An update on COVID-19 vaccine booster doses

THE LATEST ON THE COVID-19 GLOBAL SITUATION & COVID-19 VACCINE BOOSTERS
Current global situation

CASES REPORTED TO WHO AS OF 3 September 2021

- **Cases:** > 218 million
- **Deaths:** > 4.5 million

*Data are incomplete for the current week. Cases depicted by bars; deaths depicted by line*
Natural infection-induced immunity to COVID-19
Infection-induced immunity to COVID-19:

- lasts many months\textsuperscript{1,2}
- is multi-faceted and generates antibodies against the spike protein plus other non-structural proteins (Nucleoprotein (N), Matrix protein (M), Envelope protein (E))
- induces systemic immunity and mucosal immunity

https://www.bmj.com/content/373/bmj.n1605
https://www.nature.com/articles/s41586-021-03696-9
The immune system is the body’s natural ability to defend against pathogens (e.g. viruses, bacteria) and resist infections.

Two types of immunity are:
- Innate immunity
- Adaptive immunity

### Innate immune response
- First line of defence
- General immediate response to ANY infection
- The innate response activates the adaptive immune response

### 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 A ‘weaker’ innate response (e.g. in elderly people or those with underlying health problems) may result in delayed stimulation of the adaptive 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
- In addition, the mucosal immune system can produce **IgA antibodies**. This is called **mucosal immunity**
- An infection with **SARS-CoV-2 initially infects the upper respiratory tract** which triggers the production of **IgA antibodies**

**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
Vaccine-induced immunity to COVID-19
COVID-19 vaccines induce neutralizing antibodies against the spike protein.

When SARS-CoV-2 is encountered naturally, neutralizing antibodies bind to the SARS-CoV-2 spike protein and block the virus from entering and multiplying in the cell.

A ‘weaker’ immune system (e.g. in elderly people or those with underlying health problems) may result in delayed and low stimulation of the antibody response after vaccination.

Current COVID-19 vaccines induce systemic immunity only and no mucosal immunity.
Current intramuscular COVID-19 vaccines do not induce mucosal immunity. They do not induce the same multifaceted immune response as a natural infection but do protect from severe disease.

Nasal COVID-19 vaccines are being investigated to protect from infection as well as from severe disease.

Infection-induced immunity induces systemic immunity but also mucosal immunity because SARS-CoV-2 infection starts in the upper respiratory tract.

Vaccine-induced immunity induces systemic immunity only and no mucosal immunity.
Antibody based immunity after COVID-19 vaccination

- Neutralizing antibodies seem to correlate with protection from symptomatic SARS-CoV-2 infection\(^1,2\)
- Data suggest that antibodies against SARS-CoV-2 persist for at least 6 months after vaccination
- Waning of neutralizing antibodies has been reported\(^3\). However, it is unclear if declining antibody titers are indicative of declining protection
- At present, it is unknown what level of neutralizing antibodies or other immune markers are associated with a vaccine’s protection of infection, severe disease and transmission

1. Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection | Nature Medicine 2. 2021.08.09.21261290v1.full.pdf (medrxiv.org)
3. Durability of Responses after SARS-CoV-2 mRNA-1273 Vaccination (nih.gov)
Current COVID-19 vaccines prevent severe disease

- Vaccines have reported sustained effectiveness against severe COVID-19 after 6 months\(^1,2,3\)

- While breakthrough infections are expected, the vast majority are less severe than those seen in unvaccinated people\(^4\)

---

1. https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e2.htm
2. Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on covid-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study | The BMJ
COVID-19 variants and immunity
### Characteristics of global circulating SARS-CoV-2 variants of concern:

<table>
<thead>
<tr>
<th></th>
<th>Alpha</th>
<th>Beta</th>
<th>Gamma</th>
<th>Delta</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Transmissibility</strong></td>
<td>Increased transmissibility</td>
<td>Increased transmissibility</td>
<td>Increased transmissibility</td>
<td>Increased transmissibility. Similar transmissibility between vaccinated and unvaccinated individuals</td>
</tr>
<tr>
<td><strong>Disease severity</strong></td>
<td>Increased risk of hospitalization, possible increased risk of severity and mortality</td>
<td>Not confirmed, possible increased risk of in-hospital mortality</td>
<td>Not confirmed, possible increased risk of hospitalization</td>
<td>Increased risk of hospitalization</td>
</tr>
<tr>
<td><strong>Risk of reinfection</strong></td>
<td>Neutralizing activity retained</td>
<td>Reduction in neutralizing activity reported</td>
<td>Moderate reduction in neutralizing activity reported</td>
<td>Reduction in neutralizing activity reported</td>
</tr>
<tr>
<td><strong>Impact on diagnostics</strong></td>
<td>No impact on RTPCR or Ag RDTs observed</td>
<td>No impact on RTPCR or Ag RDTs observed</td>
<td>None reported to date</td>
<td>None reported to date</td>
</tr>
<tr>
<td><strong>Effectiveness of COVID-19 vaccines</strong></td>
<td>Protection retained</td>
<td>Protection retained against severe disease; reduced protection against symptomatic disease; limited evidence</td>
<td>Unclear impact; very limited evidence</td>
<td>Protection retained against severe disease; possible reduced protection against symptomatic disease and infection; limited evidence</td>
</tr>
</tbody>
</table>

https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---10-august-2021
COVID-19 booster dose?
Target groups for COVID-19 booster doses

Waning immunity

• Third doses should be prioritized for the vulnerable: those most at-risk populations when there is evidence of waning immunity against severe disease and death. They are not for the fit and healthy.\(^1\)

Poor primary response to vaccination

• Immunocompromised people may not respond sufficiently to two doses of COVID-19 vaccine. For example, in a trial with organ transplant recipients only 4% of people generated SARS-CoV-2 antibodies after one dose, increasing to 40% after two doses and 68% after three doses.\(^2\)

• Emerging data shows that immunocompromised people should receive a third dose if they did not respond sufficiently to their initial doses or if they are no longer producing antibodies. Such groups would be exempt from the booster moratorium.\(^2\)

---

1. WHO news updates
   Interim statement on COVID-19 vaccine booster doses (who.int)
Update on COVID-19 vaccine global distribution

- COVID-19 vaccination in low-income countries is lacking behind
- As of 3 September 2021, 5.4 billion vaccine doses have been administered
- 40% of the world population has received at least one dose of a COVID-19 vaccine
- Only 1.8% of people in low-income countries have received at least one dose

https://ourworldindata.org/covid-vaccinations
The COVAX Facility provides access to COVID-19 vaccines to all participating countries, regardless of income levels.

As of 24 August 2021, COVAX has shipped over 207 million COVID-19 vaccines to 138 participants.

Photo: UNICEF

* [https://www.gavi.org/vaccineswork/gavi-covax-amc-explained](https://www.gavi.org/vaccineswork/gavi-covax-amc-explained)*
Globally, many health workers and populations at risk have not yet had their first or second vaccinations

- In the context of ongoing global vaccine supply constraints, administration of booster doses will exacerbate inequities by driving up demand and consuming scarce supply while priority populations in some countries, or subnational settings, have not yet received a primary vaccination series.

- The focus for the time being remains on increasing global vaccination coverage with the primary series (either one or two doses for current EUL vaccines).

- However, if third doses are prioritized for those most at-risk while global access to vaccines is increased - such as through increasing production and donating doses to COVAX - then they should not be seen as depriving others of their first doses.

Interim statement on COVID-19 vaccine booster doses (who.int)
WHO news updates
Resources

- Coronavirus (COVID-19) Vaccinations - Statistics and Research - Our World in Data
- COVAX (who.int)
- The Gavi COVAX AMC Explained | Gavi, the Vaccine Alliance
- Weekly epidemiological update on COVID-19 - 10 August 2021 (who.int)
- Interim statement on COVID-19 vaccine booster doses (who.int)
- WHO news updates
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