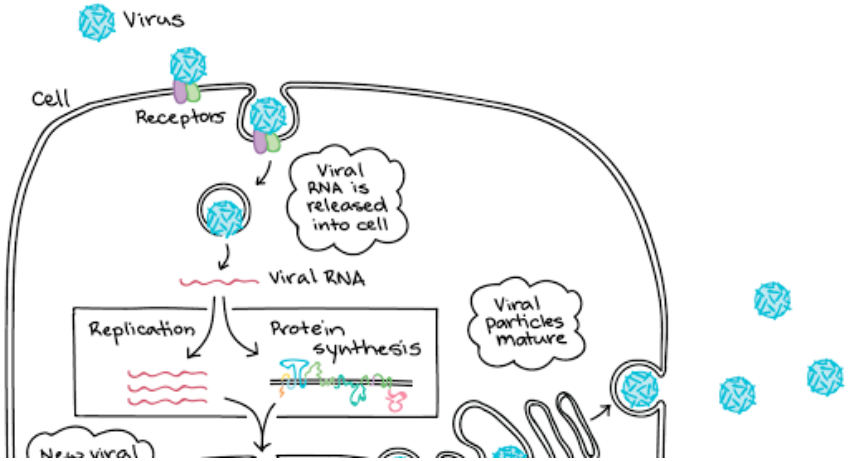
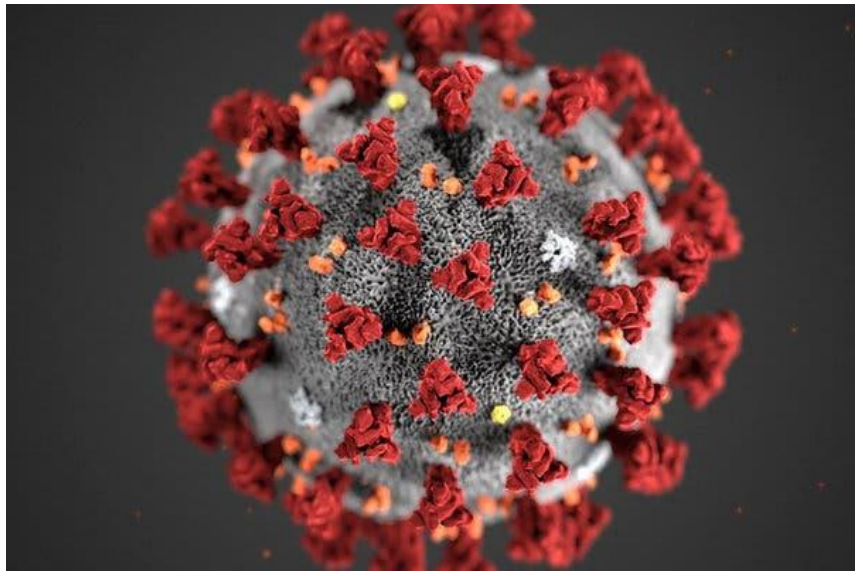
Treatment of CoVid-19

Oscar Gibson

A Simple Introduction to Viruses

- Viruses are tiny, non-living particles that are essentially a capsule of chemicals.
- When they get inside a host cell (such as inside a human):
  1. The virus coat breaks open.
  2. This releases RNA which takes over the ‘machinery’ in the nucleus of the host cell.
  3. The viral RNA causes the host cell to replicate the virus.
  4. New viral particles are released, sometimes destroying the host cell in the process.
- A virus is made up of a combination of 10-12 proteins. The variety of proteins is what changes between different types of viruses.
- CoVid-19 is caused by one such virus, a representation of which can be seen in the image to the right.





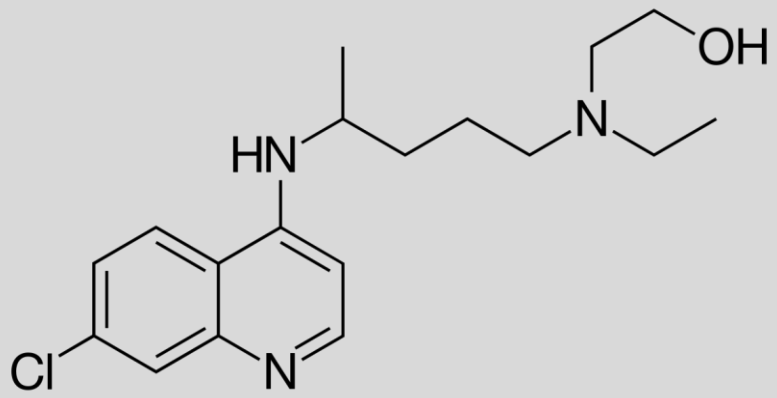
Our Bodies Defences

- Our bodies have a number of natural defences to viruses.
- Firstly, the primary mechanical defence, such as the skin, and hairs in the nose.
    - This acts as a barrier to anything attempting to enter the body.
- Next is the mucous in the respiratory tract, constantly being moved by the cilia, transporting away virus particles or generally unwanted matter.
- Finally, the immune system. This is made up of several responses, but in essence the immune system acts through: macrophages and lymphocytes.
    - Macrophages travel in bodily fluids, including lymph and blood, and destroy small particles by engulfing them and breaking them down – they do this to anything which isn't recognised as part of the body, whether it is a piece of sawdust, or a virus.
    - Lymphocytes originate in the bone marrow, and there are several types, including B, T and killer T. Essentially their role is to recognise invading organisms by their carbohydrate or protein compounds on the surface of their cells, which become antigens when recognised. There are loads of different lymphocytes for recognising different antigens. When they recognise a foreign antigen, they make antibodies, which attach to the receptors (haemagglutinin is what is found on the influenza virus) to stop replication. Usually, when you are recovered, you have memory cells which, if the virus returns, results in antibody's killing the virus.
        - Note that a virus such as influenza readily mutates with antigenic shift as it is made up of RNA, which is single stranded (rather than DNA) allowing for swift mutation. This means that it can't be recognised by the lymphocytes previously made, which is why you must have a new influenza vaccine every year.

Antiviral Treatment – Hydroxychloroquine

- It seems that a drug will be being used to treat CoVid-19 before a vaccine is for it, largely because drugs have already been tested for safety, and so efficacy only has to be proved against this virus.
- Hydroxychloroquine is one potential drug and is currently used to treat:
  - Malaria (Mosquito borne disease that causes tiredness vomiting and headaches – this drug inhibits protozoal food vacuole functioning by increasing the pH of that food vacuole).
  - Rheumatoid arthritis (long-term autoimmune disorder primarily effecting joints – it helps due to its immunomodulatory effects).
  - Lupus (autoimmune disorder when the immune system attacks healthy tissue).
  - Porphyria Cutanea Tarda (results in blistering of the skin when exposed to sun).
  - And many more.
- It was approved for medical use in 1955 by the United States. It is on the WHO's List of Essential Medicines, and in 2017 was the 128th most commonly prescribed drug in the US, therefore it a common, well-understood drug.
- The pharmacokinetics of the drug are: once orally administered (tablet) it has quick gastrointestinal absorption, a large distribution volume and is excreted via the kidneys.
- It is a hydroxylated derivative of chloroquine, with a similar mechanism of action, both of which I will look at in due course. Overall though, it has a safer profile than chloroquine, with lower ocular toxicity. This safety aspect is especially useful during pregnancy and lactation.

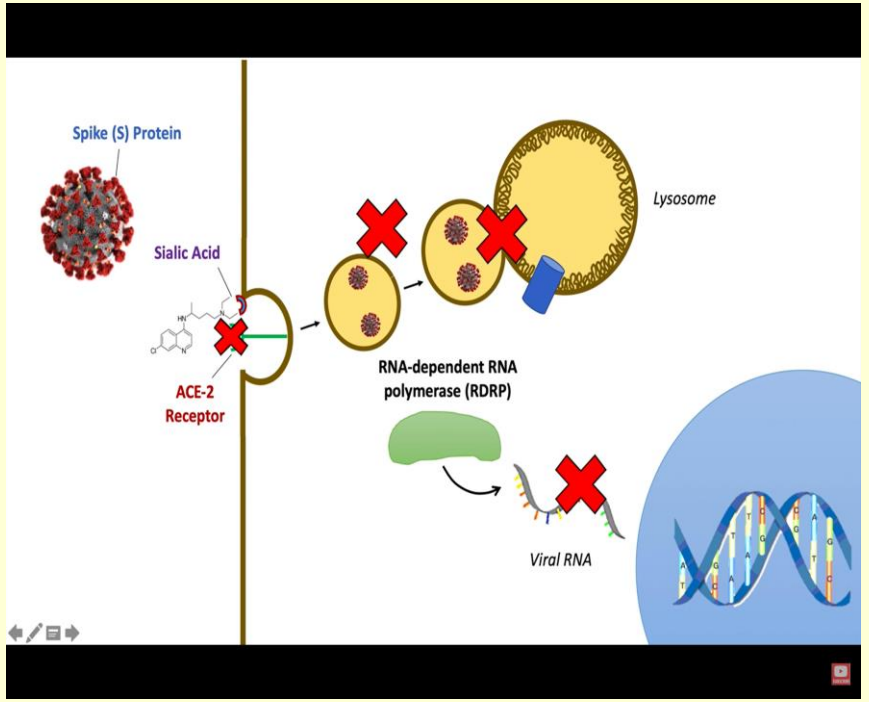
What is Hydroxychloroquine made of and what properties does it have?



- $C_{18}H_{26}ClN_3O$ is hydroxychloroquine (seen in image), whereas chloroquine is $C_{18}H_{26}ClN_3$. Most people talk about these two being one and the same, especially in the current pandemic, as they have a similar mechanism of action. But hydroxychloroquine is much safer and is used to treat different diseases.
- Hydroxychloroquine has many effects on organelle function:
  - Immunomodulatory effects (treating rheumalogical conditions) – look at this in the 'modulating immune system' part of the presentation, so not during this antiviral section.
  - **Alkalinizes lysomal pH** as it has a high pH. A lysosome is an acidified organelle responsible for the recycling of nutrients and other waste products.
  - It is a **zinc ionophore** (basically carries zinc within it through the plasma membrane of cells) allowing zinc into cells so it may have an anti-cancer effect.
  - They **bind to sialic acids**.

Mechanism of action against SARS-CoV-2

- The truth is, its precise mechanism of action is unknown, but the following have been proven in vitro.
- What is known is that it inhibits endocytosis (the process of a virus entering a cell), which works as follows:
  - Spike (S) proteins on the coat of the virus bind to ACE-2 receptors of the cell.
  - This causes it to be endocytosed into the cell, and packaged in an endosome.
  - The endosome fuses into a lysosome, where the virus is released and can infect the cell.
  - This is where hydroxychloroquine comes in.
  - It enters into the endosome and lysosome and alkalizes them preventing their function.
  - Note that it may also inhibit the action of a proton pump into the lysosome, but this isn't entirely known.
  - The alkalization stops the process of endocytosis (bringing the endosome into the cell) and stops the fusion with the lysosome.
- Furthermore, in 2010, a study showed that RNA-dependent RNA polymerase, which replicates the virus, is inhibited by zinc, therefore zinc essentially stops RNA-dependent RNA polymerase from making viral RNA. Therefore, as zinc concentrations increase, viral RNA decreases.
- Finally, around ACE-2 receptors, there is usually a lot of sialic acid on the surface of the cell. The S protein of the virus can bind to sialic acid as well. Hydroxychloroquine binds to the sialic acid so that the S protein of the virus can't and in doing so, the hydroxychloroquine also prevents proper binding of the virus to the ACE-2 receptor.



Why did you pick this drug?

- I looked at many other drugs including:
  - Lopinavir/ritonavir (kaletra – tested showing no benefit to 200 patients in China).
  - Nitazoxanide (inhibits the expression of N protein).
  - Ivermectin (discovered in late-1970s in Japan and originally a vetinary drug, it kills parasites).
  - Camostat Mesylate, Remdesivir and Favipiravir: I will look at more later on.
  - Each of these may have had clinical trials with limited success, but I don't feel that anything has had the marked improvement that hydroxychloroquine has had.
  - The exception is remdesivir, but even with positive signs, the issue is that it has to be administered early, and so it won't necessarily be lifesaving as, with the current pressure on the NHS, people are arriving at hospitals late into their time with the virus, when they need ventilators. Furthermore, the trials aren't conclusive.
- Moreover, since hydroxychloroquine has already passed safety trials and is approved for the treatment of malaria, it has already crossed this large, time consuming barrier to getting the drug onto the market.
- In addition, it is a common, mass manufactured drug that many of us take when we go to a region with malaria. It is therefore well understood and, if it shows efficacy in trials, it can be easily mass manufactured and used on mass. Furthermore, it is already showing improvement (next slide).
- Finally, it has three different methods of working against the virus, which no other drug that I looked at had, so if one fails, one of the others will hopefully work. They also all work on different aspects of the cycle, so they act as safety nets to each other.
- I suppose the obvious next question is, why not chloroquine? My reasoning is as follows (very opinion heavy):
  - Although less active, hydroxychloroquine is a much safer, less toxic drug to use.
  - Given that they both work on similar principles and the efficacy of them both seems to be similar at the moment.
  - The likelihood is that hydroxychloroquine will be more readily accepted by a greater number of patients, and so will become standard treatment.
  - More serious cases may however require chloroquine.

Trials

- The original success of the drug, which caused people to initially express an interest in it, came from reports in China, which showed that it could inhibit SARS-CoV-2 in vitro (of course, this is only in a petri dish but):
- Attempts at treating patients with CoVid-19 were then tried in China and France, which both came out with conclusions of apparent efficacy in treating COVID.
- These tests prompted the following reactions:
  - Trump preaches about how it is a game changing drug.
  - The FDA (food and drug administration in the US) has designated hydroxychloroquine for off-label, compassionate use for treating CoVid-19 (emergency use authorisation).
  - WHO added the drug to its large global SOLIDARITY trial to test a variety of potential treatments.
- Currently, there are 142 trials that have been registered across the world involving hydroxychloroquine and no results have returned as yet. However:
  - An EU based open-label non-randomized trial in which patients were given hydroxychloroquine and azithromycin is showing positive signs.
  - The same is true of an open-label randomized placebo-controlled study of hydroxychloroquine being carried out in China.

Challenges

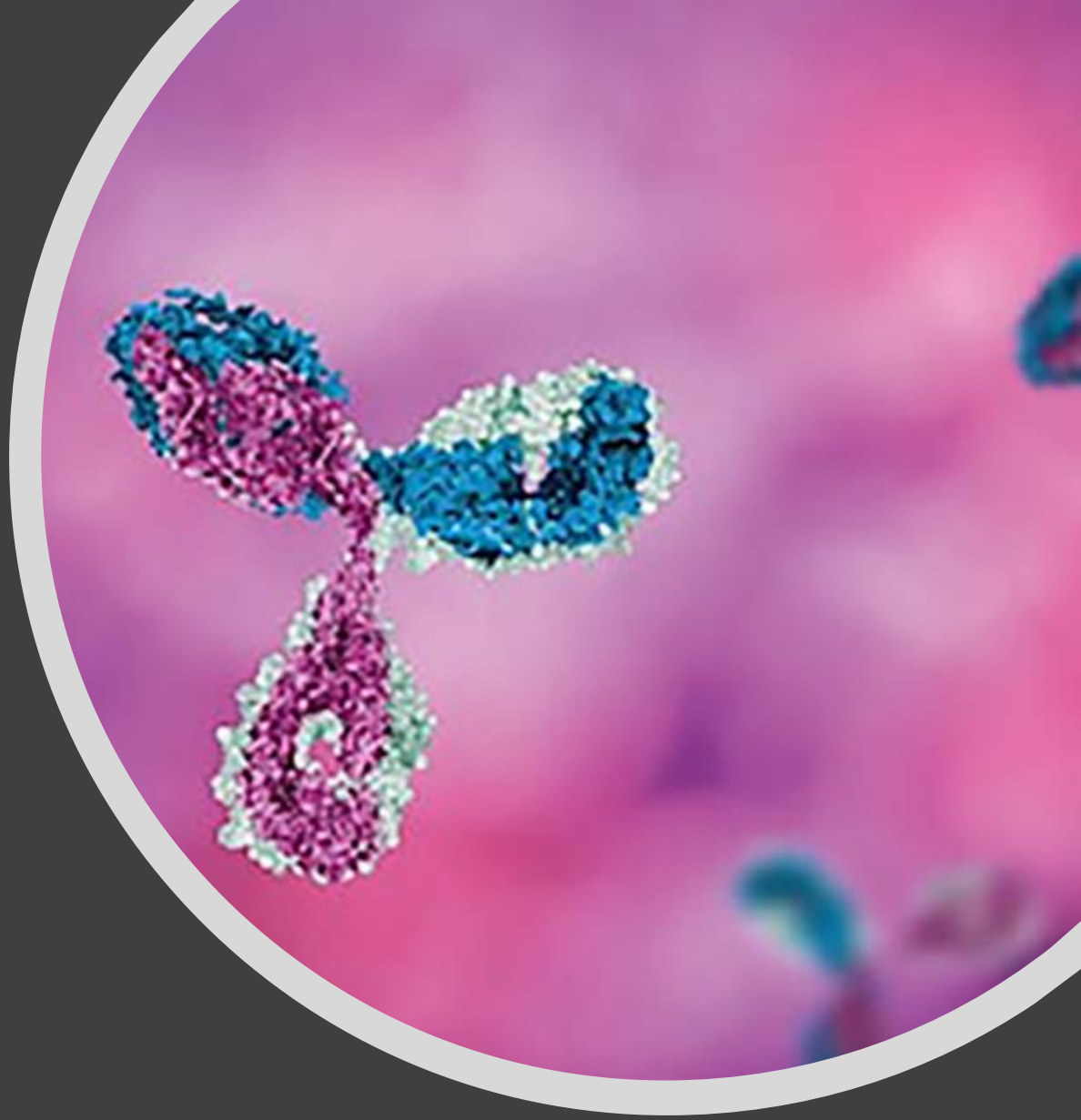
- The previous slide is slightly biased and hides the reality of the treatment. It is a drug that has been tested for many viruses and has shown good results in vitro but not translated through to the same good effects in humans. But I remain hopeful.
- Another large issue is that, as soon as people see some source of efficacy on such a well known drug as this, they begin self medicating with it, and there have been some terrible cases in Nigeria and the US of hydroxychloroquine poisoning. The purchase of this drug by people medicating with it against CoVid-19 has resulted in shortages of the drug for those that had previously been taking it to treat other conditions that it is already used for.
- As with any antiviral drug, since it has to attack something which is using the machinery of its own cells, it has some bad side effects (but we understand these and side effects are inevitable with any antiviral – furthermore, since this will only be short term use to treat COVID in any patient, it is unlikely to have some of the more serious side-effects):
    - Vomiting
    - Headache
    - Change in vision (and potentially long-term retina damage).
    - Heart Problems
    - Stomach cramps and diarrhoea.

Other interesting antivirals

- I will now look at some other antivirals which seem to have been doing well in trials lately, and so were almost ‘close seconds’ to hydroxychloroquine which I ended up choosing. I will just look at how they work, but some (especially Remdesivir) have had successful trials. I am looking at how they work just to show different ways that antiviral treatments work.
- Remdesivir
  - It is a nucleotide analog (this means that they contain a nucleic acid, sugar and phosphate - just like nucleotides that we learned about in DNA and RNA) and mimics adonine.
  - This similarity to adonine means that they can be incorporated into polymerase enzymes, meaning no more RNA sub-units can be added to that enzyme.
  - This blocks polymerase function which is needed for replication.
  - But if you take them too late, there will be too many virus particles for the slowing to help, and also, what kills people is the lungs filling with fluid.
- Favipiravir
  - It selectively and potently inhibits the RNA dependant RNA polymerase, which is an enzyme that catalyses the transcription of RNA from an RNA template; the mechanism which the COVID 19-virus uses to replicate.
  - This stops the virus' RNA chain from elongating and hence causes chain termination.
  - It is not entirely certain how it works however and other research suggests that it induces mutations.
- Camostat Mesylate
  - This blocks the virus’ entry into the cell by inhibiting the cellular host TMPRSS2.
  - This works as the virus’ entry into the cell depends on binding of the viral spike proteins (S) to cellular receptors, angiotensin converting enzyme 2 (ACE2) and on S protein priming by host proteases (TMPRSS2 - transmembrane protease, serine 2).

Passive Immunization

- There are two types of immunization: active and passive. Artificial active immunization is injecting weakened forms of the virus or bacteria into the body (or by other methods of vaccination), so that, when the immune system has recognised foreign particles, it develops a primary immune response. It then keeps memory cells which can react and make antibodies quickly if the virus comes to infect you.
    - Sadly, the vaccine will take a long time to create, as it has to be tested, therefore passive immunization offers a more practical solution in the short term.
- Passive immunization is injecting antibodies made by something or somebody into you.
    - Previously it had been called pharming as horses and cows had been injected with the virus and then had had the antibodies created were removed and injected into patients.
    - This is currently used against tetanus and rabies.
    - Note that this is only good as a short term emergency treatment as no memory cells are created and the antibodies don't hang around forever.
- Currently, there are two main forms of passive immunization:
    - Convalescent plasma insertion takes blood from a recovered person and isolates the plasma for insertion into the patient. This is because antibodies are proteins found in plasma, and thus aren't filtered out when the other red and white blood cells are filtered out of the blood.
    - Monoclonal antibody treatment works as follows:
        - You first inject an animal such as a mouse with a specific protein from the virus.
        - You then can remove the antibodies created (usually around the spleen as this is an aggregation point).
        - You can then fuse them with myeloma tumour cells which divide uncontrollably.
        - Under the correct conditions you create a tissue culture that provides a constant source of antibodies against a specific protein on the virus.



History of Convalescent Plasma Treatment

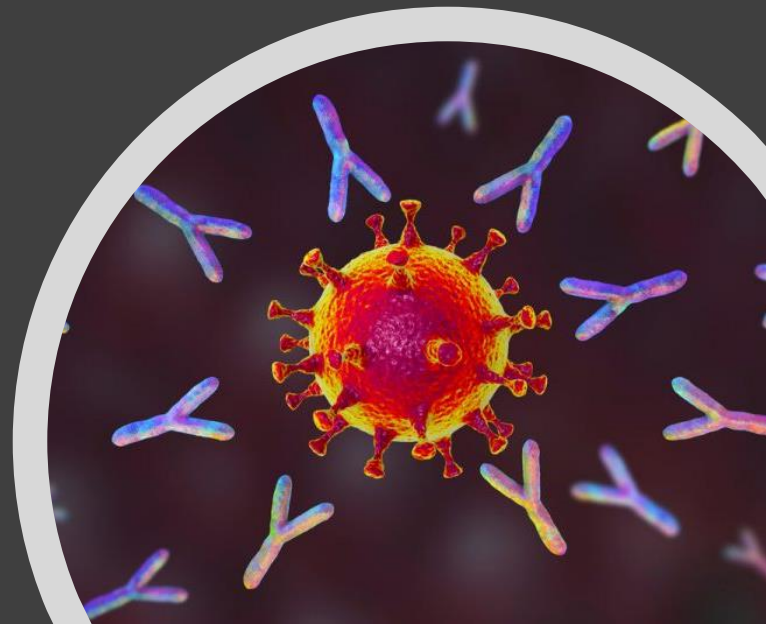
- In 1890, the first rational approach to the use of, what we now know as, convalescent plasma treatment was exploited by the physiologists Von Behring and Kitasato to treat diphtheria. They used blood serum:
  - Initially, it was produced from immunised animals.
  - Soon whole blood or serum from recovered donors with a specific humoral immunity were identified as a possible source of specific antibodies of human origin.
- Studies conducted during the Spanish influenza pandemic of 1918 to 1920 suggested that the use of convalescent plasma might be effective. In the end it had mixed results for the treatment of Spanish flu. But, after this, for the first time it was identified as a potential therapy for a number of viral infections. In the following decades, possible therapeutic efficacy was claimed for the management of:
  - Measles,
  - Argentine haemorrhagic fever,
  - Influenza,
  - Middle East respiratory syndrome coronavirus (MERS-CoV).
- There are several other examples of the use of this treatment being used for the prophylaxis or treatment of bacterial infectious diseases such as scarlet fever in the 1920–40s and pertussis until the 1970s as well.
- It also ended up as being a successful treatment for Ebola.

Current Coronavirus Passive Immunisation

- Monoclonal antibody treatments are being researched across the world, and I will look more at this on a later slide.
- The convalescent plasma transfusions are being tested (used on patients) in various countries at the moment, including in the NHS, with people including Matt Hancock donating their plasma. Michael Squire was the first to donate his plasma to the NHS.
    - The current trials have shown improvement (including two Chinese trials), but to what extent can this be scaled up? I don't think it can be a widespread solution.
    - Israel is a country that is very heavily using this treatment at the moment. In their initial trial of 37 patients, they saw improvement (though obviously this is not substantial evidence). This includes one man in his 60s who was on a ventilator who showed improvement. Furthermore, the other patients ranging from 50 to 80 all showed improvement as well, with one being discharged. Although I understand that it is hard, at this stage, to attribute this success entirely to the plasma transfusion, I feel that it shows promising signs.
    - In America, the FDA approved two nationwide clinical trials in early April. Nearly every blood centre in the country (600 centres) are working to collect convalescent plasma. The FDA allowed it to be used in 'compassionate use' cases.
    - Currently 6500 people have registered their interest for the NHS Blood and Transplant plasma donation programme as well.
    - Takeda and Vir, are two Japanese companies looking for the efficacy of convalescent plasma treatment as well.

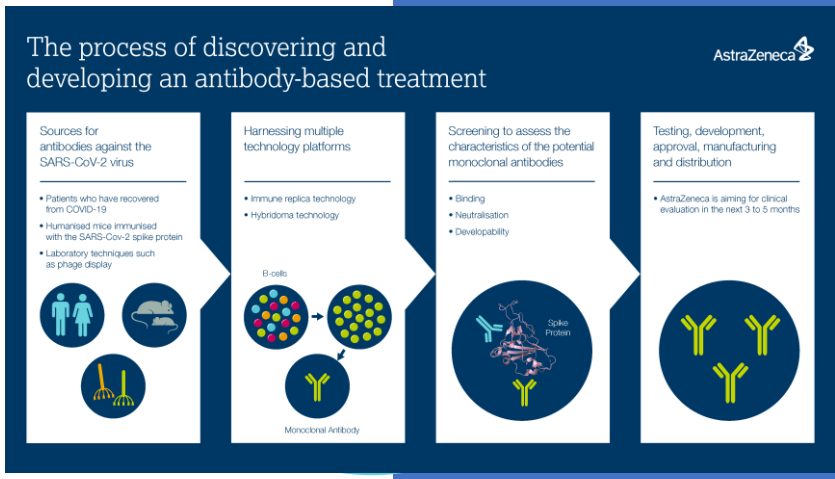
Where do you see this treatment going?

- For me, the only plausible solution is creating a monoclonal antibody treatment, as, once created, it provides an almost infinite source of antibodies. The convalescent plasma insertion is very limited, not only because there are only a limited number of patients that have had CoVid-19, but also because of those patients that have recovered from CoVid-19, only certain people in that category will be happy to give their plasma. I will look more at the research into monoclonal antibody treatment on the next slide.
- Having said this I feel that convalescent plasma treatment **will** be eventually successful, but I think it will only be given to those in the worst condition as there will only be limited availability of it. I also think that this plasma transfusion will be one of the first successful trials, but it will only be limited in number. It can however be given from the donor to the receptor as soon as 36 hours after being collected so it is quite a swift treatment. But, donors have to be symptom free for 28 days which creates a long waiting time and, at the viruses peak infection in a country, I just can't see this treating all the people that need it. What's more, you have to be the same blood type as the donor, which adds another level of challenge in distribution.
    - This issue of limited resource has already been seen, such as in New York where they were rationing plasma and having to make challenging ethical decisions on who should receive the plasma.



Monoclonal Antibody Treatment Research

- This is what I think the most effective antibody treatment will be, so where are we at the moment?
- AstraZeneca are currently partnered with governments and external academic experts to evaluate possible candidates.
  - They are trailing three different sources of antibodies: patients who have recovered from CoVid-19, immunised humanised mice and laboratory techniques such as phage display.
  - They are aiming at targeting the Spike protein on SARS-Cov-2.
  - They are harnessing its proprietary immune replica technology, which can capture and screen antibodies from millions of primary B cells. The company is also utilising hybridoma technology, which is a method for producing large numbers of monoclonal antibodies through a culture of hybrid cells that results from the fusion of B cells and immortal myeloma cells.
  - Once identified, the monoclonal antibodies will be screened against their ability to bind to the spike protein before further developability tests are carried out.
  - They are aiming for clinical evaluation in the next 3 to 5 months.
- Celltrion is another company working on this. They initially identified and secured 300 different types of antibodies that bind to the SARS-CoV-2 antigen.
  - These were then screened based on their ability to bind to the virus Spike (S) protein.
  - Celltrion was then able to capture a total of 38 potent neutralising monoclonal antibodies, of which, 14 were identified as most potent against SARS-CoV-2. They are now beginning cell line development on these and anticipate moving into the first human trails in July.
- The Pandemic Prevention Platform, supported by the Defence Advanced Research Project Agency, are currently still looking at possible antibodies that block the virus, but something interesting that they have said is:
  - The animal testing phase may take longer than usual as researchers need special, genetically modified mice to test coronavirus therapies. Normal lab mice aren't easily infected with this virus, and the susceptible mice are in short supply. So, they are trying to find other animals they might use to develop their candidate antibody. For example, researchers in China have shown the rhesus monkeys can be infected with the new coronavirus, so that's one possibility.
  - They say, best case scenario, they might have a drug in June.
- Current trials are continued onto the next slide.

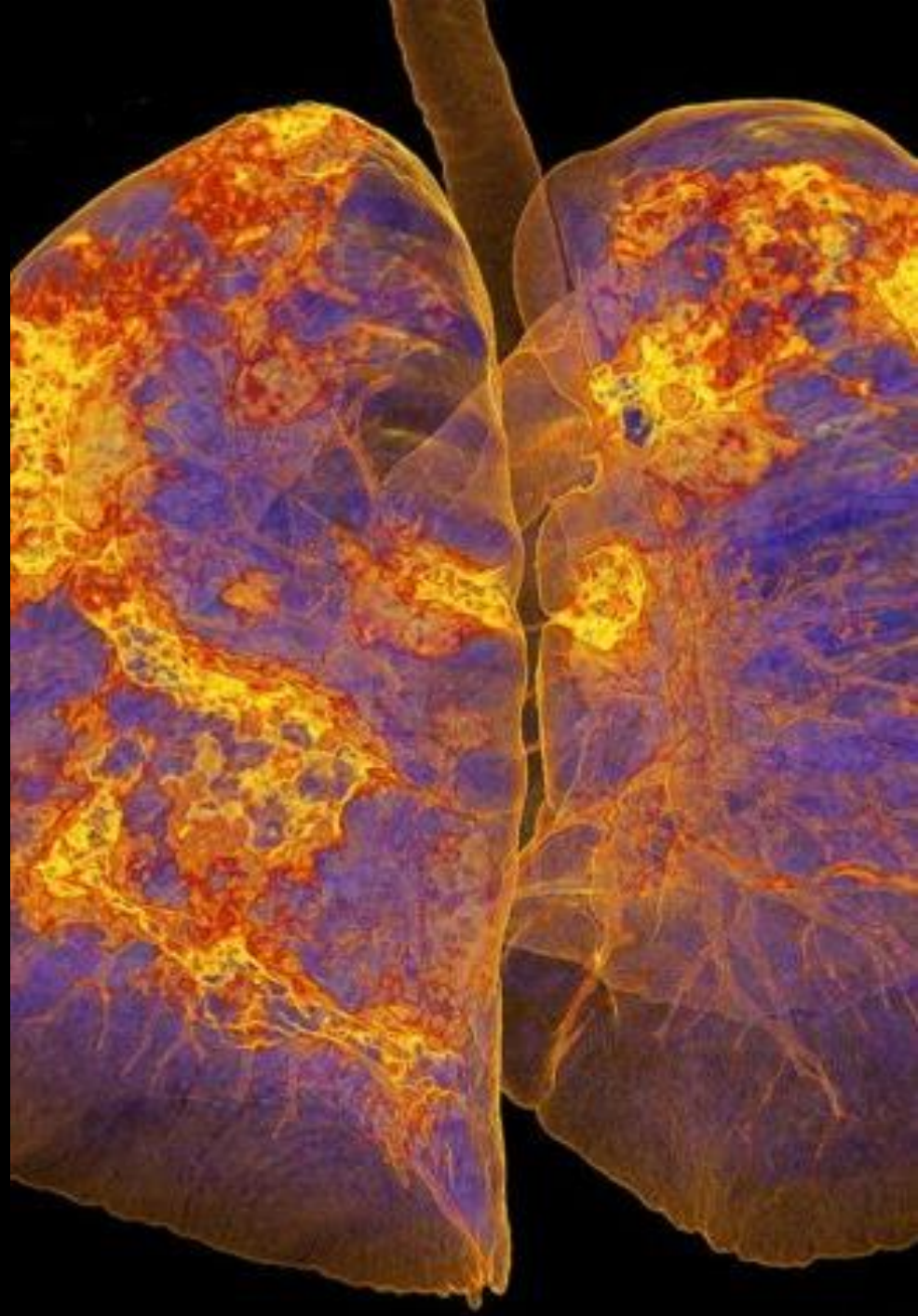


Monoclonal Antibody Treatment Research continued

- GlaxoSmithKline announced a $250 million investment in San Francisco-based, Vir Biotechnologies to support its development of a monoclonal antibody drug for CoVid.
- Regeneron scientists have isolated hundreds of neutralizing antibodies against the SARS-CoV-2 virus from a humanized mouse model as well as from humans who have recovered from CoVid-19.
  - Their goal is to select the top two antibodies for a cocktail therapy, which can either be administered to at-risk people before exposure as a vaccine or as treatment for those already infected.
  - They aim to enter clinical studies by early summer.
  - Their SARS-CoV-2 antibodies will target the spike protein in an attempt to block the interaction of the virus with the host.
  - They used their proprietary VelociSuite technologies to produce fully human antibodies against the novel coronavirus from genetically edited mice.
  - Regeneron is preparing for clinical-scale production with the goal of making hundreds of thousands of low prophylactic doses per month by the end of summer.
  - It's also working with the HHS' Biomedical Advanced Research and Defence Authority and the U.S. Department of Health and Human Services to ramp up manufacturing capacity even further.
- 3rd People's Hospital in Shenzhen began analysing antibodies from blood taken from recovered CoVid-19 patients, isolating 206 monoclonal antibodies which showed what he described as a 'strong' ability to bind with the virus' proteins, and say that their trials are looking successful at the moment.
- Eli Lilly and AbCellera have entered into an agreement to co-develop monoclonal antibody products for the treatment and prevention of CoVid-19. The collaboration will use AbCellera's rapid pandemic response platform, developed under the DARPA Pandemic Prevention Platform (P3) Program, and Lilly's global capabilities for rapid development, manufacturing and distribution of monoclonal antibodies.
- Studies in both Switzerland and the Netherlands have claimed to create antibodies that can block the spike protein on the coronavirus infection. They both claim to have neutralised the virus in a lab setting. They created it by isolating a specific plasma cell from a patient that is producing a neutralising antibody. This means that they can fuse it with a myeloma cell to make a limitless supply of the antibody.
  - These are the first countries to have this level of evidence and they describe it as a 'significant breakthrough'.
  - Israeli Prime Minister, Benjamin Netanyahu, has pledged $60 million at an international donors conference raising funds for this treatment.

CoVid-19's effect on our bodies

- CoVid-19 begins with an incubation period of 5 days.
  - This is when the virus begins to establish itself and infect the lungs, throat and airway, turning the cells in these areas into 'coronavirus factories'.
- You then move into mild disease phase for about a week.
  - Most people (8 out of ten who get it) experience mild symptoms, a fever and a cough. It can also result in body aches, sore throat and a headache.
  - It is a result of your immune response, and the release of chemicals called cytokines, who rally he immune system but cause aches, pain and a fever.
- Few (14%) people move onto the severe disease phase, if the immune system overreacts to the virus, it moves from a protective to a pathological immune response.
  - There is often too much inflammation, caused by cytokines (these reactions are 'cytokine storms'), which results in collateral damage throughout the body. This can cause pneumonia, and results in your lungs filling with water.
  - Here one may need a ventilator to help them breathe, in order to get sufficient oxygen around the body.
- Very few people (6%) move to the critical phase.
  - The immune system is moving out of control and damage is caused throughout the body as the blood doesn't have enough oxygen. This leads to organ failure in some cases, septic shock.
  - Acute respiratory distress syndrome may occur which is caused by widespread inflammation in the lungs, stopping the body from getting enough oxygen needed to survive. It can stop the kidneys from cleaning the blood and damage the lining of your intestines as well.
  - Here ECMO machines (extra-corporeal membrane oxygenation) act as artificial lungs, as they take blood out of the body and oxygenate it for you.
- If this condition gets very bad, death can occur.



Treatment of Cytokine Storms

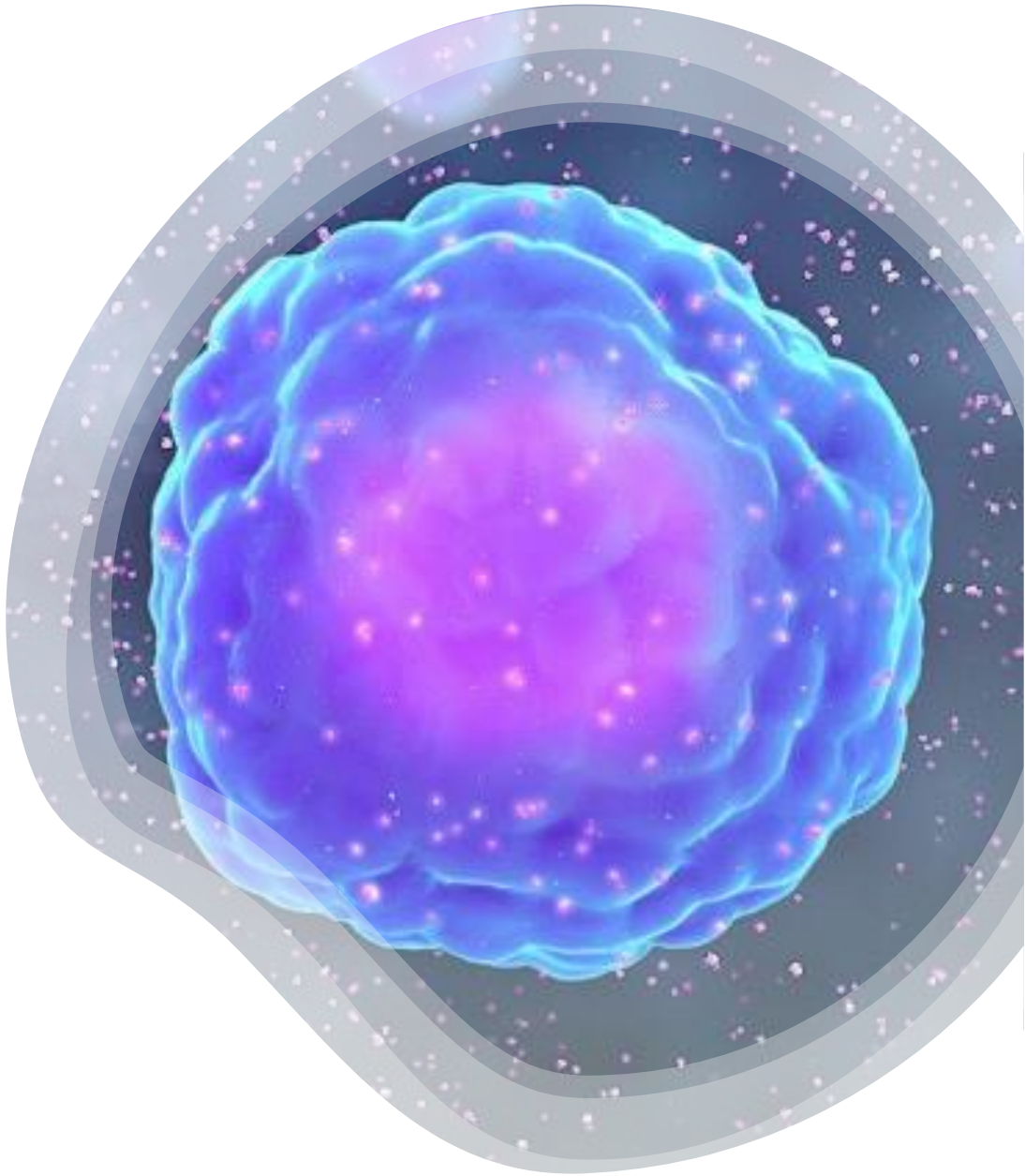
- So, how do we deal with cytokine storms? The answer is that many drugs are currently being trialled, with various mechanisms of action. Some are listed below, but I will look at a few in more detail on later slides.
- One drug that has been developed by Synairgen uses interferon beta to modulate the immune system and suppress the cytokine storm.
  - Thus far, it has been blind trialled in 10 hospitals around Britain, including Southampton University Hospital.
  - The initial results of the trial are expected by the end of June.
- Another possibility is dexamethasone which is a corticosteroid. There is some evidence that it may be successful if used in the early acute phase of infection, but other trials say that it exacerbates the symptoms of CoVid-19.
  - This drug is currently used to treat rheumatoid arthritis and multiple sclerosis as it is an anti-inflammatory.
- Finally, tocilizumab is a monoclonal antibody that is synthetically produced and binds to the IL-6 on cytokines, which cause excessive inflammation. As the monoclonal antibody binds to it, it blocks this process and stops the inflammation.

Vitamin D

- For a long time, Vitamin D has been know to increase antibody production and decrease the levels of cytokines.
- During this pandemic, there has been a strong link between vitamin D levels in the blood, and mortality rates of CoVid-19, with lower vitamin D levels corresponding to higher mortality rates.
- One study in Indonesia has shown that vitamin D has both decreased the severity and the mortality of CoVid-19. This study had 780 cases, confirmed positive by a blood test, showed decreased severity of:
  - Blood clots
  - Hypoxia
  - Respitory distress
  - But, the most interesting part of this study was as follows:
    - 49.7% of the people on this study had normal/sufficient vitamin D, of which 4 died.
    - 27.7% had insufficient vitamin D, of which 88% died.
    - 23% had deficient vitamin D, of which 99% died.
    - This shows an undoubtable trend. Therefore I think that, by spending more time out in the sun, and eating oily fish, you are at a massively reduced risk of death as it 'puts out' the cytokine storm.
    - Over 1 billion people in the world are deficient in vitamin D, and, in the immediate short term, I think that this is the most important preventative measure – getting more vitamin D into your system.
- But, the following groups, who are known to have lower levels of vitamin D, are more at risk of having a severe immune response to CoVid-19. People that are/have:
  - Obese,
  - Diabetes,
  - Dark skinned,
  - Live in the city.

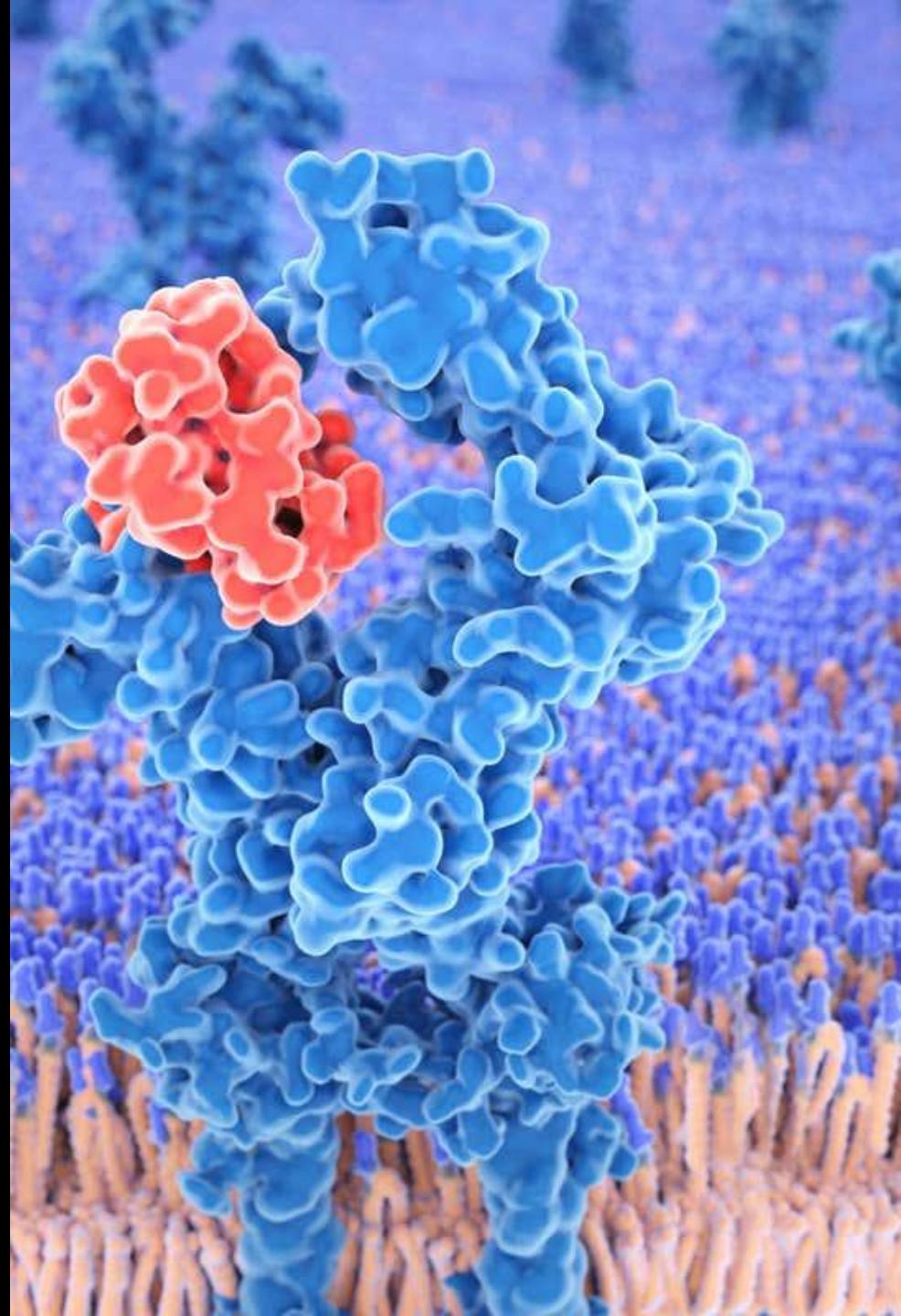
Hydroxychloroquine

- As I have already mentioned, Hydroxychloroquine has antiviral properties, but it also has anti-inflammatory properties as well that are being tested to stop cytokine storms caused by CoVid-19.
- What it does to suppress cytokine storms is decrease cytokine production by macrophages such as interleukin (IL)-1 and IL-6.
- It also has interaction with toll-like receptors and T cell receptors making it effective in different sites of the signalling cascade in the inflammatory response. These interactions prevent autoimmunity without immunosuppressing the patient, meaning that the balance is right between stopping the cytokine storm, and ensuring that the patient's immune system is still working to fight off the SARS-CoV-2 virus.
- Since several viruses upregulate the expression of IL-1, IL-6 and TNF-alpha in vitro, Hydroxychloroquine is very effective in viral infections, and could be too in this infection. Furthermore, with its doubled antiviral and anti-inflammatory properties, as well as it being a well understood drug, that is being repurposed, I really do feel that it is going to be quite successful in the treatment of CoVid-19.
- The biggest concern surrounding this drug is the effect that it has had on bone marrow in the past, leading to reduced white blood cells, platelets, and abnormal red blood cells.
- But, I will end my thoughts on this drug, with a trial by Renmin Hospital of Wuhan University, who carried out a trial on 62 patients, randomized to receive either placebo, or Hydroxychloroquine, 200mg twice daily for 5 day. Their results suggest that patients hospitalized with mild illness recovered more quickly with the addition of the drug than with the placebo at the start of a standard treatment.



Infliximab

- Infliximab is a monoclonal IgG1 antibody that is produced by a recombinant cell line cultured by continuous perfusion.
- It is an anti-TNF (tumour necrosis factor - a pro-inflammatory cytokine involved in the establishment and maintenance of tissue inflammation). Therefore, infliximab inhibits TNF's natural process, therefore stopping the inflammation. It is currently used for diseases including:
  - Crohn's disease,
  - Rheumatoid arthritis,
  - Psoriasis.
- There are other monoclonal antibodies that do the same including adalimumab and golimumab, but infliximab is currently the one being the most researched for CoVid-19.
- Currently Johnson and Johnson are doing research into the uses of infliximab in patients with CoVid-19, but this is in early stages, and no evidence has been released as yet.



Summary

Overall, I think that is undoubtable that one of these treatments will come out before a vaccine, but which one? I hope that hydroxychloroquine shows conclusive beneficial evidence, as it can then be distributed quickly on mass. However, I feel that it won't be conclusive until at least September. In the mean time, I feel that the convalescent plasma, if scaled up effectively, is showing really good improvements, and also feel that the studies done on Vitamin D should be distributed to people to (hopefully) reduce mortality this way. I feel that the monoclonal antibody treatments will take a bit longer to come out.