Vaccines

"Get immunized before you fight with the invisible enemies"

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STORYLINE

Our parents love us a lot and cannot bear to see us in tears. Right? But have you ever wondered why, when we were kids, they took us to the doctor for vaccinations despite knowing that we might develop fever for 2-3 days afterwards. It was painful for them too ☹. But they were concerned about protecting us from harmful germs first. So, what are vaccines, and why are they required? This chapter explains the importance of vaccination and their scheduled dosage through which, we are protected from several life-threatening infectious diseases. We will also learn what are the key components used to make vaccines and how our immune system fights against these germs with the help of vaccination.

"Prevention is better than cure"

As rightly said, there are many infectious diseases for which no cure is available, and hence, prevention remains our best option. We recently witnessed the widespread of Covid-19, a disease caused by the novel Coronavirus, named SARS-Cov2 (initially referred to as 2019-CoV). One of the most effective ways to reduce the spread of this disease is through preventive measures such as distancing. This disease was first detected in Wuhan, China, in December, 2019 and was declared a pandemic by the World Health Organization (WHO) on March 11, 2020.

WHEN IS A DISEASE CALLED AS A PANDEMIC OR AN EPIDEMIC?

Endemic diseases are those that are consistently present in a particular population, region or country. An endemic disease becomes an **outbreak** when the number of cases exceeds the expected level. If the disease spreads further and affects a large population within one or few countries it is called an epidemic. However, But if the infectious disease is not controlled in time and spreads across multiple countries or continents, the disease becomes a **pandemic** **(Fig. 1)**.

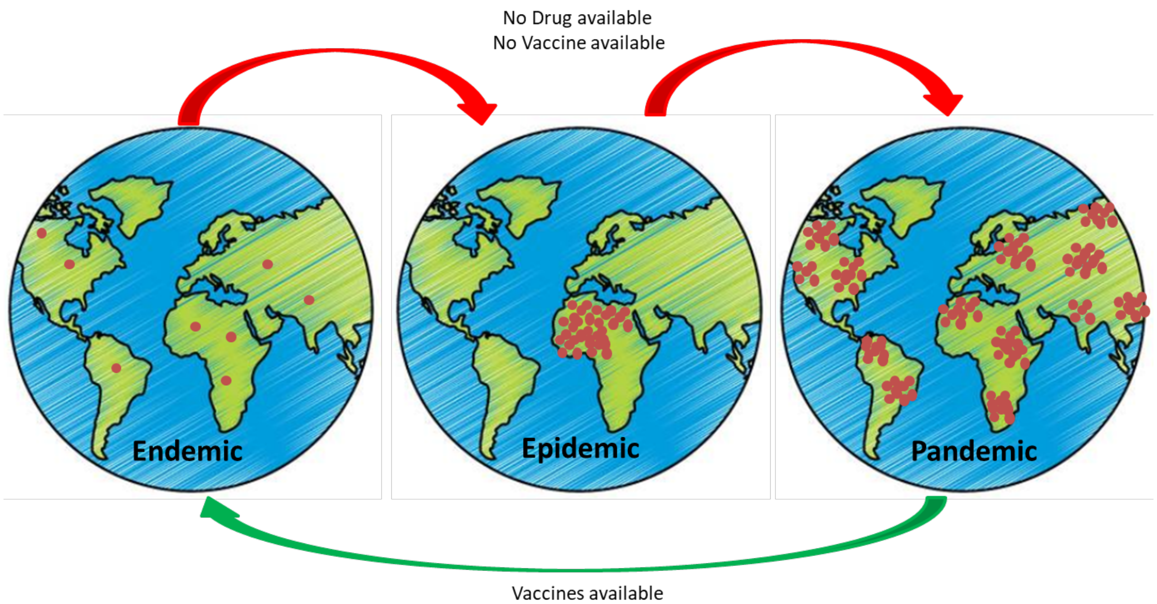


Fig. 1: An infectious disease may progress from endemic to epidemic and then to pandemic. However, the availability of vaccines can reverse this sequence, and can even lead to disease eradication.

WHICH DISEASES ARE EPIDEMIC OR PANDEMIC?

For centuries, many diseases have caused epidemics and pandemics, claiming thousands to millions of lives worldwide. Some examples are cholera, Ebola, avian influenza, leptospirosis, meningitis, MERS, pandemic influenza, plague, Rift Valley fever, seasonal influenza, yellow fever, dengue, Zika (Table 1).

Table 1: Some common pandemic/epidemic diseases (listed as per World Health Organization)

Disease	Causative agent	Cure	Vaccine
Chikungunya	Virus	No specific drug	No Vaccine
Cholera	Bacteria	Rehydration therapy and improved sanitation	Oral cholera vaccines
Dengue	Virus	No specific drug	Dengvaxia

Ebola virus disease	Virus	immune and drug therapies	rVSV-ZEBOV
Meningitis	Bacteria	penicillin, ampicillin, chloramphenicol and ceftriaxone	Polysaccharide, conjugate, and protein-based vaccines
MERS-CoV	Virus	No specific drug	No vaccine
Nipah virus infection	Virus	No specific drug	No vaccine
Novel coronavirus (2019-nCoV)	Virus	No specific drug	Several vaccines, including mRNA
Plague	Bacteria	treated with antibiotics	Vaccine not widely used
SARS	Virus	No specific drug	Several vaccines
Smallpox	Virus	ERADICATED	
Yellow fever	Virus	No specific drug	Vaccine available
Zika virus disease	Virus	No specific drug	No vaccine

Smallpox is the only human disease that has been declared 'eradicated' through vaccination. Poliomyelitis was once a widespread epidemic, but due to extensive vaccination programs, it is now endemic in a few regions of the world (Fig. 2).

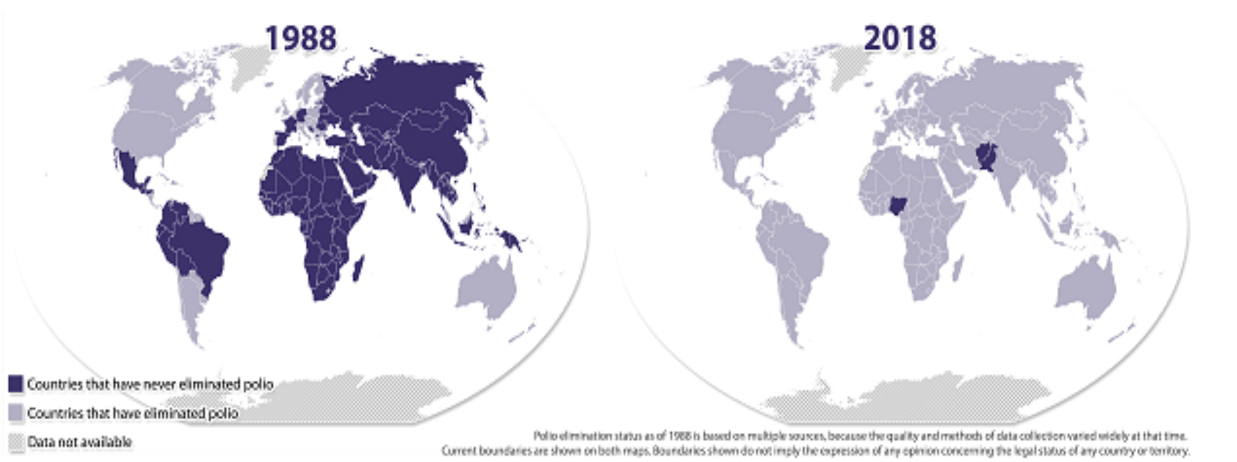


Fig. 2: Poliomyelitis: An epidemic disease which has now become endemic due to availability of vaccines. Blue regions indicate where polio remains endemic (Resource: https://www.cdc.gov/polio/progress/index.htm)

GERMS AND OUR BODY

Anything foreign to our body is recognized and eliminated by our immune system. Immunity is the body's ability to resist the entry or invasion of pathogens. When a germ (pathogen or antigen) enters our body, it is attacked by the body' defense cells. These warriors are the immune cells that constitute our immune system. Immune cells are present in our blood as white blood cells (WBCs), that defend our body against infections (Fig. 3). Specific type of WBCs (also called **leucocytes**) produce antibodies in response to antigens. These antibodies recognize and help kill the invading germs. After killing the germs, some of these WBCs retain memory of them, enabling the body to respond more quickly if the same germ enters again. However, if the germ succeeded in escaping the immune response, infection occurs (Fig. 4).

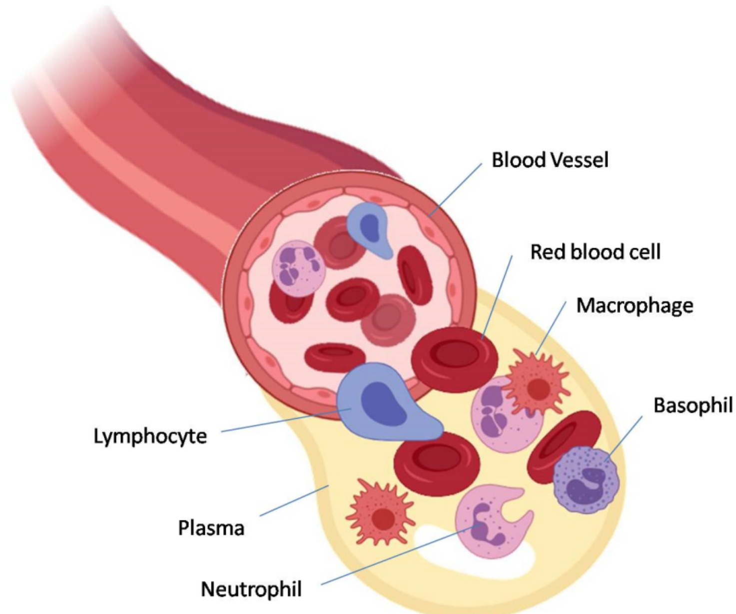


Fig. 3: Blood vessel containing red blood cells and white blood cells. White blood cells are the body's defenders and are important part of our immune system.

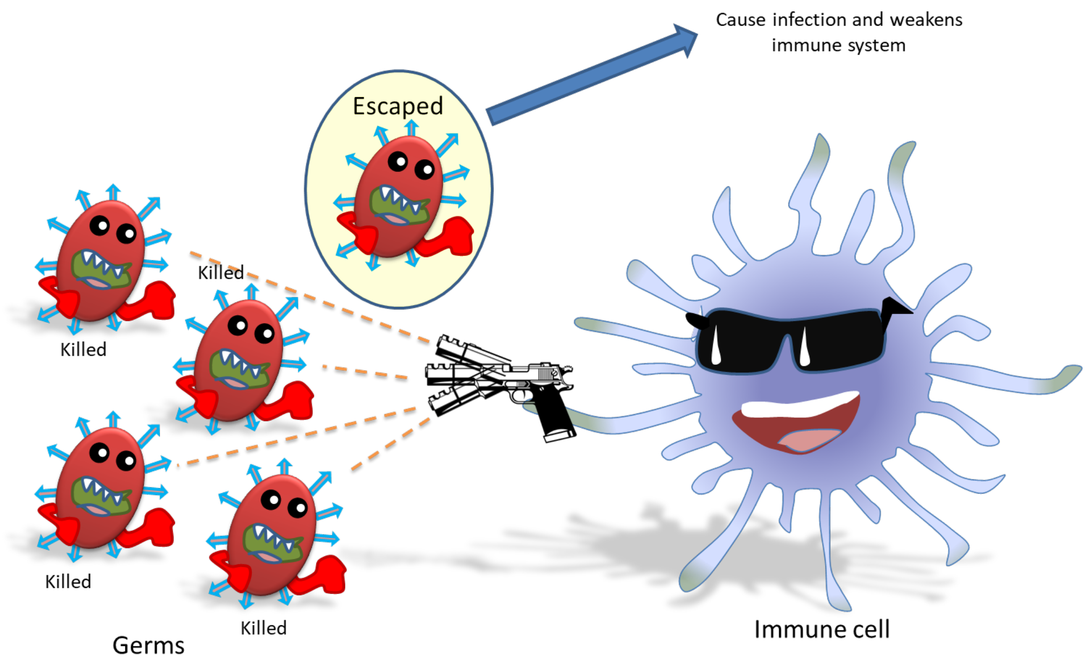


Fig. 4: Immune cells fighting invading germs. Even a few germs that escape destruction can and cause infection.

WHAT ARE ANTIBODIES AND HOW DO THEY WORK?

Among various immune cells, B-cells secrete antibodies that interact with antigens. Antibodies (also called immunoglobulins) are the Y-shaped proteins that neutralize pathogens such as viruses and bacteria. But do antibodies recognize the entire antigen? No, antibodies identify only specific regions on antigens called epitopes. The paratope (the antigen binding region of an antibody) specifically interacts with the epitope of an antigen. But antibodies are highly specific, each antibody recognizes only a particular epitope. Hence, an antigen with multiple epitopes will be identified by different antibodies. And if two different pathogens or antigens share the same epitope, they can both be recognized by the same antibody (Fig. 5).

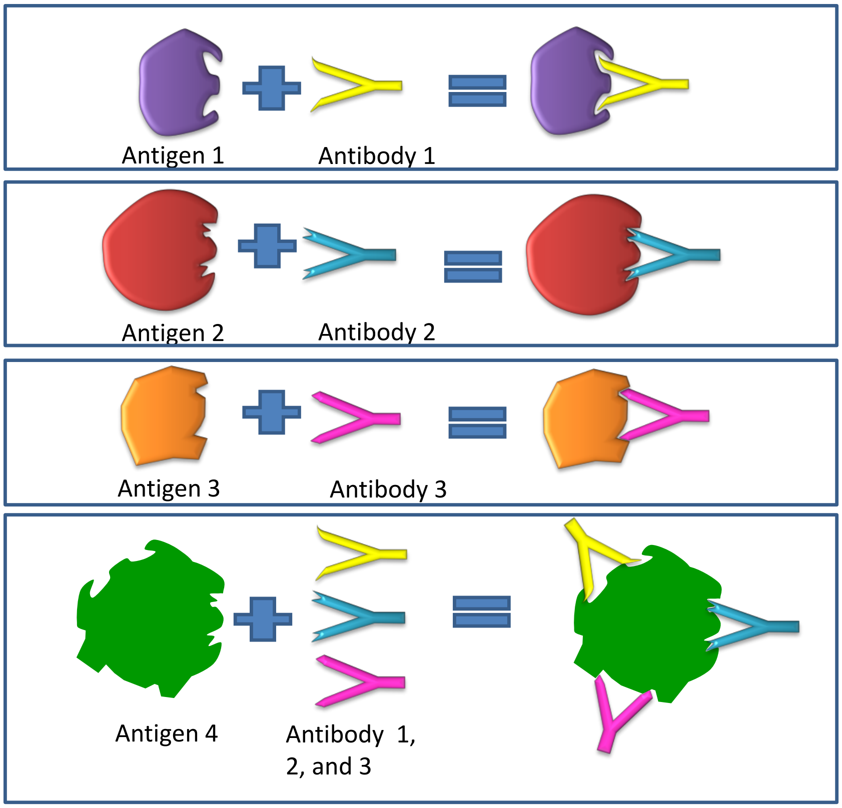


Fig. 5: Antigenic determinants (epitopes) are specifically recognized by antibodies. Antigen 1 is recognized by antibody 1 only. Likewise, antigen 2 and 3 are recognized by antibodies 2 and 3, respectively. But, antigen 4 contains all three epitopes and is therefore recognized by antibodies 1, 2 and 3.

HOW DO WE ATTAIN IMMUNITY?

Immunity can be attained **directly** or **indirectly**. Direct immunity requires exposure to a pathogen or its antigen. Immunity is conferred lifelong only if memory cells are formed. A person is considered immune if they have **previously exposed to a disease** and succeeded in eliminating the pathogen. Another way of immunization is through **vaccination** against the disease (discussed later). In both the cases, the body generates its own antibodies.

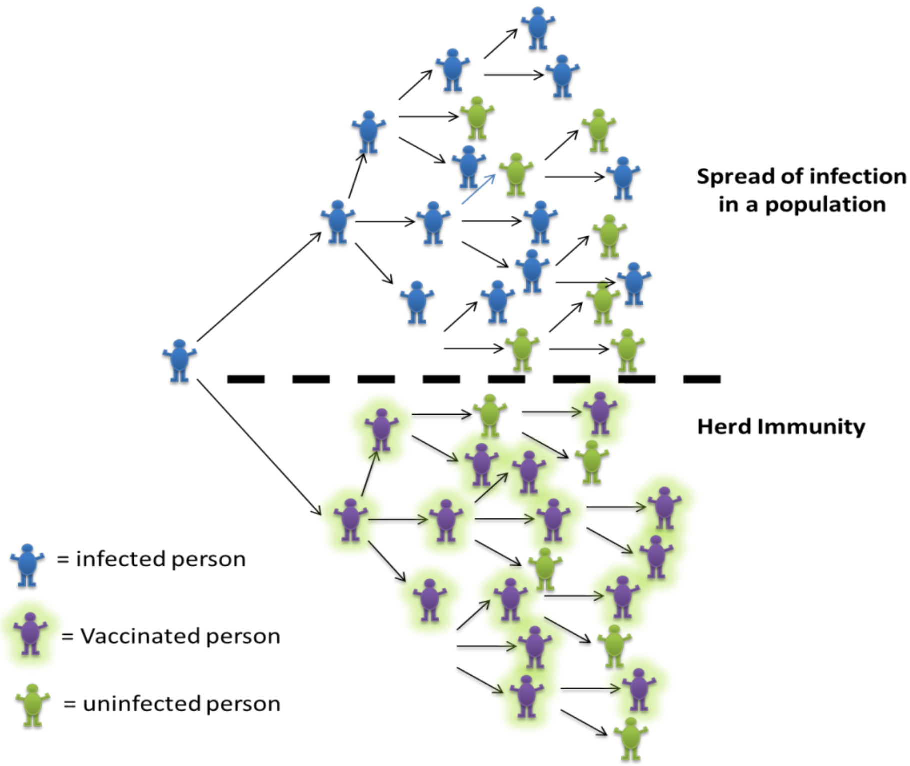


Fig. 6: Herd Immunity: When an infected person comes into contact with others in a community, the infectious disease can spread rapidly. But if the majority of people in the community are vaccinated, they act as safeguards to and protect those who are not immunized.

On the other hand, indirect immunity can be attained either through **passive** immunity or **herd** (=community) immunity.

- **Passive immunity** is acquired when antibodies against a pathogen are received from another individual. For example, a mother transfers antibodies through the placenta or her infant through breast milk
- **Herd immunity** is attained when a large proportion of a community is immunized., here leaving only a small number of susceptible individuals. These susceptible persons are indirectly protected by vaccinated persons, as pathogen is not transferred from the immunized person and therefore, such persons act as insulators for susceptible persons (Fig. 6).

WHAT ARE VACCINES?

In recent years, we witnessed social distancing and lockdowns across the world as measures to prevent the spread COVID-19. However, lockdowns do not prepare our immune system to fight the infection. Vaccines are another preventive measure that trains our immune system ready to fight with germs. A vaccine is a biological formulation that enhances our acquired immunity (acquired immunity is the one that develops after the exposure to a pathogen). Vaccines often contain the same pathogen in a killed or or weakened form, or only a part of it, so that our white blood cells can recognize it in advance (Fig. 7). This exposure does not cause the disease but helps our immune system to develop memory. If the pathogen enters our body later, our immune system quickly identifies and kills it immediately.

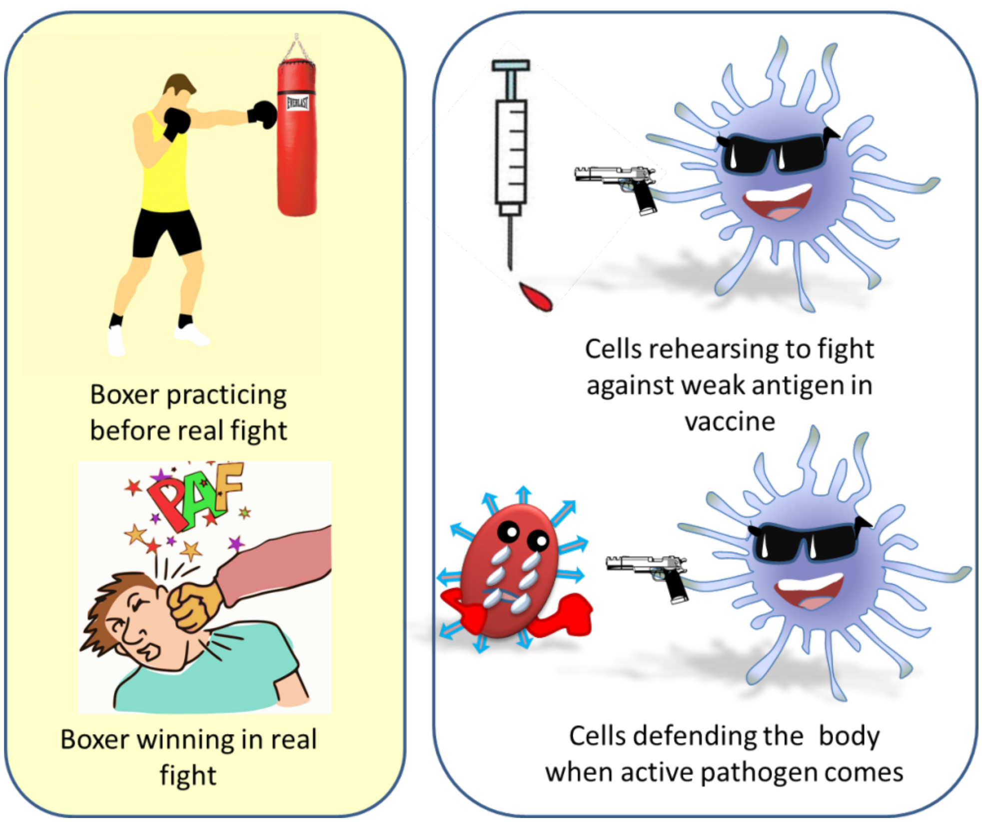


Fig. 7: Like a boxer practices with a punching bag before the actual fight, our immune cells practice with the weakened or inactivated pathogen present in a vaccine. When the real pathogenic strain enters the body, our white blood cells recognize and eliminate it rapidly t due to their previous exposure.

HOW ARE VACCINES DESIGNED?

a vaccine is prepared from pathogen, itself, either as the whole organism or as a part of it (Fig. 8). Therefore, it is necessary to assure that the pathogen or its component used in the vaccine is non-pathogenic and only mimics the actual pathogen sufficiently to elicit an immune response. making Vaccines can be prepared by using the whole pathogen, either after inactivation (killing by heat or chemicals) or attenuation (weakening so that it loses its virulence) the pathogen. Alternatively, only antigenic parts of the pathogen may be used to stimulate an immune response without causing infection. These parts could be carbohydrates (polysaccharides) present on pathogen's surface; proteins or the genetic material of pathogen. Even these molecules help our immune cells to rehearse fighting these harmless mimics. As a result, when the actual pathogen infects our body is prepared for the real fight.

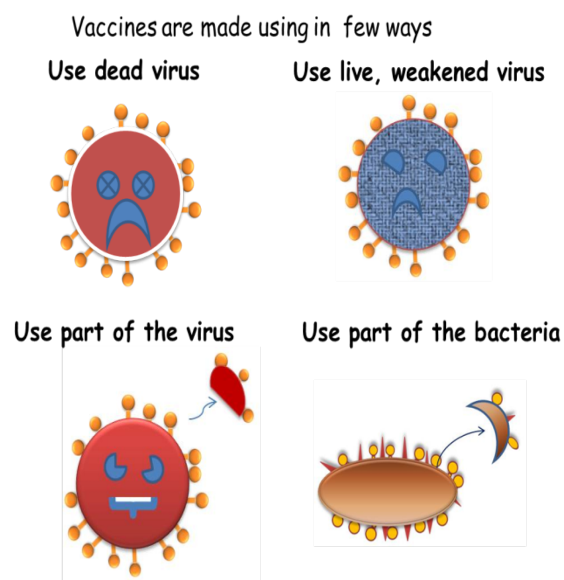
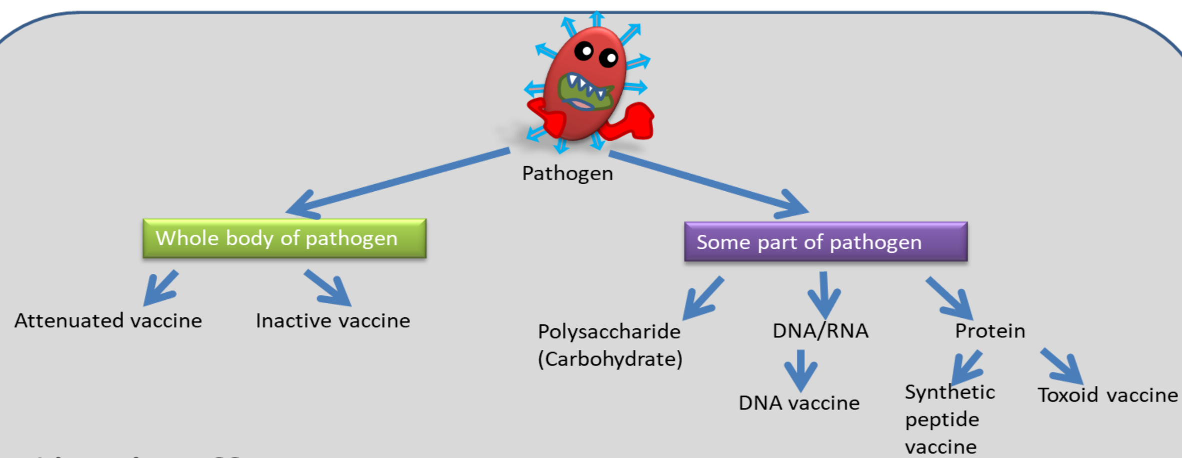


Fig. 8: Vaccines can be made by either using the whole pathogen or only a part of it, but in both the cases it should not cause infection inside the body.



Did you know??

- ✓ Polio vaccine, hepatitis A vaccine, rabies vaccine and some influenza vaccines are inactivated vaccines.
- ✓ BCG, IPV, MMR, Yellow fever vaccines are live attenuated vaccines.
- ✓ Vaccines used for Tetanus and diphtheria are toxoid based vaccines
- ✓ PCV13, Hepatitis B and HiB are subunit vaccines.

SMALL POX VACCINE: THE FIRST VACCINE IN THE WORLD

Although many attempts were made to develop vaccines, it was Edward Jenner who successfully developed the first vaccine against smallpox in 1796. It had been observed that milkmaids, who suffered cowpox once in their lifetime, rarely get infected with smallpox. Based on this observation Jenner collected fluid from cowpox pustules, and inoculated it into a healthy boy, James Phipps. Later, the boy was intentionally exposed smallpox, but the child did not develop smallpox and became immune to it (Fig. 9). In fact, the term vaccine is originated from Latin word "*vacca*", meaning cow.

Reason: Cowpox infection generated immune memory. When the smallpox virus entered the body, it was identified by the same memory cells, allowing the immune system to destroy the virus rapidly.

Similar experiments were later done by Louis Pasteur who developed vaccines against cholera, anthrax and rabies.

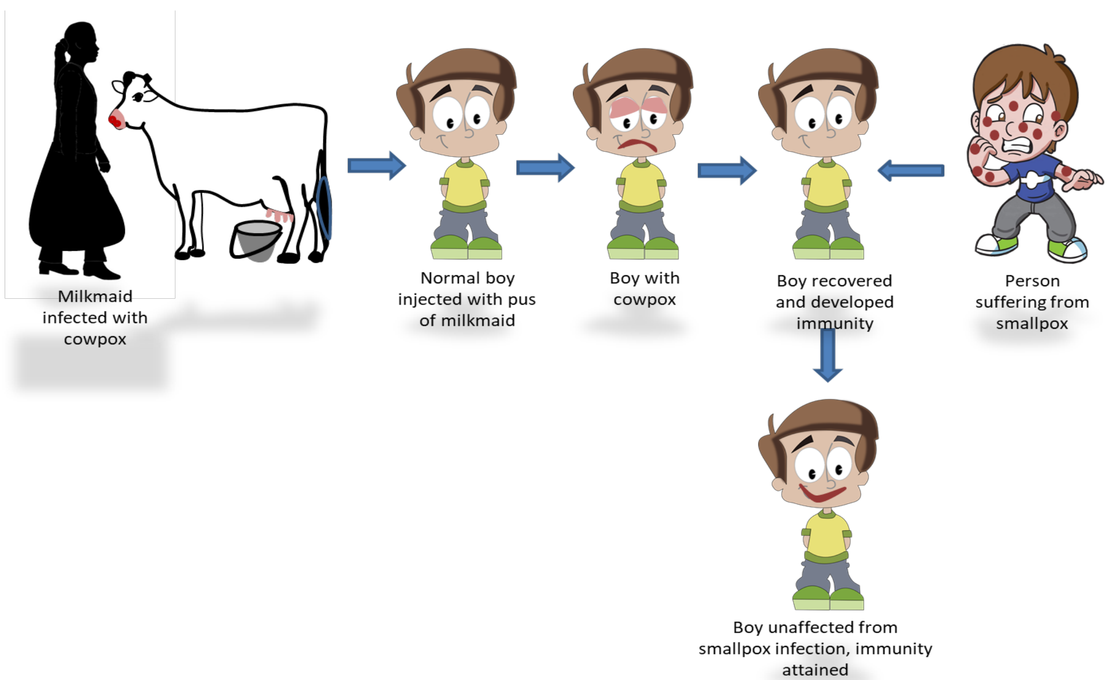


Fig. 9: A milkmaid who recovered from cowpox developed immunity. . Since cowpox and smallpox share similar antigens, antibodies and memory cells identifies smallpox virus, therefore when fluid from milkmaid recovered from cowpox was injected in healthy boy, the person develops immunity against smallpox.

BCG Vaccine for tuberculosis

The Bacille Calmette-Guerin (BCG) vaccine was developed by Albert Calmette and I. Camille Guerin in 1921. To prepare this vaccine, they repeatedly grew a bovine strain (*Mycobacterium bovis*) in a medium containing high concentration of of bile. With repeated sub-culturing over several years, the bacteria became less virulent while remaining capable of stimulating an immune response. Hence, BCG is a live attenuated vaccine.

WHAT VACCINES ARE RECOMMENDED FOR INFANTS AND CHILDREN

Table 2: Vaccines administered for respective diseases for children up to the age of six.

Vaccine	Disease
Varicella	Chickenpox
DTaP	Diphtheria
	Tetenus
	Pertussis
Hib	Haemophilus influenzae type b (Hib)
HepA	Hepatitis A
HepB	Hepatitis B
Flu vaccine	Influenza (Flu)
MMR	Measles
	Mumps
	Rubella
IPV	Polio
PCV13	Pneumococcal
RV	Rotavirus

According to the Advisory Committee on Immunization Practices (ACIP), recommended schedule worldwide for some common vaccines for diseases that are known for severe infections. These diseases may be caused by bacteria or viruses and vaccines have been created for some of them. Although every country has their own schedule for vaccines, but WHO and CDC has listed few of them mandatory for children. Nevertheless, there are vaccines which are recommended for adults as well. **But why is this schedule necessary?**

Our immune system responds differently to vaccines at different ages; moreover children's susceptibility to a particular disease depends on their age and the like hood of exposure to specific pathogens. Therefore, CDC has recommended 10 vaccines that protect against 14 diseases (Table 2). The scheduled plan for administering the vaccine is shown in Table 3.

Table 3: Vaccines recommended for Infants and Children (up to 6 years of age).. Red arrows indicate the recommended age range during which a vaccine may be administered. Figure adapted from https://www.cdc.gov.

<table>
<tr><th>Birth</th><th>1 month</th><th>2 months</th><th>4 months</th><th>6 months</th><th>12 months</th><th>15 months</th><th>18 months</th><th>19-23 months</th><th>2-3 years</th><th>4-6 years</th></tr>
<tr><td>HepB</td><td colspan="2">HepB</td><td></td><td colspan="4">HepB</td><td></td><td></td><td></td></tr>
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<tr><td></td><td></td><td></td><td></td><td></td><td colspan="2">Varicella</td><td></td><td></td><td></td><td>Varicella</td></tr>
<tr><td></td><td></td><td></td><td></td><td colspan="7">Influenza (Every year)</td></tr>
</table>

WHAT ARE BOOSTER DOSES?

Sometimes, after the primary vaccination, one or more booster doses are given several years later. This can be considered as a re-exposure to the immunizing antigen, reminding the immune system and strengthening immune memory against the antigen is so that protection is maintained a for longer period (Fig. 10).

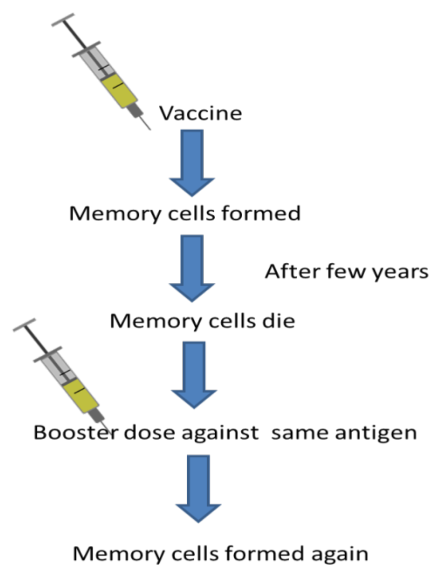
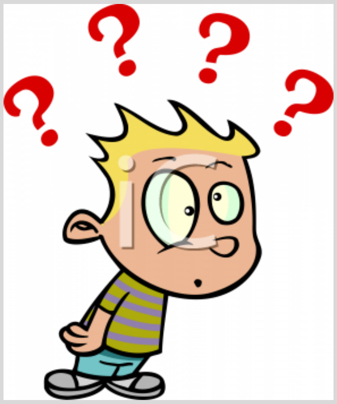


Fig. 10: Booster dose are administered several years after othe primary vaccination to reinforce immune protection.

Why do even adults get tetanus injection on injury?

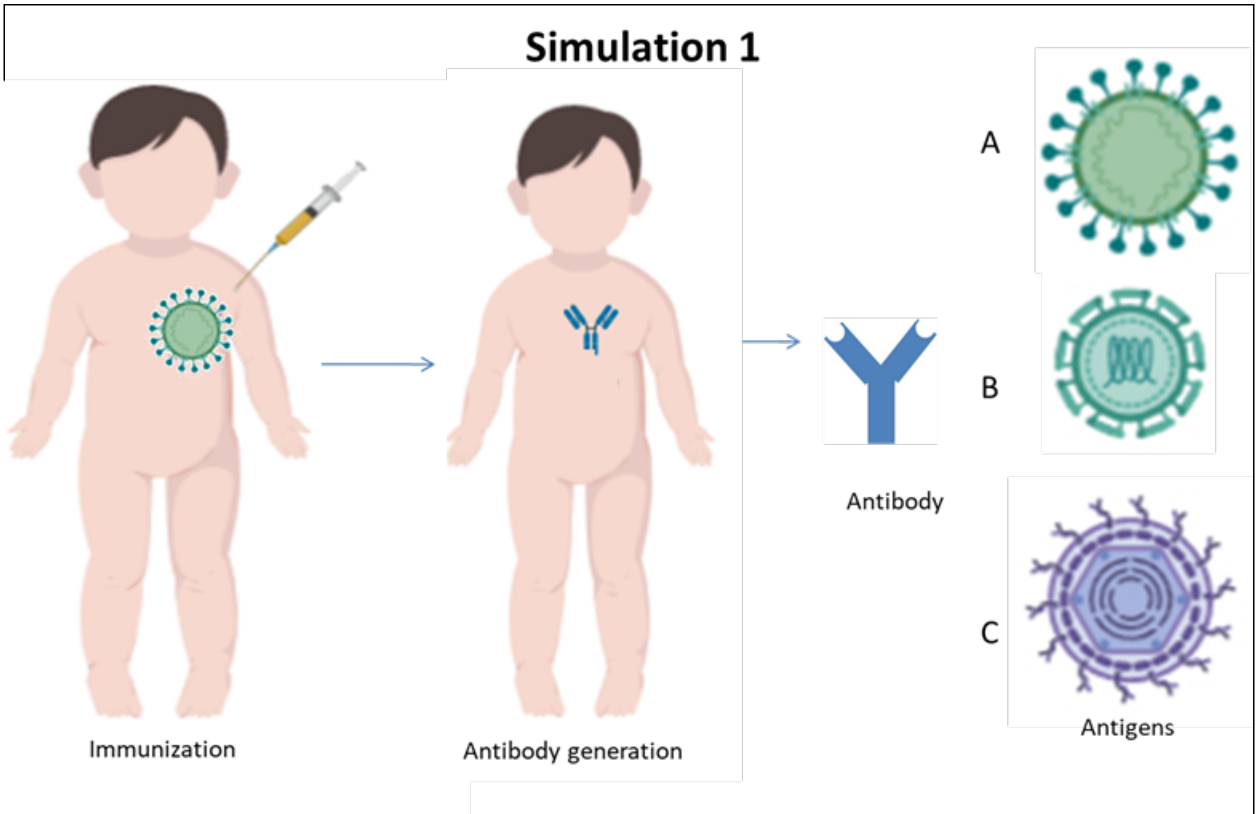


Tetanus, an infection caused by *Clostridium tetani*, is prevented in childhood by the DTaP (Diphtheria, tetanus, and pertussis) vaccine However, if an adult is not protected against this bacterium, the microorganism may enter the body, through a wound and it produces a toxin that causes severe stiffness and painful spasms. Therefore, in adults are given the TdaP (tetanus, diphtheria, and pertussis) vaccine, which differs slightly from the childhood DTa vaccine. Even if an adult was immunized in childhood, a booster dose every 10 years will maintain protection.

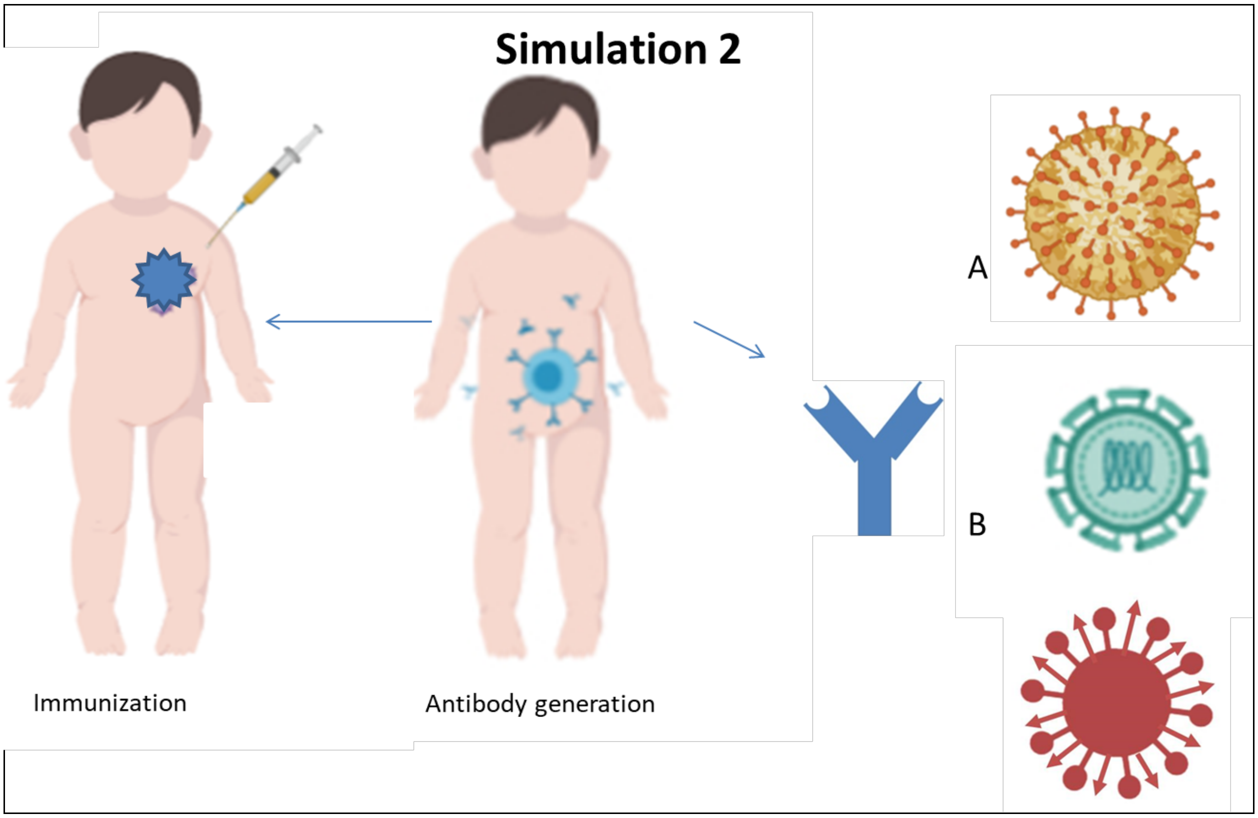
LETS' LEARN WITH ACTIVITIES

ACTIVITY 1

- **Simulation 1:** A child was vaccinated against one of the virus (A, B, C) and developed antibodies. Identify the virus against which the child is protected due to vaccination. (Clue=Antigen-antibody binding)
- **Simulation 2:** Identify the virus or viruses against which the child is protected after vaccination. (Clue=look at the structures antigen and antibody and relate to their interactions)



Simulation 1
A
B
C
Immunization
Antibody generation
Antibody
Antigens



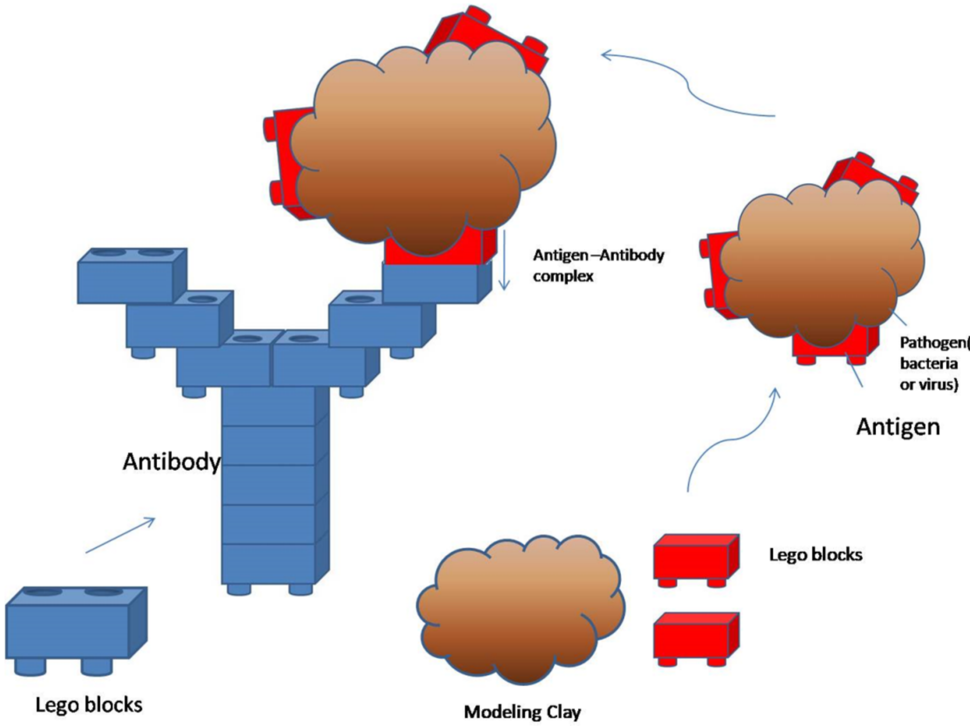
ACTIVITY 2 LEGO GAME : MAKE YOUR OWN ANTIBODY AND ANTIGEN COMPLEX

Requirements: You will need- 2 long and 2 short plastic straws, pencil or glass rod, modeling clay, and a rubber band

Procedure:

- **To make an antibody model:** Use Lego blocks to construct a Y-shaped antibody molecule. Your model should look something like diagram below. Each antibody has two antigen-binding sites, which are highly specific.
- **Specificity:** The antigen-binding sites fit only a particular antigen present on a disease causing bacteria or virus.
- **To prepare a pathogen model:** Use modeling clay to make a a bacterium or virus. Insert two LEGO Lego blocks on the surface to represent the antigens.

- **To demonstrate antigen-antibody complex**, bring the two models together and attach the Y shaped ends of the antibody to the matching Antigen (RED LEGO)

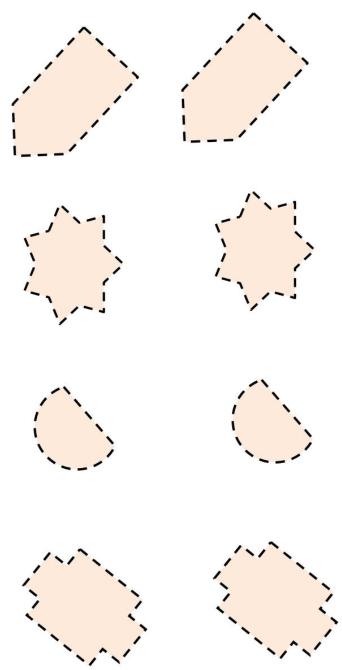


ACTIVITY 3: Antigen – antibody interaction

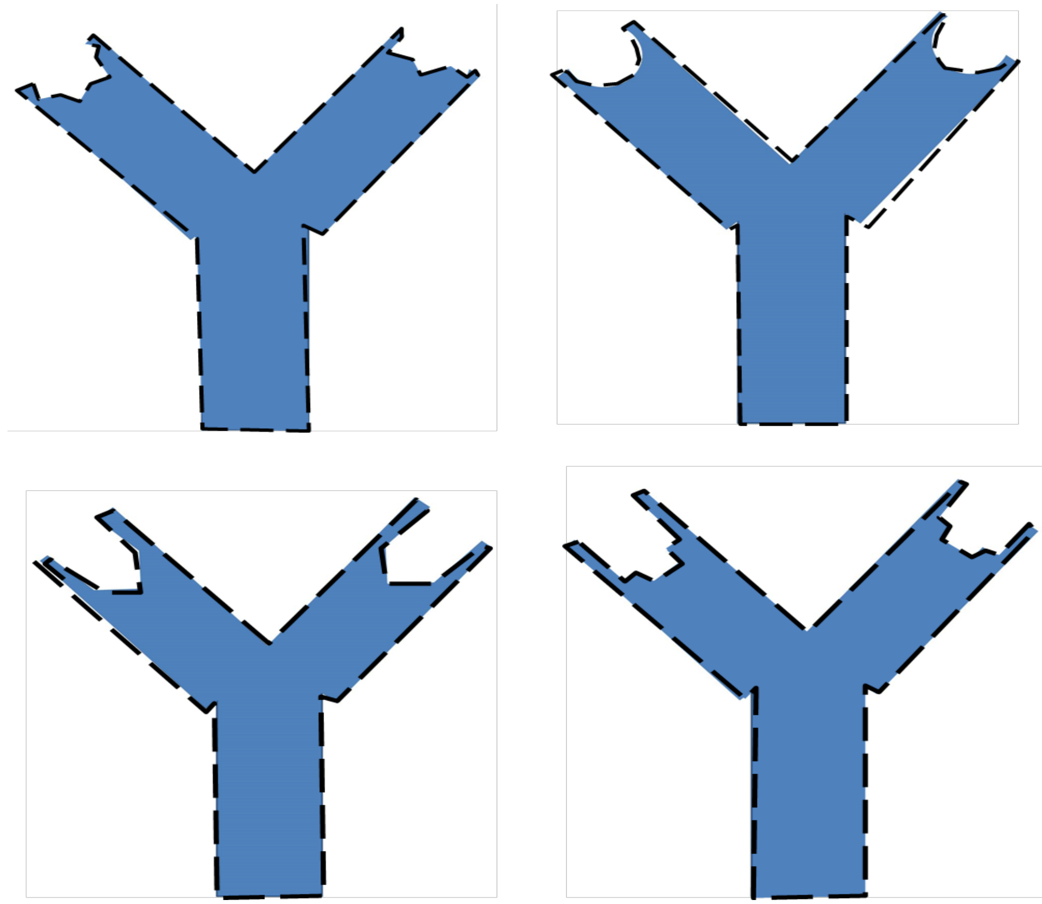
- In this activity, students will learn about antibody diversity and antibody-antigen binding. They will investigate the binding of different antibodies to antigen templates and determine if a match occurs. This activity demonstrates the "lock-and –Key" biological relationships between antidies and antigens

How to play

- Choose the antibody that best fits the given antigen.
- Print the antigen templates and match each one with the correct antibody.



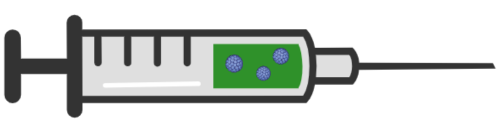
Antigen Structures



ACTIVITY 4: Know your family

As new infectious diseases emerge, more vaccines are added to immunization. Our grandparents generally received fewer vaccines than we do today. Take a survey of your family to learn about the vaccines received by different generations and diseases they are protected. Also learn from your grandparents how people coped with infectious diseases such as Chickenpox, Smallpox etc. before vaccine became widely available. .

Vaccine	Grand Pa	Grand Mom	Dad	Mom	Me	My sibling
Varicella						
DTaP						
HepA						
HepB						
Flu vaccine						
IPV						
PCV13						
RV						
Hib						
MMR						



The Vaccine QUIZ

1. What is the name of the scientist who discovered the first vaccine?

2. Which of the following is true about vaccines?
   a. Vaccines prompt white blood cells to make antibodies to protect a specific illness

b. Vaccines contain a harmless version of the invader.

c. Vaccines help to prevent future illnesses

d. All of the answers are correct

3. Which vaccine is given soon after birth?

   A. Polio

   B. Hepatitis B

   C. Measles, mumps, and rubella (MMR)

   D. Varicella

4. The first vaccine developed was against smallpox.

   A. True   B. False

5. Vaccines work by teaching your immune system to know what the real infection looks like

   A. True   B. False

6. Bacille Calmette-Guerin (BCG) is injected to get immunity from

   A. Polio

   B. Cholera

   C. Small pox

   D. Tuberculosis

7. Vaccines contain antibodies which help defend against a pathogen?

   A. True   B. False

Glossary

Antibody Antibody is a Y-shaped protein which is produced by a type of White blood cell called B-cells (plasma cells) that recognizes a specific region of antigen

	and helps in its elimination from our body. It is also known as an immunoglobulin (Ig).
Antigen	Any foreign substance which is capable of inducing an immune response in the body.
Attenuated vaccine	An attenuated vaccine is a vaccine where the virulence of a pathogen is reduced while its viability is maintained.
Booster dose	It is the re-exposure of body to the previously immunized antigen by extra administration of a vaccine after a primary dose. The extra dose helps to recreate the memory cells.
Epidemic	When an infectious disease occurs prevalently in a community at a particular time.
Epitope	Specific region of antigen (and not the complete antigen) which is identified by the antibody.
Herd immunity	A type of indirect immunity where a large percentage of a population is immunized to a particular disease, and these individuals act as a shield to those people in a population who are not immune.
Immune system	The defense system of our body involving white blood cells (also called leukocytes) and proteins that are used to evade any foreign material from our body. Many organs like thymus, bone marrow and spleen are involved for defending against any antigen.
Pandemic	When the epidemic disease spreads further, occurring over a wide geographic area and affects very large population.
Paratope	Also called an antigen-binding site, is that part of antibody which interacts with epitope of an antigen.
Toxoid	If the toxins produced from bacteria are inactivated or suppressed, it becomes toxoid which is not toxic but efficient to generate immune response.
Vaccination	It is the administration of a vaccine to a body due to which our immune system develops immunity to protect from a disease.

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