LAST UPDATE: 10 FEBRUARY 2021

CORONAVIRUS
UPDATE
49

An update on

Immune response to SARS-CoV-2 & viral infections

THE LATEST ON THE COVID-19 GLOBAL SITUATION
& THE IMMUNE RESPONSE

World Health Organization | EPI•WiN | infodemic MANAGEMENT

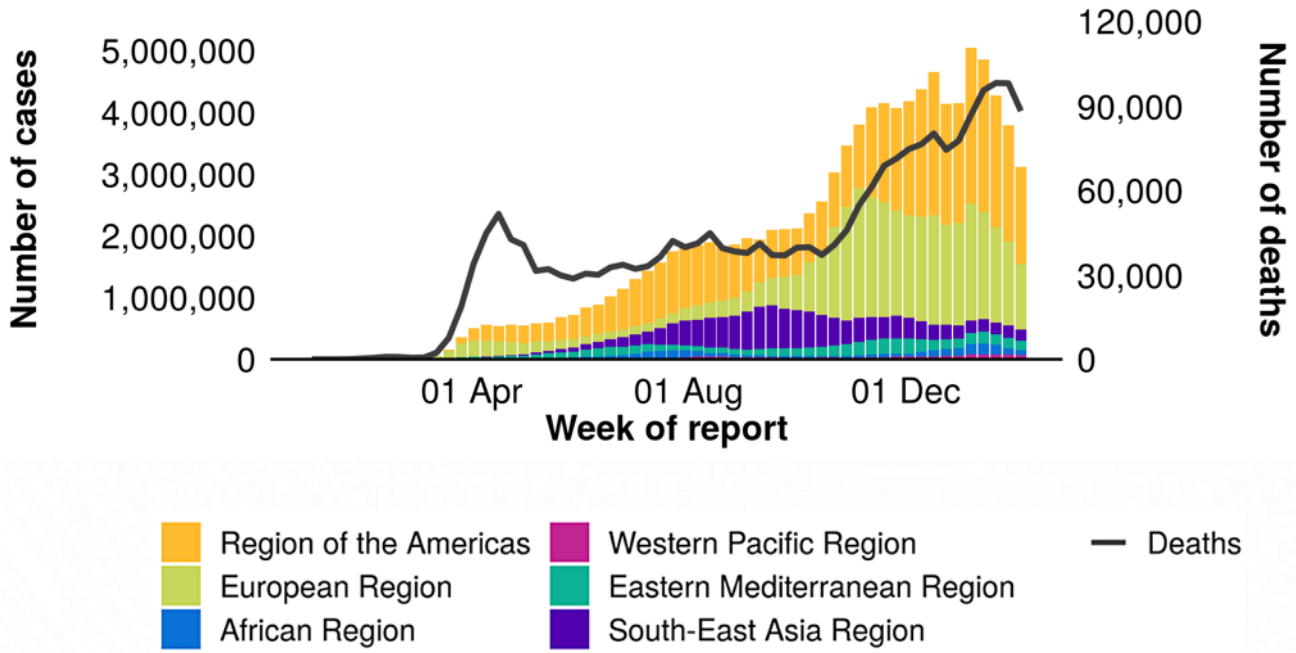
Overview

- Global situation 3
- Immune response to viral infections 4
- Innate immune response 6
- Adaptive immune response 7
- Re-infection of SARS-CoV-2 12
- SARS-CoV02 variants and COVID-19 vaccines 14
- COVID-19 protective measures 15
- WHO resources 16

Current global situation

Cases reported to WHO as of 07 February 2021, 10:00AM CEST

- **> 105 million cases**
- **> 2.3 million deaths**



CHECK OUT
THE LATEST GLOBAL SITUATION

WHO Coronavirus Disease (COVID-19) Dashboard

* Data are incomplete for the current week. Cases depicted by bars; deaths depicted by line

Immune response to viral infections

- The immune system is the body's natural ability to defend against pathogens (eg. viruses, bacteria) and resist infections
- Two types of immunity are:
  - **innate immunity** and
  - **adaptive immunity**

Innate immune response

- First line of defence
- General immediate response to ANY infection
- Innate immune response cells secrete interferons[1] and other chemicals (cytokines)
- Interferons interfere with virus replication
- The innate response activates the adaptive immune response[2]

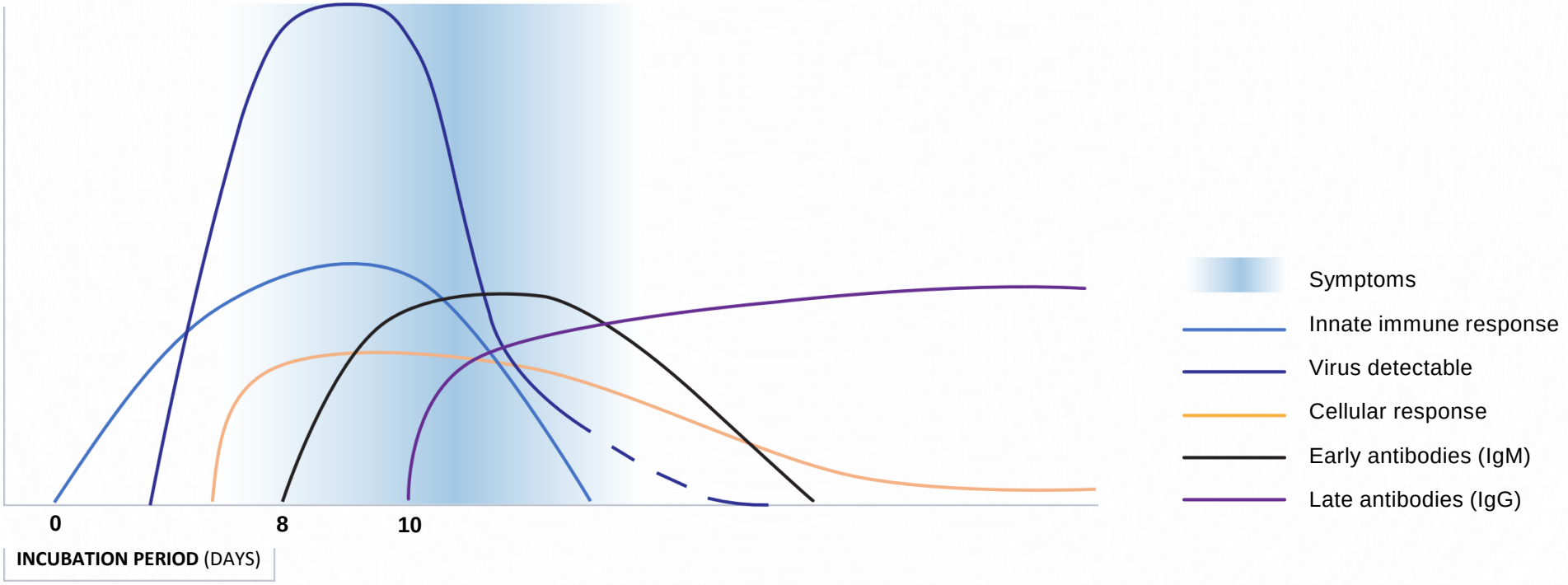
Adaptive immune response

- Second line of defence
- Specific response to the infection
- Starts after 6 - 8 days
- Involves two types of white blood cells
  - **T cells** (cellular response)
  - **B cells** (antibody response)

[1] Interferons and cytokines cause fever, muscle aches, etc – the typical early symptoms of infection
[2] A 'weaker' innate response (e.g. in elderly people or those with underlying health problems) may result in delayed stimulation of the adaptive response

Immune response to viral infections

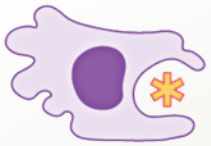
- The innate immune response is immediate, whereas the cellular and antibody response usually starts after 6 to 8 days



Innate immune response

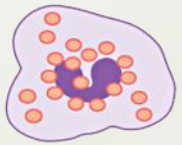
- When a virus enters the body, **cells can recognize markers** present on the virus
- This results in non-specific antiviral activity
- **Cells of the innate system** (such as marcophages, neutrophils, dendritic cells and others) **are activated to remove pathogens and foreign cells** from the body and activate the adaptive immune response

Cells involved in the innate immune response



Marcophage
Phagocytic cell that consumes foreign pathogens; Stimulates response of other immune cells

Neutrophil
First responder at site of infection. Most common type of white blood cells. Releases toxins that kill bacteria and recruits other immune cells to site of infection



Natural killer cell
Kills virus infected cells and tumor cells

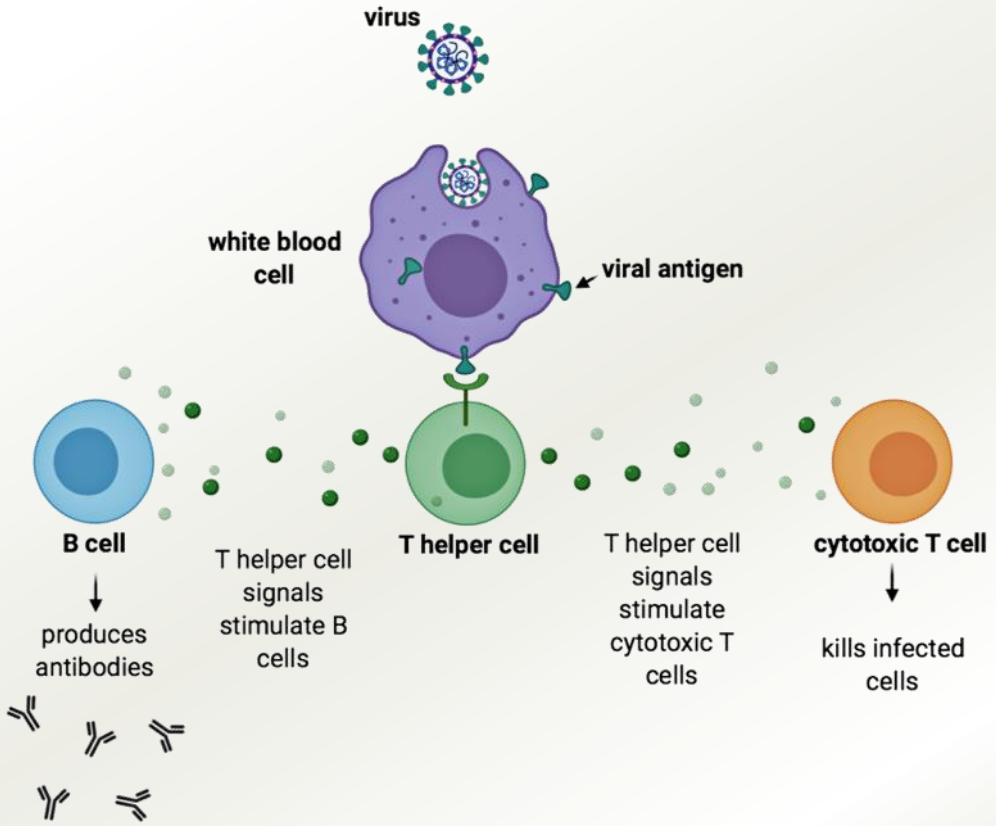
Dendritic cell
Presents antigen on its surface, thereby triggering the adaptive immune response

https://opentextbc.ca/biology/chapter/23-1-innate-immune-response/

Adaptive immune response: T cells

T cells (cellular response)

- **T cells recognize cells that are infected with a specific virus** and rapidly increase in number to tackle the infection
- Types of T cells:
  - **CD4+ helper T cells** bring in other cells of the immune system and stimulate B-cells to produce antibodies specific to that virus
  - **CD8+ cytotoxic T cells** kill the cells in which the virus is multiplying and help to slow down or stop the infection

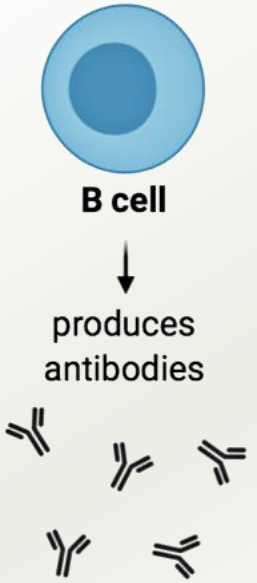


https://www.virology.ws/2020/11/05/t-cell-responses-to-coronavirus-infection-are-complicated/

Adaptive immune response: B cells

B cells (antibody response)

- **B cells produce antibodies** that are specific to the virus
- **IgM antibodies** are produced first and disappear after a few weeks
- **IgG antibodies** are produced at the same time or a couple days later, and titres (levels) usually remain for months or years

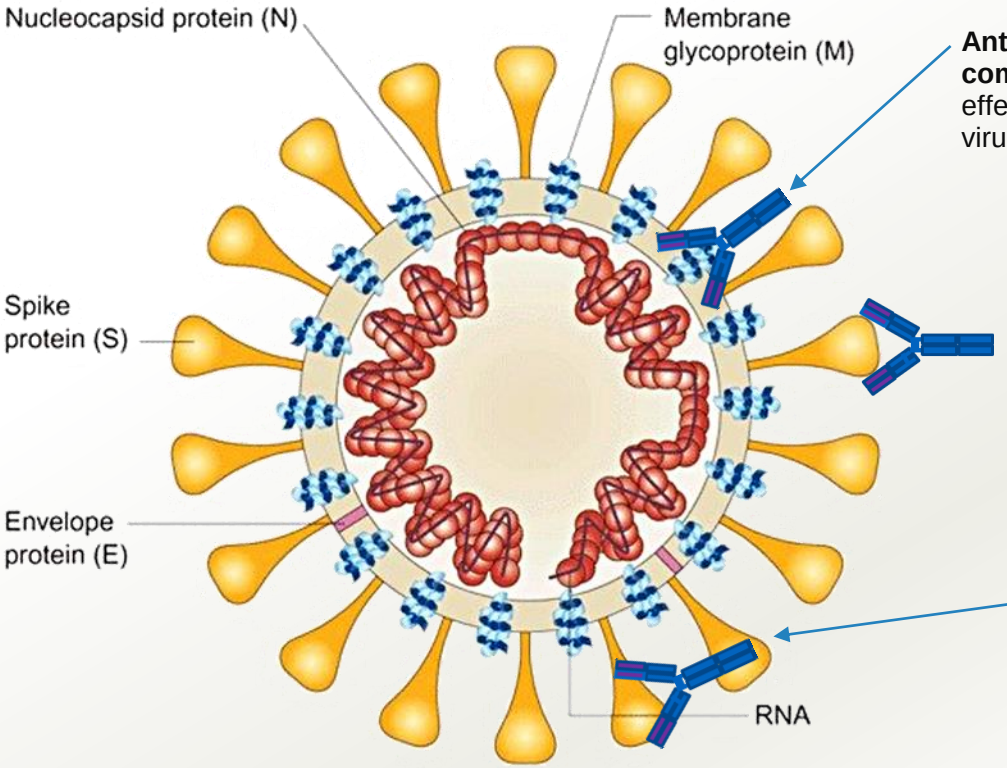


Memory cells

- **Once the infection is over**, the T cells and B cells decline in number, but some cells will remain (memory cells)
- Memory cells respond rapidly if they come in contact with the same virus again, killing the virus and accelerating an antibody response

Neutralizing antibodies bind to viral proteins

Components of the SARS-CoV-2 virus



Antibodies to other components may not effectively neutralize the virus

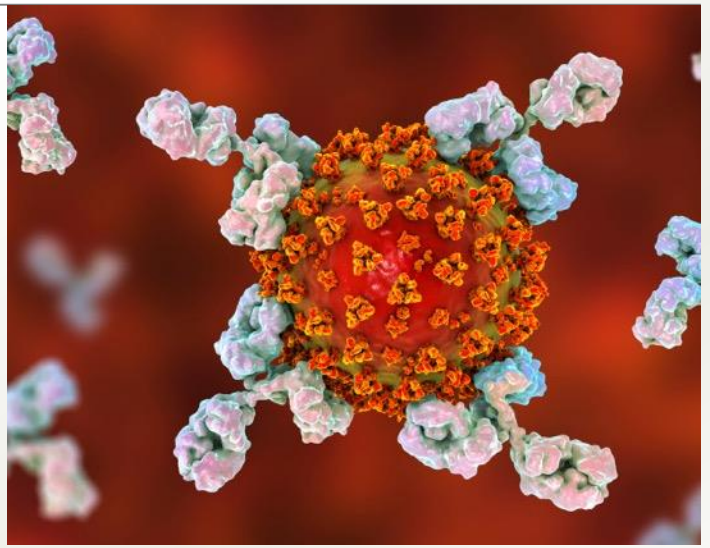
Neutralizing antibody hypothesis: the antibody changes the viral spike protein and prevents entry of the virus via the ACE2 receptor into a targeted cell

Antibodies that attach differently may not effectively neutralize the virus

Sources for *hypothesis* (5 June 2020) and *image* (16 July 2020)

Antibody response to SARS-CoV-2

- **Most COVID-19 patients who recover have antibodies** to SARS-CoV-2 detectable in their blood
- Most COVID-19 patients develop antibodies about 1-3 weeks after symptoms appear. Many patients start to recover during this time
- **Patients who have had more severe disease appear to have higher levels of neutralizing antibodies.** While, patients who had mild or asymptomatic COVID-19 have lower levels of neutralizing antibodies
- Several studies* show that antibodies **remain for several months in individuals who tested positive**, for example a study of more than 30,000 individuals with mild to moderate COVID-19 found that neutralizing antibody titers persisted for at least 5 months after SARS-CoV-2 infection



https://science.sciencemag.org/content/370/6521/1227#:~:text=used%20a%20cohort%20of%20more,least%205%20months%20after%20infection
https://immunology.sciencemag.org/content/5/54/eabf3698.full
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7756220/
https://www.gov.uk/government/statistics/uk-biobank-covid-19-antibody-study-final-results/uk-biobank-covid-19-antibody-study-final-results
https://wwwnc.cdc.gov/eid/article/27/3/20-4543_article

*The studies referenced are not an exhaustive list

T cell response to SARS-CoV-2

- It is possible that in persons with **low levels of neutralizing antibodies**, the innate immune response and the T cell response clears the virus
- Some studies show that persons exposed to SARS-CoV-2 may develop virus-specific T cell responses without detectable circulating antibodies
  - ➢ This may mean that persons who have had mild COVID-19 or were asymptomatic can generate memory T-cell responses to prevent recurrent infection in the absence of antibodies
- Some T cells in persons without exposure to SARS-CoV-2 have been found to cross-react with SARS-CoV-2 (possibly due to prior exposure to other coronaviruses)
  - ➢ This may mean that persons with reactive T-cells will get less severe disease if exposed to SARS-CoV-2

https://wwwnc.cdc.gov/eid/article/27/1/20-3611_article
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7427556/

Re-infection of SARS-CoV-2

- Generally, a person who recovered from a viral infection is protected against a new infection
- It is not yet known how long protection will last after a SARS-CoV-2 infection
- To date, re-infection with SARS-CoV-2 seems rare but several cases of repeat SARS-CoV-2 infection have been reported
- Preliminary results from the *SARS-CoV-2 Immunity and Reinfection Evaluation (SIREN)* study conclude that **past SARS-CoV-2 infection reduces the risk of re-infection by 83% for at least 5 months** and that **fewer than 1% of 6,600 study participants who had COVID-19 were re-infected**

SIREN
SARS-CoV2 Immunity & Reinfection Evaluation

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30783-0/fulltext
https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30764-7/fulltext
https://www.medrxiv.org/content/10.1101/2021.01.13.21249642v1

SARS-CoV-2 variants & re-infection

- **Changes in the virus genomic sequence**, called mutations, **can make prior immunity less effective** (e.g. as with the influenza virus)
- Recently, several SARS-CoV-2 variants have emerged that involve genetic mutations of the spike protein
- Studies are ongoing to investigate if some of these variants can evade the immune response to a previous SARS-CoV-2 infection and make people more vulnerable to re-infection
- In lab experiments, one of the mutations present in the variants identified in South Africa and Brazil has helped the virus evade antibodies generated after an initial infection
- In Brazil, studies are ongoing to determine if a new variant called P.1 may lead to more cases of re-infection

https://www.who.int/docs/default-source/coronaviruse/risk-comms-updates/update47-sars-cov-2-variants.pdf?sfvrsn=f2180835_4
https://elifesciences.org/articles/61312#content
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00183-5/fulltext?s=08

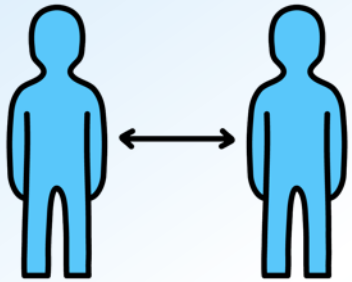
SARS-CoV-2 variants & COVID-19 vaccines

- Current variants involve mutations to the gene for the spike protein that is targeted by COVID-19 vaccines
- Several COVID-19 vaccines have reported reduced efficacy to protect against mild to moderate disease in people infected with SARS-CoV-2 variants, however the vaccines are still expected to protect against severe disease and death
- Studies are ongoing to examine if some vaccines may be more susceptible to effects of the variants than others
  - those using smaller epitopes (the **receptor binding domain** on the spike protein) may be more susceptible than those using a larger part of the virus such as the **spike protein** or the **whole inactivated virus**

https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

COVID-19 protective measures

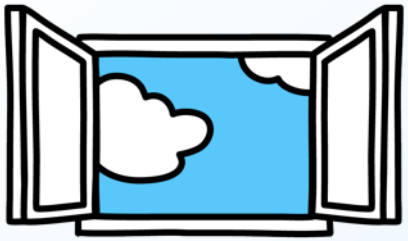
Protect yourself & others



Keep your distance

Wash your hands frequently

Cough & sneeze into your elbow



Ventilate or open windows

Wear a mask

WHO resources

- **Draft landscape and tracker of COVID-19 candidate vaccines**
  https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

- **An update on SARS-CoV-2 virus mutations & variants**
  https://www.who.int/docs/default-source/coronaviruse/risk-comms-updates/update47-sars-cov-2-variants.pdf?sfvrsn=f2180835_4

- **Disease outbreak news SARS-CoV-2 variant**
  https://www.who.int/csr/don/31-december-2020-sars-cov2-variants/en/

- **WHO weekly epidemiological update on SARS-CoV-2 variants of concern**
  https://www.who.int/publications/m/item/weekly-epidemiological-update---9-february-2021

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infodemic
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www.who.int/epi-win