The Big, Wonderful Immune System

Basics of Immunology & Vaccinology

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Today we'll learn…

- General anatomy and function of the human immune system
- Types of immunity
- Types of vaccines and how they differ

Icebreaker

Where does the word “vaccine” come from?

The word “vaccine” comes from vaccinia, which derives from the Latin word “vacca,” meaning cow.

Definitions

Definitions

- **Vaccine-preventable**
  - **Bacteria:** small single-celled organisms
    - Humans have more bacteria in and on themselves than human cells!
    - Living
  - **Virus:** infectious microbe consisting of a segment of nucleic acid surrounded by a protein coat
    - Cannot replicate on its own - must infect cells and use components of the host cell to make copies of itself
    - Not “alive”
- **No vaccines currently available**
  - **Prion:** abnormal, pathogenic agents that are transmissible and are able to induce abnormal folding of specific normal cellular proteins called prion proteins that are found most abundantly in the brain
    - Mad Cow Disease, Creutzfeldt-Jakob, Scrapie, Kuru, chronic wasting diease
  - **Fungi:** single-celled or very complex multicellular organisms
    - Found in just about any habitat
    - Some are pathogenic
    - Includes mushrooms, yeast, mold, mildew

Definitions

- **Immunity:** protection from an infectious disease. If you are immune to a disease, you can be exposed to it without becoming infected or ill.
- **Vaccine:** a preparation that is used to stimulate the body's immune response against a specific disease
- **Vaccination:** the act of introducing a vaccine into the body to produce protection from a specific disease
- **Immunization:** a process by which a person becomes protected against a disease through vaccination. This term is often used interchangeably with vaccination or inoculation
- **Immunology:** study of the immune system

The Immune System

What is the immune system?

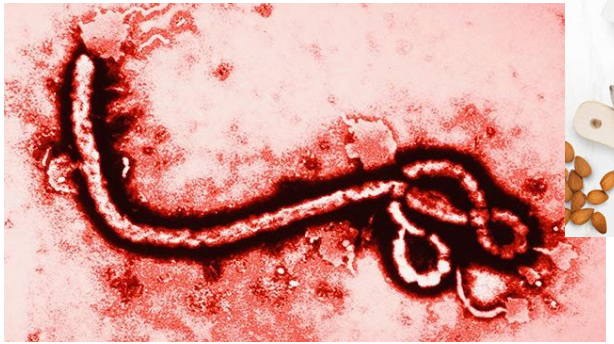
The immune system is awesome!!!

What is the immune system?

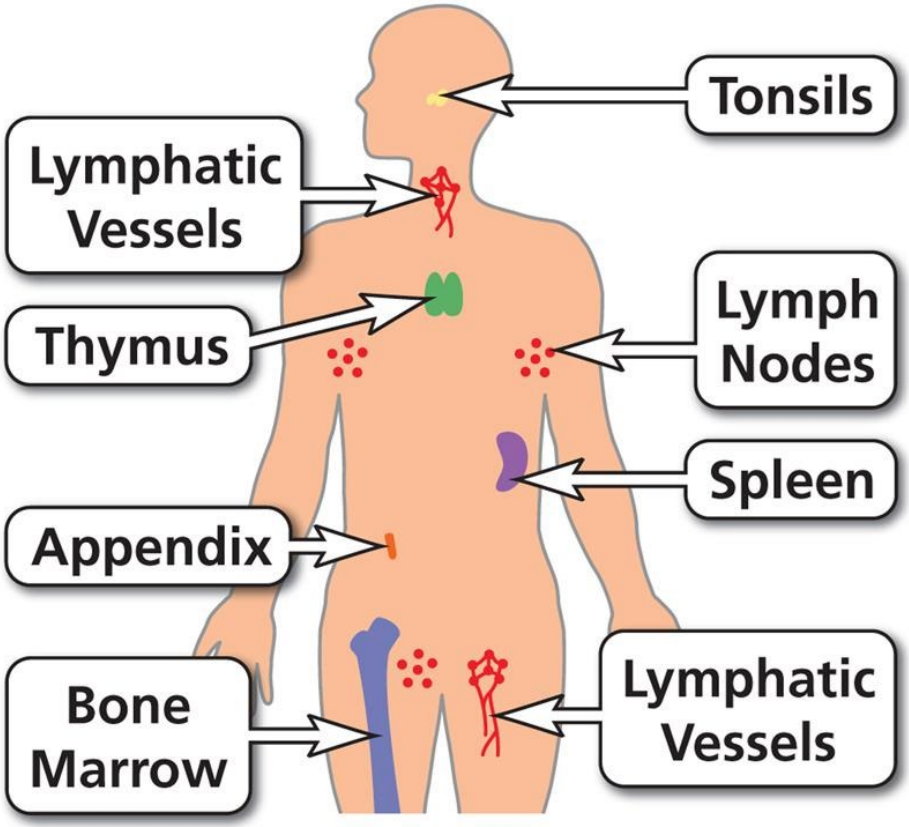
- A complex system of interacting cells that identifies foreign substances and develops a defense against those substances
- Two key principles:
  - Specificity
  - Memory

Antigen

- Substance capable of producing an immune response
- Recognized as “non-self,” or foreign
- Two types:
  - Exogenous
  - Endogenous



Immune System

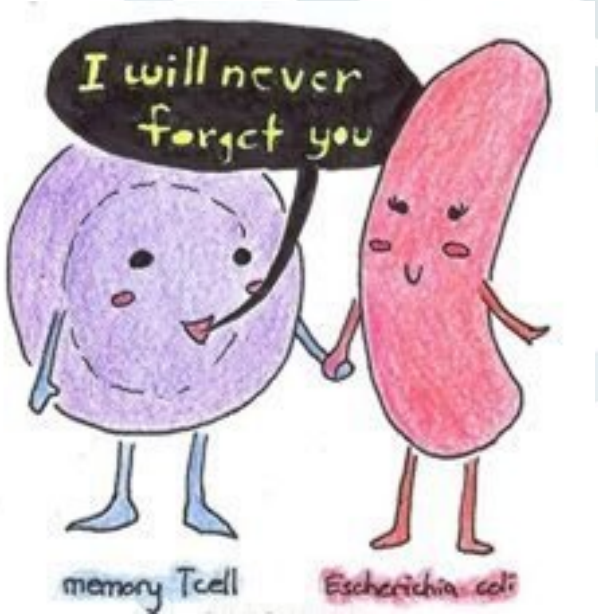


Innate immunity

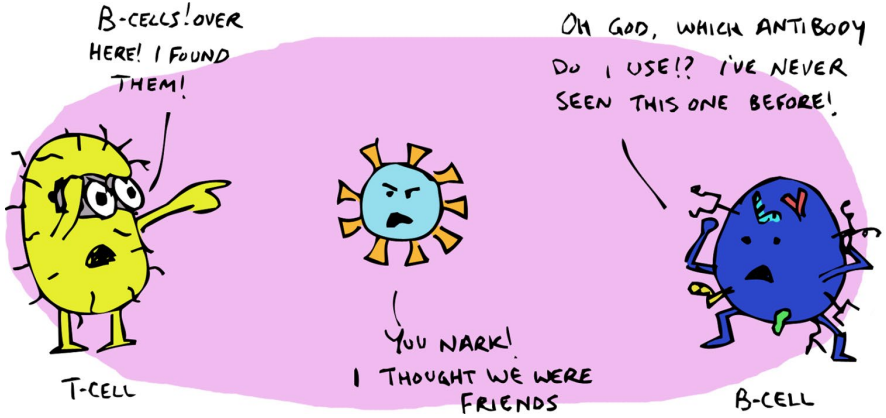
- Anatomical barriers
  - Physical or chemical
  - Skin, mucous membranes, saliva, and tears
- Cellular responses
  - Phagocytic cells, dendritic cells, and natural killer cells
- Soluble proteins
  - Complement components, cytokines, lysozyme, and interferons
- Inflammatory responses
  - Fever
- Cough reflex

Adaptive immunity

- Types:
  - Humoral vs. cell-mediated
  - Active vs. passive
- High degree of specificity with memory
- Self/non-self recognition
- Not independent from innate immunity
  - Poorly effective without innate immunity



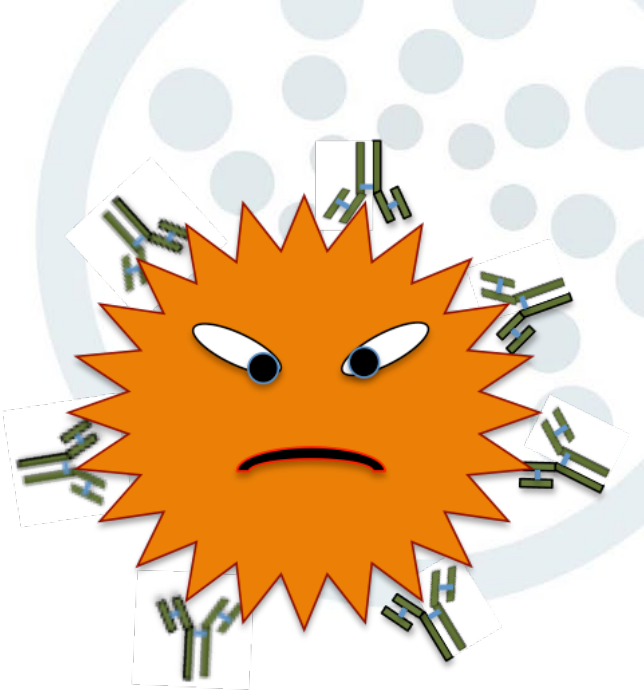
Humoral immunity



- Important against bacteria, parasites, toxins, and extracellular virus particles
- B lymphocytes
  - Mature in the bone marrow
  - Memory B cells
    - Long lifespan
    - Membrane-bound antibodies
  - Effectors B cells (plasma cells)
    - Antibodies in secretory form
    - Live only a few days
- Antibodies
  - Also called immunoglobulins
  - A Y-shaped protein with antigen binding sites
  - 5 types

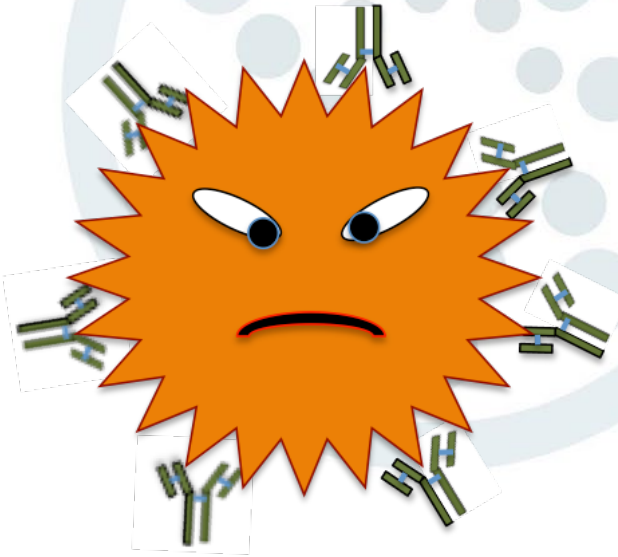
Antibodies

- IgA
  - Found on mucous membranes, and in saliva, tears, and breastmilk
  - Important first line of defense against certain pathogens
- IgD
  - Antigen receptor on mature B cells
  - Activates basophils and mast cells to produce antimicrobial factors
- IgE
  - Hypersensitivity reactions
    - Triggers histamine release
  - Important in parasitic worm infections

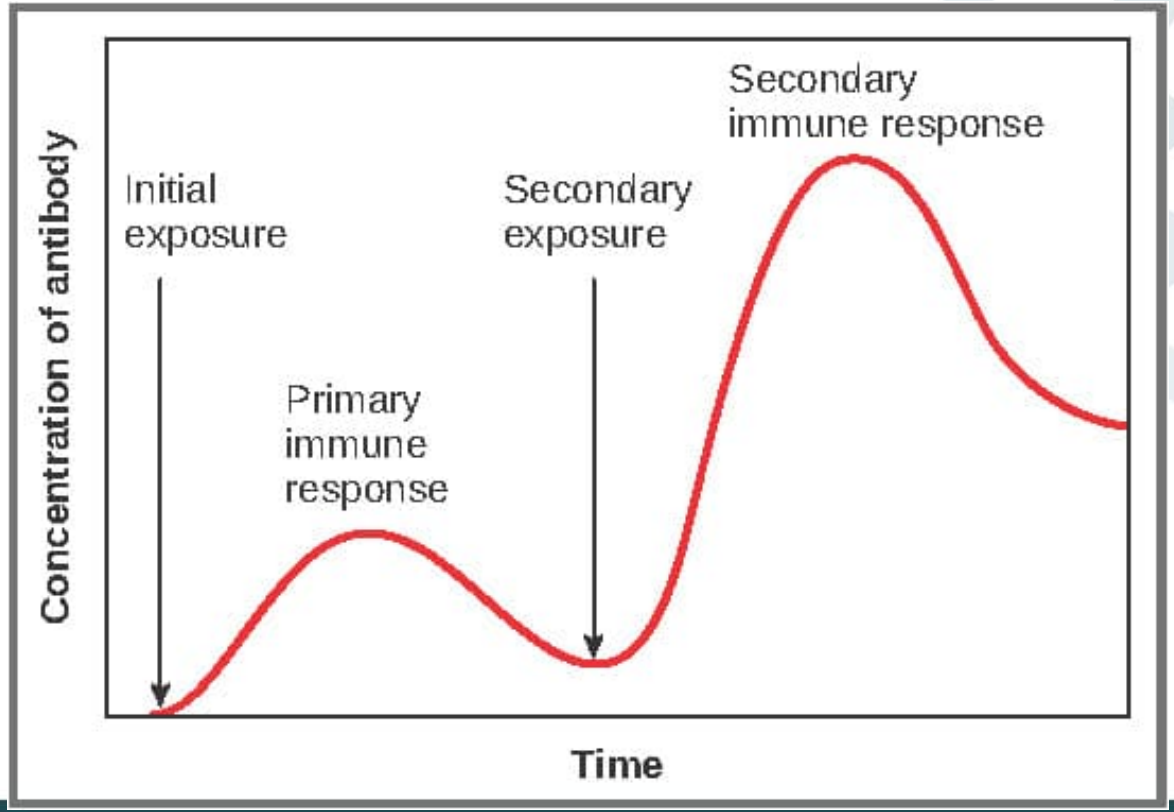


Antibodies

- IgG
  - Most abundant type
  - Majority of antibody-based immunity
  - Crosses the placenta during pregnancy
- IgM
  - First type of antibody produced in a primary immune response

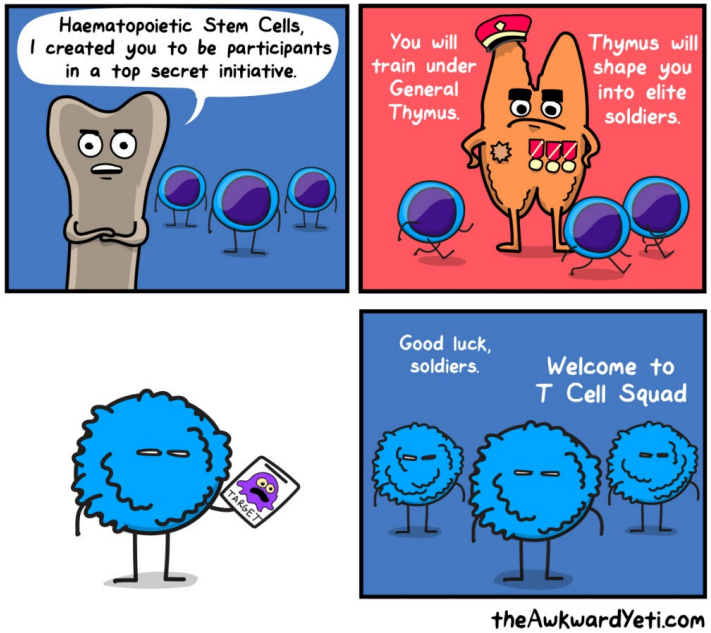


Primary vs. secondary immune response



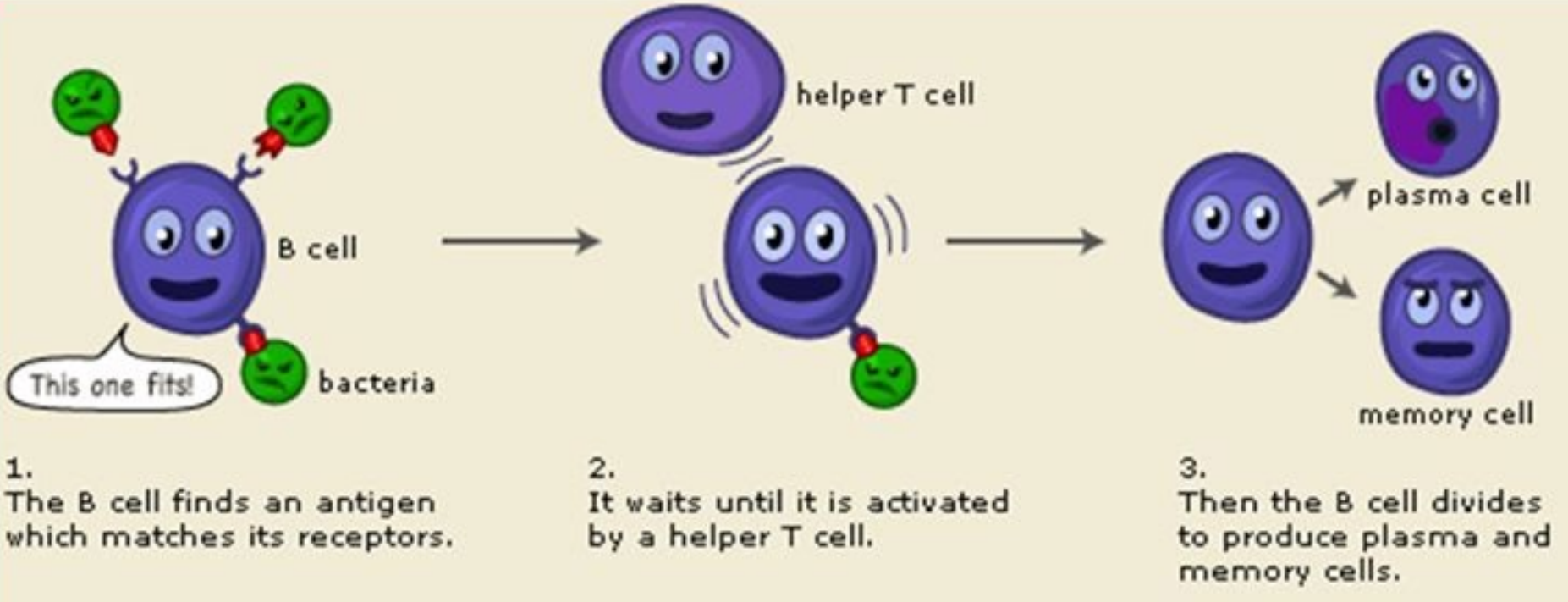
Cell-mediated immunity

- Important against virus infected cells, cancer cells, and transplanted cells
- T-lymphocytes
  - Arise in the bone marrow but mature in the thymus
  - T-helper CD4 cells
    - Recognizes and interacts with antigen-molecule complexes
      - B cells and antigen, for example
    - Becomes activates and secretes cytokines
  - T-cytotoxic CD8 cells
    - Exhibits cell killing activity once activated

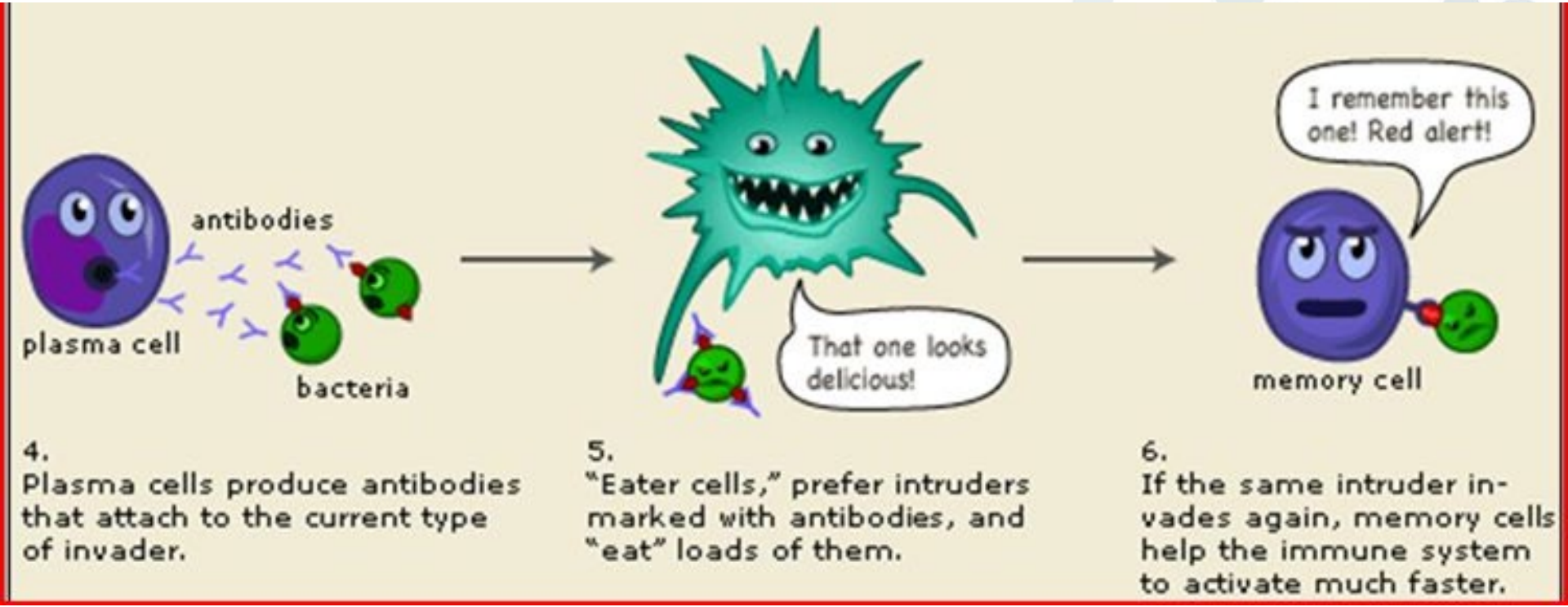


Now let's put it all together…

Humoral response: Part 1



Humoral response: Part 2

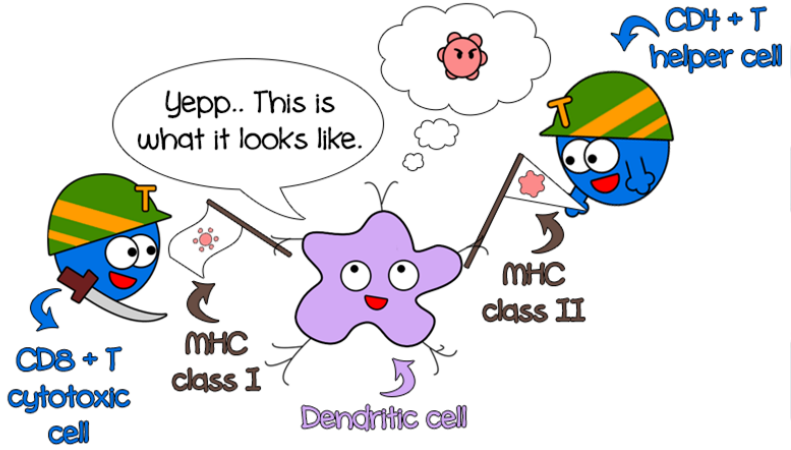


4.
Plasma cells produce antibodies that attach to the current type of invader.

5.
"Eater cells," prefer intruders marked with antibodies, and "eat" loads of them.

6.
If the same intruder invades again, memory cells help the immune system to activate much faster.

Cell-mediated response



- Antigen presenting cells
  - B cells
  - Macrophages
  - Dendritic cells
  - Langerhans cells
- Major Histocompatibility Complexes (MHC)
  - Class I - found on the surface of all nucleated cells
    - CD8 T-cytotoxic cells
      - Kills virus infected cells, cancer cells, and intracellular bacteria
  - Class II - found on the surface of antigen presenting cells
    - CD4 T-helper cells
      - Extracellular antigens

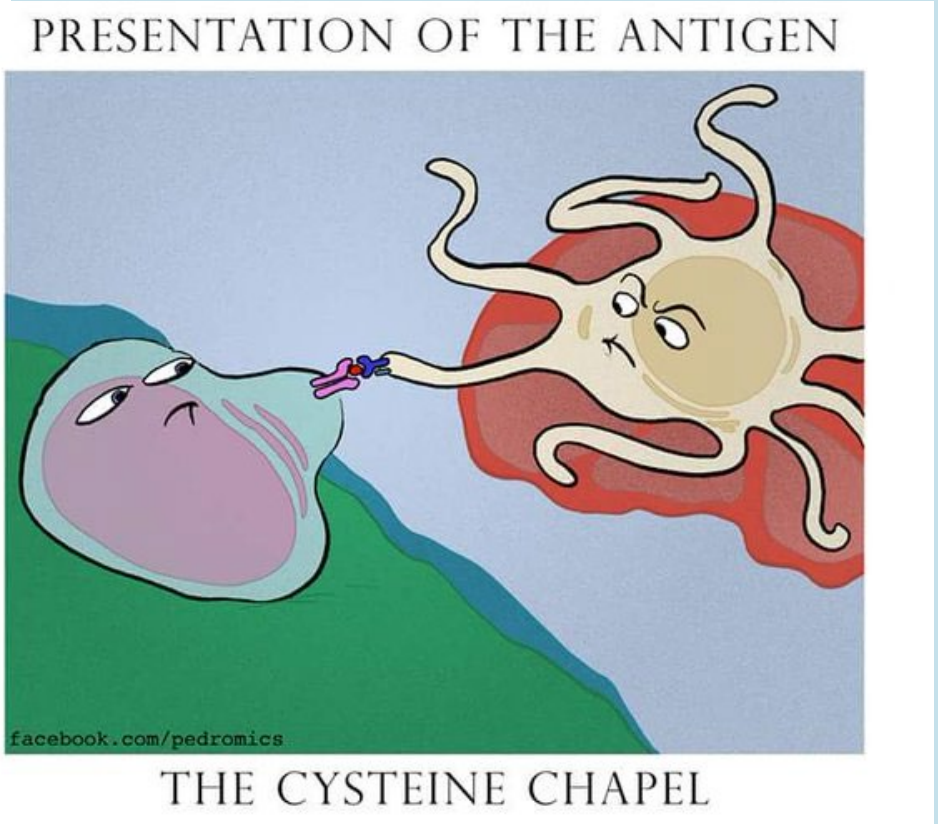
Passive vs. active immunity

- Passive immunity
  - Protection derived from products by an animal or human and that are transferred to another human
  - Protection wanes, often within a few weeks or months
  - Most common forms are
    - Maternal antibodies
    - Pooled antibodies
    - Antitoxins
    - Monoclonal antibodies

Passive vs. active immunity

- Active immunity
  - Protection produced by a human's own immune system
  - Lasts for many years, sometimes a lifetime
- Two types
  - Survive infection from the disease causing organism
  - Vaccination

Questions?


PRESENTATION OF THE ANTIGEN
facebook.com/pedromics
THE CYSTEINE CHAPEL

Vaccines

History of vaccines - a tale of smallpox

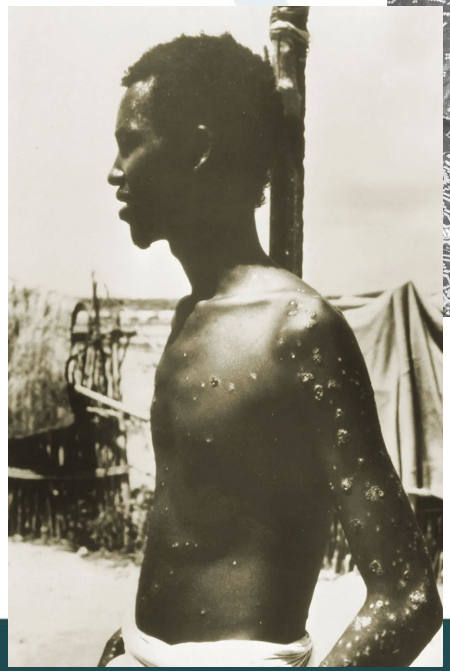
- Variolation
  - Started somewhere in Asia as early as 200 BCE
    - China: scabs from smallpox pustules would be dried in the sun and then inhaled by people
    - India: smallpox pustule was lanced and same lance was used to transfer some of the pus into the arm of a healthy person
- Edward Jenner
  - Observed that milkmaids who had acquired cowpox were immune to smallpox even when exposed multiple times
  - May 14, 1796 tested first vaccine on eight-year-old James Phipps
    - Inoculated with matter from a cowpox sore on the hand of Sarah Nelmes
    - In July, Jenner inoculated Phipps with matter taken from a fresh human smallpox sore. Phipps remained healthy.

History of vaccines - a tale of smallpox

- Massachusetts became the first U.S. state to encourage the use of smallpox vaccine in 1802
  - In 1855, MA became the first state mandating vaccination for school children
- Last cases of naturally occurring smallpox in the U.S. developed in Hidalgo County, Texas in 1949
- Routine U.S. smallpox vaccination ceased in 1972

History of vaccines - a tale of smallpox

- Last wild case of variola major identified on October 16, 1975 in Rahima Banu in Bangladesh. She recovered completely.
- Last naturally occurring smallpox (variola minor) case EVER identified October 26, 1977 in Ali Maow Maalin in Somalia. He became an advocate for polio vaccination and worked as a vaccinator.
- Smallpox declared eradicated on May 8, 1980



Vaccination

- Active immunity without the risk of actual disease
- Two types of vaccines
  - Inactivated
  - Live, attenuated
- General rule
  - The more similar a vaccine is to the disease-causing form of the pathogen, the better the immunity response is to the vaccine
- Factors influencing the immune response to vaccines
  - Maternal antibodies
  - Dose of antigen
  - Route of administration
  - Adjuvant
  - Host factors

Inactivated vaccines

- Cannot cause any form of disease
- Less affected by circulating antibody
- Always require multiple doses to induce an immune response
- Mostly a humoral response
- Antibody titers will diminish with time
  - This is called “waning”

Types of inactivated vaccines

- Whole cell: contain whole bacteria or virus that have been killed through a physical or chemical process
  - Polio, hepatitis A, rabies, and whole cell pertussis
- Subunit, recombinant, polysaccharide, and conjugate: use specific pieces of the germ, like its protein, sugar, or capsid
  - Create a strong immune response that is targeted to key parts of the germ
  - May need boosters for ongoing protection
  - Hib, hepatitis B, HPV, acellular pertussis, pneumococcal disease, meningococcal disease, COVID-19, and shingles

Types of inactivated vaccines

- Toxoid: use a toxin made by the germ that causes a disease that has been made harmless
  - Immune response is targeted to the toxin
  - May require booster shots for ongoing protection
  - Diphtheria and tetanus
- Messenger RNA (mRNA): mRNA created in a laboratory teaches cells how to make a protein that triggers an immune response. The mRNA is broken down within a few days after vaccination
  - COVID-19, RSV
- Viral vector: use a modified version of a different virus as a vector to deliver instructions to stimulate immune response
  - Ebola Zaire

Live, attenuated vaccines

- Virus or bacteria is weakened using laboratory techniques
- Must grow and replicate in vaccinated person
  - Fragile
- Humoral and cell-mediated response occurs
- Usually produce immunity with one dose
- Vulnerable to interference from circulating antibody
- Cannot be used in immunocompromised persons

Live, attenuated vaccines

- Measles, mumps, rubella (MMR)
- Varicella
- Rotavirus
- Intranasal influenza
- Yellow fever
- Vaccinia (smallpox - ACAM2000)
- Oral typhoid
- Oral polio

Questions?


WHITE BLOOD CELL VS. THE COMMON COLD
NOBODY IN OR OUT. GOT THAT? IT'S CHILLY OUT AND THIS KID DOESN'T HAVE A JACKET.
WOAH. COLD VIRUS HAS HOT CHOCOLATE!
EXIT
eh?
LET HIM IN.
THEAWKWARDYETI.COM

Vaccine components

- Antigens
  - Stimulates the immune response towards the specific antigen
- Stabilizers
  - Maintains effectiveness in storage
  - $MgCl_2$, $MgSO_4$, lactose-sorbitol
  - Gelatin
    - Gelatin contained in most vaccines is porcine in origin
      - Rabavert rabies vaccine is bovine gelatin
    - All major religious groups have approved the use of gelatin-containing vaccines for their followers
    - Vegans may refuse products with gelatin

Vaccine components

- Antibiotics
  - Help prevent bacterial contamination during the manufacturing process
  - Neomycin, streptomycin, polymyxin B, chlortetracycline, amphotericin B
    - Rarely cause human allergies

Vaccine components

- Adjuvants
  - Help stimulate the production of antibodies against the antigen
  - Makes vaccines more effective by enhancing, accelerating, and prolonging the immune response
    - Adjuvants allow for lesser quantities of the vaccine and fewer doses
  - Important in inactivated vaccines
  - Several hundred different types
    - Aluminum
    - Monophosphoryl A
    - QS21
    - Squalene

Aluminum

- Natural element that is present in our environment
  - Found in plants, soil, water, and air
- Used as an adjuvant in vaccines since the 1930s
- Quantity found in vaccines is small
  - Adults ingest 7-9mg/day
  - 1 liter of infant formula contains as much as 1 vaccine
- Processed the same in the body whether ingested or injected

Vaccine components

- Preservatives
  - Added to multi-dose vials to prevent bacterial or fungal growth
  - Thimerosal
    - Removed from all routine childhood vaccines in the late 1990s
  - Phenol, benzethonium chloride, 2-phenoxyethanol currently used in the U.S.

Vaccine components

- Formaldehyde
  - Used to inactivate viruses and detoxify bacterial toxins
  - A by-product of protein and DNA synthesis, so it is commonly found in the bloodstream
    - The quantity found in the blood is 1500 times greater than that found in any vaccine
    - Pears contains 38.7-60mg/kg

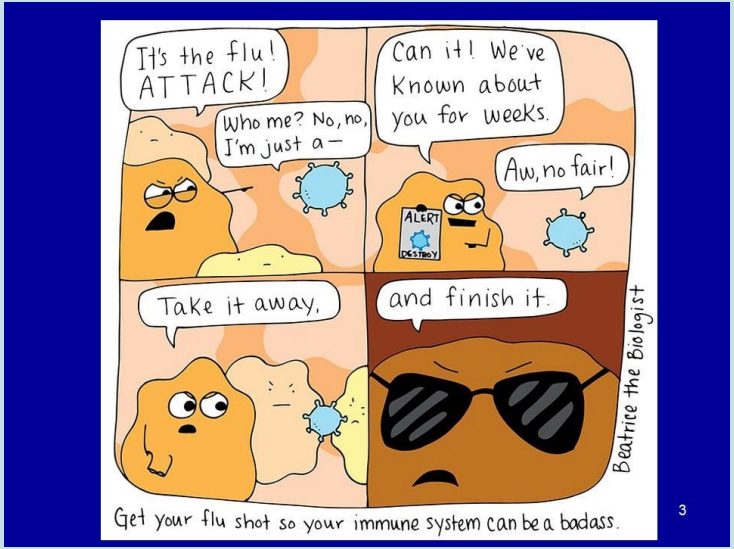
Fetal cells

- Fetal cell lines
  - Fetal cells are virtually immortal, and can reproduce many times
  - Human viruses require cells to grow and human cells are better than animal cells at supporting the growth of human viruses
  - Used to make rubella, varicella, hepatitis A, and rabies (one version, Imovax) vaccines
  - Cells were obtained from two elective abortions performed in the early 1960s
    - Fetal cell lines do not require ongoing abortions

What vaccines do not contain

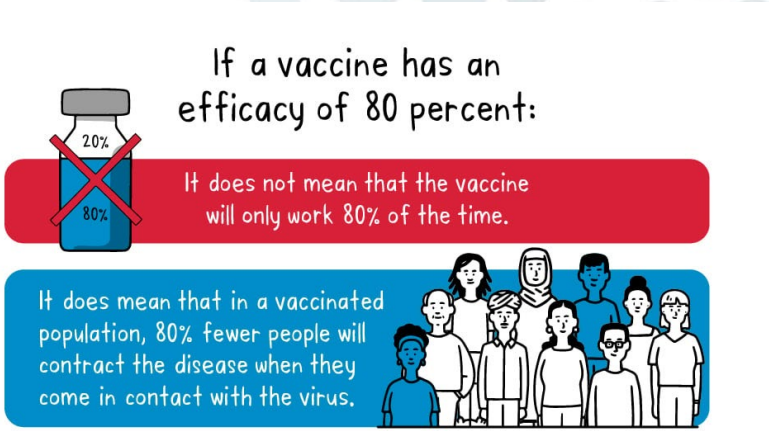
- Corn or peanut oils
- Parts of fetuses

Questions?

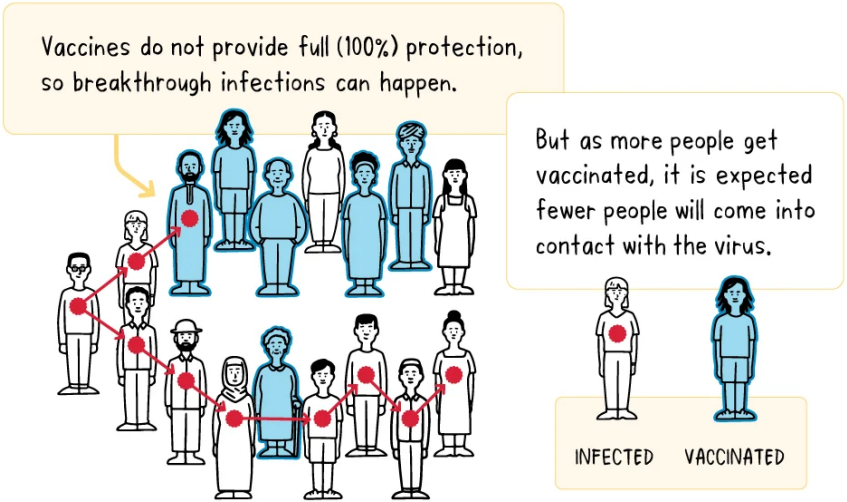

It's the flu! ATTACK!
Who me? No, no, I'm just a—
Can it! We've known about you for weeks.
Aw, no fair!
ALERT
DESTROY
Take it away,
and finish it.
Beatrice the Biologist
Get your flu shot so your immune system can be a badass.
3

Understanding vaccine efficacy & effectiveness

- Vaccine efficacy
  - A measure of how much the vaccine lowered the risk of getting sick
  - Measured in a controlled clinical trial and is based on how many vaccinated people developed the “outcome of interest” (usually disease) compared with how much people who received the placebo developed the same response



Understanding vaccine efficacy & effectiveness

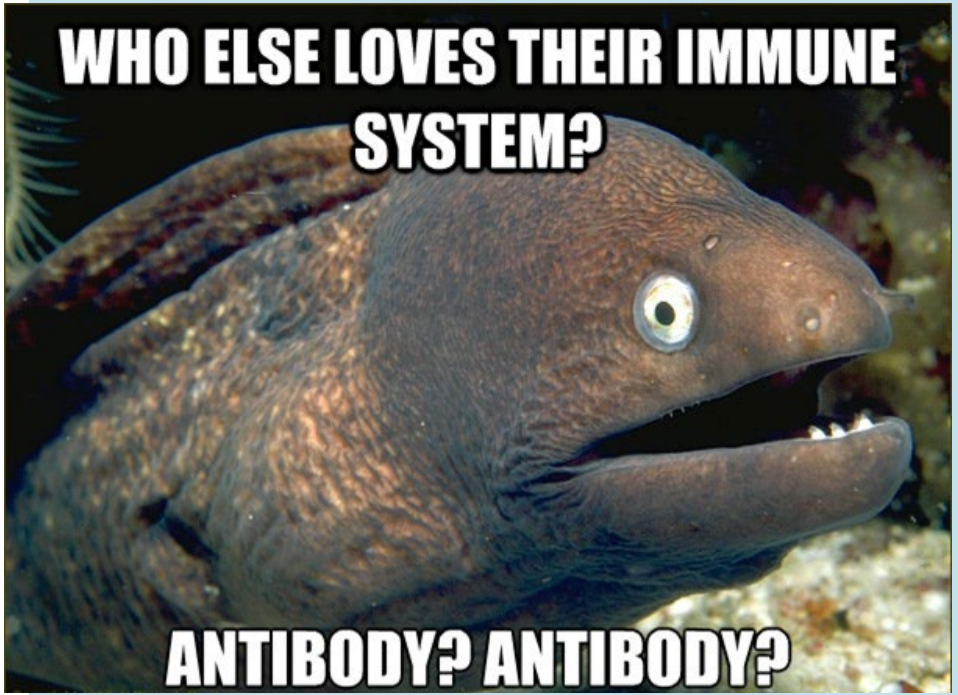


- Vaccine effectiveness
  - Measure of how well vaccines work in the real world
  - If vaccinated people do get sick, they are likely to have milder symptoms
  - It is very rare for someone vaccinated to experience severe illness or die from the disease the vaccine is for

Vaccine “failure”

- Circumstances fail, not necessarily the vaccine
- Primary
  - Failure to launch an adequate immune response
  - Can result from several factors
    - Interference of virus replication by circulating antibody
    - Compromised vaccine from storage and handling errors
    - Hepatitis B chronic infection
- Secondary
  - Gradual loss of immunity after an initial immune response over a period of time after vaccination
    - This is calling waning

Questions



Thank you!

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