Vaccines

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Vaccines

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Course Objectives

- Prevention and Control of Vaccine Preventable diseases
- Global Impact of vaccines: Successes and challenges
- Vaccine fundamentals
  - Basic Immunology
  - Introduction to Vaccinology
Strategies for Prevention and Control

**Eradication:** Worldwide interruption of transmission. No disease anywhere.

**Elimination:** Interruption of transmission in a substantial geographic area. No endemic cases in the area, but still cases elsewhere.

**Control:** Reduction of cases in the geographic area of interest.
Ingredients for Eradication/Elimination Programs

- Easily recognizable disease
- No non-human reservoir
- Pathogen is genetically stable
- No subclinical infection
- Usually not highly communicable
Ingredients for Eradication/Elimination Programs

- An effective, safe (and cheap) intervention
- Bold vision and determination
- Resources, administrative skill, flexibility
  Cooperation of the affected populations
SMALLPOX (Eradication)
Ingredients for Control

- Very distinctive disease
- Humans only reservoir
- Stable virus
- No sub-clinical infection
- Transmitted slowly
- Vaccine was cheap, easy to administer
- Strong vision
SMALLPOX

Global mass vaccination campaign

Surveillance and containment
  Smallpox spreads slowly
  Ring vaccination

Administrative barriers
  Effective surveillance
1977  Last naturally-occurring case
      Ali Maow Maalin
      Cook/ Healthcare Worker, Somalia

1978  Birmingham, UK
      Research photographer died
      Poor laboratory safety

1980  Declared eradicated by WHO

2014  Vials of smallpox virus found
      NIH cold room being renovated

2019  Gas explosion and fire
      State Research Center of Virology
      Koltsovo, Siberia

2019  Continuing debate whether two stocks
      of smallpox virus (US, Russia) should be destroyed
POLIO
Ingredients for Control

- Easily recognized disease
- No non-human reservoir
- 3 pathogens genetically stable
- \textbf{MUCH} sub-clinical infection
- Very transmissible
- Vaccine effective –
  - needs several doses
  - easy to administer (oral drops)
  - Cheap
  - but can revert to virulence
- International commitment
Three individual and immunologically-distinct wild polio virus strains (WP1, WP2, WP3)

Symptomatically all the same, however genetic differences that require each one to be eradicated

OPV is a weakened but live virus vaccine, meaning you are giving the recipient a polio virus. In very small number every year, reverts to full virulence and causes Vaccine Derived Polio Virus (VDPV)
1988    Global Polio Eradication Initiative launched
2012    WPV3 last time seen, presumed eradicated
2015    WPV2 declared eradicated globally
2016    tOPV replaced with bOPV (serotypes 1 & 3)
2019    WPV3 declared eradicated

Wild poliovirus (WPV1) continues to circulate
OPV-derived viruses circulating in Africa, SE Asia, China

2016    IPV being introduced into vaccine programs globally
Global POLIO Eradication

- Political instability, wars
- Religious and political opposition
- Immunization fatigue
Africa declared free of wild polio in 'milestone'

By Naomi Scherbel-Ball
BBC News
Published
25 August
Wild polio eradicated in Africa

Countries with polio cases in the past 12 months

- **Vaccine-derived poliovirus**
- **Wild poliovirus**

*Afghanistan and Pakistan also have cases of vaccine-derived poliovirus*

Source: WHO (data up to 19 August 2020)
Role of Inactivated Polio Vaccine (IPV)

- Every country that has eliminated polio used OPV to do it; because it induces local immunity in the intestinal tract against polio.

- IPV induces only very low-level immunity and cannot interrupt wild type transmission in the environment.
Three children with a rash

- Fever to 40°C
- Rhinorrhea
- Cough
- Rash (as pictured)
- Conjunctivitis (as pictured)
Which virus is MOST likely cause of symptoms?

- Rubella
- Varicella
- Lassa fever
- Measles
- Yellow Fever
- Ebola
Rubella
Varicella
Lassa fever
Measles
Yellow Fever
Ebola

Which virus is MOST likely cause of symptoms?
Measles
Ingredients for Control

- Distinctive disease
- No non-human reservoir
- Virus is genetically stable
- No subclinical infection

Right conditions for elimination or eradication programs
Measles

- One of the most contagious viral infections. Infecting 90% of susceptible contacts
- Spread during asymptomatic phase
- Can live 2 hours or longer in the air after an infected person coughs or sneezes
- Much more easily spread than COVID-19
Complications of measles

- Otitis media ~1 in 10
- Pneumonia ~1 in 10
- Diarrhea ~1 in 10
- Acute encephalitis ~1-1000
- Death ~2 per 1000
**Prevention**

- Education of health care personnel and community
- Vaccination
- Nutrition (*Vitamin A supplementation*)
- Treatment of underlying disease (eg. HIV)
Yellow Fever

- An acute viral hemorrhagic fever
- Originated in Central Africa
- Spread by *aedes aegypti* mosquito
- Monkeys can also be infected
Incubation period is 3-6 days
- Sudden onset fever, chills
- Yellow eyes
- Headache
- Backache
- Vomiting
- Bleeding
- Death can occur on days 7-12 of illness
Non-distinctive febril illness at beginning

Non-human reservoirs
  - Monkeys
  - Mosquitos

Highly effective vaccine

Could be compatible for elimination or control strategies

1851 First International Sanitary Conference (international cooperation regarding quarantine to prevent cholera and other problems)

1905 Yellow Fever and Malaria control Panama (William Crawford Gorgas)

Yellow Fever and Malaria
Diseases such as yellow fever, malaria, pneumonia, diarrhea, and other, aided by poor nutrition caused thousands of deaths. By the late 19th century, the French were victims of these diseases that killed 22 thousand of its workers.
# National Immunization Schedule

## Liberia

**Recommended routine immunization**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Description</th>
<th>Schedule</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Primary Infant Vaccination Schedule</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BCG</td>
<td>Bacille Calmette-Guérin vaccine</td>
<td>Birth</td>
<td></td>
</tr>
<tr>
<td>OPV</td>
<td>Oral polio vaccine</td>
<td>Birth; 6, 10, 14 weeks</td>
<td></td>
</tr>
<tr>
<td>DTwPHibHepB</td>
<td>Diphtheria and Tetanus and Pertussis and Haemophilus influenzae and Hepatitis B vaccine</td>
<td>6, 10, 14 weeks</td>
<td></td>
</tr>
<tr>
<td>Pneumo_conj</td>
<td>Pneumococcal conjugate vaccine</td>
<td>6, 10, 14 weeks</td>
<td></td>
</tr>
<tr>
<td>Rotavirus</td>
<td>Rotavirus vaccine</td>
<td>6, 10, 14 weeks</td>
<td></td>
</tr>
<tr>
<td>IPV</td>
<td>Inactivated polio vaccine</td>
<td>14 weeks</td>
<td>From January 2018</td>
</tr>
<tr>
<td>Measles</td>
<td>Measles vaccine</td>
<td>9 months</td>
<td></td>
</tr>
<tr>
<td>YF</td>
<td>Yellow fever vaccine</td>
<td>9 months</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Adolescents and Adult Vaccination Schedule</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td>Human Papillomavirus vaccine</td>
<td>10 years (2 doses)</td>
<td>Not available in all parts of the country</td>
</tr>
<tr>
<td>TT</td>
<td>Tetanus toxoid vaccine</td>
<td>14 years; +4 weeks; +6, +12 months</td>
<td>And pregnant women</td>
</tr>
</tbody>
</table>
Global Impact of Vaccines: Successes and Challenges
Substantial Advancement in Vaccine Innovation in last 15 years...and more to come

- 1920-1939: 1 vaccine
- 1940-1959: 3 vaccines
- 1960-1979: 4 vaccines
- 1980-1999: 3 vaccines
- 2000-2018: >12 vaccines
**Fig. 1.** Historical and projected vaccination coverage rates. The graph shows expansion of global vaccination rates over the past 50 years for vaccines against DPT, poliomyelitis, and measles and the BCG (Bacillus Calmette-Guérin) vaccine for TB, all of which were recommended in 1984 by the WHO EPI. In 2000, the establishment of Gavi allowed the acceleration and global expansion of vaccination efforts against hepatitis B virus (HBV), *Haemophilus influenzae* type b (Hib), pneumococcus, and rotavirus. Licensed vaccines exist for protection against human papillomavirus (HPV), malaria, typhoid fever, and dengue, but large-scale vaccination against these diseases in low-income countries has not yet been implemented. Vaccines against TB, HIV, shigella, group B streptococcus (GBS), respiratory syncytial virus (RSV), antimicrobial-resistant pathogens (AMR), and emerging infectious diseases (EIDs) are likely to reach the late stages of development during the next 3 to 10 years. EIDs refer to about 30 different pathogens that have the possibility to cause outbreaks and pandemics and for which we do not yet have vaccines (31).
Progress and Challenges with Achieving Universal Immunization Coverage

(Data as of July 2019)

Sources:
- Member states reports to WHO and UNICEF.
- The 2019 World Bank Development Indicators Online
- United Nations, Population Division, 2019 revision

unicef

World Health Organization
Almost 9 out of 10 children reached in 2018, almost 20 million children un or under vaccinated

Coverage of a third dose of vaccine protecting against diphtheria, tetanus, and pertussis (DTPv-3) remains at 86% in 2018, leaving 19.4 million children vulnerable to vaccine preventable diseases.

The key goal of the Immunization Agenda 2030 is to make vaccination available to everyone, everywhere, by 2030.

While immunization is probably the most successful public health intervention, reaching 86% of infants is not enough. The upward trend in coverage has increased by only 5% in the past decade and has plateaued.
The gap between the best performer, the European Region, and the lowest performer, the African Region, is 18 percentage points.

The Western Pacific Region and especially the Region of the Americas experience drops in coverage.

The biggest gains have been made by the African Region (over a 20 year period), and the South East Asian Region (over a ten year period).
Just 10 countries account for 60% of unprotected children

Countries with most unprotected children

10 countries account for 11.7% of the 19.4 million under and unvaccinated children in the world (60%). This list includes some countries with moderate coverage and very large birth cohorts, and other countries with substantially lower coverage.

*N Preliminary survey suggests lower coverage and higher number of unvaccinated children.
However, many countries that previously had attained high coverage levels backslided in the last few years.

Many countries that had previously reached at least 90% coverage with a first dose of measles containing vaccine, dropped back in the last few years. The chart shows 19 selected countries with significant drops in coverage (10 percentage points or more).

Reasons for backsliding include complacency, lack of investment in public health, conflict, and in some places lack of trust in vaccines.

Measles elimination requires sustained very high coverage in all age and population groups.
GAVI’S IMPACT

- **Increased childhood survival**
  - Halved childhood mortality by preventing approximately 13 million deaths
  - Marked decline in incidence of deadly and debilitating infectious diseases.

- **National Development thrives.**
  - For every US$ 1 invested in vaccines in Gavi-supported countries, there is a US$ 54 return in savings from averted illness and broader societal benefits.

- **Global health security improves.**
  - In the face of global challenges, such as climate change, urbanization, human migration, fragility and conflict, Gavi has helped countries broaden vaccine coverage and improve health systems.
Coverage for newer vaccines in Gavi countries is now better than average

The trajectories for Pneumococcal Conjugate and Rotavirus Vaccines are especially noteworthy, as lower income countries have been able to achieve higher coverage than the global average thanks to support from the Gavi Alliance. Non-Gavi Middle Income countries are falling behind.
Success in scaling up new vaccines and increasing coverage in Gavi countries

Breadth of protection Gavi 68

Coverage in 2018

Rapid scale up of new vaccines in Gavi supported countries

Coverage of select antigens now higher in Gavi supported countries vs. global
Significant coverage gains since Gavi’s inception yet children being missed

- In last ~20 years, succeeded in vaccinating 4 in 5 children in Gavi supported countries
- Keeping pace with population growth will increasingly be a challenge
- Reaching 5 in 5 children will require new thinking and new approaches

Source: WUENIC 2019 update
Major Challenges to GVAP

- Accelerating urbanization
- Migration and displacement
- Conflict and political instability
- Vaccine unaffordability in middle-income countries
- Unexpected vaccine supply shortages both locally and globally
- Rising vaccine hesitancy
Measles Highlights Challenges in Vaccine Delivery
Measles program has prevented tens of millions of deaths in less than 2 decades, 2000 - 2017

- Estimated measles deaths averted through Routine Immunization and SIAs
- Estimated measles deaths still occurring

Measles vaccination has averted **21.1 million** estimated deaths 2000-2017

Measles contribution to U5 mortality has dropped from 6% to 2%

Figure 2. Measles notification rate per million population by country, EU/EEA, 1 January 2019–31 December 2019

Notification rate of measles (per million), January 2019–December 2019
- 0
- 0.01–0.99
- 1.00–9.99
- 10.00–19.99
- ≥20.00
- Not included

Ten deaths (case-fatality rate (CFR): 0.09%) attributable to measles were reported to TESSy during the 12-month period in Romania (5), France (2), Hungary (1), Italy (1) and United Kingdom (1) (see Figure 3). Over the 12 month period, the case fatality rates by age group ranged between 0 and 0.09% (Table 2).
Figure 4. Vaccination coverage for first (left) dose of a measles- and rubella-containing vaccine and second (right) dose of a measles-containing vaccine, EU/EEA, 2018
Philippines measles outbreak is deadliest yet as vaccine scepticism spurs disease comeback

The sharp drop came in the wake of a political battle over Sanofi’s dengue vaccine Dengvaxia, which was discontinued in the Philippines last year over safety concerns despite the company’s protests, as politicians traded blame.
US measles outbreak concentrated among unvaccinated children

As 2019 begins, a measles outbreak has been reported in Washington state, and the number of cases has been steadily increasing. As of Feb 11, there have been 54 confirmed cases, according to the Washington State Department of Health (DOH) and all but one have occurred in Clark County, which borders on the state of Oregon. There are an additional 11 unconfirmed cases plus four confirmed related cases in Oregon.

As of Feb 7, four other outbreaks been reported in the USA in 2019: three in New York, and one in Texas.

www.thelancet.com/infection Vol 19 March 2019
Measles Outbreaks from Imported Cases in Orthodox Jewish Communities — New York and New Jersey, 2018–2019

FIGURE. Number of measles cases, by date of rash onset — New York (n = 242)* October 1, 2018–April 30, 2019, and New Jersey (n = 33) October 17, 2018–November 30, 2018

* Excludes New York City.
A behaviour, influenced by a number of factors including issues of confidence [do not trust vaccine or provider], complacency [do not perceive a need for a vaccine, do not value the vaccine], and convenience [access]. Vaccine-hesitant individuals are a heterogeneous group who hold varying degrees of indecision about specific vaccines or vaccination in general. Vaccine-hesitant individuals may accept all vaccines but remain concerned about vaccines, some may refuse or delay some vaccines, but accept others; some individuals may refuse all vaccines.
Figure 3: The majority of the EU public agree that vaccines are important, safe, and effective. Most of the EU public either strongly or tend to agree that vaccines – including the MMR and seasonal influenza vaccines – are important, safe, and effective. However, the seasonal influenza vaccine is viewed as both less important and less safe than the MMR vaccine and vaccines generally.
Immunity - the ability of an organism to resist an infection or toxin. The human body must be able to differentiate “self” from “non-self” (eg: bacteria, viruses, pollens).

Antigen - anything that triggers an immune response
- entire pathogen (bacteria, virus);
- toxin expressed by pathogen;
- piece of a pathogen (capsular polysaccharide)

Immune system has two overlapping subsystems:
- Innate immune system
- Adaptive immune system
Also called “non-specific” or “inborn” immune system
Functions as the first line of defense against infection
Response is non-specific
Components of the Innate Immune System

- Non-specific barriers
  - Skin, saliva, mucous
- Soluble factors
  - Complement proteins,
  - Cytokines (responsible for inflammation)
- Cellular components
  - Neutrophils, basophils
  - Macrophages
  - Dendritic cells
Constantly evolves as we encounter new antigens
Creates targeted response (antigenic specificity) to antigens
Takes longer to develop than innate immunity because it is antigen-specific
Said to have “memory” because it learns by experience and responds to previously seen antigens
Components of the Adaptive Immune System

- **B-Cells**
  - Secrete antibodies
  - Become memory cells

- **T-Cells**
  - Cell mediated immunity
  - Various roles
    - Hunt and destroy abnormal cells (cytotoxic t-cells)
    - Help activate B-cells (helper T-Cells)

- **Antigen-presenting cells**
What is a Vaccine?

- A substance used to stimulate production of antibodies and provide immunity against one or several diseases
- Prepared from the causative agent, its products, or a synthetic substitute
- Treated to act as an antigen without inducing disease

Vaccines stimulate B and T-Cells (adaptive immunity) to produce long-lasting immunity
Inactivated vs. Live-attenuated Vaccines

**Inactivated:**
- Vaccine that is not live
- May be composed of toxoids, killed viruses, or recombinent proteins
- Not infectious, but still antigenic

**Live-Attenuated:**
- Weakened microbes
- Mimic natural infection without causing the disease
Inactivated vs. Live-attenuated Vaccines

**Inactivated:**
- Vaccine that is not live
- May be composed of toxoids, killed viruses, or recombinent proteins
- Not infectious, but still antigenic

**Examples**
- Pneumococcal conjugate
- DTwPHibHepB
- Inactivated polio (IPV)
- HPV

**Live-Attenuated:**
- Weakened microbes
- Mimic natural infection without causing the disease

**Examples**
- BCG
- Rotavirus
- Measles
- Oral Polio
- Yellow Fever
Inactivated Vaccines

**Advantages:**
- Cannot replicate, so cannot cause infection
- Safe even in immunocompromised persons

**Disadvantages:**
- Produce weaker immune response than a live vaccine
- Induce mostly humoral response (Abs) with little cellular immunity
- Require multiple doses (a priming dose and additional doses to induce adequate immunity)
- Immunity may wane over time, requiring booster doses
Advantages:
- Induce strong, long-lasting immune cellular and humoral response
- Schedules often have repeat dosing to ensure a large percent of population is truly immunized (measles needs 95% for herd immunity)
  - People may miss dose or some people may not respond well to first dose

Disadvantages:
- Generally need caution when giving to immunocompromised patients
- May cause mild versions of the disease you are trying to prevent (e.g., varicella vaccine may cause a rash 10 days after vaccination)
- Oral polio vaccine can rarely revert to a virulent form and cause disease
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Live Vaccines</th>
<th>Not Live (Inactivated) Vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune response</td>
<td>Humoral and cell-mediated</td>
<td>Mostly humoral&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Dosing</td>
<td>One or 2 doses usually sufficient&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Multiple-dose series usually necessary&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Adjuvant</td>
<td>Not necessary</td>
<td>May be necessary&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Route of administration</td>
<td>Intranasal, oral, subcutaneous</td>
<td>Intramuscular, subcutaneous, intradermal&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>Duration of immunity</td>
<td>Potentially lifelong</td>
<td>Booster doses may be necessary&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Person-to-person transmission</td>
<td>Possible&lt;sup&gt;g&lt;/sup&gt;</td>
<td>Not possible</td>
</tr>
<tr>
<td>Effect of passively acquired antibodies</td>
<td>Inactivation possible</td>
<td>Interference possible</td>
</tr>
<tr>
<td>Use in immunocompromised hosts</td>
<td>May cause disease</td>
<td>May be less immunogenic</td>
</tr>
<tr>
<td>Use in pregnancy</td>
<td>Fetal damage theoretically possible&lt;sup&gt;h&lt;/sup&gt;</td>
<td>Fetal damage theoretically unlikely</td>
</tr>
<tr>
<td>Rationale for storage requirements</td>
<td>Maintain viability</td>
<td>Maintain stability</td>
</tr>
<tr>
<td>Administration on the same day</td>
<td>Acceptable&lt;sup&gt;i&lt;/sup&gt;</td>
<td>Acceptable&lt;sup&gt;j&lt;/sup&gt;</td>
</tr>
<tr>
<td>Interval between doses of the same vaccine given in sequence</td>
<td>Minimum intervals apply&lt;sup&gt;k&lt;/sup&gt;</td>
<td>Minimum intervals apply&lt;sup&gt;l&lt;/sup&gt;</td>
</tr>
<tr>
<td>Interval between doses of different vaccines given in sequence</td>
<td>Minimum intervals apply&lt;sup&gt;k&lt;/sup&gt;</td>
<td>No minimum intervals</td>
</tr>
</tbody>
</table>

<sup>a</sup> Inactivated vaccines may stimulate limited cell-mediated immune responses through cross-presentation.

<sup>b</sup> RVV and typhoid Ty21a are given orally in multiple-dose series; cholera vaccine is given as a single oral dose. Although 1 dose of MMR or VAR may be sufficient to induce long-lasting immunity, second doses are given before school entry to ensure that children who did not seroconvert to the first dose have another chance to do so. Since immunity to varicella zoster virus can wane after immunization, the second dose of VAR may also serve as a booster.

<sup>c</sup> Older adults may respond well to a single dose of an inactivated vaccine because they have been previously primed by natural exposure. This might apply, for example, to PPSV23—adults who receive this vaccine have probably had prior exposures to S pneumoniae.

<sup>d</sup> HibT, IV, MenACWY-D, MenACWY-CRM, PPSV23, IPV, and RAB do not contain adjuvants.

<sup>e</sup> Flu vaccine intradermal (idiRV) was discontinued in 2017.

<sup>f</sup> Long-term protection has been demonstrated for some inactivated vaccines, such as HepA and HepB, in the absence of booster doses.

<sup>g</sup> This is relevant for OPV, where horizontal transmission contributes to immunity at the population level, but also on rare occasion leads to disease in contacts. Transmission of vaccinia represents a real risk to susceptible close contacts. Transmission of cholela vaccine, LAIV, RV, and VAR has been documented, but is rare. Transmission of MMR, Ty21a, and YFV has not been documented.

<sup>h</sup> The possibility of fetal infection leads to the general recommendation that live vaccines not be given during pregnancy (see Chapter 6: Vaccination in Special Circumstances—Pregnancy, Postpartum, and Breast-Feeding).

<sup>i</sup> Separate sites are always used for simultaneous administration. The only example of two live vaccines that cannot be given at the same time are VAR and smallpox (the concern is increased complications from smallpox vaccine).

<sup>j</sup> Separate sites are always used for simultaneous administration. Examples of two inactivated vaccines that cannot be given at the same time are MenACWY-D and PCV13 in anatomically or functionally asplenic children (the concern is reduced response to pneumococcal antigens) and PCV13 and PPSV23 (the concern is interference).

<sup>k</sup> Replication of the first live vaccine can interfere with replication of a second live vaccine that is given within 4 weeks.

<sup>l</sup> Proper spacing between the doses is necessary to maximize the immune response.
Get The App!

You can download The Vaccine Handbook mobile app for FREE from the app store (iphone users only)!

The app is fully searchable, allows for bookmarking, highlighting and annotation, and contains hyperlinks to valuable content from nonprofit and governmental sources.

The Vaccine Handbook, print edition, is also available for purchase. The 9th edition will be released May 2020.
Polysaccharide vaccines are made using a sugar molecules from the outer coating of a bacterium (part of its capsule)

Stimulates antibody response to capsule of the bacterium, which aids the immune system removing the bacteria

**Limitations**
- Not immunogenic in children <2 years
- Do not induce long-lasting immunity
- Repeated doses may not provide boost
  - Repeated doses (>3 in a lifetime) or too close together (<5 years) may actually reduce the immune response

**Pneumococcal-23**
- Reserved for children >2yrs with asplenia
- Or persons >65 years of age
Conjugate vaccines are made by combining a protein (antigen or toxoid) from a pathogen with the polysaccharide. Conjugation helps promote a more robust immune response. No worries giving to immunocompromised patients.

**Advantages**
- Immunogenic in kids <2 years and good in adults >65 years
- Do induce long-term immune memory
- Repeated doses “boost” the immune response

Eg: Pneumococcal conj; Diptheria, Tetanos, HIB,
Vaccine Components

- **Antigens (active components)**
- **Additives**
  - Adjuvants
  - Antibiotics
  - Stabilizers
  - Preservatives
- **Residuals (Trace components)**

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**COMMON COMPONENTS OF VACCINES**

As well as the active components, vaccines contain a number of other substances. This graphic examines these and the reasons for their inclusion.

### ACTIVE COMPONENTS

A form of the virus, bacteria or toxin that causes the disease is used as the antigen. This antigen is modified from the original form so it no longer causes disease, but still elicits an immune response from the body. To modify the disease causing agent, it can be treated with specific chemicals so it cannot replicate. It can also be treated so it does not cause serious disease, or only parts of the disease-causing agent that do not cause serious symptoms can be used.

### ADJUVANTS

- **Al(OH)₃**
  
  **Aluminium Hydroxide**

  Added to enhance the body’s immune response to the vaccine. How they work isn’t entirely understood, but it’s thought they help keep antigens near the site of injection. This means they can be easily accessed by the immune system cells. There is no evidence of any serious adverse effects from adjuvants, though they can cause some minor reaction near the injection site.

- **AlPO₄**
  
  **Aluminium Phosphate**

### STABILISERS

- **MgSO₄**
  
  **Magnesium Sulphate**

  Vaccines need to be stable, so stabilizers are added to ensure the various components remain stable and effective. A variety of different stabilizers are used; either inorganic magnesium salts such as magnesium sulphate or magnesium chloride, or mixtures of lactose, sorbitol and gelatin. Monosodium glutamate and glycine are also used in some cases.

### PRESERVATIVES

- **Thiomersal**

  **Phenol**

  **Phenoxyethanol**

  Preservatives help prevent contamination of vaccines. They are used particularly in multi-dose vaccines. Thiomersal is a common preservative, though its use declined in the late 1990s when vaccines were falsely linked to child autism. This link was later shown to be an elaborate medical hoax, and there is no link between thiomersal and autism.

### TRACE COMPONENTS

- **Formaldehyde**

  These are left over from the vaccine production process. Though they are purposefully removed, residual amounts remain. Formaldehyde is one such agent, used to deacetylate viruses and detoxify bacteria, but amount remaining is several hundred times lower than the smallest amount known to cause harm in humans.
**Antigens** are the components of a vaccine that induce immunity.

- Portion of disease-causing organism
- Modified toxin from the organism
- Live but weakened virus
Adjuvant: help generate a stronger immune response. By using adjuvant you can use less antigen or give fewer vaccine doses for the same effect.
  ○ *Aluminum salts and oil-in-water emulsions* most common

Stabilizers: maintain vaccine potency during storage. Protect against extreme cold or heat. Provide a bulking matrix so the small amount of antigen does not stick to the vial wall.
  ○ *Sugars (sucrose), amino acids (glycine), and proteins (gelatin-bovine)* are most common
Preservatives: Keep vaccines safe for injection. Includes antimicrobial agents added to inactivated vaccines to prevent growth of bacteria or fungi, especially in a multi-dose vial of vaccine.

- *Thimerosal* is a common preservative. Causes concern due to mercury content. However, made from *ethylmercury* and not *methylmercury* (the mercury found in fish and toxic at high levels)
Leftover products from the manufacturing process that may be present in final vaccine.

Examples include formaldehyde or antibiotics, such as streptomycin.
Some individuals have a bad reaction to a vaccine, just as some people have reactions to medicines or foods.

- **Common AE**
  - Fever
  - Soreness at injection site
  - Prolonged crying

- **Serious AE’s** can be found in the insert for the vaccine.
Contraindications and Precautions
Advisory Committee on Immunization Practices (ACIP)

www.cdc.gov
Prolonged Crying

- Defined as 3+ hours of crying within 2 days of being vaccinated

- Neither a precaution or contraindication for future vaccinations
Hypotonic Hyporesponsive Episode (HHE)

- Worrisome shock like reaction following vaccination, where child becomes hypotonic and unresponsive for a brief period then returns to baseline.

- Originally associated with whole-cell pertussis vaccine.

- No long-term consequences. Not a contraindication for future vaccinations.
Saliva

- Innate Immunity
- Adaptive Immunity
Innate Immunity

• Saliva

Adaptive Immunity
Innate Immunity

Adaptive Immunity

- Saliva

Helper T-cell
Innate Immunity

• Saliva

Adaptive Immunity

• Helper T-cell
Neutrophil

- Innate Immunity
  - Saliva
- Adaptive Immunity
  - Helper T-cell
Innate Immunity

- Saliva
- Neutrophil

Adaptive Immunity

- Helper T-cell
Innate Immunity

- Saliva
- Neutrophil

Adaptive Immunity

- Helper T-cell
Innate Immunity

- Saliva
- Neutrophil
- Macrophage

Adaptive Immunity

- Helper T-cell
Innate Immunity
- Saliva
- Neutrophil
- Macrophage

Adaptive Immunity
- Helper T-cell

IgG antibody
Innate Immunity
- Saliva
- Neutrophil
- Macrophage

Adaptive Immunity
- Helper T-cell
- IgG antibody
Innate Immunity
- Saliva
- Neutrophil
- Macrophage

Adaptive Immunity
- Helper T-cell
- IgG antibody

Complement
Innate Immunity

- Saliva
- Neutrophil
- Macrophage
- Complement

Adaptive Immunity

- Helper T-cell
- IgG antibody
Which vaccine is made of only sugars?

- Polysaccharide vaccine
- Conjugate vaccine
Which vaccine is made of only sugars?

Polysaccharide vaccine
Which can be given to children < 2 years of age?

- Polysaccharide vaccine
- Conjugate vaccine
Which can be given to children < 2 years of age?

Conjugate vaccine
Which vaccine *does not* induce long-term immunity?

- Polysaccharide vaccine
- Conjugate vaccine
Which vaccine does not induce long-term immunity?

Polysaccharide vaccine
COVID Vaccines

- mRNA
  - Pfizer-BioNTech
  - Moderna

- Adenovirus vector vaccines
  - Chimpanzee adenovirus vector
    - AstraZeneca-Oxford
  - Human adenovirus
    - Johnson and Johnson
    - Sputnik (Russian vaccine)
mRNA Vaccines

Delivery and translation
In some formulations, a lipid nanoparticle protects mRNA and ferries it into cells, where it directs ribosomes to make protein.

*Secreted*
- Growth factors, cytokines

*Intracellular*
- Metabolic enzymes

*Membrane*
- Receptors, channel proteins