Introduction to Immunology, Vaccinology, and COVID-19 Trials

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Housekeeping

• Participant lines muted during the webinar
• Type questions in the “Question” pane of your Dashboard
• Q & A session at the end of the webinar.
Continuing Nursing Education

Upon full participation in this webinar & completion of an evaluation, participants will be awarded 1.0 contact hours.

The Association of Nurses in AIDS Care (ANAC) is accredited as a provider of nursing continuing professional development by the American Nurses Credentialing Center's Commission on Accreditation.
Disclosures

The speaker has no relevant conflict of interest to disclose.
Learning Objectives

At the conclusion of today’s activity, participants will be able to:

• Describe the basics of Immunology
• Discuss how a vaccine is developed
• Identify the different types and mechanisms of the COVID-19 vaccines currently under clinical trial
Agenda

1. Introductions
2. Speaker presentation
3. Question & Answer
Introduction to Immunology

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Innate Response

• First line of defense
• Prevents infection? No!
• NK cells activated when cells are infected
• Activation of innate response is required before the adaptive response can happen
• No immunological memory
• We don’t think vaccination will help with immunological memory
• NK cells work by causing infected cells to burst, like a dart bursting a water balloon
Adaptive = Acquired

• Antigen-specific defense mechanism

• Takes several days to become protective

• Develops throughout life
Adaptive – Part 1
(also known as humoral or antibodies)

- Antibodies are made by B cells in the first 2 days after infection, but usually takes 2 weeks for full effect
- Antibodies have three simultaneous functions:
  - neutralize or stop the virus
  - eliminate the virus through opsonization
  - sensitize the immune system to engage other functions
- Antibodies can prevent infection
- Antibodies have immunological memory
How Do Antibodies Prevent Infection?

1st way: Neutralization
How Do Antibodies Prevent Infection?

2nd way: Eliminate the virus

Opsonization uses other cells of the immune system to destroy HIV
Binding antibodies sensitize the immune system

Antibody Dependent Cellular Cytotoxicity (ADCC)

- NK cells may also be able to act like a CD8 killer T cell ("a hitman")
- They need a binding antibody attached to the HIV to act like a "lookout"
- With the lookout in place, the NK cell can identify HIV and kill it
Humoral Response – Summary

• Antibodies attach to the virus at sites that are used by the virus for entry into cells.
• Neutralizing antibodies can work alone to block a virus from entering cells.
• Vaccines designed to elicit neutralizing antibodies against HIV have not worked very well in trials so far.
• Recent discoveries of several broadly neutralizing antibodies are very exciting, and designing a vaccine to produce these antibodies is underway!
• Binding antibodies can attach to HIV and call other parts of the immune system into action to help destroy it.
Adaptive Part Two - Cellular

- Cellular response involves two types of cells:
  1) Helper T lymphocytes (CD4⁺)
  2) Cytotoxic T lymphocytes (CTL or CD8⁺)
- Have memory!
- Activated once infection occurs
The Two Types of Cells

- CD4\(^+\) cells recognize HIV and help cells communicate with each other, calling the killers into action

- CD8\(^+\) cells are the killers
How Does the Adaptive Response Work?

- **T-cell function: immunosurveillance**
- Checks other cells of the body (are they infected or abnormal?)
- Destroys infected or abnormal cells
CD8 Cells May Need Binding Antibodies – More sensitization!

**Antibody Dependent Cell-mediated Viral Inhibition**

- CD8 cells may also be able to do a better job of killing if they have an antibody acting as the “lookout”
- Their role is already to kill infected cells, but having the antibody in place amplifies their success
Adaptive Response – Summary

Cellular = Cytotoxic T lymphocytes (CTL or CD8+) and helper T lymphocytes (CD4+)

• Cannot prevent infection
• T cells are activated when cells become infected
• T cells can eradicate an established infection
• T cells have immunological memory
• T cells can be primed by vaccination
Questions?
Introduction to Vaccinology
History of Preventive Vaccines

• Used for decades around the world, most commonly in children
• Safe when manufactured and used properly
• Cost-effective compared to treatment
• Eliminated smallpox worldwide
• 2008: 1st vaccine for girls and young women against a cancer-causing virus, human papilloma virus (HPV), and 2009-10 approval for boys and young men
# Vaccine Research in Perspective

<table>
<thead>
<tr>
<th>VACCINE</th>
<th>DISCOVERY OF VIRUS</th>
<th>VACCINE DEVELOPED FOR HUMAN USE</th>
<th>YEARS TO VACCINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>H. Influenzae-B</td>
<td>1892</td>
<td>1985</td>
<td>93</td>
</tr>
<tr>
<td>Herpes (HSV-1)</td>
<td>1919</td>
<td>Not available</td>
<td>&gt;90</td>
</tr>
<tr>
<td>Pertussis</td>
<td>1906</td>
<td>1926</td>
<td>20</td>
</tr>
<tr>
<td>Polio</td>
<td>1909</td>
<td>1954</td>
<td>47</td>
</tr>
<tr>
<td>Yellow Fever</td>
<td>1900</td>
<td>1935</td>
<td>35</td>
</tr>
<tr>
<td>Influenza</td>
<td>1933</td>
<td>1945</td>
<td>12</td>
</tr>
<tr>
<td>Measles</td>
<td>1911</td>
<td>1957</td>
<td>46</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>1973</td>
<td>1995</td>
<td>22</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>1967</td>
<td>1984</td>
<td>17</td>
</tr>
<tr>
<td>HPV</td>
<td>1974</td>
<td>2007</td>
<td>33</td>
</tr>
<tr>
<td>HIV</td>
<td>1983</td>
<td>Not available</td>
<td>&gt;30</td>
</tr>
</tbody>
</table>
# The Impact of Vaccines in the United States

<table>
<thead>
<tr>
<th>DISEASE</th>
<th>BASELINE 20(^{\text{TH}}) CENTURY PRE-VACCINE ANNUAL CASES</th>
<th>2008 CASES*</th>
<th>PERCENT DECREASE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles</td>
<td>503,282</td>
<td>140</td>
<td>99.9%</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>175,885</td>
<td>0</td>
<td>100.0%</td>
</tr>
<tr>
<td>Mumps</td>
<td>152,209</td>
<td>454</td>
<td>99.7%</td>
</tr>
<tr>
<td>Pertussis</td>
<td>147,271</td>
<td>10,735</td>
<td>92.7%</td>
</tr>
<tr>
<td>Smallpox</td>
<td>48,164</td>
<td>0</td>
<td>100.0%</td>
</tr>
<tr>
<td>Rubella</td>
<td>47,745</td>
<td>16</td>
<td>99.9%</td>
</tr>
<tr>
<td><em>Haemophilus influenzae type b, invasive &lt;5 yrs.</em></td>
<td>20,000</td>
<td>30</td>
<td>99.9%</td>
</tr>
<tr>
<td>Polio, paralytic</td>
<td>16,316</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Tetanus</td>
<td>1,314</td>
<td>19</td>
<td>98.6%</td>
</tr>
</tbody>
</table>

*Provisional Source: MMWR 4/2/99, 12/25/09, 3/12/2010
What are Vaccines?

Vaccines teach your body to recognize and fight invaders.
How Does a Vaccine Work?

By teaching the body to recognize and fight invaders.

Body recognizes HIV virus

Body – Sounds Alarm

Fighter cells and proteins go into action

GOAL - HIV is controlled or killed
Vaccine and Related Designs

- Whole-Inactivated (Inactivated HIV)
- Live-Attenuated (Weakened HIV)
- Synthetic Peptide (Laboratory-Made Piece of Protein)
- Recombinant Sub-Unit (HIV Protein Made in a Lab)
- Recombinant Viral Vector (Another Virus Carries Pieces of HIV)
- Recombinant Bacterial Vector (Bacteria Used to Carry Pieces of HIV)
- Broadly Neutralizing Antibodies (Non-Vaccine) (Circulate in the Body and Attach to and Neutralize Many HIV Strains)
- DNA (DNA Carries Pieces of HIV)
- Virus-Like Particles (Same Shape as HIV, Insides Changed)
HOW AN HIV VACCINE MIGHT WORK
What Might a Preventive HIV Vaccine Do?

Benefits for the person who gets the vaccine:
- Prevent infection
- Prevent disease
- Delay disease progression

Benefits for the entire community:
- Prevent further transmission
- Create “herd immunity”
Potential Impact of a Vaccine

Even a vaccine with low efficacy and limited coverage can impact the epidemic and play a role in preventing future infections

HIV-1 Diversity Worldwide

HIV-1 group M: 9 subtypes & several circulating recombinant forms

HIV genomes differ by 10-30%
Human genomes differ by about 0.1%

Hemelaar et al. 2004. WHO/UNAIDS.
CoVPN Overview

Stephaun E. Wallace, PhD, MS
Director of External Relations, COVID-19 Prevention Network
Staff Scientist, Vaccine and Infectious Disease Division, Fred Hutch
Clinical Assistant Professor, Dept of Global Health, UW
What is the COVID-19 PREVENTION NETWORK?

The HVTN was formed 2 decades ago by Dr. Anthony Fauci of the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health, to address HIV and other global vaccine needs. The network quickly pivoted to COVID-19 and studies to ensure a safe and effective COVID-19 vaccine. Comprised of the foremost infectious disease and vaccine experts in the country, the research network and its global partners are working hand in hand to address this urgent need in our fight against the pandemic.

Dr. Anthony Fauci, Director of the National Institute of Allergy and Infectious Diseases
We need to develop multiple vaccine platforms.

No single vaccine platform can be manufactured at enough scale to immunize the 4.4 billion adult population on the planet and 3 billion children, 220 million adults in US alone.

Use known platforms to cover the field scientifically. Manufacturing scalability is a key factor.

Coordinated USG effort to involve global vaccine manufacturing companies.

There must be an unprecedented coordinated approach to test, manufacture the vaccine at scale, and deliver the vaccine into peoples' arms throughout the world.
CoVPN Operations Center

- Built around structure of the HIV Vaccine Trials Network founded in 1999 at Fred Hutchinson Cancer Research Center
- Academically based CRO with Operations Center (Corey and Kublin), Statistical Data Management Center (Peter Gilbert PI) and centralized world class immunology and virology labs (Julie McElrath PI)
  - McElrath T cell Lab; Montefiori Pseudovirus Lab; Tomaras Binding Antibody Lab; and UW Virology/ Jerome Lab are all HVTN Laboratories; all validated in the HIV assays they perform and are now involved in OWS
Vaccine Designs

- **SARS-CoV-2**
  - **TIVATED** (SARS-CoV-2)
  - **LIVE-ATTENUATED** (WEAKENED SARS-CoV-2)
  - **RECOMBINANT NANO PARTICLE** (SARS-CoV-2 PROTEIN MADE IN A LAB)
  - **VIRUS-LIKE PARTICLES** (SAME SHAPE AS SARS-CoV-2, INSIDES CHANGED)
  - **MONOCLONAL ANTIBODIES** (CIRCULATE IN THE BODY AND ATTACH TO AND NEUTRALIZE MANY SARS-CoV-2 STRAINS)

- **SYNTHETIC PEPTIDE** (LABORATORY-MADE PIECE OF PROTEIN)
  - **Modern Pfizer**
  - **AstraZeneca Janssen**
  - **Novavax Sanofi**

- **mRNA** (mRNA DELIVERS SARS-CoV-2 SPIKE PROTEIN INSTRUCTIONS, WHICH IS MADE BY HOST CELL AND PRESENTED ON SURFACE)
<table>
<thead>
<tr>
<th>Protocol Name</th>
<th>Concept Name</th>
<th>Study N</th>
<th>Protocol Open</th>
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</thead>
<tbody>
<tr>
<td>Moderna phase 3</td>
<td>Moderna phase 3</td>
<td>30000</td>
<td>7/27/2020</td>
</tr>
<tr>
<td>AstraZeneca phase 3</td>
<td>AstraZeneca phase 3</td>
<td>30000</td>
<td>8/29/2020</td>
</tr>
<tr>
<td>Janssen phase 3</td>
<td>Janssen phase 3</td>
<td>60000</td>
<td>9/21/2020</td>
</tr>
<tr>
<td>Novavax phase 3</td>
<td>Novavax phase 3</td>
<td>30000</td>
<td>10/12/2020</td>
</tr>
<tr>
<td>Sanofi phase 3</td>
<td>Sanofi phase 3</td>
<td>30000</td>
<td>12/1/2020</td>
</tr>
</tbody>
</table>
Interested in volunteering for a COVID-19 Prevention Clinical Study?

Thank you for your interest in our studies. Science can't move forward without your help!

Selecting the button below will take you to the CoVPN Volunteer Screening Registry.

The purpose of this screening registry is to create a list of potential volunteers who want to take part in current or future COVID-19 prevention clinical trials. You must be 18 years or older to participate. Participation involves completing a short online survey that includes some personal questions. Your participation is voluntary.

Volunteer Now!

www.preventcovid.org
www.coronaviruspreventionnetwork.org
Engagement and Participation Foci with Priority Populations

PRIORITY POPULATIONS

• Native/Indigenous
• African American/Black
• Latinx
• Occupational Engagement
• People with pre-existing health conditions
• Communities experiencing health disparities
• Older Adults/Veterans Administration
  • Nursing Home (mAb trials)
  • Assisted Living Facility residents (vaccine trials)

• All activities are tailored for each of these vital priority populations
• Priority populations require varying:
  • Outreach
  • Engagement
  • Recruitment approaches
• Building and maintaining relationships with experts working with these groups
Community Engagement Activities

I. **Materials for participants/potential participants** *(English & Spanish)*
   A. Community-based presentation of trial specific principles
   B. CoVPN public website w/ registry – [www.PreventCOVID.org]

II. **Materials for sites** *(English & Spanish)*
   A. Standardized informational tools for site staff involved in community engagement
   B. Great ideas for community engagement
   C. FAQs – *incorporated in website*
   D. COVID inequities slide set
   E. General recruitment materials for use across vaccine studies: poster, flyer, postcard, palm cards
   F. Site training/Preparation/Q&A calls in advance of each study
   G. Educational Videos
   H. National Heart, Lung, and Blood Institute Partnership w/ site specific support
Community Engagement Activities

III. Priority Population Expert Panels
   A. Scientists from and working with priority populations
      • Modeled after NIH review committees
      • Convene and discuss each protocol and related materials
      • Generate reports on significance, impact, ethics, etc. for larger priority population community
   B. Native/Indigenous
   C. African American/Black
   D. Latinx
   E. Older Adults/Veterans Administration

IV. Convening Community Working Groups with research familiarity for discussion
   A. Utilizing Community Advisory Board and Community Action Board Models
   B. Community Working Group convened and meeting regularly
V. Stakeholder Engagement and Building Trust

A. Convening Community Listening Sessions (ongoing and iterative)
   • Opportunities for community to hear research updates
B. Virtual Town Halls/Webinars
   • Education sessions presenting and discussing community-level considerations for research engagement
C. Trade Unions
   • Meat/Poultry Industry, Restaurants, Factories
D. Grass Roots Organizations working on COVID and Social Justice
   • ThriveSS, BYP100, Urban Indian Health Institute
E. National Organizations
   • AARP, ANAC, NAACP, National Urban League, YWCA/YMCA, UnidosUS
F. Political Entities
   • Black Caucus, Hispanic Caucus, Progressive Caucus
G. CoVPN Faith Initiative - faith-based engagement
H. National Magazines
I. National Scientific Panels highlighting scientists of color
## CoVPN Virtual Town Halls/Webinars

<table>
<thead>
<tr>
<th>Date</th>
<th>Title</th>
<th>Organizations</th>
</tr>
</thead>
<tbody>
<tr>
<td>6/30/2020</td>
<td>The Blacker the Plan: Our People, Our Problem, Our Solution: Facts Only: How to Survive and Thrive During a Time of Pandemics</td>
<td>Black AIDS Institute, American Medical Association, CoVPN/HVTN</td>
</tr>
<tr>
<td>7/1/2020</td>
<td>COVID-19 Community Conversation Webinar</td>
<td>HANC CP, AVAC, TAG, CoVPN</td>
</tr>
<tr>
<td>7/8/2020</td>
<td>Fred Hutch Town Hall</td>
<td>Fred Hutch including HVTN and CoVPN</td>
</tr>
<tr>
<td>7/16/2020</td>
<td>NMAC Webinar</td>
<td>NMAC, CoVPN</td>
</tr>
<tr>
<td>7/16/2020</td>
<td>A ‘We the People’ Research Discussion on Medical Mistrust</td>
<td>BAI, CoVPN, HVTN, TAG</td>
</tr>
<tr>
<td>7/21/2020</td>
<td>Introduction to Vaccinology/Immunology</td>
<td>BAI, CoVPN, HVTN</td>
</tr>
<tr>
<td>7/23/2020</td>
<td>A ‘We the People’ Research Discussion on Vaccine Clinical Research</td>
<td>BAI, CoVPN, HVTN, Emory, Vanderbilt, HANC</td>
</tr>
<tr>
<td>8/19/2020</td>
<td>Community-Campus Partnerships for Health</td>
<td>CCPH, CoVPN</td>
</tr>
<tr>
<td>9/24/2020</td>
<td>COVID in Black: Honest Conversations about COVID-19 in Black Communities (Ep.1)</td>
<td>CoVPN</td>
</tr>
<tr>
<td>10/14/2020</td>
<td>Intersections: How Do We Grapple With The Disproportionate Impact On Communities Of Color With COVID-19 In The Midst Of The Battle To End HIV By 2030?</td>
<td>Indiana University, Black AIDS Institute, CoVPN, TruEvolution</td>
</tr>
<tr>
<td>10/27/2020</td>
<td>CoVPN Overview and Introduction to Immunology/Vaccinology</td>
<td>Association of Nurses in AIDS Care, CoVPN</td>
</tr>
</tbody>
</table>
CoVPN Faith Initiative

• Faith Ambassadors & Clergy/Faith Leaders
  • Geographically distributed across the US
  • Speaking to the intersection between faith and science
  • Establishing and enhancing networks of faith leaders to conduct COVID & CoVPN educational activities

• Establish and Maintain a faith-based advisory council
  • Provide guidance and direction for CE activities

• Implementation of National faith-focused COVID & CoVPN Education program
  • Educators will represent diverse faith, racial and ethnic identities
  • Program will integrate anti-racist, anti-xenophobic, anti-homophobic and Good Participatory Practice principles
Community Engagement Activities

VI. Communications Creatives & Community Influencers
   I. Lift up voices of people with lived experiences
   II. Celebrity Champions
   III. Marketing Campaign launched September 2020

VII. Sponsor CE Advisory Committees
Thank You

COVPN Executive Committee
Larry Corey and Kathy Neuzil
David Stephens and Myron Cohen
Study Chairs

NIH Executive Team
• Mary Marovich
• Emily Erbelding
• Carl Dieffenbach
• Hilary Marston
• Cliff Lane

VRC
• John Mascola
• Barney Graham
• Julie Ledgerwood
• Sandra Sitar

CoVPN Staff
Merlin Robb

HHS
Oracle

NIH
• Tony Fauci
• Francis Collins
• Doug Lowy

Fred Hutch
Resources


Q & A Discussion

Additional questions?
Email Erin at erin@anacnet.org
Continuing Nursing Education

To be awarded contact hours for this webinar, complete the evaluation found at

https://www.classmarker.com/online-test/start/?quiz=h6f5f7f385f49cc2

You will also receive an email with this link after the webinar

Additional questions?
Email Erin at erin@anacnet.org

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