Update on COVID-19 vaccines & immune response
Current global situation

CASES REPORTED TO WHO AS OF 2 February 2022

- Cases: > 380 million
- Deaths: > 5.6 million

* Data are incomplete for the current week. Cases depicted by bars; deaths depicted by line
COVID-19 vaccines continue to provide strong protection against severe disease and death

- COVID-19 vaccines work through different platforms (different mechanisms, delivery methods, processes) and in different ways to protect us from disease

- Some vaccine technologies, such as the mRNA vaccines, have been licensed for use for the first time for COVID-19

- As of 2 February 2022, there are 8 COVID-19 vaccines in the WHO Emergency Use List (EUL), using different types of vaccine platforms

- Current COVID-19 vaccines continue to provide strong protection against severe disease and death; however, vaccines are less effective against Omicron symptomatic disease

- This slide set explains the immune response and how the vaccine platforms work

Enhancing Readiness for Omicron (B.1.1.529): Technical Brief and Priority Actions for Member States (who.int)
Immune response to a viral infection

Two types of immunity are:

- **Innate immunity**
  - General immediate response to ANY infection

- **Adaptive immunity**
  - Specific response to an infection
  - Involves the **cellular response** (T cells) and the **antibody response** (B cells)

- Innate immune response is immediate; whereas cellular & 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 macrophages, 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:

- **Macrophage**: 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.
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.

[Image: Diagram of the immune response showing T cells, B cells, virus, and viral antigen]

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
Response in an immunized person

- When adaptive immune cells (B cells and T cells) encounter the same virus again, they respond rapidly and the immune system can effectively clear an infection before it causes disease.

- Vaccines use this immune memory to protect us from infection.

- Immune memory can result from a prior infection or from an effective vaccine.

Figure. Immune response in an immunized person
An immune response is induced by vaccines

- **Vaccines safely deliver an immunogen** (antigen able to elicit an immune response) to the immune system in order to train it to recognize the pathogen when it is encountered naturally by activating:

- **CD4+ helper T cells** that in turn stimulate:
  - B-cells to produce neutralizing antibodies specific to the virus
  - CD8+ cytotoxic T cells to recognize and kill cells infected by the virus

Kylie Quinn; https://theconversation.com/could-bcg-a-100-year-old-vaccine-for-tuberculosis-protect-against-coronavirus-138006
## COVID-19 vaccines with an approved WHO emergency use listing

As of 2 February 2022

<table>
<thead>
<tr>
<th>VACCINE PLATFORMS</th>
<th>MANUFACTURER &amp; BRAND NAME</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Messenger Ribonucleic acid (mRNA)</strong></td>
<td>Comirnaty (Pfizer/BioNtech)</td>
<td>mRNA vaccines provide the instructions to human cells to make part of the SARS-CoV-2 spike protein</td>
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<tr>
<td></td>
<td>Spikevax (Moderna)</td>
<td>The spike protein triggers the recipient’s immune system to develop a protective response which defends against future exposure to SARS-CoV-2</td>
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<tr>
<td><strong>Recombinant viral vector</strong></td>
<td>Vaxzevria (Astra Zeneca)</td>
<td>A modified virus (the viral vector), other than the virus causing COVID-19, is used to deliver the instructions to human cells to make part of the SARS-CoV-2 spike protein</td>
</tr>
<tr>
<td></td>
<td>Covishield (Serum Institute of India)</td>
<td>The spike protein triggers the recipient’s immune system to develop a protective response which defends against future exposure to SARS-CoV-2</td>
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<tr>
<td></td>
<td>Janssen</td>
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<tr>
<td><strong>Inactivated virus</strong></td>
<td>Coronavac (Sinovac)</td>
<td>An inactivated vaccine consists of killed virus or particles that are recognized by the immune system to elicit an immune response (examples of other vaccines are influenza vaccines)</td>
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<tr>
<td></td>
<td>Sinopharm</td>
<td></td>
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<td></td>
<td>Covaxin (Bharat)</td>
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<tr>
<td><strong>Recombinant spike protein nanoparticle</strong></td>
<td>Novavax and Serum Institute of India</td>
<td>Subunit vaccines contain specific fragments of the SARS-CoV-2 spike protein, which have been carefully selected to produce combinations of these molecules likely to produce a strong and effective immune response (examples of other vaccines are pertussis, HPV and HepB)</td>
</tr>
</tbody>
</table>
mRNA vaccines

- mRNA vaccines are antigen-coding strands of **messenger RNA (mRNA)** delivered inside a lipid coat
- Once inside cells, the mRNA is translated into **the protein antigen**
- The antigen is recognised, inducing an immune reaction
- Seen by the body as if a virus is inside a cell, T-helper, cytotoxic T-cells and antibodies are induced
- mRNA is recognized by cells as a ‘pathogen’ stimulating a strong immune response
- WHO EUL COVID-19 mRNA vaccines are Comirnaty (Pfizer/BioNtech) and Spikevax (Moderna)
Viral vector vaccines

- Viral vector vaccines use a non-coronavirus vector (e.g., adenovirus) modified to include a gene that encodes a target antigen.
- Can be replicating or non-replicating.
- **Replicating**: upon infection produces SARS-CoV-2 antigen in that cell and new virus, which infects other cells.
- **Non-replicating**: infects a cell and produces SARS-CoV-2 antigen in that cell but does not produce new virus.
- The SARS-CoV-2 antigen inside the cells is seen by the body as if this is a SARS-CoV-2 infection and induces T helper cells and cytotoxic T cells.
- WHO EUL viral vector vaccines are Vaxzevria, Covishield (AstraZeneca and Serum Institute of India) and Janssen.
- All WHO EUL viral vector COVID-19 vaccines are non-replicating viral vector vaccines.
Inactivated virus vaccines

- In inactivated virus vaccines, the genetic material of the virus has been destroyed to stop disease producing capacity.
- Inactivated virus cannot replicate inside the body, so higher doses are needed.
- Sometimes, an adjuvant (molecules that stimulate the immune system) is used to help strengthen the immune response.
- Inactivated virus vaccines generally only induce antibody-mediated immunity.
- WHO EUL inactivated virus COVID-19 vaccines are Coronavac (Sinovac), Sinopharm and Covaxin (Bharat).
Viral subunit vaccines

- Subunit vaccines use the antigen of the virus without any genetic material, usually with an adjuvant to give a better immune response.
- Usually made using a recombinant expression system (made in a cell without using the virus).
- With the help of antigen-presenting cells, the antigens are recognised by T helper cells as with a real viral infection.
- Subunit vaccines generally induce antibody-mediated immunity.
- WHO EUL viral subunit COVID-19 vaccines are Nuvaxovid and Covovax (Novavax and Serum Institute of India).
All WHO EUL listed COVID-19 vaccines protect against severe disease and death

- WHO Emergency Use Listing (EUL) involves careful and rigorous assessment of quality, safety and efficacy data of COVID-19 vaccines
- The EUL process consists of a ‘preparedness, an emergency and a post-listing phase

**Preparedness phase**
- Establish assessment platform to assess vaccine
- Establish essential requirements that a vaccine must meet on quality, safety and efficacy

**Emergency phase**
- Conduct rigorous assessment to determine quality, safety and efficacy of the vaccine
- Issue a recommendation whether a vaccine should receive WHO Emergency Use Listing

**Post-listing phase**
- Continue to collect and assess safety, efficacy and effectiveness data on the vaccine
- Actively monitor for side effects of the vaccine
- Reassess validity of listing when new data is generated

*Regulation and Prequalification (who.int)*
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
- Get vaccinated when it is your turn