COVID-19 Conversations

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COVID Vaccine Development: From Discovery to Impact

Kathleen Neuzil, MD, MPH
10 June 2020
Vaccine Development: A Continuum from Discovery to Impact

Public Health Need / Market Need

Discovery & Exploratory Stage  Preclinical Stage  Phase I  Phase II  Phase III  Regulatory Approval  Policy  Financing  Launch Phase IV  Delivery

Impact!

Political Will

Vaccines as a tool for healthy equity
The Case for a Vaccine: WHO Coronavirus Dashboard

- 7,258,842 cases
- 411,694 deaths

https://covid19.who.int/
Clinical Vaccine Development: Where Do We Begin? What is the Goal?

- Indication
- Target population
- Safety, reactogenicity
- Immunogenicity
- Efficacy
- Co-administration
- Duration of protection

http://www.mdpi.com/2076-393X/1/3/204/htm
What Do We Know About Immunity in Humans?

• Immune response post-infection to spike protein
  • Neutralizing responses
• Level of antibody needed to prevent re-infection?
• Duration of protection from natural immunity?
• Importance of T cell immunity?
• Phase 1 human trials in SARS, MERS
  • Broadly neutralizing antibodies
Rapid COVID-19 vaccine development

By Barney S. Graham

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Finding the fastest pathway to vaccine availability includes the avoidance of safety pitfalls

**Potential risks associated with vaccine development for COVID-19**

Antibodies that bind virus without neutralizing infectivity can cause disease through increased viral replication or formation of immune complexes that deposit in tissue and activate complement pathways associated with inflammation. T helper 2 cell (Th2)-biased responses have also been associated with ineffective vaccines that lead to enhanced disease after subsequent infection. Antibody-dependent enhancement (ADE) of viral replication has occurred in viruses with innate macrophage tropism. Virus-antibody immune complexes and Th2-biased responses can both occur in vaccine-associated enhanced respiratory disease (VAERD).

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<thead>
<tr>
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<th>Antibody-mediated</th>
<th>T cell-mediated</th>
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<tr>
<td><strong>Mechanism</strong></td>
<td>Fc-mediated increase in viral entry</td>
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<td><strong>Effectors</strong></td>
<td>Macrophage activation and inflammatory cytokines</td>
<td>Complement activation and inflammatory cytokines</td>
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<td><strong>Mitigation</strong></td>
<td>Conformationally correct antigens and high-quality neutralizing antibody</td>
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Is There a Role for Controlled Human Infection Models?

**PANDEMIC VACCINE DEVELOPMENT MODEL – Overlapping Phases**
*Shorten Development Time*
- Define target product profile, pre-clinical, assay development
- Large-scale production
- Clinical Development
  - Phase I
  - Phase 2/3
- Licensure
  - Regulatory pathway

**HYBRID MODEL – Adding New Controlled Human Infection Model (CHIM)**
*Provides supporting data; does not accelerate initial timeline*
- Manufacture SARS-CoV-2 challenge strain, engage communities/ethicists
- Develop SARS-CoV-2 CHIM when disease characteristics better known and rescue drug available
- Begin testing of vaccines in model
Vaccine Development: A Continuum from Discovery to Impact

Vaccines as a tool for healthy equity
ACCESS TO COVID-19 TOOLS (ACT) ACCELERATOR
A Global Collaboration to Accelerate the Development, Production and Equitable Access to New COVID-19 diagnostics, therapeutics and vaccines

24 April 2020

COMMITMENT and CALL TO ACTION

Our Vision and Mission
Grounded in a vision of a planet protected from human suffering and the devastating social and economic consequences of COVID-19, we, an initial group of global health actors (BMGF, CEPI, Gavi, Global Fund, UNITAID, Wellcome Trust, WHO) and private sector partners and other stakeholders, are launching a landmark, global and time-limited collaboration to accelerate the development, production and equitable global access to new COVID-19 essential health technologies.

Our Mission is not only accelerated development and availability of new COVID-19 tools – it is to accelerate equitable global access to safe, quality, effective, and affordable COVID-19 diagnostics, therapeutics and vaccines, and thus to ensure that in the fight against COVID-19, no one is left behind.

Our Commitment
1. We commit to the shared aim of equitable global access to innovative tools for COVID-19 for all.
Reported Adult Immunization Programs by World Bank Income Category in 2018

- ≥1 policy reported
- HepB policy
- HZV policy
- Influenza Policy
- PCV policy
- PPSV policy

- Low-income (n=34)
- Lower middle-income (n=45)
- Upper middle-income (n=55)
- High-income (n=58)
Summary

• Safe and effective vaccines are needed for COVID-19; must be accessible, affordable and globally available

• Vaccine development is a staged, deliberate and careful process
  • Many challenges – New disease, poorly understood immunity, uncertain trajectory of outbreak
  • Vaccine safety will be meticulously assessed
  • If enhanced disease occurs it will be carefully assessed and immune mechanisms investigated