How can vaccine research further contribute to achieve the control of the pandemic everywhere?

Meeting objectives

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Meeting conclusions

South Africa: high pre-omicron seroprevalence, which provided high protection vs. infection. Fourth wave with steeper rise in cases but lower percentage of hospital admissions with severe disease, apparent increased risk of reinfection.

Globally: differences among countries in seroprevalence, waves driven by policies, misinformation and variants. Unvaccinated are primary drivers of the pandemic. Surveillance is detecting omicron in many countries.

WHO advisory groups, including TAG- COVAC are providing recommendations to WHO. Key topic is vaccine composition.

Transmissibility is critically important even if disease is less severe. Need to consider capacity to respond and impact on herd immunity. PHSM (especially reducing superspreader events), reaching higher vaccination rates will be needed. Need data on disease in groups with different levels and types of immunity. Balance rapid decisions with need for data. Potential threat is high, so we need to be prepared.
Meeting conclusions
Although many studies suffer from confounding, vaccines are still working quite well against severe disease caused by delta variant.

After previous infection, there is a biphasic decay in antibody to virus; memory B cells do not decay, modest decay in circulating responsive T cells, importance of N protein in CD8 response.

For vaccines, while NAbs are lower with some variants, cellular responses are less variable. Vaccines will likely continue to prove protective against severe disease caused by new variants. Boosting can increase both humoral and cellular responses.

The laboratory research community is coordinating efforts and sharing reagents needed to rapidly assess the threat from omicron. Key results will take some time—e.g., many studies will need to wait for availability of virus stocks. Shipping restrictions (affected by travel bans) can be an impediment.
Meeting conclusions

The WHO International Standard for anti-SARS-CoV-2 immunoglobulin has been widely distributed and is an invaluable reagent for reducing variability and comparing studies. Replacement primary standard will be established 10/22. Variant-specific neutralizing curves, secondary standards can be used.

Variant-specific vaccines will need validated and well-controlled manufacturing processes with appropriate testing plans and facility-specific systems and data. Some variant-specific product characterization assays (e.g., potency, identity) may need to be validated.

Importance of validated, controlled assays and making sure that assays are reliable for evaluating immunity against new variants. Animal models (possibly also organoid systems) will provide valuable data on phenotypes of variants. Importance of facilitating research including reagent exchange– does the virus still need to be BSL-3? Multivalent vaccines may be useful, but may need additional characterization and evaluation. Value of antigenic sin studies.
Meeting conclusions

Can we be better prepared for new variants by including different antigens or making chimeric spike proteins?

Challenges are posed by original antigenic sin and multivalent vaccines. There may be more technical difficulties in making new inactivated or recombinant protein vaccines vs mRNA or vectored vaccines.

Balance between speed and reliability, but sequence data alone may not be sufficient to support introduction of variant-specific vaccines. Regulators support immunobridging (to known effective prototype vaccine) as an approach to develop variant-specific vaccines. Manufacturers can have candidates ready for testing in 60-90 days.

WHO is revising the COVID vaccines TPP to reflect new data and needs.
Meeting conclusions

People with higher neutralizing antibody responses directly after vaccination tend to be better protected against symptomatic illness. Cutoffs that guarantee protection don’t exist, but immunobridging using neutralizing responses is a useful predictor of vaccine effectiveness that have already been used for COVID vaccines. We don’t need a full correlate of protection.

Neutralizing antibody levels similar to or superior to those associated with efficacy of known effective vaccines could be considered as a basis for authorizing new vaccines (whether as primary series or boosts), subject to availability of supportive data (e.g., CMI, animals) plus follow-up effectiveness studies.

Randomization (whether individual or small cluster) during deployment could yield essential information about vaccine effectiveness to meet these needs. Lead time plus lack of immediate availability makes randomized deployment more feasible.
Key knowledge gaps

Specific information about omicron variant - transmissibility, virulence, adaptive immune avoidance for various vaccines

Omicron exposed gaps in global seroepidemiology

Still need more information on best vaccine regimens

New vaccines might be needed, and manufacturers are getting started. This is easier for mRNA and vectored vaccines. This will also require at least some new assays.

Standardization of assays is critical

Other research needs: original antigenic sin, role of T cells in severe disease, more broadly protective vaccines, improved effectiveness studies (e.g., operational research during deployment), vaccine effectiveness against severe disease

In all decisions, consider likely consequences among the unvaccinated, the previously infected, and the vaccinated. Global access to vaccines is critical.