genes - 4 structural proteins (spike, matrix, nucleoprotein, envelope), plus an RNA dependant RNA polymerase Park
- Has 80% similarity to SARS-CoV and shares most of its genetic code including the S glycoprotein, RNA polymerase and proteases Zhu
- Different 'strains' exist - L and S with slight differences at one point in genome- but no evidence of differences in infectivity or aggressiveness MacLean
- In 5700 samples, minimal viral diversity was found - suggests a vaccine should work across global strains Dearlove
- ChAdOx1 vaccine has been developed by University of Oxford
  - Phase I trials in 1000 healthy adults ongoing (safety trial)
  - Phase II and III trials ongoing across the country to assess the immune response generated, and protection against infection offered

How SARS-CoV2 infects a human

- Virus enters the body via the nose or mouth
- Travels to the upper respiratory epithelium and alveoli
- Viral spike protein binds to ACEII receptor on type-2 epithelial cells, allowing the virus to enter the cell Cevik
- Virus hijacks cell machinery to make copies of its own RNA, and assemble new virus
- New viruses are transported to the cell membrane in vesicles and are released by exocytosis and can infect other cells Fehr
- Cell death caused by virus infection by necrosis causes the release of new viruses and damages host tissue.
- This induces inflammation and triggers an immune response:
  - Macrophages
    - Take up virus and dead cells
    - Release cytokines to recruit immune cells
    - Cause vasodilation, causing fluid to enter lungs (oedema)
  - Neutrophils
    - Release reactive oxygen species to destroy infected cells
    - This damages alveoli (can result in ARDS)
  - Dendritic cells
    - Present virus proteins to T cells, activating the adaptive immune response
  - Complement
    - Helps co-ordinate further immune activation and pro-inflammatory responses. It may also lead to ARDS. Risitano 2020
  - T cells
    - CD8+ - Release cytotoxic factors to kill infected cells
  - B cells
    - Generate antibodies to neutralise virus

Viral load in human samples

Viral RNA has been found in (does not indicate live virus): Wolfel, Wang, Yang, Li, Han, To

Throat and nasal swabs	Saliva	Sputum	Bronchoalveolar lavage
Feaces	Urine	Blood	Sperm

Live, replicable virus has been found in:

Throat and nasal swabs	Saliva	Sputum	Bronchoalveolar lavage

- High rate of false negative PCR tests - early disease and low viral load often show negative which later becomes positive - must assume positive and retest 2-3 days later Li
- Detection of RNA does no indicate live virus
    - In 9 mild patients, no live virus was cultured from throat swabs or sputum despite high PCR viral load - supports 7-14 day isolation is sufficient Wolfel

Serology

- Antibodies neutralise virus by preventing the virus from entering the cell, or from uncoating within the cell
- Antibodies
    - IgM is produced after day 5-10 of infection
    - IgG is produced after 7-11 days of infection and peaks on day 21
    - IgA is produced after 7-11 days of infection
- Measuring antibodies can tell us if a person has been infected and recovered from SAR-CoV2, and if they are immune to the virus
- Antibody test measured IgG - best time to test is 14 days after symptom onset
- In SARS-CoV patients
    - IgG detected after 14 days, IgM correlated with virus neutralisation titre (To - n=16)
    - IgA and IgM peaked after 16-20 days after illness onset. IgG peaked at 21-25 days - IgA serum correlates with COVID-19 severity (n=9) Ma
- SARS-CoV2 serology study In HCW at UHB Shields
    - 554 asymptomatic had PCR - 2.39% positive
    - 516 had serum
        - 26% had prior COVID-19 like illness
            - of which, 37.5% had seroconversion and higher levels than asymptomatic
        - 17% asymptomatic had seroconversion
    - Highest staff rates - housekeeping (34.5%), acute medicine 933%), general internal medicine (30.3%), lowest rates in intensive care (14.8%), emergency medicine (13.3%) and general surgery (13%).
    - Shows that asymptomatic seroconversion occurs, but prior illness results in higher antibody responses.