





# **THE BASIC SCIENCE OF VACCINES**

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# AGENDA

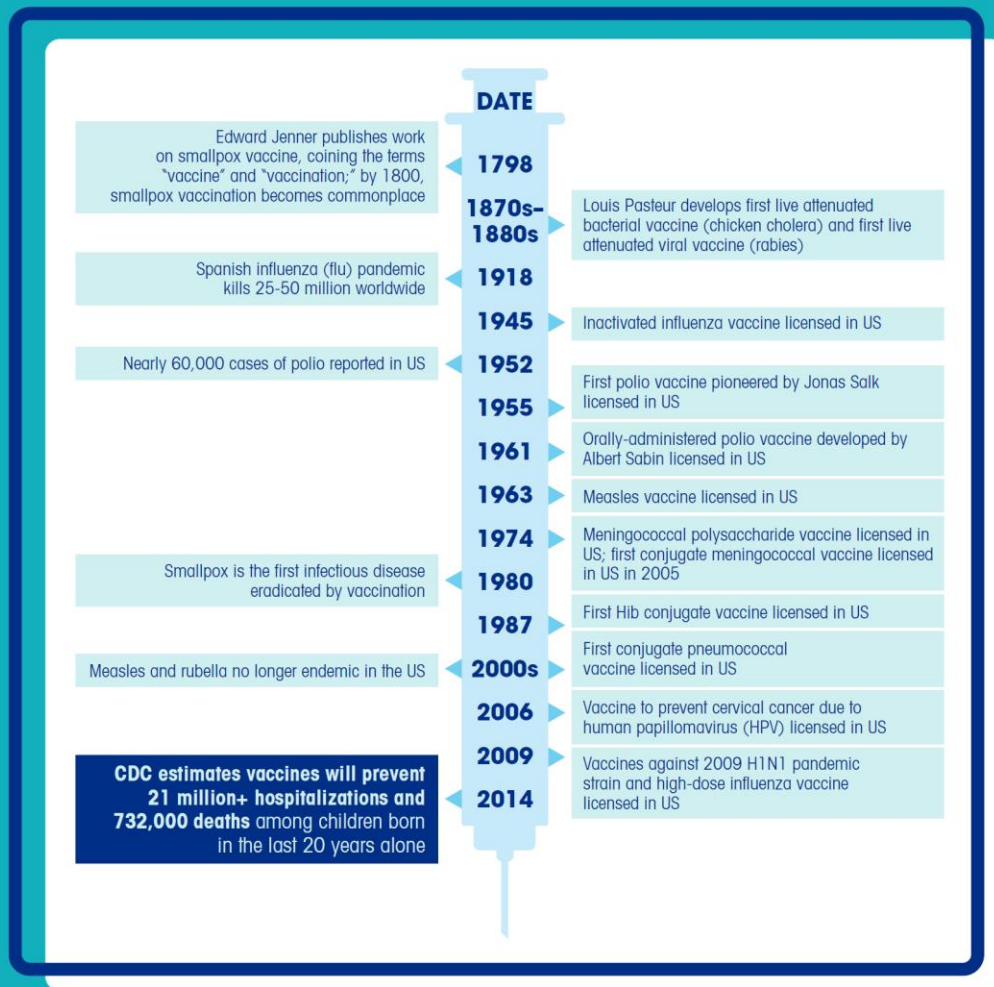
- What is a vaccine?
- A brief history of vaccines
- Types of vaccines
- How does a vaccine work?
- What is herd immunity?
- What are the ingredients of vaccines?
- How is a vaccine developed?
- HPRU Vaccine Trials: Successes and challenges

# WHAT IS A VACCINE?

- A vaccine trains your immune system to produce antibodies (proteins that fight disease), exactly like it would if you were exposed to the disease.
- But vaccines work without making us sick from the infection because vaccines typically contain pieces of dead, weakened, or lab-made substances that stimulate your immune system.

# A BRIEF HISTORY OF VACCINES

## A SHOT OF SCIENCE: BRIEF HISTORY OF VACCINE ACCOMPLISHMENTS\*

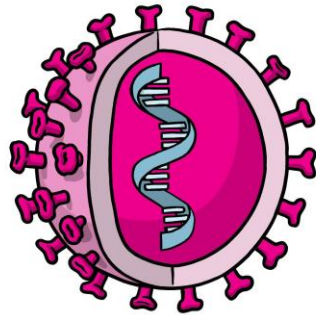


Reference:  
<https://www.nfid.org/2017/04/19/shot-of-science-a-brief-history-of-vaccine-accomplishments/>

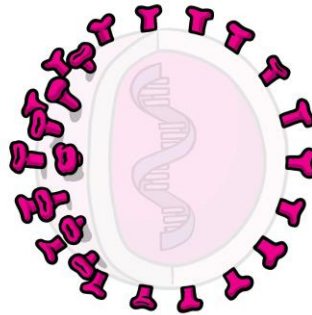
\*Timeline for illustrative purposes only; references available at [nfid.org/vaccine-science](http://nfid.org/vaccine-science)

# TYPES OF VACCINES

There are three main approaches to making a vaccine:



Using a whole virus  
or bacterium



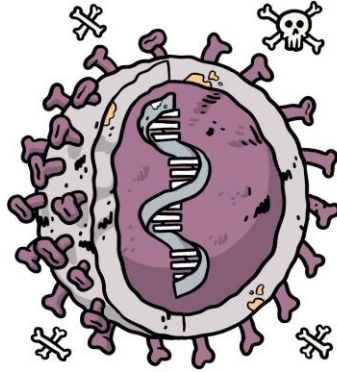
Parts that trigger  
the immune system



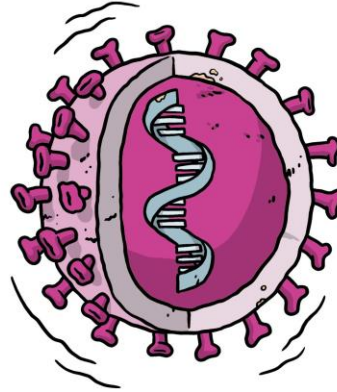
Just the  
genetic material

# THE WHOLE MICROBE APPROACH

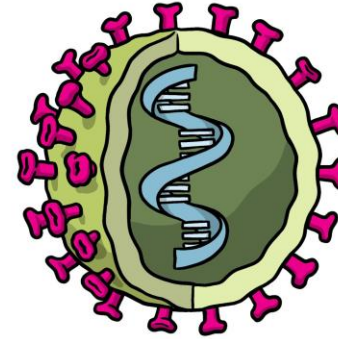
The whole-microbe approach



Inactivated vaccine



Live-attenuated vaccine



Viral vector vaccine

Reference: <https://www.who.int/news-room/feature-stories/detail/the-race-for-a-covid-19-vaccine-explained?fbclid>



Only uses the very specific parts  
(the subunits) of a virus or bacterium that  
the immune system needs to recognize.

# THE SUBUNIT APPROACH

- A subunit vaccine is one that only uses the very specific parts (the subunits) of a virus or bacterium that the immune system needs to recognize.
- It doesn't contain the whole microbe or use a safe virus as a vector.
- The subunits may be proteins or sugars.
- Most of the vaccines on the childhood schedule are subunit vaccines, protecting people from diseases such as whooping cough, tetanus, diphtheria and meningococcal meningitis.





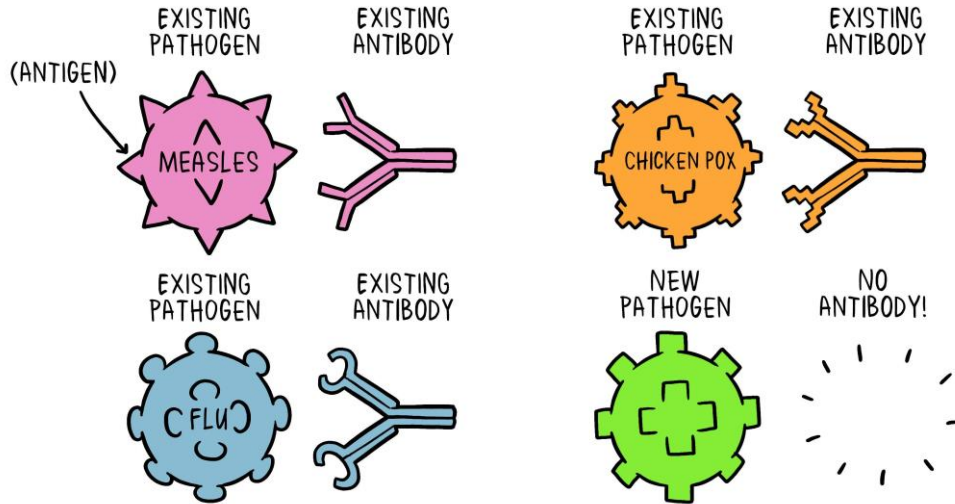
Uses the genetic material for specific proteins - the DNA or RNA.

# THE GENETIC APPROACH

- A nucleic acid vaccine delivers a specific set of instructions to our cells, either as DNA or mRNA, for them to make the specific protein that we want our immune system to recognize and respond to.

# HOW DOES A VACCINE WORK?

The body's natural response:



When a new pathogen or disease enters our body, it introduces a new antigen. For every new antigen, our body needs to build a specific antibody that can grab onto the antigen and defeat the pathogen.



A VACCINE is a tiny weakened non-dangerous fragment of the organism and includes parts of the antigen. It's enough that our body can learn to build the specific antibody. Then if the body encounters the real antigen later, as part of the real organism, it already knows how to defeat it.

# HOW DOES A VACCINE WORK?

- Vaccines contain weakened or inactive parts of a particular organism (antigen) that triggers an immune response within the body.
- Newer vaccines contain the blueprint for producing antigens rather than the antigen itself.
- Regardless of whether the vaccine is made up of the antigen itself or the blueprint so that the body will produce the antigen, this weakened version will not cause the disease in the person receiving the vaccine, but it will prompt their immune system to respond much as it would have on its first reaction to the actual pathogen.

# HOW DOES A VACCINE WORK CONTINUED...

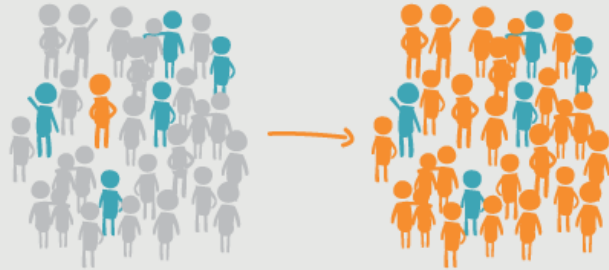
- Some vaccines require multiple doses, given weeks or months apart.
- This is sometimes needed to allow for the production of long-lived antibodies and development of memory cells.
- In this way, the body is trained to fight the specific disease-causing organism, building up memory of the pathogen so as to rapidly fight it if and when exposed in the future.

# HOW DOES A VACCINE WORK CONTINUED...

- When you get a vaccine, your immune system responds. It:
  - Recognizes the invading virus or bacteria.
  - Produces antibodies. Antibodies are proteins produced naturally by the immune system to fight disease.
  - Remembers the disease and how to fight it. If you are then exposed to the virus or bacteria in the future, your immune system can quickly destroy it before you become unwell.
  - The vaccine is therefore a safe and clever way to produce an immune response in the body, without causing illness.

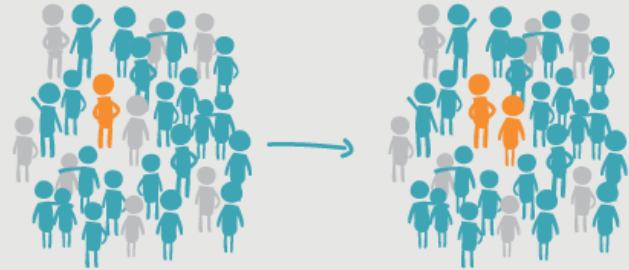
# What is 'herd immunity'?

If only a few people are **vaccinated**...



...then one **person** is infected...  
the disease spreads very fast

But if lots of people are **vaccinated**...

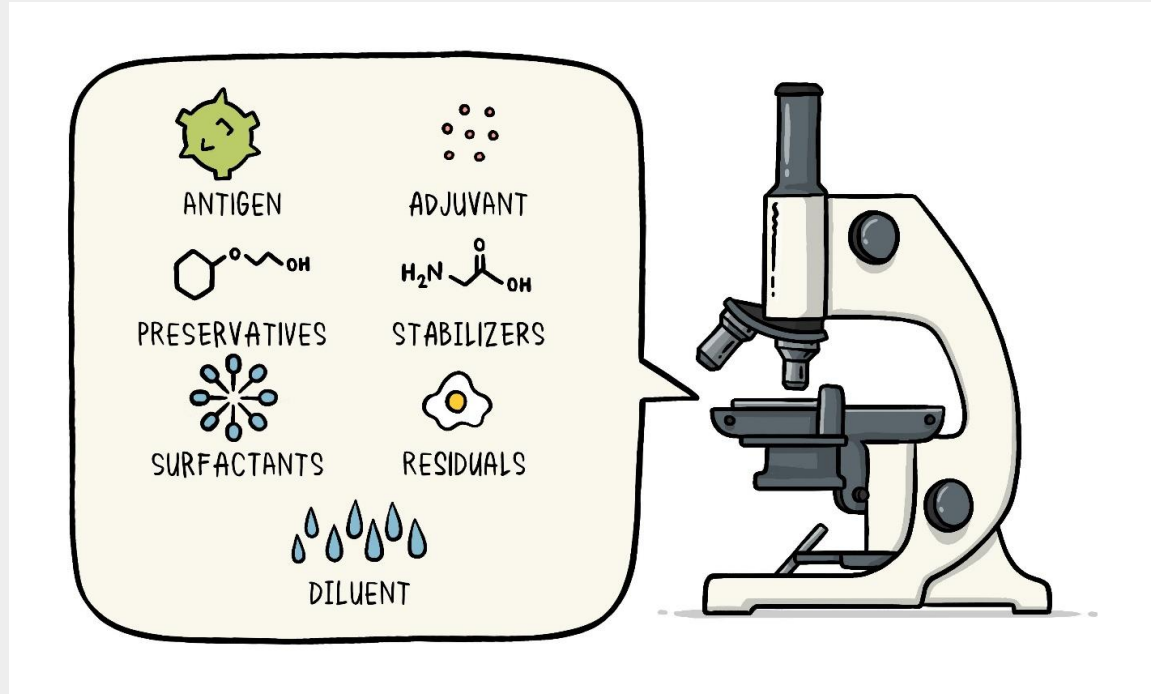


...then the **disease** can't spread very far,  
so the whole community stays safe.  
**This is 'herd immunity'**

**#CelebrateVaccines**

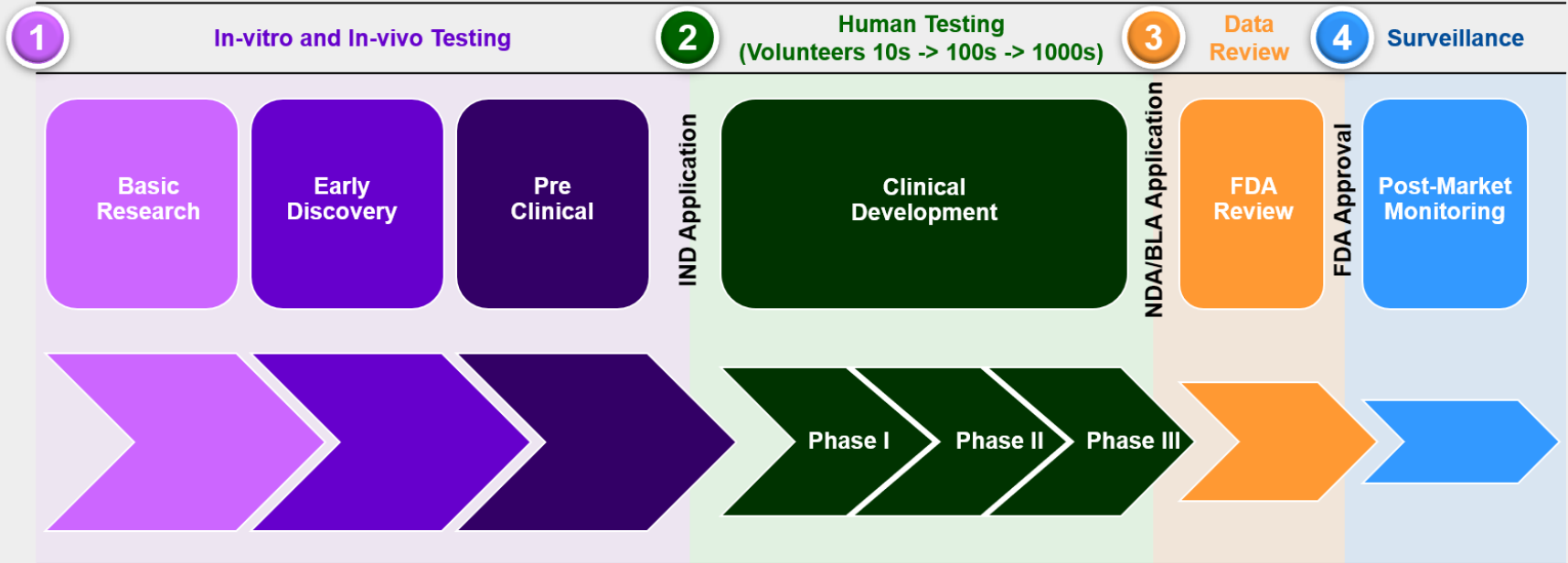
British Society for  
**immunology**  
www.immunology.org

# WHAT ARE THE INGREDIENTS IN A VACCINE?



Reference : <https://www.who.int/news-room/feature-stories/detail/how-are-vaccines-developed>

# VACCINE DEVELOPMENT







# **HPRU VACCINE TRIALS – SUCCESSES AND CHALLENGES**

# HIV VACCINE TRIALS

## PHASE 1-2

Study	Success/Challenge
<p><b>HVTN 100</b> A phase 1-2 randomized, double-blind, placebo-controlled clinical trial of <b>clade C ALVAC-HIV (vCP2438) and Bivalent Subtype C gp120/MF59®</b> in HIV-uninfected adults at low risk of HIV infection.</p>	<p>The regimen elicited robust immune responses that appeared to be stronger than those reported in the RV144 trial, in Thailand. Interim results met all GO criteria to continue with the phase II/III efficacy trial i.e. HVTN 702.</p> <p><i>L. G. Bekker et al., Lancet HIV (2018).</i></p>
<p><b>HVTN 108</b> A phase 1/2a clinical trial to evaluate the safety and immunogenicity of <b>HIV clade C DNA, and of MF59® - or AS01B- adjuvanted clade C Env protein in various combinations</b>, in healthy, HIV-uninfected adult participants.</p>	<p>All groups demonstrated acceptable safety profiles. Further, all groups had high IgG response rates and improved CD4 response rates and magnitudes.</p> <p><i>N. Garrett et al., In: Conference on retroviruses and opportunistic infections Boston USA (2020).</i></p>
<p><b>HVTN 111</b> A phase 1 clinical trial to evaluate the safety and immunogenicity of <b>HIV clade C DNA and of MF59- adjuvanted clade C Env protein</b>, in healthy, HIV uninfected adult participants.</p>	<p>Both the prime/boost and coadministration regimens were safe and may be advanced into efficacy trials depending on whether cellular or humoral responses are desired.</p> <p><i>M.C. Hoissienipour et al., Clin Infect Dis (2020).</i></p>



# HIV VACCINE TRIALS

## PHASE 2-3

Study	Success/Challenge
<p><b>HVTN 702</b> A pivotal phase 2b/3 multi-site, randomized, double-blind, placebo-controlled clinical trial to evaluate the safety and efficacy of <b>ALVAC-HIV (vCP2438) and bivalent subtype C gp120/MF59</b> in preventing HIV-1 infection in adults in South Africa.</p>	<p>The trial was stopped as the data and safety monitoring board found that the vaccine was ineffective in preventing HIV acquisition.</p> <p><i>P. Adepaju et al., Lancet HIV (2020).</i></p>
<p><b>HVTN 705</b> A multicenter, randomized, double-blind, placebo-controlled efficacy study of <b>heterologous prime/boost vaccine regimen of Ad26.Mos.4HIV aluminum phosphate adjuvanted clade C gp 140</b> in preventing HIV-1 infection in adult women.</p>	<p>Ongoing</p>
<p><b>HPTN 084</b> A phase 3 double blind safety and efficacy study of <b>long-acting injectable cabotegravir compared to daily oral TDF/FTC</b> for Pre-exposure prophylaxis in HIV-uninfected women.</p>	<p>In Nov 2020, DSMB, recommended that the sponsor stop the blinded phase of the trial and share results - the PrEP regimen of long-acting cabotegravir injections once every 8 weeks was found to be safe and superior to daily oral TDF/FTC for HIV prevention.</p> <p><a href="https://www.hptn.org/news-and-events/announcements/hptn-084-study-demonstrates-superiority-of-injectable-cabotegravir-">https://www.hptn.org/news-and-events/announcements/hptn-084-study-demonstrates-superiority-of-injectable-cabotegravir-</a></p>

# HIV VACCINE TRIALS

## PHASE 2-3

Study	Success/Challenge
<p><b>PREPVacc</b> A phase IIb three-arm, two-stage HIV prophylactic vaccine trial with a second randomization to compare <b>TAF/FTC to TDF/FTC</b> as pre-exposure prophylaxis.</p>	<p>Upcoming study</p>

# COVID VACCINE TRIALS

Study	Success/Challenge
<p><b>Novavax</b> A phase 2a/b, randomized, observer-blinded, placebo-controlled study to evaluate the efficacy, immunogenicity, and safety of a <b>SARS-CoV-2 recombinant spike protein nanoparticle vaccine (SARS-CoV-2 rS) with matrix-m1™ adjuvant</b> in South African adult subjects living without HIV; and safety and immunogenicity in adults living with HIV.</p>	<p>The vaccine administered demonstrated 60% efficacy in South Africa and 80% efficacy in UK. In SA, the 60% efficacy in prevention of mild, moderate and severe COVID-19 was observed in 94% of HIV uninfected participants.</p> <p><i><a href="https://ir.novavax.com/news-releases/news-release-details/novavax-covid-19-vaccine-demonstrates-893-efficacy-uk-phase-3">https://ir.novavax.com/news-releases/news-release-details/novavax-covid-19-vaccine-demonstrates-893-efficacy-uk-phase-3</a></i></p>
<p><b>Ensemble</b> A randomized, double-blind, placebo-controlled phase 3 study to assess the efficacy and safety of <b>Ad26.COV2.S</b> for the prevention of SARS-CoV-2-mediated COVID-19 in adults aged 18 years and older.</p> <p><i><a href="https://www.jnj.com/johnson-johnson-initiates-second-global-phase-3-clinical-trial-of-its-janssen-covid-19-vaccine-candidate">https://www.jnj.com/johnson-johnson-initiates-second-global-phase-3-clinical-trial-of-its-janssen-covid-19-vaccine-candidate</a></i></p>	<p>Among all participants, across different geographies and including those infected with emerging viral variants, the vaccine candidate was 66% effective overall in preventing moderate to severe COVID-19, 28 days after vaccination. The onset of protection was observed as early as day 14. The level of protection against moderate to severe COVID-19 infection was 72% in USA, 66% in Latin America and 57% in SA post-vaccination.</p>
<p><b>CROWN Coronation</b> An international, Bayesian platform adaptive, randomized, placebo-controlled trial assessing the effectiveness of candidate interventions in preventing COVID-19 disease in adults.</p>	<p>Ongoing</p>



