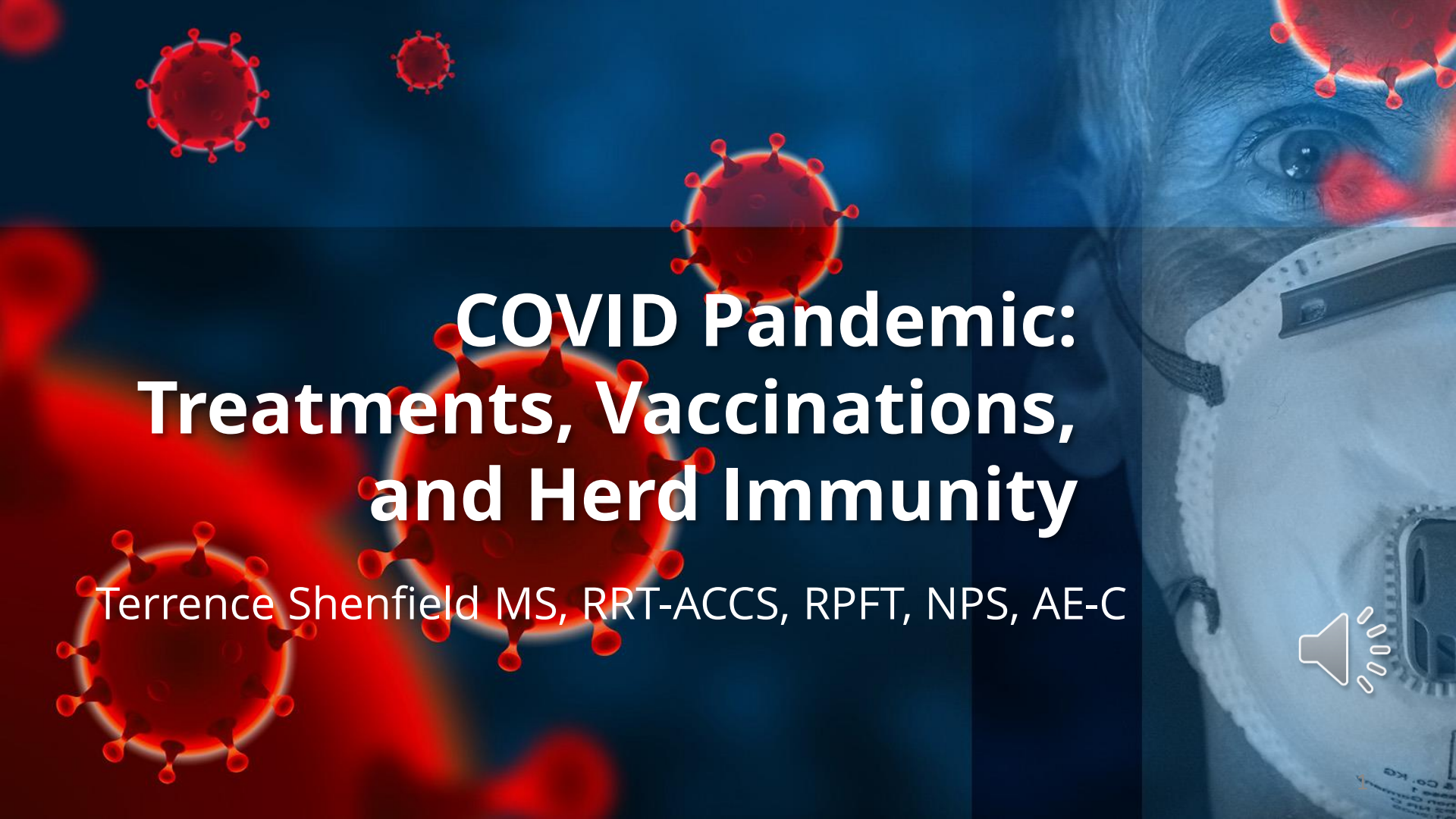
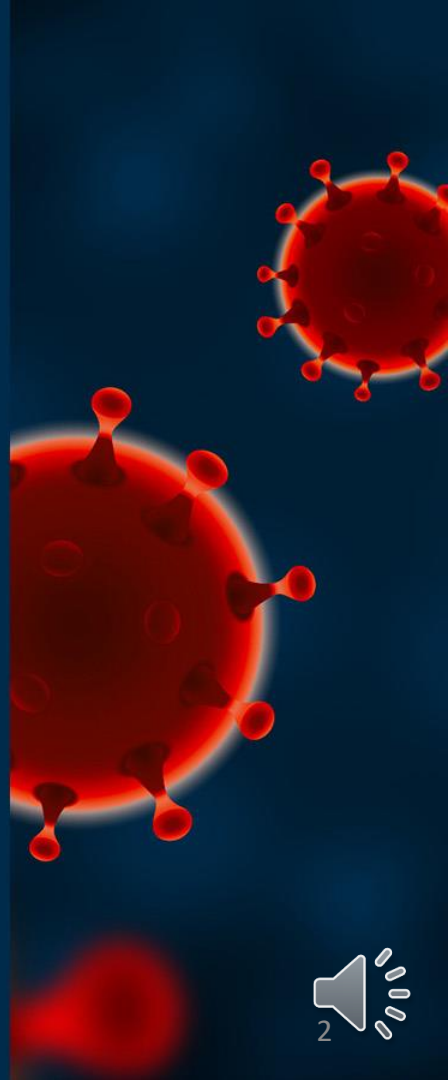


COVID Pandemic: Treatments, Vaccinations, and Herd Immunity

Terrence Shenfield MS, RRT-ACCS, RPFT, NPS, AE-C

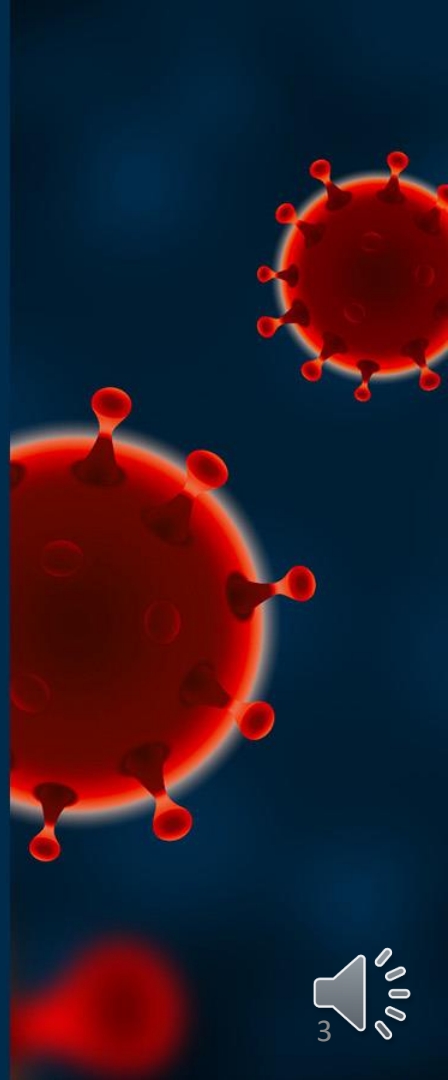
Objectives

- Background of the SARS-COV-2
- Virus characteristics
- Cytokine storm
- Understanding Immunity
- Current treatment options
- Vaccines
- Herd Immunity



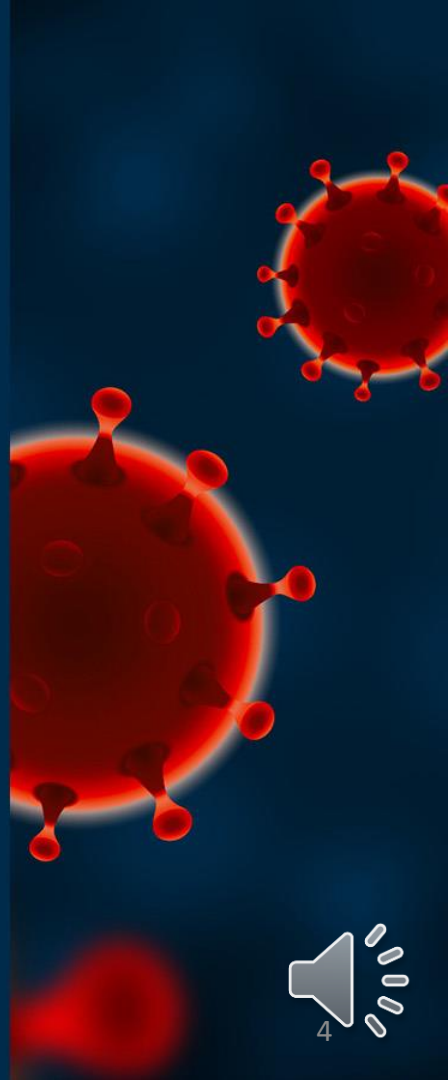
Background of SARS-CoV-2

- December 2019, the seventh member of the human coronavirus family was recognized.
- Several pneumonia cases of unknown etiology were first reported in December 2019 in Wuhan, China
- The natural reservoir for betacoronaviruses are bats and rodents.
- As of April 2021, we now have 149,000,000 cases worldwide

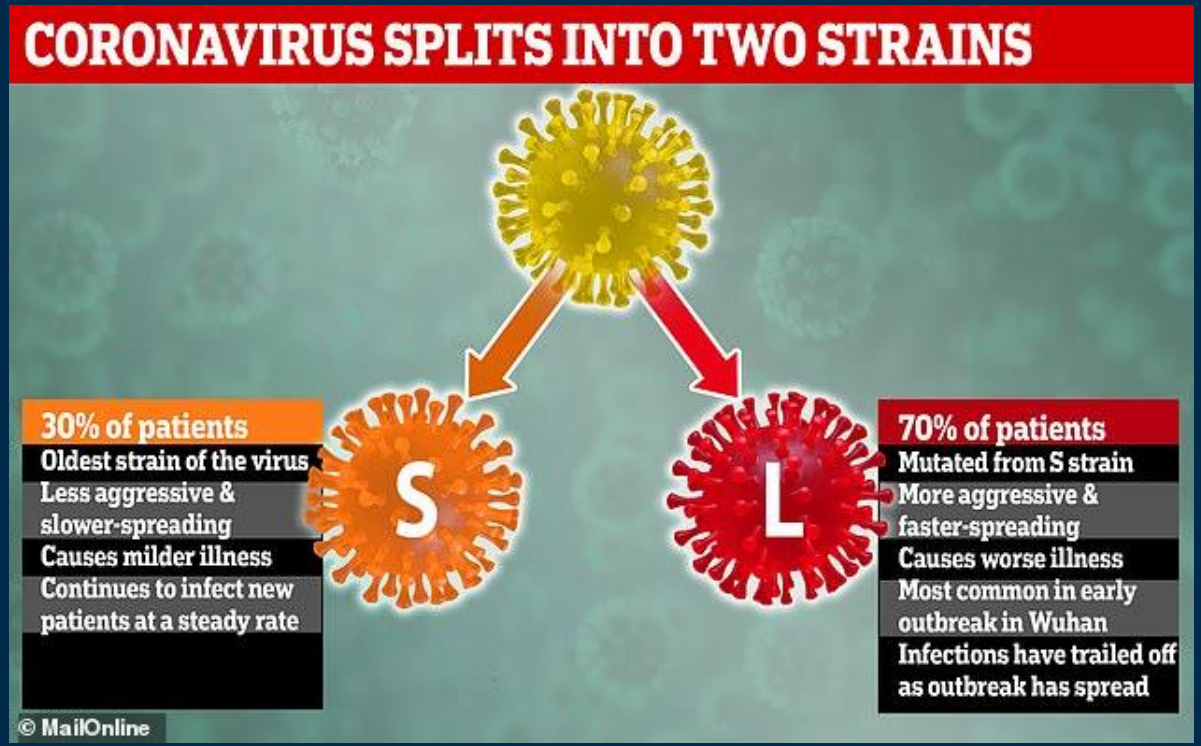


Virus Characteristics

- Severe acute respiratory syndrome coronavirus
  - SARS-CoV-2 is the virus name
  - COVID-19 is the disease
- These two types of SARS-CoV-2 and are defined by means of two different SNPs
- SNP= Single Nucleotide Polymorphisms
- Major types “L” and “S”



Viral types and differences

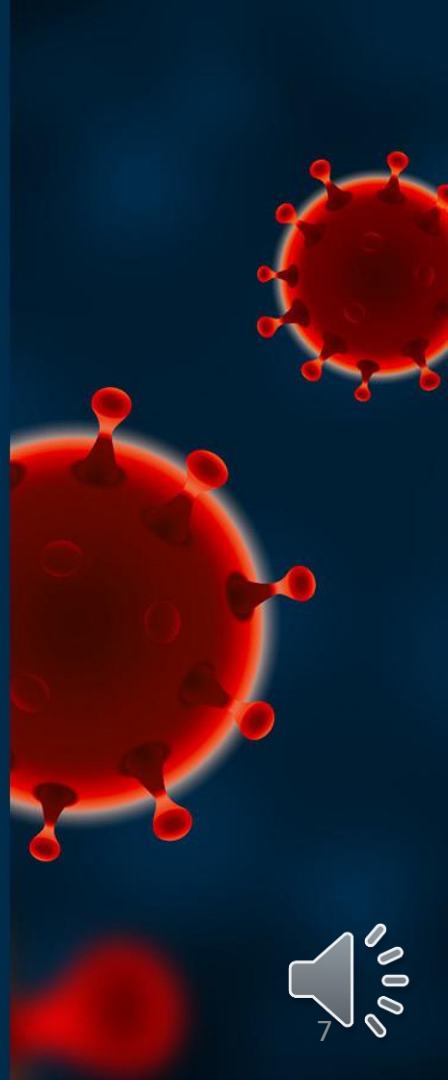


More background on the virus

- Primary mode of infection is human-to-human transmission through close contact, which occurs via spraying droplets from infected individual through their cough or sneeze

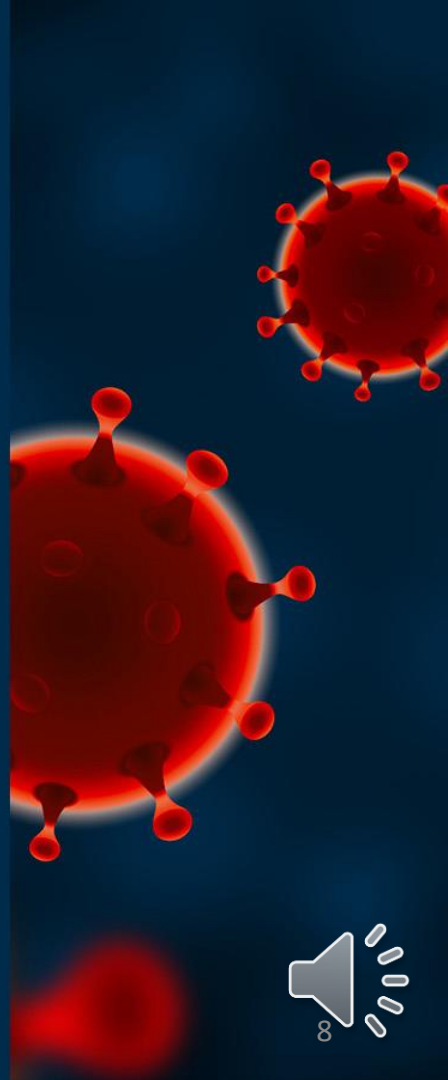
ACE2 Receptor

- Angiotensin-converting enzyme 2 (ACE2) is considered as the major determinant of the pathogenesis for SARS-CoV-2
- ACE2 is an expressed protein on the cell membrane
- ACE2 is expressed in type 2 alveolar cells
- Spikes of the SARS-CoV-2 fit perfectly into this receptor
- Once gaining entry to cell, it makes copies of itself
- Patients with comorbidities have greater expression of ACE2



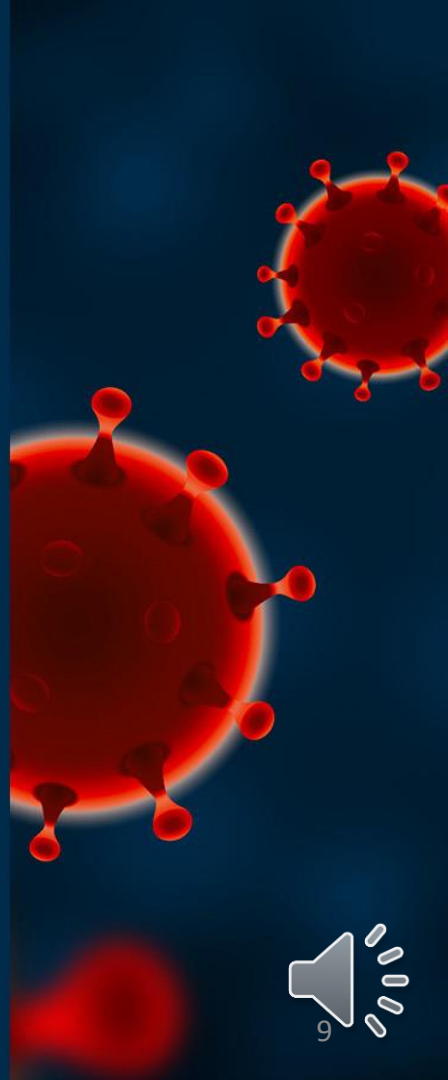
Cytokine storm

- Inflammatory-induced lung injury
- IL-2, IL-6, IL-7, IL-10, G-CSF, IP-10, MCP-1, MIP-1A, and TNFα
- Treatments are being studied that lessent these pro-inflammatory mediators



Immunity to COVID-19

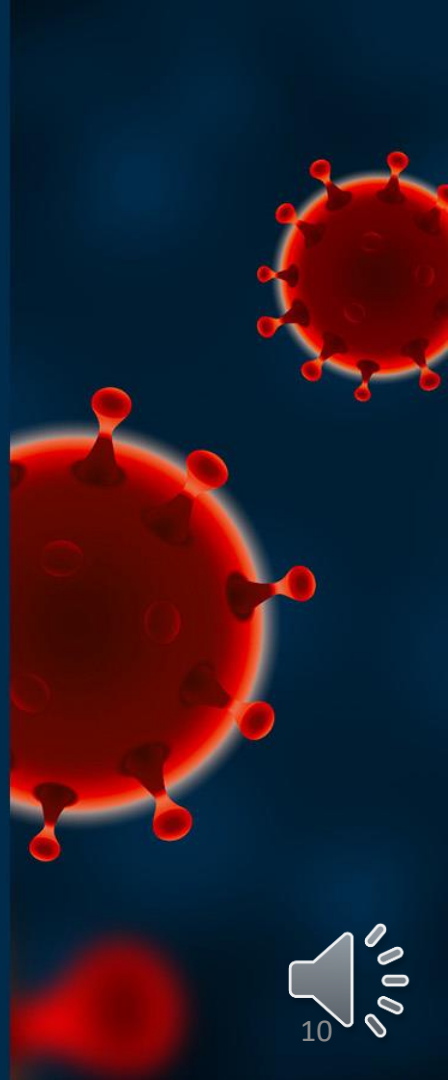
- Studies have demonstrated that COVID 19 dampens the immune response leading to “impaired immunity”
- Impaired immunity can lead to virus dissemination and destruction of the affected tissues, particularly in organs with high ACE2 expression such as the lungs



Understanding Immunity

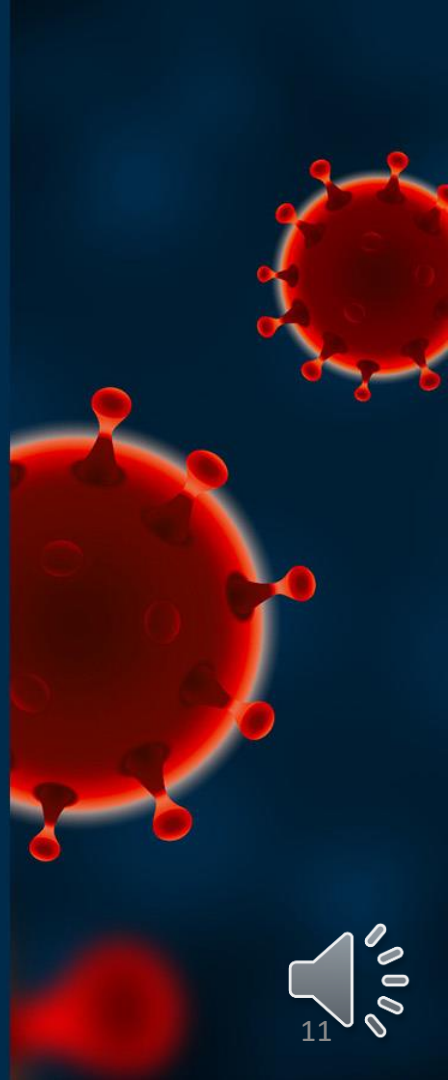
- Innate immunity
  - recruiting immune cells to sites of infection through the production of chemical factors, including specialized chemical mediators called cytokines

- Acquired or Adaptive immunity
  - established at the level of the individual, either through natural infection with a pathogen or through immunization with a vaccine



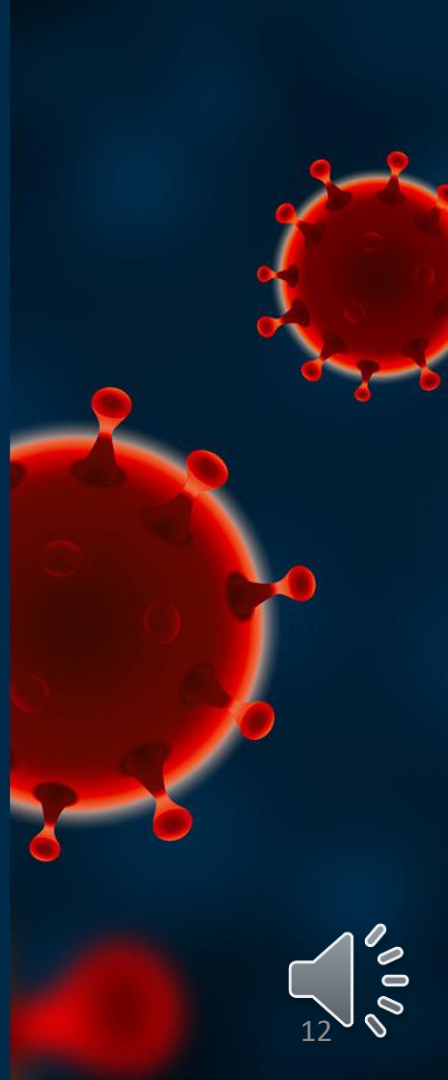
Innate response to SARS-CoV

- To mount an antiviral response, innate immune cells need to recognize the invasion of the virus
- Normally RNA replication is prevented via specific pathogen-associated molecular patterns (PAMPS) and viral loads are kept under control
- Expression of type I IFN and other pro-inflammatory cytokines is suppressed in leading to greater disease severity



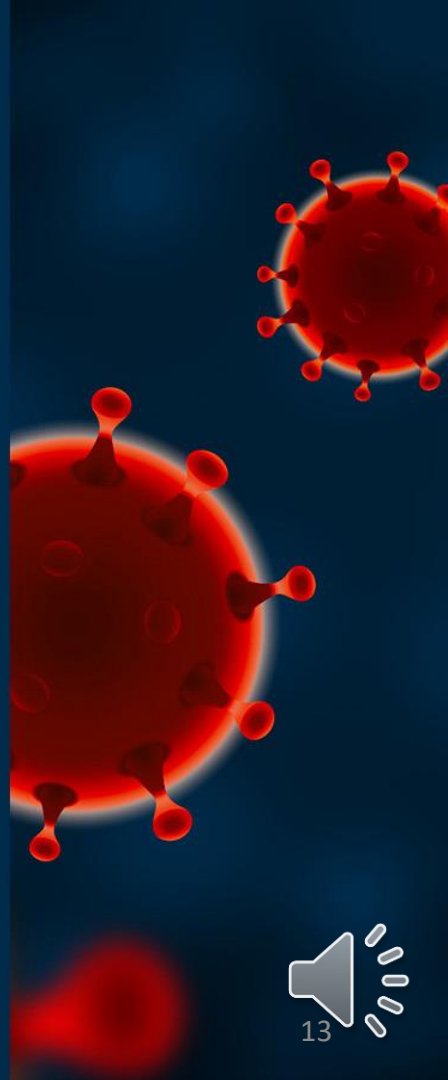
Difference between innate and adaptive immune

- The key difference between innate and adaptive immunity is that innate immunity is a fast-immune response that provides the first line of immunological defense against infections while adaptive immunity is a slow immune response mediated by the T and B lymphocytes.



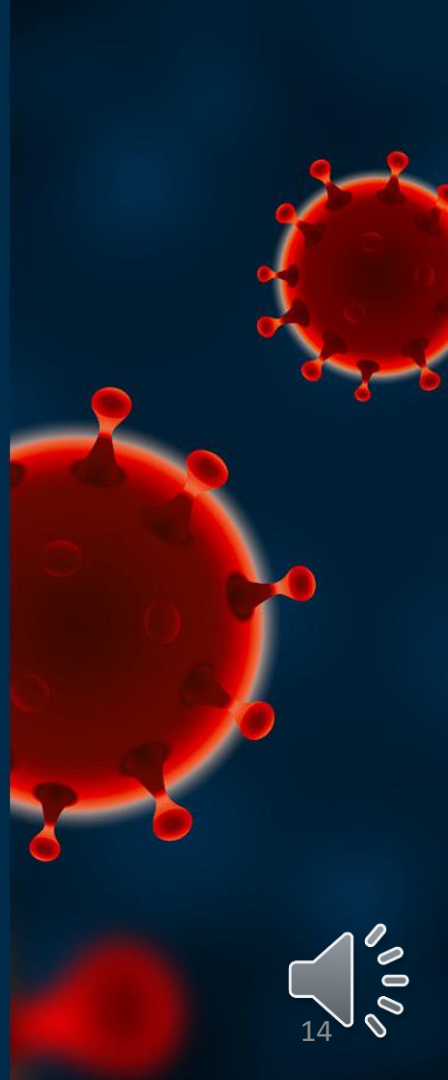
Adaptive or Acquired Immune Response

- After initial infection antibodies appear 7-10 days
- B-cell– and T-cell–mediated adaptive immunity to SARS-CoV-2 is essential
- Adaptive immunity creates immunological memory
- Type 1 helper cells immune response plays a dominant role in an adaptive immunity to viral infections
- Type 1 helper cells secrete interferon-γ (IFN-γ) and tumor necrosis factor-α (TNF-α) and mainly protect the organism against intracellular pathogens
- Cytotoxic T cells are essential in killing of viral infected cells



Potential Immune Evasion Mechanisms

- Current observations indicate that coronaviruses are particularly adapted to evade immune detection and dampen human immune responses
- Impaired immunity can lead to virus dissemination and destruction of the affected tissues, particularly in organs with high ACE2 expression



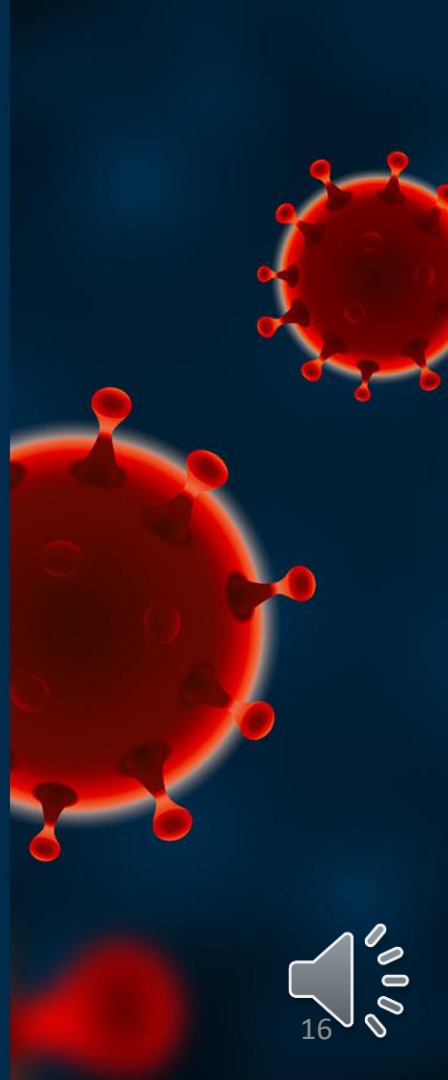
Potential Treatment Options of COVID-19

- Small Molecules
- Anti-inflammatory Drugs
- JAK Inhibitors
- Chloroquine and Hydroxychloroquine
- Phosphodiesterase 4 (PDE4) Inhibitors
- Methotrexate
- Angiotensin-Converting Enzyme Inhibitors (ACEI) or Angiotensin Receptor Blockers (ARBs)
- Nucleoside Analogs

- Protease Inhibitors (PIs)
- Type I IFNs
- Monoclonal Antibodies
- Melatonin as a Potential Adjuvant Treatment
- GM-CSF Inhibitors
- IL-6 Inhibitors
- IL1-Inhibitors
- TNF-α Inhibitors
- Convalescent Plasma
- Vitamin D

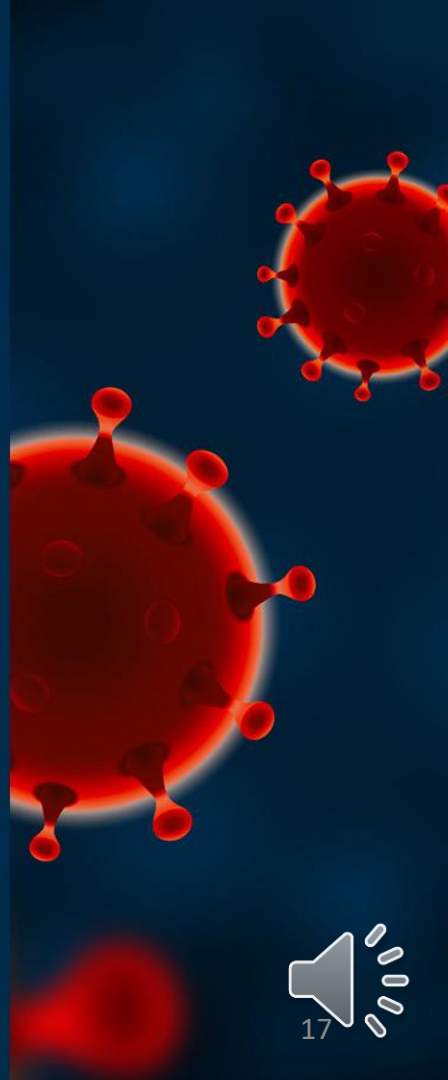
Arbidol™

- Viral entry to the cell and replication within the cell can be considered as a target for designing the antiviral drugs
- Inhibits viral entry into host cells through inhibition of viral membrane fusion
- A recent clinical pilot trial in China reported viral load reduction and decreased mortality rate in COVID-19 patients received Arbidol (400 mg; three times; nine days) as compared to the control group.



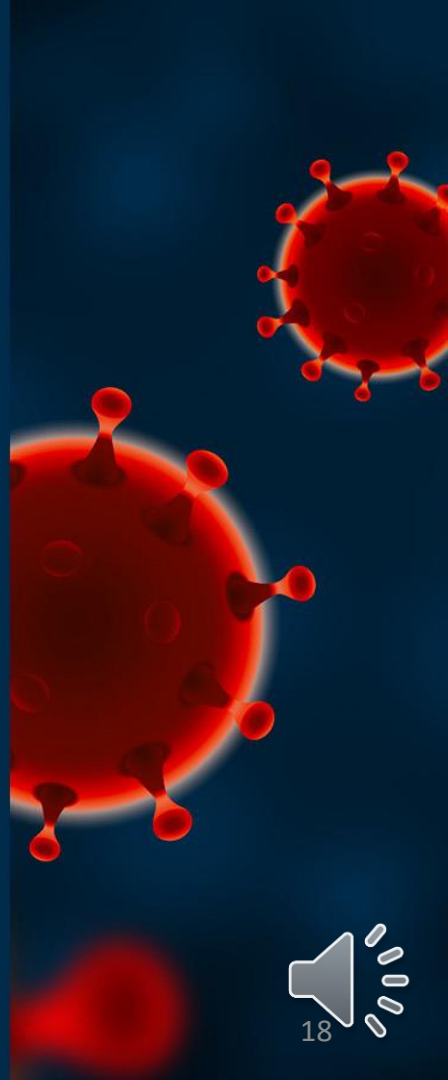
Chloroquine and Hydroxychloroquine

- Used either for prevention and treatment of malaria or for the treatment of rheumatoid arthritis
- Considered as an immunomodulator rather than immunosuppressant
- Contributes to the suppression of the “cytokine storm”
- HCQ 400 mg per day for 5 days plus conventional treatments
- Conclusions: The prognosis of COVID-19 moderate patients is good.



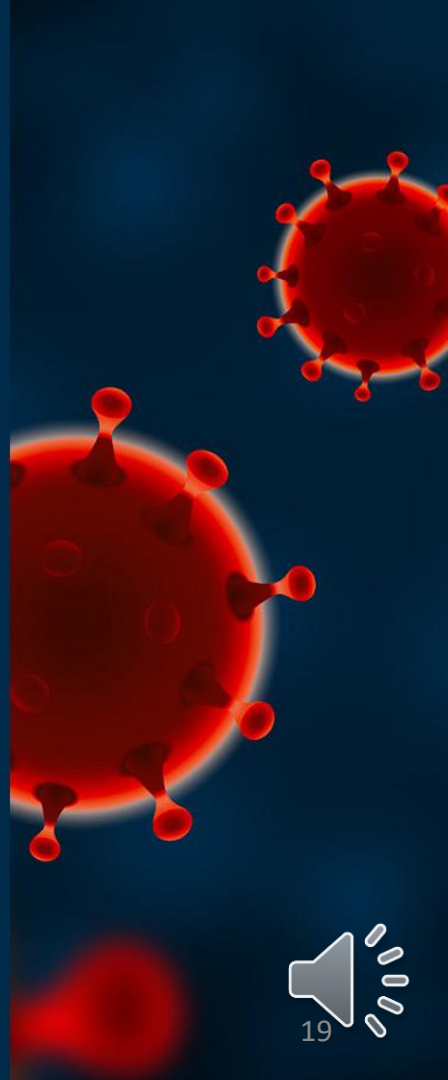
Hydroxychloroquine and Azithromycin

- Study in Brazil
- 447 patients were enrolled from March 28 to May 19, 2020. COVID-19 was confirmed in 397 patients
- **Findings:** In patients with severe COVID-19, adding azithromycin to standard of care treatment (which included hydroxychloroquine) did not improve clinical outcomes.
- Our findings do not support the routine use of azithromycin in combination with hydroxychloroquine in patients with severe COVID-19.



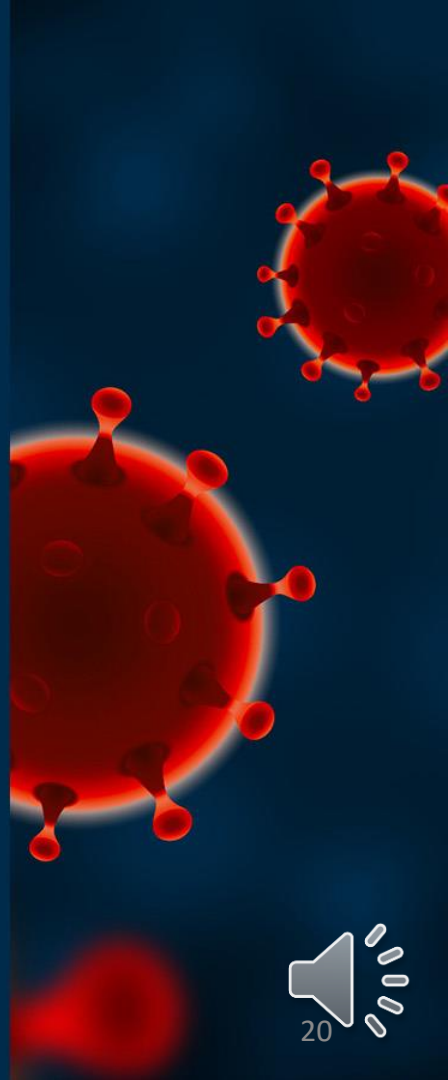
Remdesivir

- Originally developed to treat Ebola virus
- Can block replication of different coronaviruses such as SARS-CoV
- Double blinded study 1063 patients
- Remdesivir (200 mg loading dose on day 1, followed by 100 mg daily for up to 9 additional days)
- Remdesivir was superior to placebo in shortening the time to recovery in adults hospitalized with Covid-19 and evidence of lower respiratory tract infection.



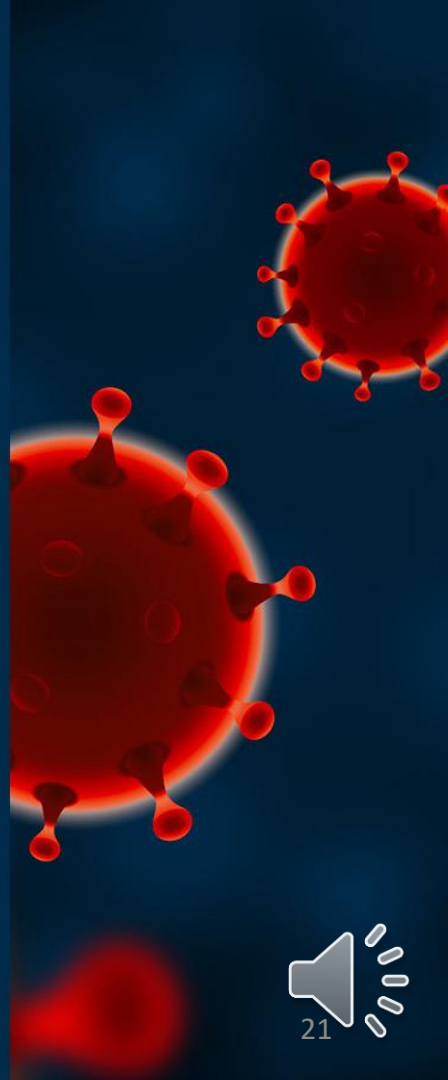
Therapeutic Plasma Exchange (TPE)

- **Study**
  - **Therapeutic Plasma Exchange (TPE) for Covid-19**
- **Results**
  - **Patients in the plasma group had a shorter hospital stay (p 0.001) and lower mortality (p 0.049) than the comparator group.**
  - **No immediate adverse effects were observed following plasma infusion.**



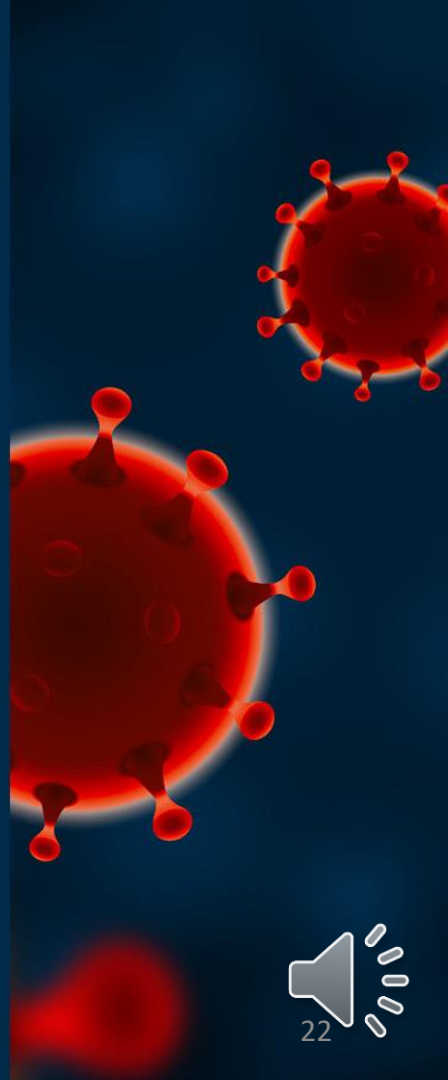
Anti-Inflammatory Drugs

- Extreme release of pro-inflammatory cytokines is the most serious presentation of COVID-19 infection and known as “cytokine storm”
- Primary inhibition of inflammatory pathways may be considered as a treatment for COVID-19
- Several anti-inflammatory drugs are currently available including nonsteroidal anti-inflammatory drugs (NSAIDs), glucocorticoids, chloroquine/hydroxychloroquine, and immunosuppressants to prevent or diminish the progression of inflammation



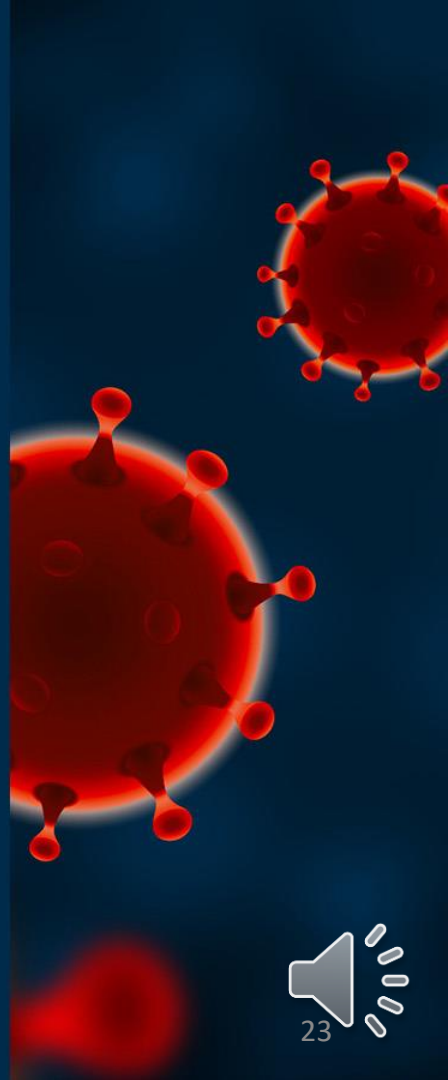
Vaccines

- Whole Virus Vaccines
- Recombinant Subunit Vaccine
- DNA Vaccines
- mRNA Vaccines



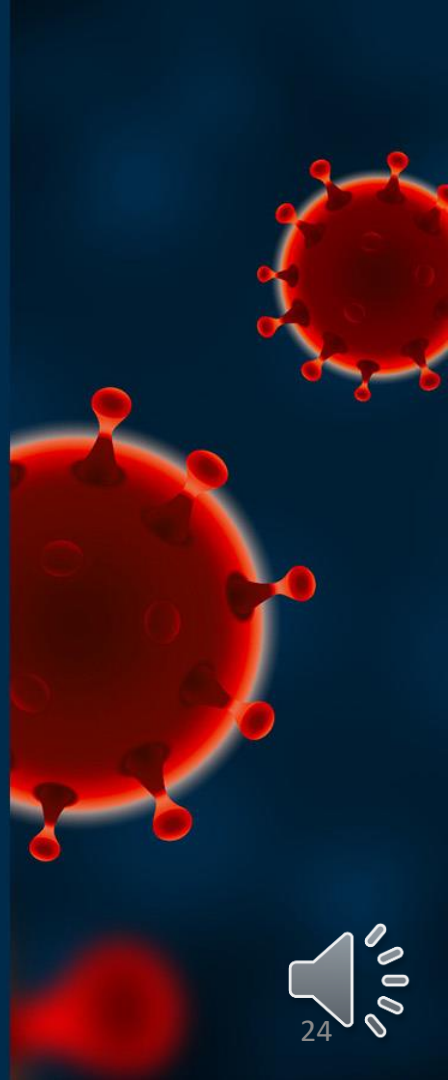
Vaccine types

- **Live-attenuated virus**
  - Advantage
    - Excellence in induction of T and B cells responses
    - Site-directed mutagenesis can be tailor made
  - Disadvantage
    - Risk of reversion to a virulent strain
    - Cold chain required
    - Not suitable or sensitive population such as infants, immunocompromised or elderly individuals



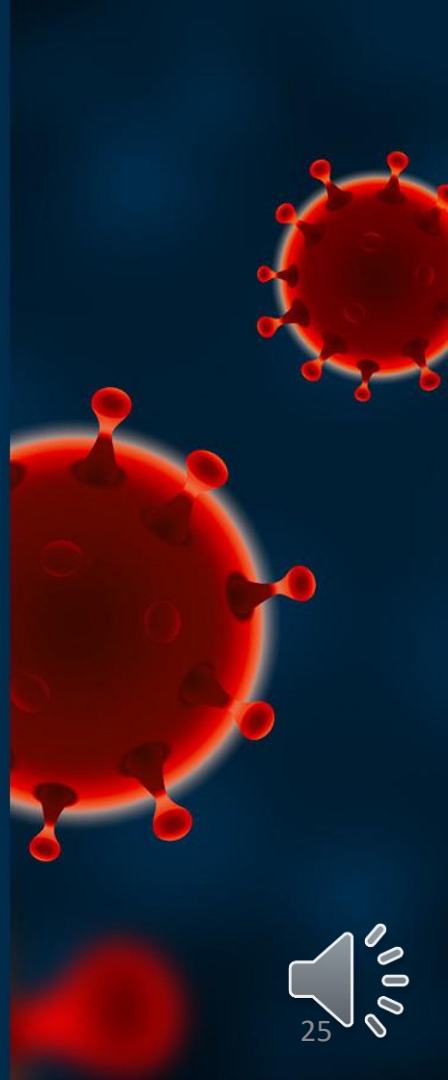
Vaccine types

- **Inactivated**
  - Advantage
    - Preserve virus particle structure
    - Rapid development
    - Excellence in neutralizing Ab induction
    - Can be formulated with various adjuvant
  - Disadvantage
    - Possible cause hypersensitivity
    - Possible Th2-bias



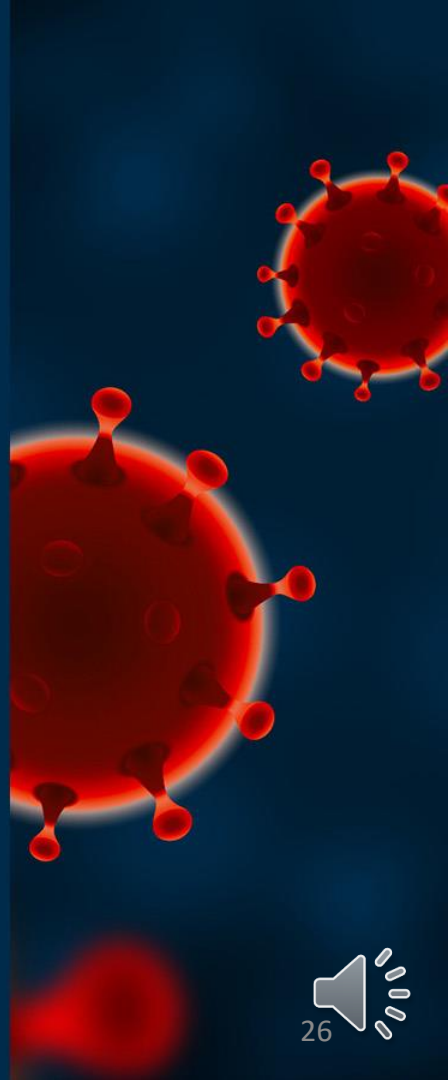
Vaccine types

- **DNA**
  - Advantage
    - Rapid production
    - Easy design and manipulation
    - Induce both B and T cells responses
  - Disadvantage
    - Efficient delivery system required
    - Induce lower immune responses when compare with live vaccine



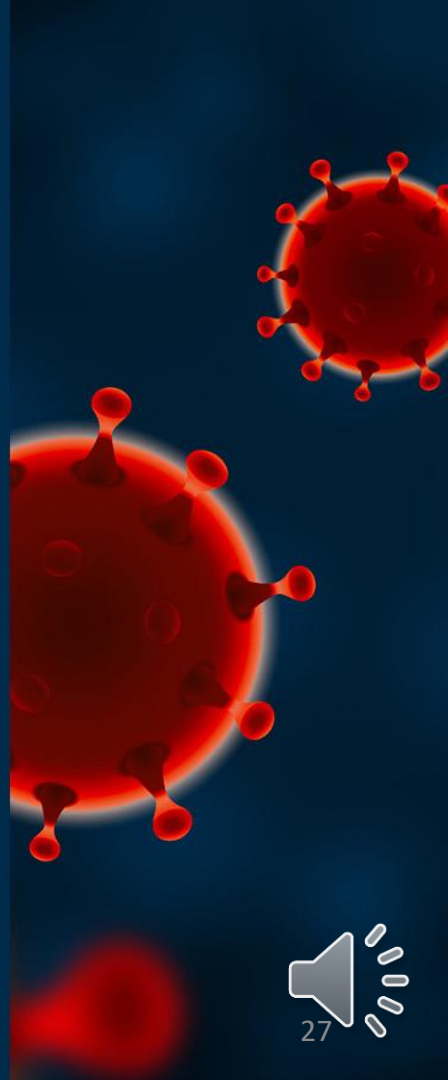
Vaccine types

- **MRNA (Pfizer and Moderna Vaccines)**
  - Advantage
    - Teach cells how to make a protein that triggers an immune response
    - Tells the cells to start making the same protein that is found in the COVID-19 virus
    - Vaccine does not expose you to the virus that causes COVID-19
    - Induce both B and T cells responses
  - Disadvantage
    - Less stable and requires cold storage (-80 Pfizer and -20 Moderna)



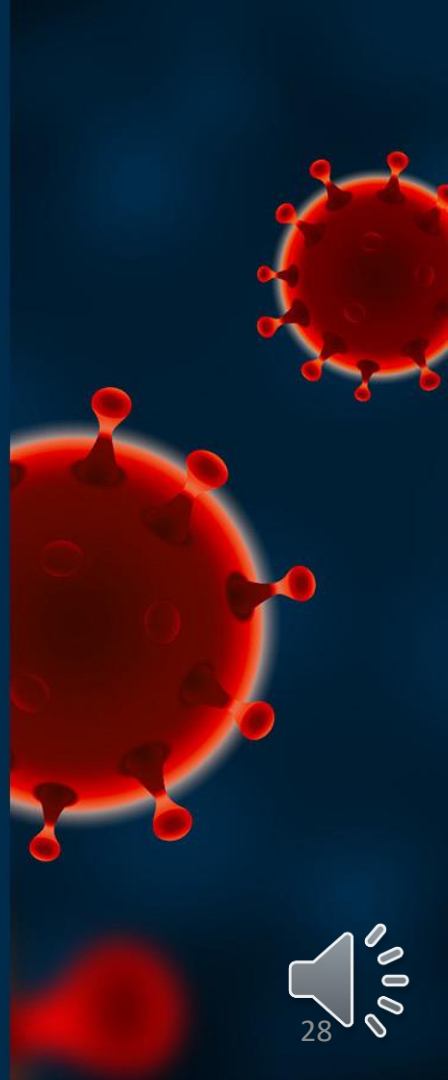
Vaccine types

- **Viral vector**
  - Advantage
    - Excellence in immune induction
  - Disadvantage
    - Varies inoculation routes may produce different immune responses
    - Possible TH2 bias

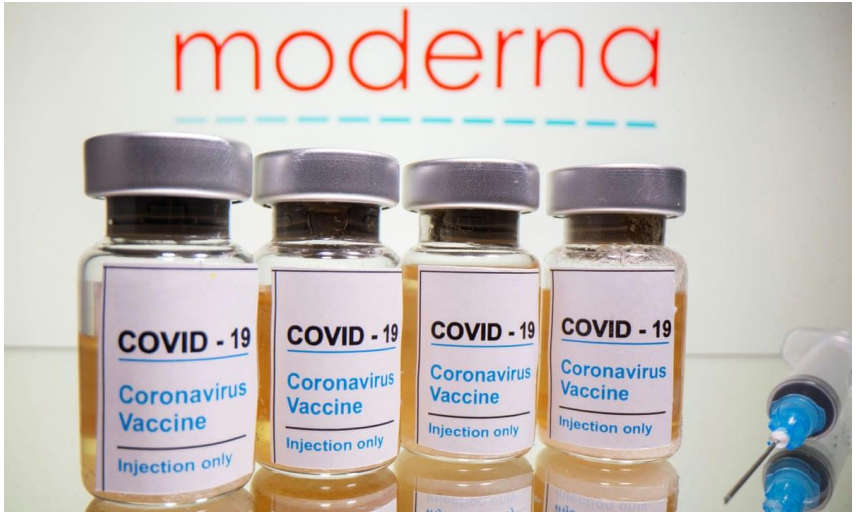


Vaccine types

- **Subunit**
  - Advantage
    - High safety profile
    - Consistent production
    - Can induce cellular and humoral immune responses
  - Disadvantage
    - Need appropriate adjuvant
    - Cost-effectiveness may vary



Moderna Vaccine



- MRNA vaccines teach our cells how to make a protein that triggers an immune response inside our bodies.
- The benefit of mRNA vaccines, like all vaccines, is those vaccinated gain protection without ever having to risk the serious consequences of getting sick with COVID-19.
- 2 shots, one month (28 days) apart
- 95% effective

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/Moderna.html

Pfizer Vaccine

- MRNA vaccines teach our cells how to make a protein—or even just a piece of a protein—that triggers an immune response inside our bodies.
- The benefit of mRNA vaccines, like all vaccines, is those vaccinated gain protection without ever having to risk the serious consequences of getting sick with COVID-19.
- 2 shots, 21 days apart
- 95% effective

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/Pfizer-BioNTech.html

Johnson and Johnson Vaccine

- Viral vector vaccines use a modified version of a different virus (the vector) to deliver important instructions to our cells.
- Modified virus (the vector) to deliver genetic code for antigen, in the case of COVID-19 spike proteins found on the surface of the virus, into human cells.
- By infecting cells and instructing them to make large amounts of antigen, which then trigger an immune response, the vaccine mimics what happens during natural infection with certain pathogens - especially viruses.
- The benefit of viral vector vaccines, like all vaccines, is those vaccinated gain protection without ever having to risk the serious consequences of getting sick with COVID-19.
- One dose
- 72% effective

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/janssen.html

Vaccines around the world

- Oxford-AstraZeneca Vaccine
  - DNA Vaccine
  - Used in Europe (35million in UK)
  - 76% effective
  - Reported blood clot issues and bleeding (held now)
- China
  - Sinopharm and Sinovac's vaccines
  - Inactivated dead virus
  - 243 million people inoculated
  - 79% effective
- Russia Sputnik V
  - Vector Vaccine
  - 79% effective
  - 3.8 million Inoculated March 2021

Delta Variant

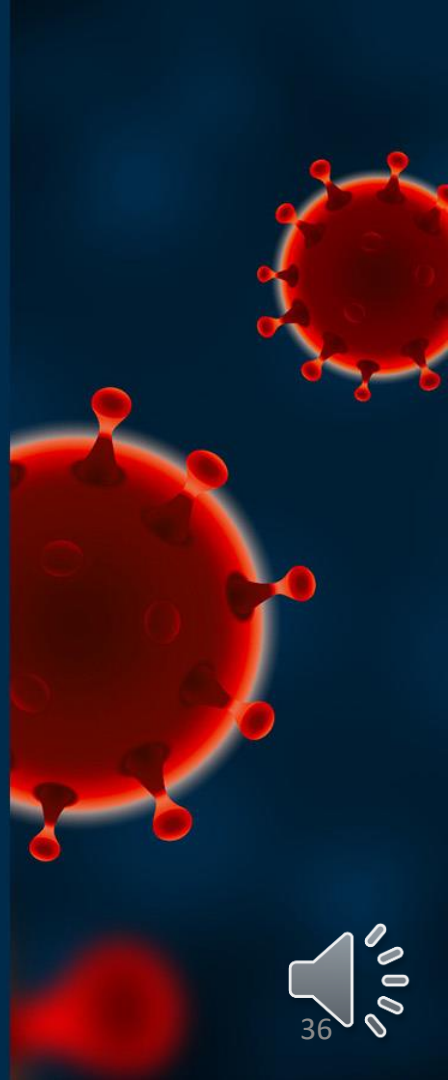
- Early cases originated in India and spread to UK first
- Most new cases of COVID19 are the Delta Variant
- Delta variant causes more severe infections and more hospitalizations
- 2 doses of vaccine give >90% immunity or the 1 dose Johnson and Johnson vaccine
- Most hospitalizations are for unvaccinated patients
- Delta variant symptoms are the same
- COVID-19 tests can detect whether you're infected with COVID-19, but might not be able to differentiate the delta variant specifically unless PCR testing is performed

Types of people in “herd immunity”

- Not immunized but still healthy
  - Not have been in contact with anyone who is sick and didn’t get vaccine
- Immunized and healthy
  - Encountered sick person and got better or received the vaccine
- Not immunized
  - Sick and contagious

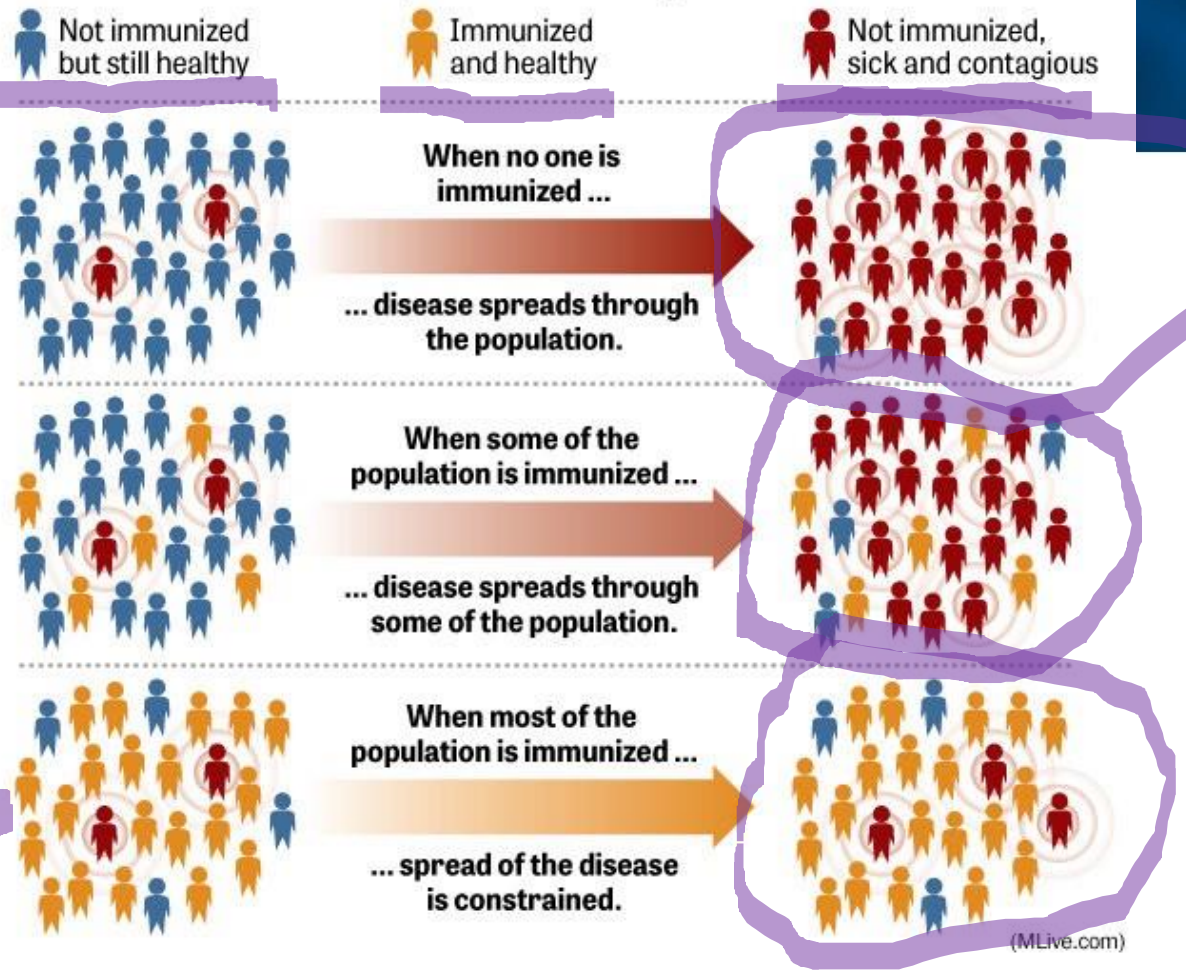
R0 Value

- Incubation is between 2-14 days
- R0 Value & Herd Immunity
- R0 of 2.2-2.6
  - meaning that on average, each individual has the potential to spread the infection to 2.2 other people



WHY DOES MY CHOICE MATTER TO OTHERS?

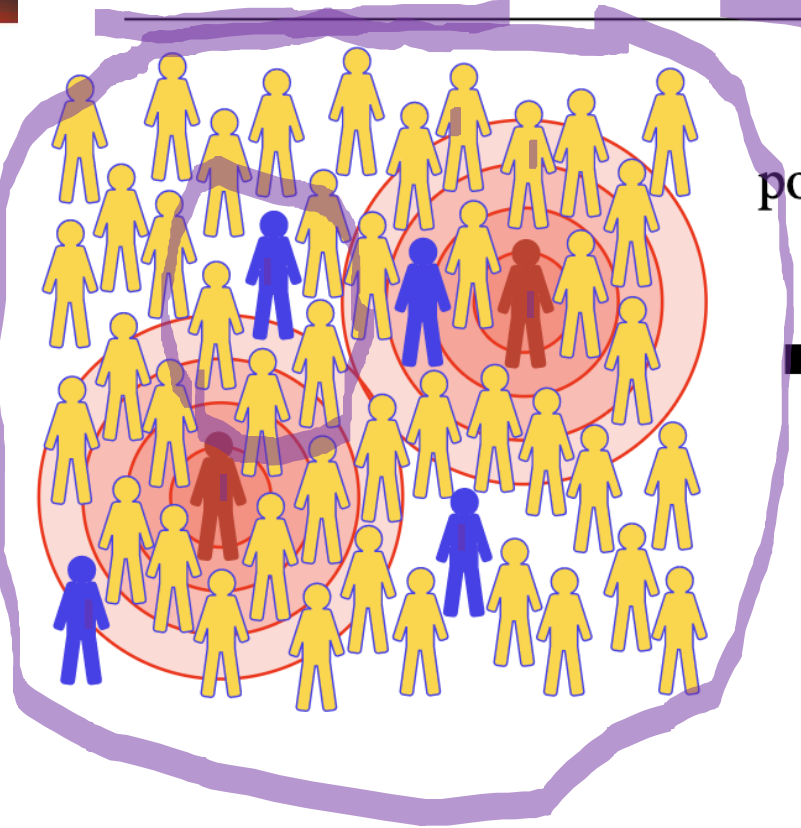
It matters because of the concept of "herd immunity." Here's how it works:



= not immunized, but still healthy

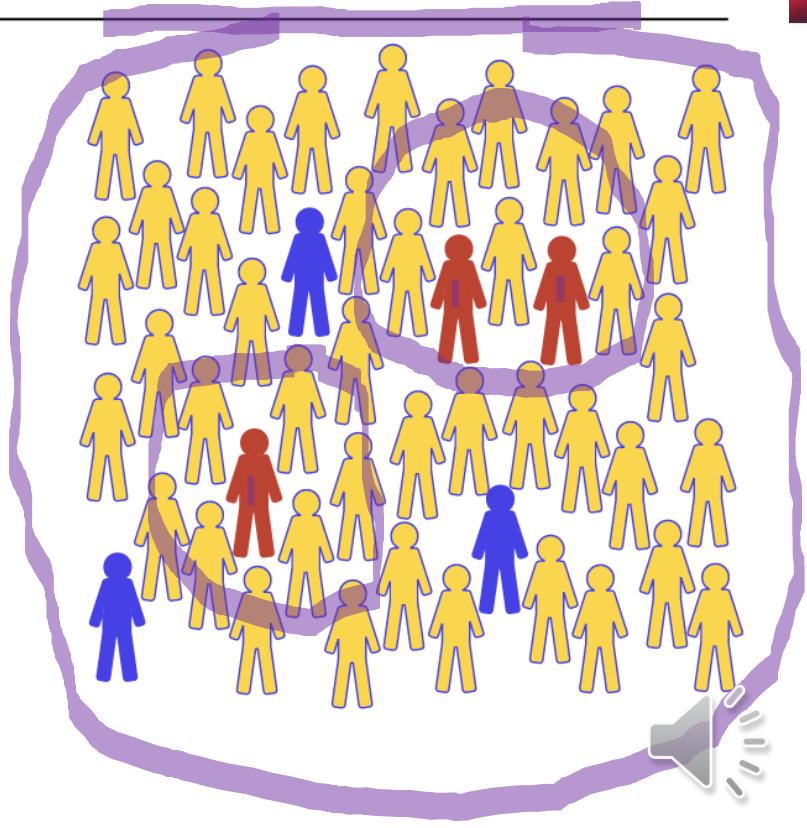
= immunized and healthy

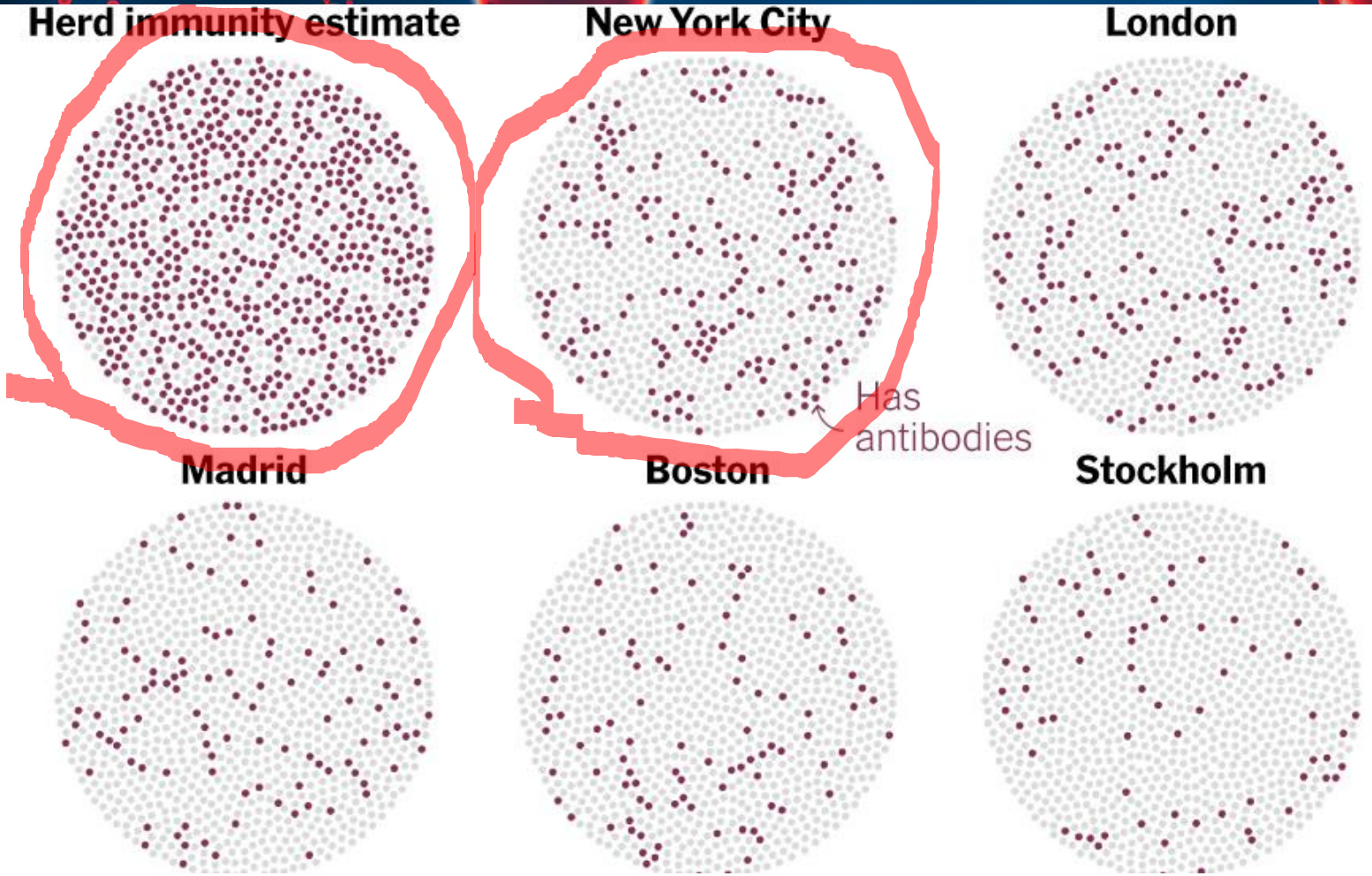
= not immunized, sick, and contagious



Most of the population gets immunized.

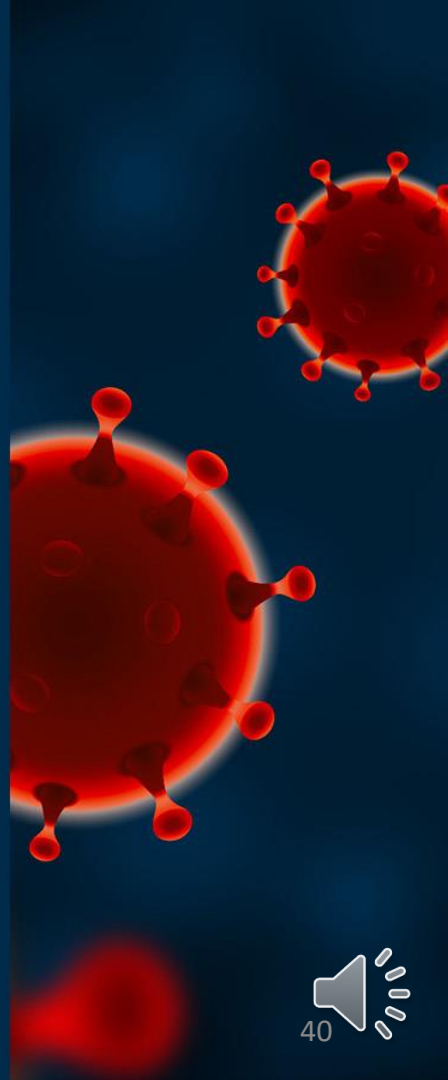
Spread of contagious disease is contained.




Herd immunity estimate
New York City
London
Has antibodies
Madrid
Boston
Stockholm

Summary

- Keep safe
- People who don’t get the vaccine are benefitting from herd immunity
- Still a problem in our world and we are a small place



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