

Vaccination Against COVID-19: What Have We Learned?

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A novel human to human transmissible Corona virus emerges



Sars-CoV-2 infection: is there protective immunity after natural infection?



- 90 % of protective antibody mediated immunity is directed against the spike protein
- Protective role of cell mediated immunity unclear, but likely to be involved
- Rare cases of Sars-CoV-2 reinfection, but reinfection cases tend to be mild

The rise of mRNA based vaccine technology

Delivery vehicle:

Nucleoside modified RNA (modRNA) Uridine containing mRNA (uRNA)

Principle:

Delivery of well-defined, optimized mRNA molecules to the cytosol of human cells followed by translation of mRNA into the specifically encoded protein sequence

Generation of antigenic structures that have "native-like" conformation, mimicking the natural antigen

mRNA is non-infectious, non-integrating into host cell genome, degraded shortly after inoculation by physiological cellular processes

More than 10 mRNA vaccines were already at different stages of clinical testing before the beginning of the Sars-CoV-2 pandemic!

Manufacture is chemically defined, with consistent processes:

- versatile platform for different vaccines, considerably shortening production
- quality control and scale up, regardless of the antigen encoded

How to develop an efficacious Sars-CoV-2 vaccine, without compromising on safety following international regulatory procedures

Which vaccine is best in which context?

Vaccine	Manufacturer /Developer	Vaccine type	Antigen	Dose	Dosage	Current approvals (Emergency use authorization)
mRNA-1273	Moderna/NIH	mRNA	Full-length spike protein	100 µg	2 doses, 28 days apart	US, EU, Canada, UK
BNT162b2	Pfizer-BioNTech	mRNA	Full-length spike protein	30 µg	2 doses, 21 days apart	US, EU, Canada, UK
Ad26.CoV2.S	Janssen/ Johnsen&Johnsen	Viral vector	Replication incompetent human Adenovirus carrying full-length spike protein	5 x 10 ¹⁰ viral particles	1 dose	US, EU, Canada
ChAdOx1	AstraZeneca/ Oxford	Viral vector	Replication deficient chimpanzee Adenovirus carrying full-length spike protein	5 x 10 ¹⁰ viral particles	2 doses, 28 days apart	India, UK, Mexico, EU

More Sars-CoV-2 vaccines are in the development pipeline:

Large-scale deployment of BNT162b2 in Israel

- Cumulative incidence of five different vaccination outcomes assessed in 596,618 vaccinated, versus 596,618 non-vaccinated matched volunteers between December 20, 2020 and February 1, 2021
- Estimated vaccine effectiveness during the follow-up period starting 7 days after the second dose was:
 - 92% for documented infection
 - 94% for symptomatic Covid-19
 - 87% for hospitalization
 - 92% for severe Covid-19

Vaccine diplomacy: the political dimension of Sars-CoV-2 vaccines

- Massive rollout of four vaccines against Sars-CoV-2 began January 2021 in rich countries, priority groups covered by mid 2021
- Vaccine production is currently the main hurdle
- Costs associated with mass immunisation programmes will be significant
- Vaccine diplomacy will play a role in determining which countries get access to vaccine in coming months
- Russia and China will use the rollout of their own coronavirus shots to advance their interests
- For most middle-income countries, vaccination timeline will stretch to late 2022
- In poorer economies, widespread vaccination coverage will not be achieved before 2023, if at all

Do vaccines protect against novel Sars-CoV-2 variants?

Current frequency of breakthrough infections at around 0.01 %

Causes of breakthrough infections:

- weak or ineffective immune response after complete vaccination
- waning of immunity over time
- Sars-CoV-2 virus evolution, particularly in the spike protein
- Constant monitoring of breakthrough infections to understand immune evasion

Surveillance of Sars-CoV-2 in Equatorial

Rapid switch from cutting edge research laboratory infrastructure, to public health surveillance corner stone

Human resource, equipment and infrastructure already available based on active research partnerships

Private-public partnerships secured funding for acquisition of reagents: February 2020

- Implementation of Sars-CoV-2 testing: February 20^{th,} 2020
- First Sars-CoV-2 case identified: March 16^{th,} 2020
- WHO endorsed laboratory as competence centre: February 24^{th,} 2020
- Transfer of laboratory based detection to other parts of the country: August 2020
- More than 150 000 Sars-CoV-2 tests conducted so far
- Development of biobank of Sars-CoV-2 positive samples

Genomic surveillance of Sars-CoV-2 circulating in Equatorial Guinea

Swiss TPH Hosch et al., unpublished

Genomic surveillance of Sars-CoV-2 in Africa: large steps forward

Swiss TPH 😏

Taken from: medRxiv 2021.05.12.21257080; https://doi.org/10.1101/2021.05.12.21257080

What have we learned...and what next?

Unprecedented speed and success of SARS-CoV-2 vaccine development is credited to combined and timely efforts of open science, industry partnerships, harmonization of clinical trials, massive financial support of governments and altruism of study participants But:

- Durability of vaccine induced protection: regular booster vaccinations required?
- Global, robust, real-time and deep genomic surveillance for Sars-CoV-2 variants needed
- Broad and equitable global vaccination campaign to prevent spread of novel Sars-CoV-2 variant
- Vaccines are not magic bullets: non-pharmaceutical interventions should continue

