# Immunizations

2021

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## Outline of Presentation

1. Basic Principles
2. Safety
3. Individual Vaccines
4. GPRA / CRS
5. Resources

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## Why is it Important?

- The 2 Things responsible for adding to Life Expectancy in the XX Century:
  - Sanitation
  - Immunizations

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## Edward Jenner

## The Father of Immunization

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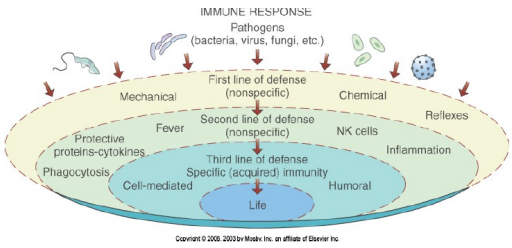
## *Protection from infection*

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## Three lines of protection

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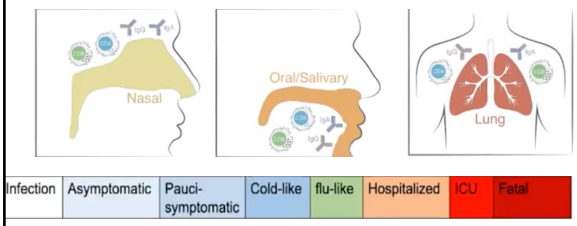
## COVID-19: the race of the immune mechanism against viral infection

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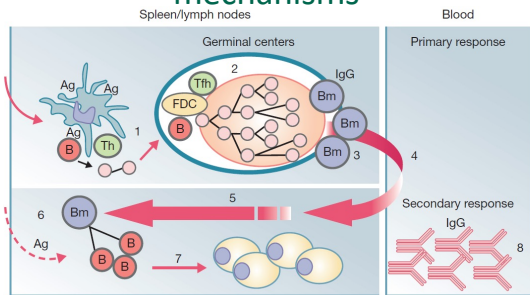
## vaccinations use natural immunity mechanisms

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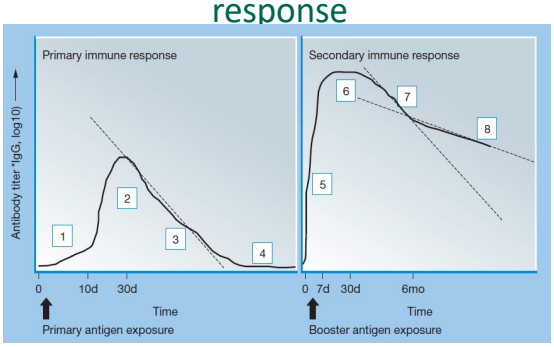
## Primary and secondary immune response

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**Immunity: 2500 years ago**

- Greek physicians: variola one in life
- Variola confers immunity

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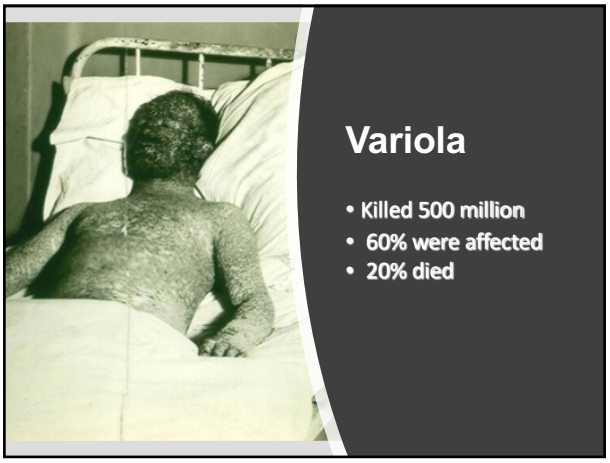

**Variola**

- Killed 500 million
- 60% were affected
- 20% died

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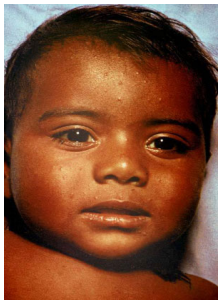
**Day 1.**



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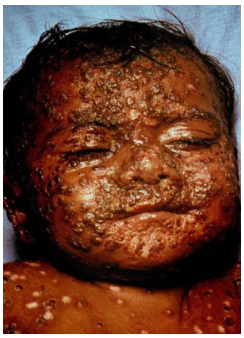
## Day 13.



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## Treatment?

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## Variolization

Deliberate, conscious infection with pox
To gain natural immunity
To avoid the disease in the future

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## 1721: Variolization in England

- **Lady Mary Montagu wearing a turkish outfit**

Canvas Pałac na wodzie, Łazienki, Jean-Etienne Liotard 1756

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milkmaids were generally immune to Smallpox

Edward Jenner - 1770s speculated that Cowpox could give immunity against Smallpox

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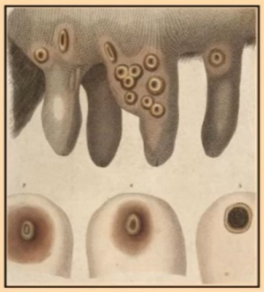
## Cowpox prevents smallpox



"I cannot take smallpox, for I have had cowpox."

*Anonymous milkmaid to Edward Jenner Chipping Sodbury, ca. 1768*

The start of a 30-year experiment ...

Milkmaids' disease and legend

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## James Phipps

*14th May 1796*
Inoculated with cowpox pus
– small sore, mild fever

*1st July*
Variolated
– no reaction

i.e. immune to smallpox

**Eureka!**

... But the Royal Society rejected Jenner's paper

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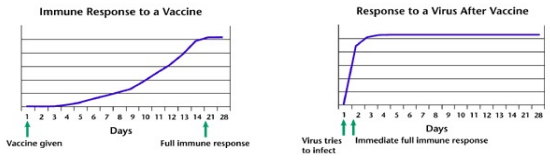
## What do we gain from vaccination?




**- przebieg odpowiedzi immunologicznej**

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## Basic Principles of Vaccination

- Immunity – the ability of the body to tolerate "self" and eliminate foreign material ("non-self")
- Immunity to a microbe is usually indicated by the presence of antibody
- Very specific to a single organism
- Two basic mechanisms for acquiring immunity – active and passive

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## Active vs. Passive Immunity

- Active Immunity
  - Protection produced by the person's own immune system
  - Usually permanent
- Passive Immunity
  - Protection transferred from another person or animal as antibody

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## The Immune Response

- Antigen – foreign substance ("non-self")
  - A live or inactivated substance (protein, polysaccharide) capable of producing an immune response
- Immune Response – production of antibodies (humoral immunity) or specific cells (cell-mediated immunity)
- Antibody
  - Protein molecules (immunoglobulin) produced by B lymphocytes to help eliminate antigens

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## Adaptive Immunity

Immunity which is acquired or developed by an individual only after a specific challenge is encountered.

The resulting adaptive immune products are effective only against the specific challenge.

Immunologic memory in adaptive immunity provides greater efficiency should there be subsequent exposure to the same challenge.

There is a time lag for development of adaptive immunity but secondary response is almost immediate.

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## Characteristics of Adaptive Immunity

In recent years, with increased knowledge of the molecular processes underlying the function of cells, it has become possible to explain at a cellular and molecular level the features that are the hallmark of acquired immune responses.

- Specificity and diversity.
- Memory.
- Regulation.
- Self / non-self discrimination.

The acquire immune processes that lead to the elimination of foreign material involve the concerted efforts of a number of different cells and molecules and can be divided into three stages.

- Recognition stage.
- Activation stage.

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## Classification of Adaptive Immunity

The two major arms of effective specific immunity are humoral immunity and cell mediated immunity. While historically these are quite distinct, current knowledge suggests that each time adaptive immunity is activated, both arms are activated. It becomes a matter of the degree to which each arm is activated.

Adaptive immunity may be classified based on the host's role in developing the adaptive specific immunity.

- Active immunity is generated when an immunocompetent host is exposed to the foreign challenge and the host's native immune cells respond by generating specific immune products.
- Passive immunity is bestowed to the host when preformed immune products are administered to the host.
- In adoptive immunity, immunocompetent cells are transplanted to an immunoincompetent host to restore the immune system.

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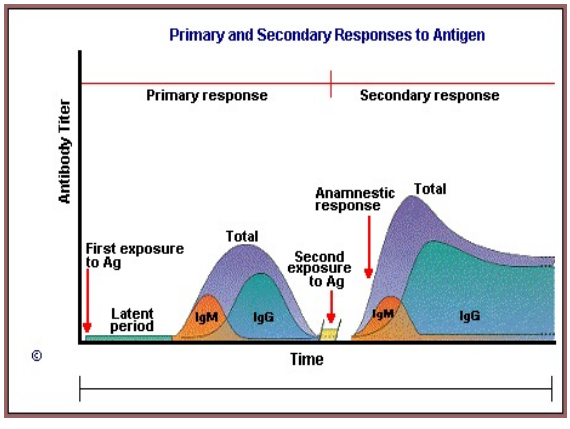


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## Principles of Vaccination

The primary goal in vaccination is to provide protective immunity by inducing a memory response to an infectious microorganism using a non-toxic antigen preparation. It is important to produce immunity of the appropriate kind: antibody / or cellular immunity.

Antibodies produced as a result of immunization are effective primarily against extracellular organisms and their products e.g., toxins. Passively administered antibodies have the same effect as induced antibodies.

Cell-mediated immunity (T cells, macrophages) induced by vaccination is important particulary in preventing intracellular bacterial and viral infections and fungal infections.

The ultimate goal of any immunization program is the eradication of the disease.

This requires that the infection is limited only to humans, with no animal or environmental reservoir, and the absence of any subclinical or carrier state in humans.

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## Principles of Vaccination

Achieving elimination requires a high level of herd immunity to prevent person to person spread.

This requires considerable infrastructure support to ensure that all at-risk populations are targeted for immunization.

This has been achieved for small pox, although we are close to the elimination of polio.

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## Passive Immunity

- Transfer of antibody produced by one human or other animal to another
- Temporary protection
- Transplacental most important source in infancy

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## Active Immunity - Vaccination

- Active immunity produced by vaccine
- Immunologic memory – mediated by memory B-cells
- Immunity and immunologic memory similar to natural infection but without risk of disease

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## Classification of Vaccines

- Live attenuated
  - viral
  - bacterial
- Inactivated

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## Live Attenuated Vaccines

- Attenuated (weakened) form of the "wild" virus or bacterium
- Must replicate to be effective
- Immune response similar to natural infection
- Usually effective with one dose

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## Live Attenuated Vaccines

- Severe reactions possible
- Interference from circulating antibody
- Fragile – must be stored and handled carefully

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## Live Attenuated Vaccines

- Viral — measles, mumps, rubella, varicella/zoster, yellow fever, rotavirus, intranasal influenza, vaccinia, oral polio*
- Bacterial — BCG, oral typhoid

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## Inactivated Vaccines

- Whole
  - virus or bacterial
- Fractional
  - Protein based
    - Subunit
    - toxoid
  - Polysaccharide based
    - Pure
    - Conjugate

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## Inactivated Vaccines

- Cannot replicate
- Less interference from circulating antibody than live vaccines
- Generally require 3-5 doses
- Immune response mostly humoral
- Antibody titer may diminish with time

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## Inactivated Vaccine – Whole Cell

- Viral: polio, hepatitis A, rabies, (influenza)
- Bacterial: (pertussis), (typhoid), (cholera), (plague)

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## Inactivated Vaccine – Fractional (protein based)

- Subunit: hepatitis B, influenza, HPV, acellular pertussis, anthrax, (Lyme)
- Toxoid: diphtheria, tetanus

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## Pure Polysaccharide Vaccines

- Not consistently immunogenic in children younger than 2 years of age
- No booster response
- Antibody with less functional activity
- Immunogenicity improved by conjugation

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## Inactivated Vaccine - Polysaccharide

- Pure polysaccharide
  - pneumococcal
  - Meningococcal
  - *Salmonella typhi* (Vi)
- Conjugate polysaccharide
  - Pneumococcal
  - Meningococcal
  - *Hemophilus influenzae* type b

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## Vaccine Administration

- There is no contraindication to the simultaneous administration of any vaccines
- Live parenteral vaccines not administered simultaneously should be separated by at least 4 weeks
- Increasing the interval between doses of a multidose vaccine does not diminish the effectiveness of the vaccine
- Decreasing the interval may cause problems with antibody response and protection

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## Vaccine Adverse Reactions

- Adverse reaction
  - extraneous effect *caused by vaccine*
  - side effect
- Adverse event
  - *any* event following vaccination
  - may be true adverse reaction
  - may be only coincidental

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## Vaccine Safety

- Contraindications
  - Severe allergic reaction to vaccine/component
  - Encephalopathy within 7 days of pertussis
- Pregnancy
- Immunosuppression
- Severe illness
- Recent blood product
- ASK SCREENING QUESTIONS

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## Invalid Contraindications to Vaccination

- Mild illness
- Antimicrobial therapy
- Disease exposure or convalescence
- Pregnant or immunosuppressed person in the household
- Breastfeeding
- Preterm birth
- Allergy to products not present in vaccine or allergy that is not anaphylactic
- Family history of adverse events
- Tuberculin skin testing
- Multiple vaccines

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## DTaP

- Diphtheria
- Tetanus
- Pertussis (acellular)
- Schedule: 2, 4, 6, 15-18 months
- DTaP vs Tdap

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## Polio

- IPV (inactivated polio vaccine)
- OPV (oral) no longer used
- Schedule: 2, 4, 6-18 months
- 4th dose at 4 – 6 years
- *Pediarix* contains DTaP, IPV, and pediatric hepatitis B

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## MMR

- Measles
- Mumps
- Rubella
- Schedule: 1 dose at 12-15 months
- 2 dose at 4 – 6 years
- MMRV (*ProQuad*)

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# Hib

- Haemophilus influenzae type b (invasive H. flu)
- 2 different vaccines licensed in the US: PRP-T and PRP-OMP
- Schedule: 2, 4, (6), 12-18 months
- *TriHIBit* and *Comvax* are combination products (complicated schedule)

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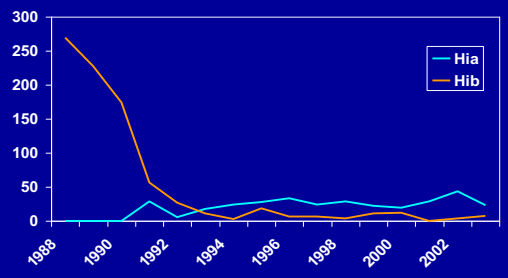
## Hib and Hia Among Navajo and White Mountain Apache, 1988-2003




Millar EV, et al. Clin Infect Dis 2005; 40:823-30

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# HepB

- Hepatitis B virus
- Schedule: birth, 2, 6-18 months
- First vaccine made with recombinant genetic technology

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## But Wait! There's More!

- There are some other vaccines for this age group:
- Rotavirus
- Pneumococcal
- Varicella
- Hepatitis A
- Influenza

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## Varicella

- Live attenuated vaccine to prevent chicken pox
- Schedule: 12 – 15 months
- 2 dose at 4 – 6 years
- New zoster vaccine for adults 60 or >

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## Hepatitis A

- 2 products exist (*HAVRIX* and *VAQTA*)
- Routine vaccination at 12 – 23 months; booster dose given at 6 – 18 months after first dose
- Pediatric and adult dosing is different

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## Rotavirus

- Rotavirus kills a half-million children per year worldwide
- *Rota-Shield* withdrawn from market due to association with intussusception
- *Rota Teq* – pentavalent, oral, 3 doses
- *Rotarix* – monovalent, oral, 2 doses

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## Meningococcal Vaccine

- MPSV – *Menomune* – usually used for patients >55
- MCV – *Menactra* – usually given at age 11 to 12
- Quadrivalent – A, C, Y, W-135

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## Human Papillomavirus

- HPV serotypes 6, 11, 16, 18
- Quadrivalent HPV vaccine (*Guardasil*)
- Series of 3 – recommended for 11 – 12 yr old females

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## Pneumococcal Vaccine

- PCV – pnemococcal conjugate vaccine
- Dose: 2, 4, 6, 12 – 15 months
- Septavalent
- PPV23 – *Pneumovax* – polysaccharide vaccine

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## Influenza

- QIV – quadrivalent influenza vaccine – given annually
- LAIV – intranasal, for use in persons 2 to 49 years of age
- Influenza causes about 36,000 excess deaths per year
- Recommended for everyone 6 to 59 months and >50

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## Resources

- CDC: www.cdc.gov
- The Pink Book – *Epidemiology and Prevention of Vaccine-Preventable Diseases*
- Nashville Area Immunization Team – Nicole Blackfox, John Mosely-Hayes, Michelle Ruslavage, Harry Brown
  615-467-1557

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