
بسم الله الرحمن الرحيم
Designed by

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Immunology outline

A. Introduction

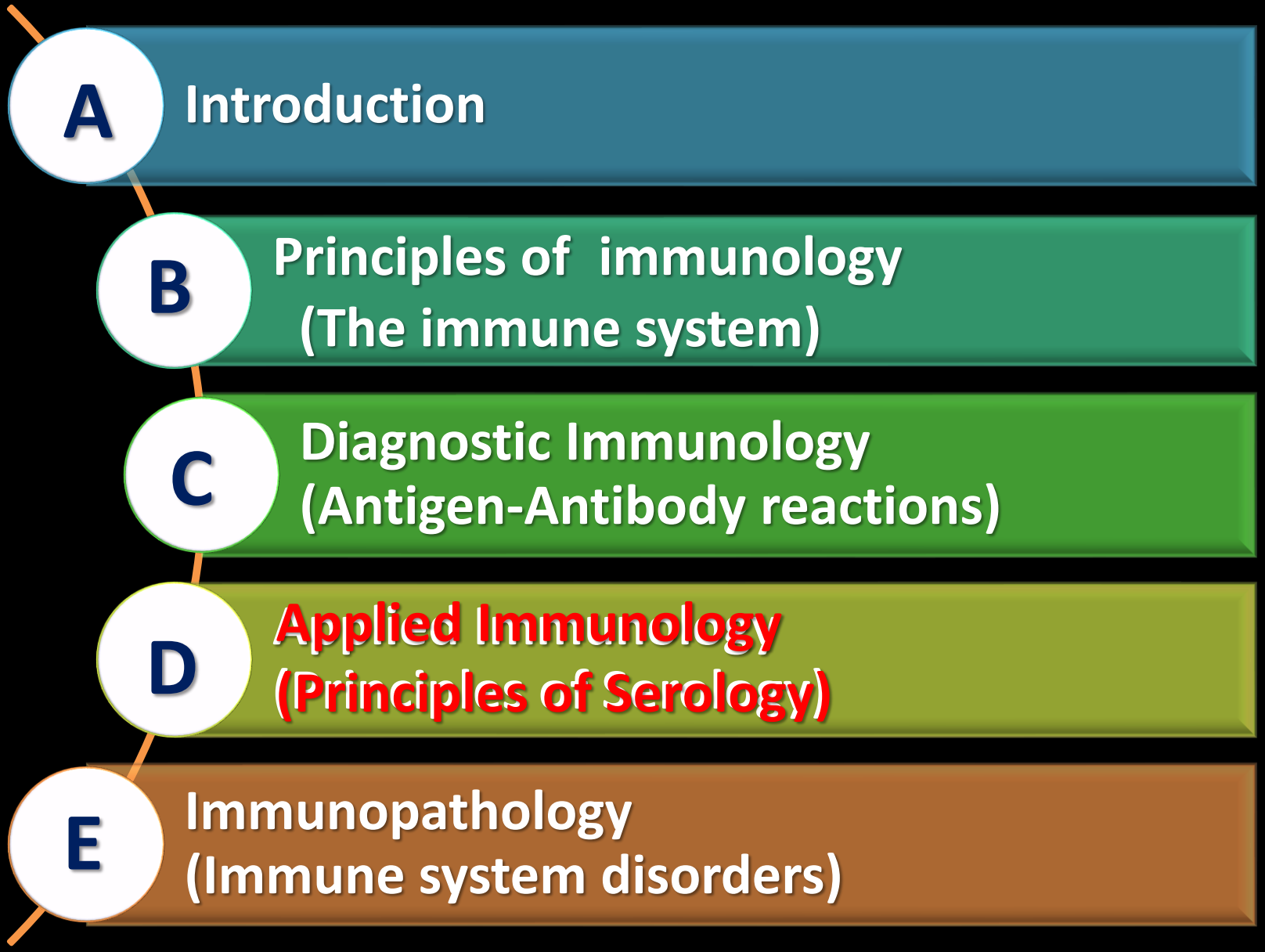
B. Principles of immunology (The immune system)

C. Diagnostic Immunology (Antigen-Antibody reactions)

D. Applied Immunology (Principles of Serology)

E. Immunopathology (Immune system disorders)

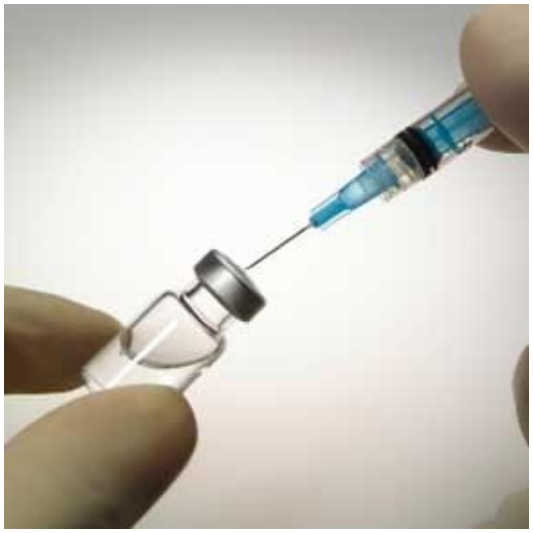
Immunology outline



Human Assist

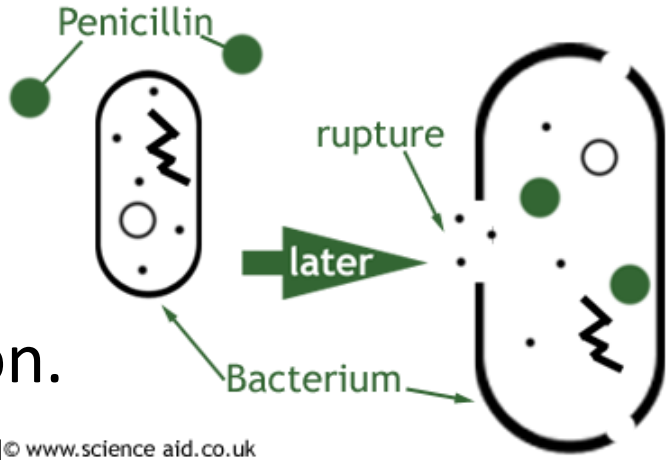
Helping the immune system

- Medical science has created to systems for augmenting the human immune system:
  - Antibiotics (NOT the same as antibodies)
  - Vaccines



How antibiotics work

- Antibiotics help destroy bacteria (but not viruses).
- Antibiotics work in one of several ways:
  - Slowing bacteria reproduction.
  - Interfering with bacterial cell wall formation.

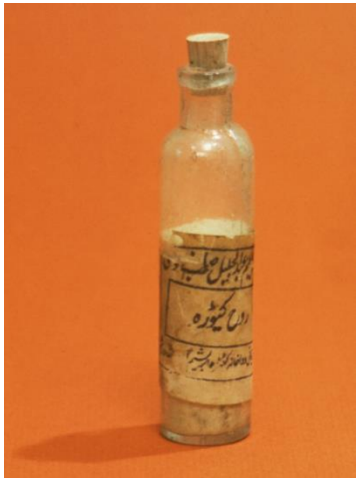


Antibiotic myths

- Antibiotics are not antibodies.
- Antibiotics do not weaken our immune system. They help it by weakening bacteria.
- Humans do not become “immune” to antibiotics. Bacteria that resist antibiotics and are not completely destroyed may multiply, producing more antibiotic-resistant bacteria.

Vaccine history

- Variolation: The deliberate inoculation of people with secretions from smallpox (*Variola*) sores, by inhaling the dried secretions or rubbing them on broken skin. Used for centuries in Asia and Africa.



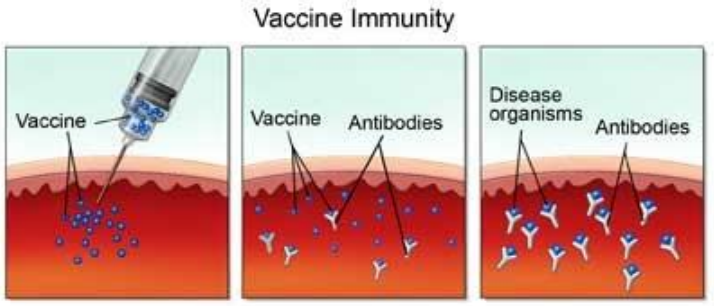
Vaccine history

- Vaccination: (From *vacca*, Latin for cow.) Invented by Edward Jenner in 1796. Jenner knew that dairy maids who had contracted cowpox never got smallpox. He inoculated a boy with secretions from cowpox sores, and showed the boy was immune to smallpox.

Not that everyone accepted the process. Cartoons like this created widespread fear of the “cow pock” vaccine.

How vaccines work

- Modern vaccines are created from killed bacteria or viruses, or fragments of proteins from these microbes.
- The proteins are recognized as antigens by our immune systems. This causes a mild immune response. Memory T-cells and B-cells remain ready to fight off the illness if it is encountered again.

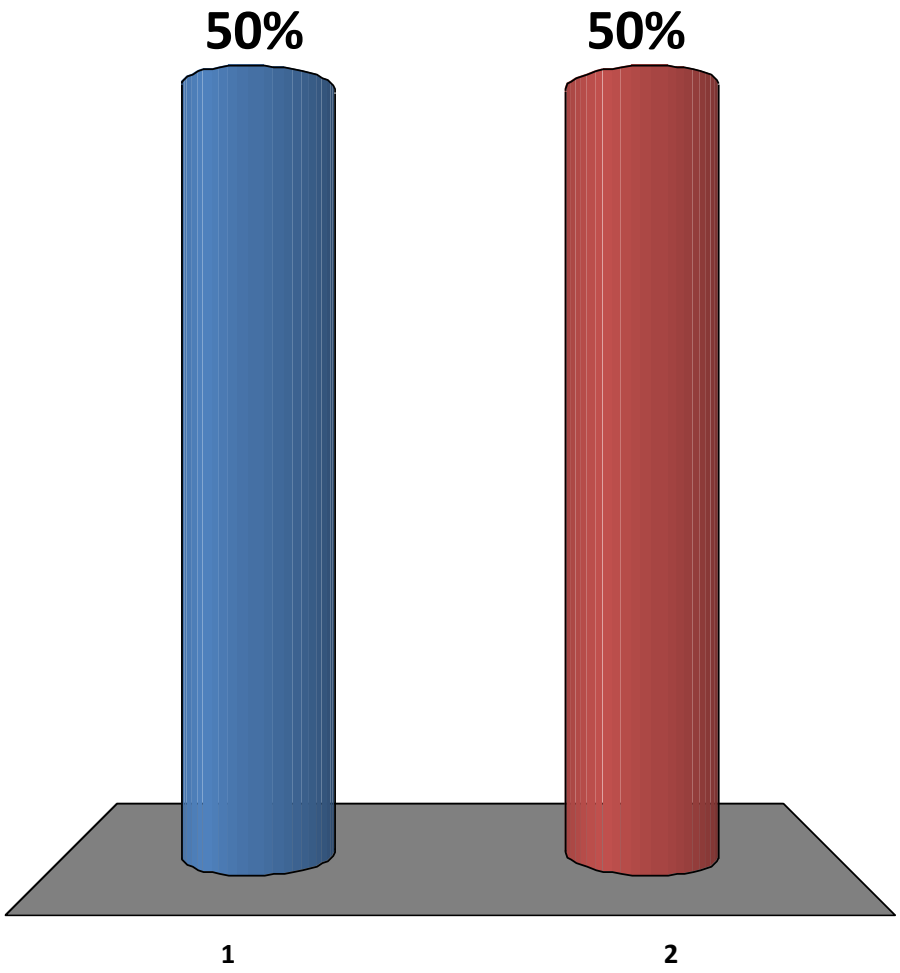


Vaccine myths

- The flu vaccine does not give you the flu. Some people get the vaccine too late, or catch a cold and think they have the flu.
- Vaccines are not less effective than a “natural” infection with the illness. The immunity is the same, and a mild response to a vaccine is much less risky than a full-blown infection of measles.
- The proposed link between vaccines and autism turns out to have far less experimental support than was originally reported.

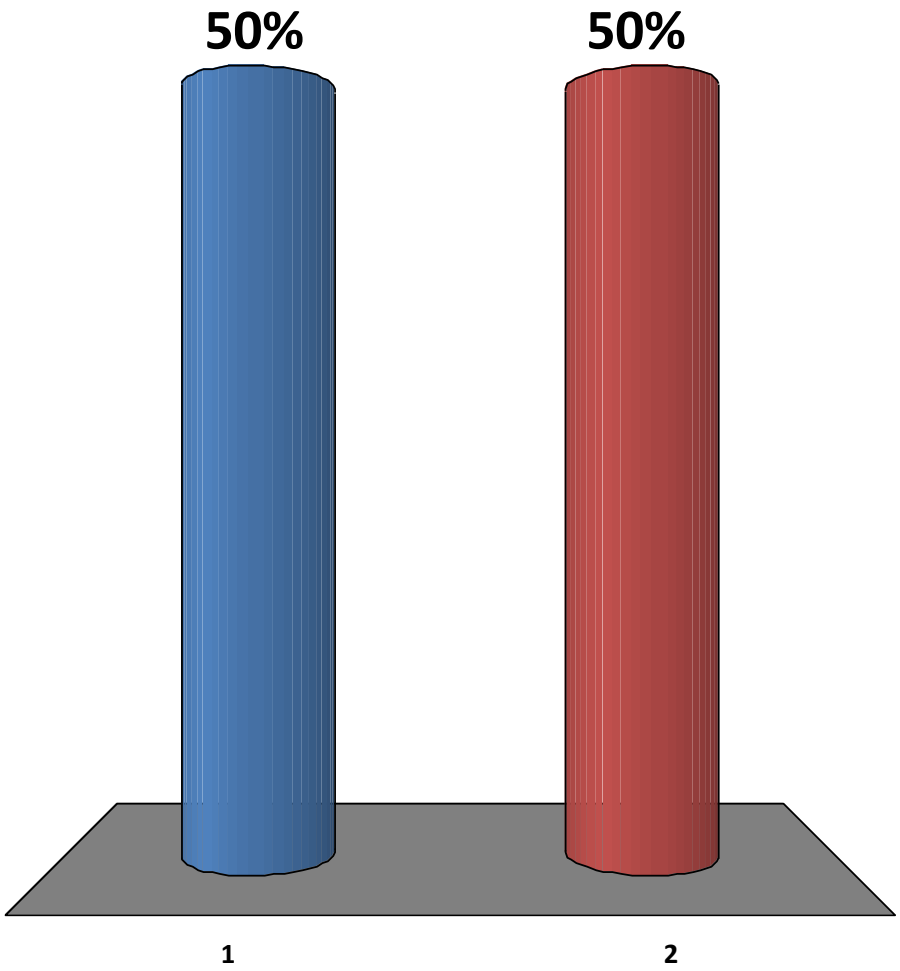
True or false: Antibiotics weaken the immune system because your body doesn't learn to make enough antibodies.

1. True. Antibiotics are a type of antibody.
2. False. Antibiotics are not antibodies.



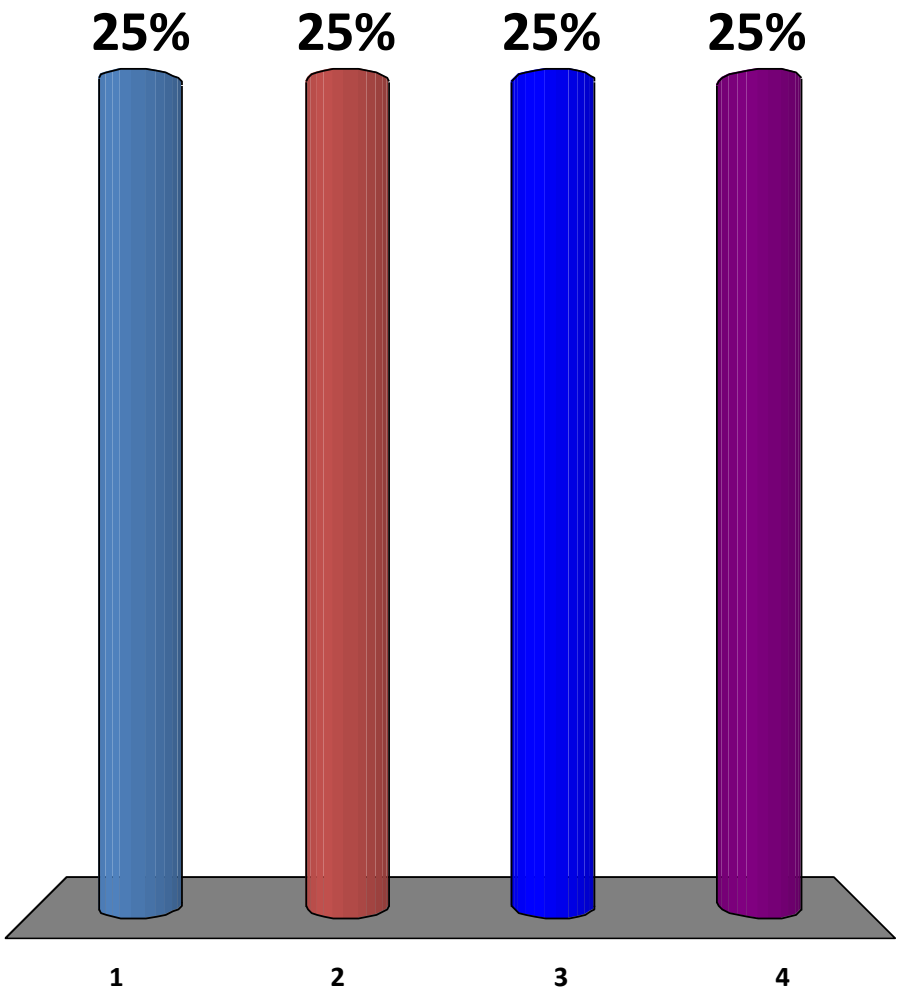
True or false: Vaccines weaken the immune system because the body doesn't learn to defend itself without help.

1. True. The immune system needs to exercise itself or it won't get strong.
2. False. Vaccination causes the body to learn to defend itself.



Vaccines stimulate the production of:

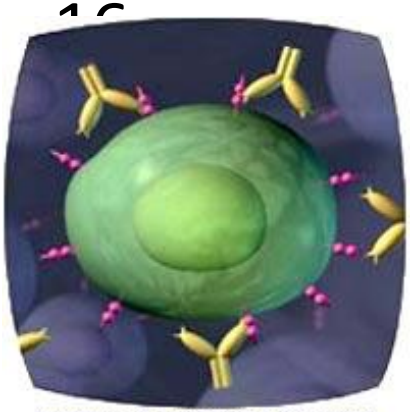
1. Antibodies.
2. Helper T-cells.
3. Antigens.
4. Memory cells.



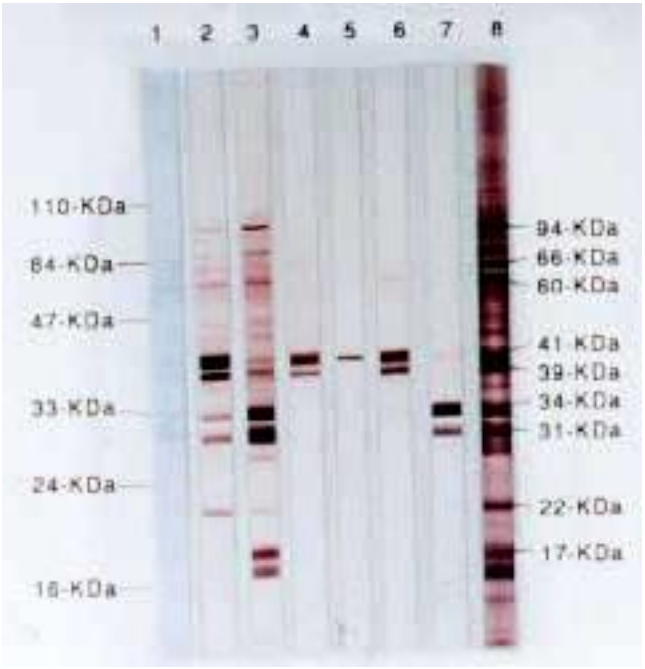
- Why will antibiotics work against bacteria but not viruses?
- Why don’t antibiotics kill your own cells?

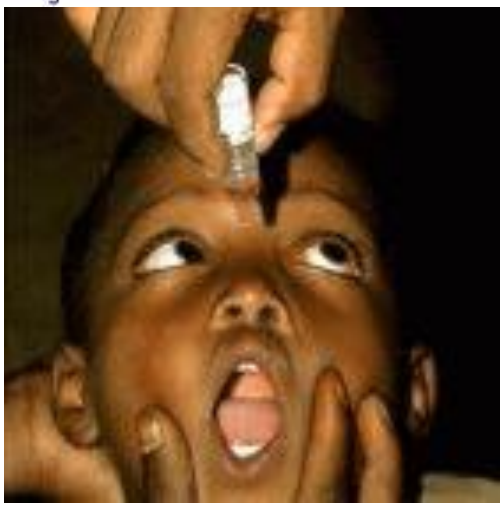
Applications of Immunology

Talaro Chapter 16



Monoclonal antibodies targeting a HER2 protein overexpressing cell



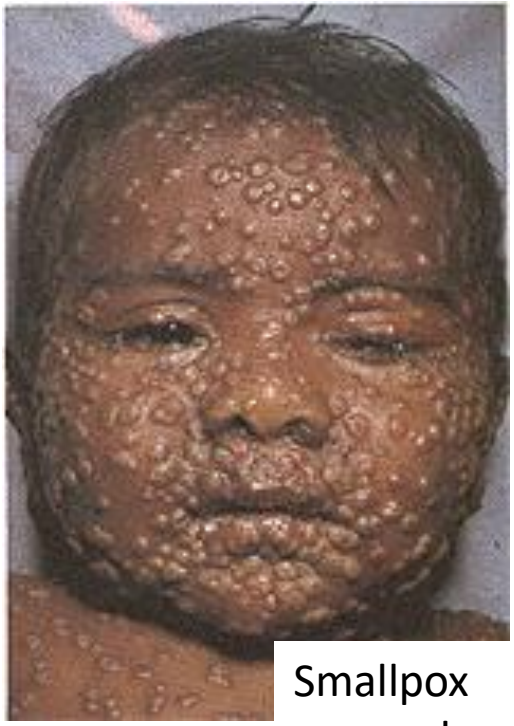


Vaccines

- Provide an antigenic stimulus that does not cause disease
  - Attenuated strain
    - Tissue culture or unnatural / unusual host
    - Hypovirulent
  - Dead whole cells or inactivated viruses
    - Heat, formalin, UV irradiation
  - Purified antigen subunits from cells or viruses
  - Surface antigens produce via rDNA technology
  - DNA vaccines
- Produces long lasting protective immunity
- Edward Jenner (page 476)
  - www.sc.edu/library/spcoll/nathist/jenner2.html
  - Cowpox
  - Smallpox
    - Variola
  - Controlled experiments
- Vaccinia virus
  - Cultured cow pox virus for many years
- Small pox eradicated in 1973

Why did the vaccinia virus work?

Immunization using a closely related, less pathogenic organism to give protection against a more pathogenic one.



Smallpox
www.cdc.gov

Cowpox on human forearm
www.cdc.gov

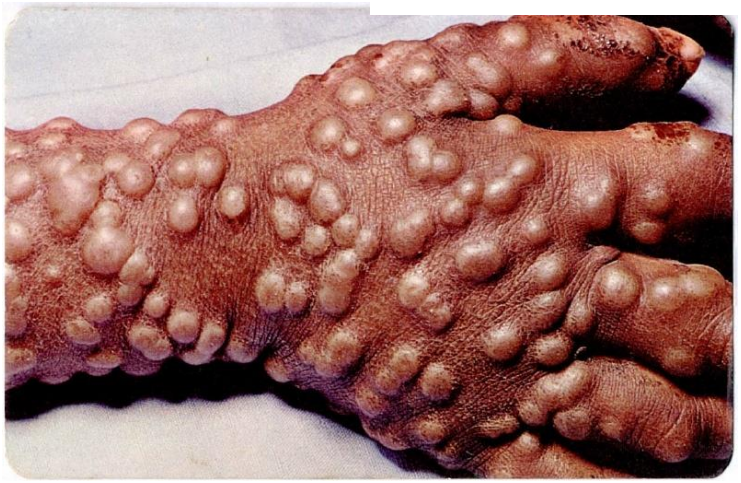


TABLE 16.1

Checklist of Requirements for an Effective Vaccine

- It should have a low level of adverse side effects or toxicity and not cause serious harm.
- It should protect against exposure to natural, wild forms of pathogen.
- It should stimulate both antibody (B-cell) response and cytotoxic (T-cell) response.
- It should have long-term, lasting effects (produce memory).
- It should not require numerous doses or boosters.
- It should be inexpensive, have a relatively long shelf life, and be easy to administer.

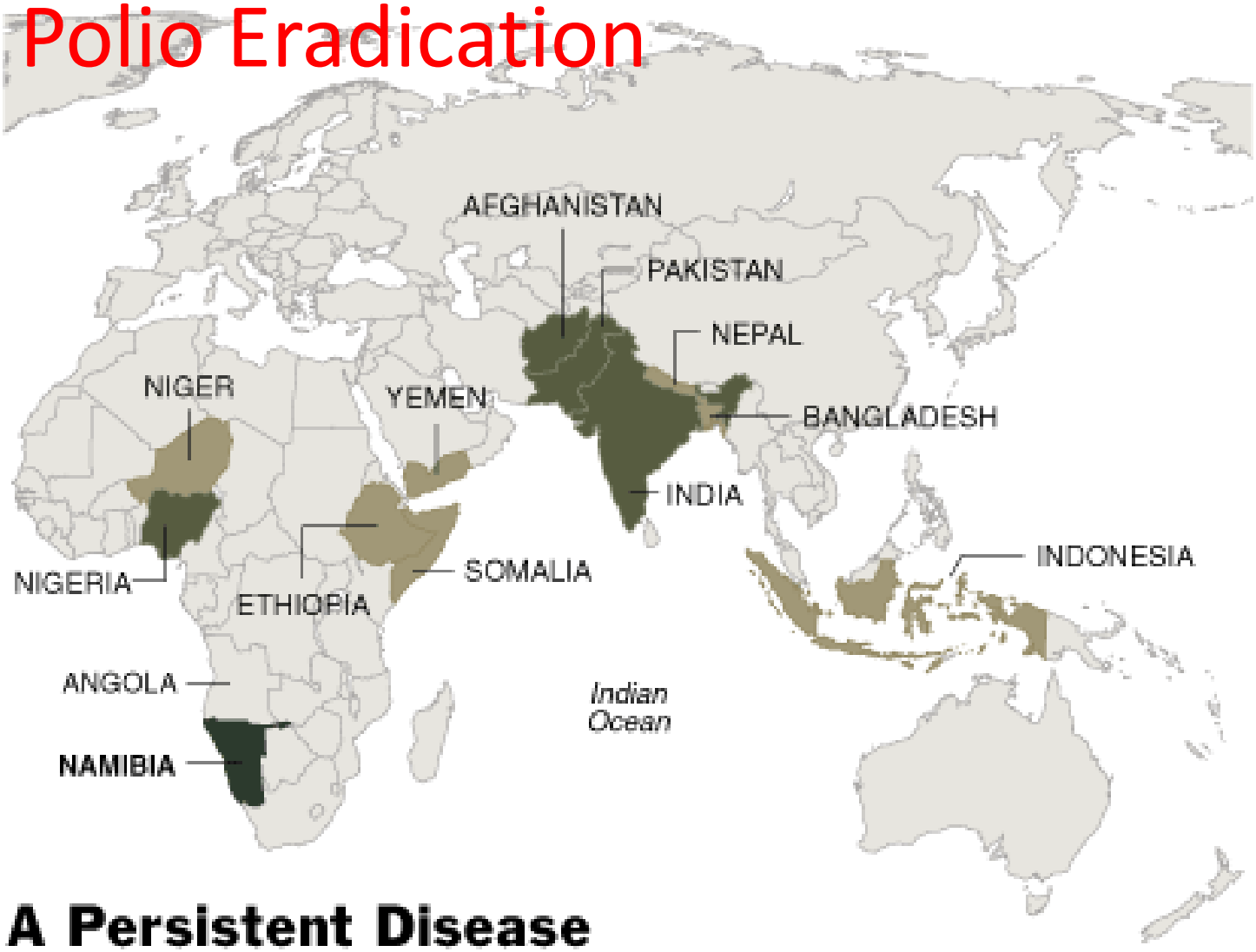
Vaccination Success

www.who.int/immunization_safety/en/
www.cdc.gov

- Small pox
  - ≅ 2 million people a year died from small pox until 1967
  - The World Health Organization initiated an immunization campaign that eradicated small pox in 12 years
- Poliomyelitis (polio)
  - This virus attacks the motor neurons of the brain and spinal cord
  - Causes paralysis and death
  - Immunization campaigns since the 1950s have virtually eradicated polio in developed countries

news.bbc.co.uk

Polio Eradication



A Persistent Disease

An unusual polio outbreak in Namibia has killed 7 people and paralyzed 33.

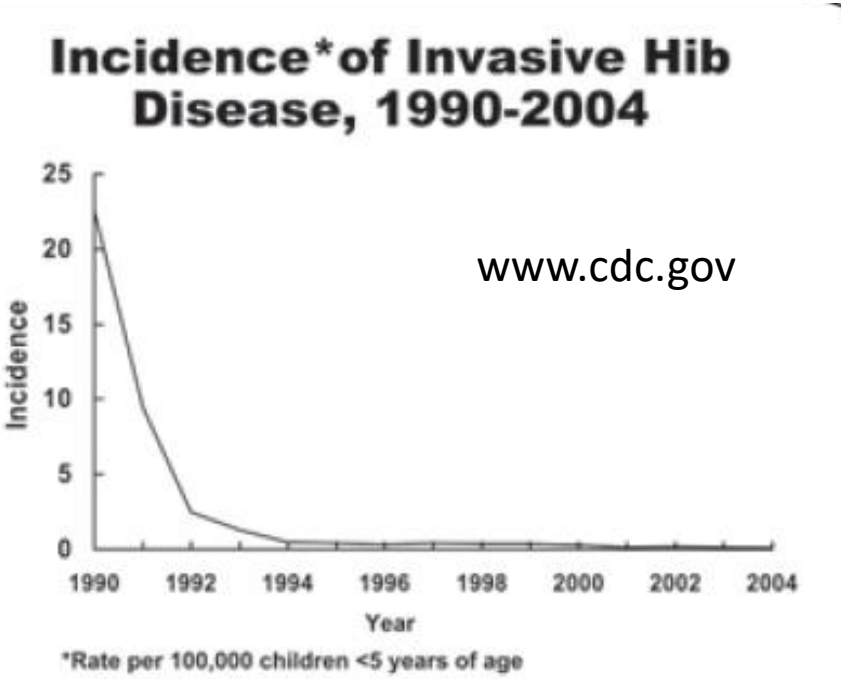
Countries where polio has yet to be eradicated.

Previously polio-free countries that were reinfected in 2006.

Sources: Global Polio Eradication Initiative; World Health Organization

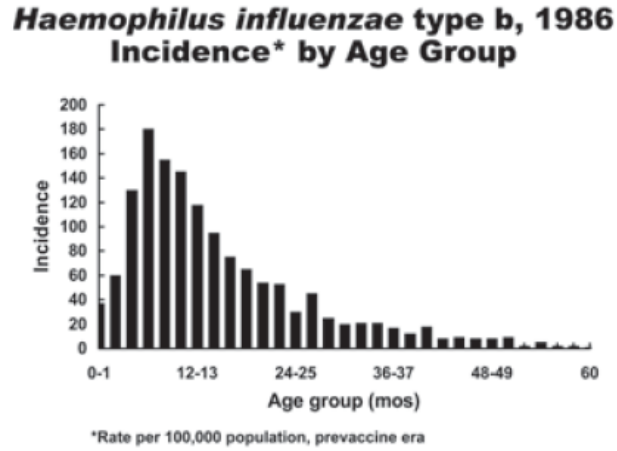
The New York Times

- *Haemophilus influenzae* type b
  - Mistakenly believed to have caused influenza
  - Type b strains accounted for majority of bacterial meningitis
- Meningitis, pneumonia, and epiglottitis
- Was the leading cause of bacterial meningitis of children 5 years or younger
  - 1/200 children contracted Hib
  - Incidence has decreased 99% since the vaccine was introduced



20,000 cases per year in the early 1980's

1,247 in 2000



www.who.int/immunization_safety/aefi/immunization_misconceptions/en/index.html

Vaccines cause disease
Disease is no longer a threat in my country
Cost of vaccination
Difficulty reaching vaccination center
Not recommended by my physician
Safety concerns
- Side effects
- SIDS

Autism
Depress the immune system
- Mercury Poisoning

Religious beliefs

Herd Immunity

Protection from a disease among unvaccinated individuals occurs when ≅ 90% of a population is immunized.

% depends on the disease & vaccine

Content and Design Attributes of Antivaccination Web Sites
Robert M. Wolfe, MD; Lisa K. Sharp, PhD; Martin S. Lipsky, MD
JAMA 2002 287:3245-3248.

Polio Outbreak Occurs Among Amish Families In Minnesota

by David Brown

Washington Post Staff Writer

October 14, 2005

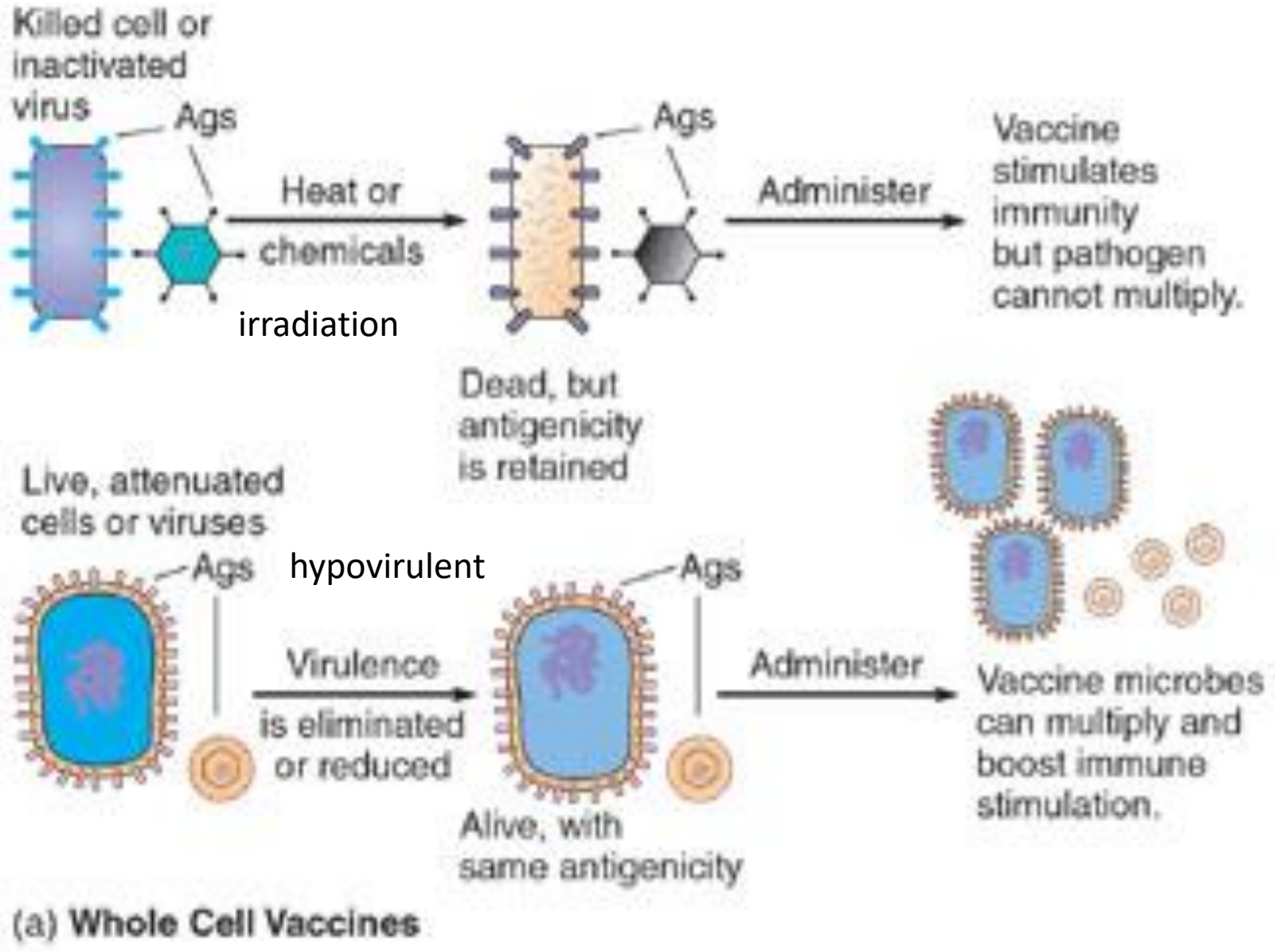
The first outbreak of polio in the United States in 26 years occurred earlier this fall in an Amish community in central Minnesota, state and federal health officials reported yesterday. Four children have been infected with the virus, although none has become paralyzed. The Amish typically decline to vaccinate their children. The last large outbreak of polio occurred in numerous Amish communities in several states in 1979.

Fears Rising Over Measles Outbreaks

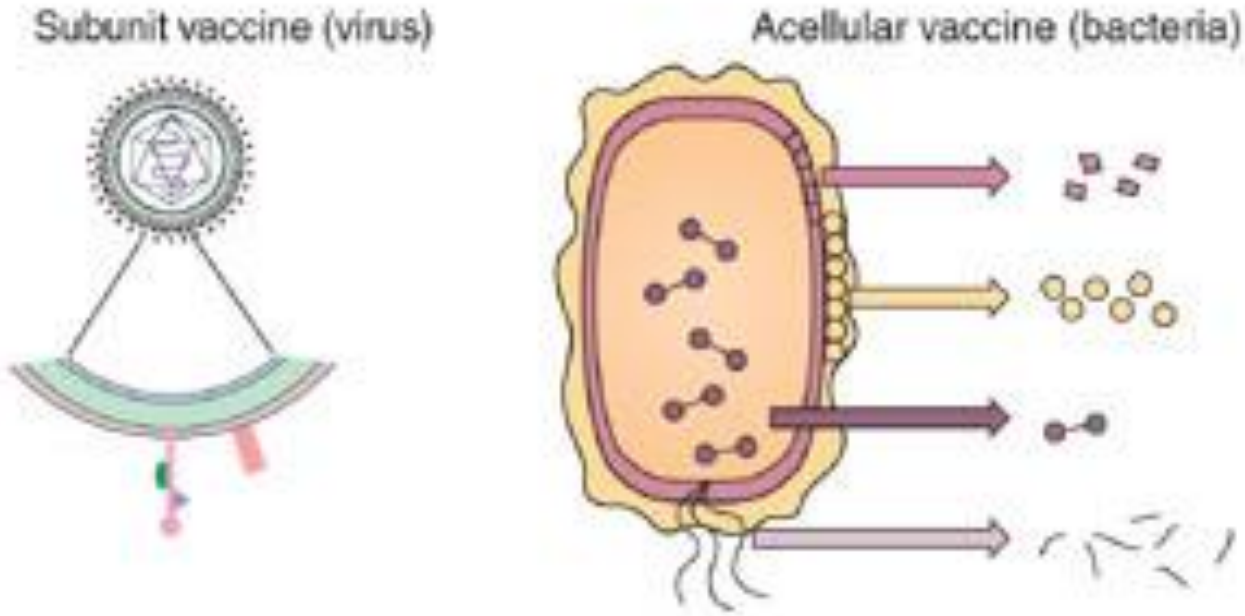
by ROBERT A. HAMILTON

STATE health officials are preparing for what they fear could be ''a major outbreak'' of measles when students who attend Boston University return home next week for spring break. Last week, a measles case was reported in Fairfield, an 18-year-old Boston University freshman who returned home eight days ago with cold symptoms and by Tuesday was in the hospital. ''We expect a lot more students will be returning to Connecticut next week, for the spring break,'' the program director of the state immunization program, Dr. Charles H. Alexander, .

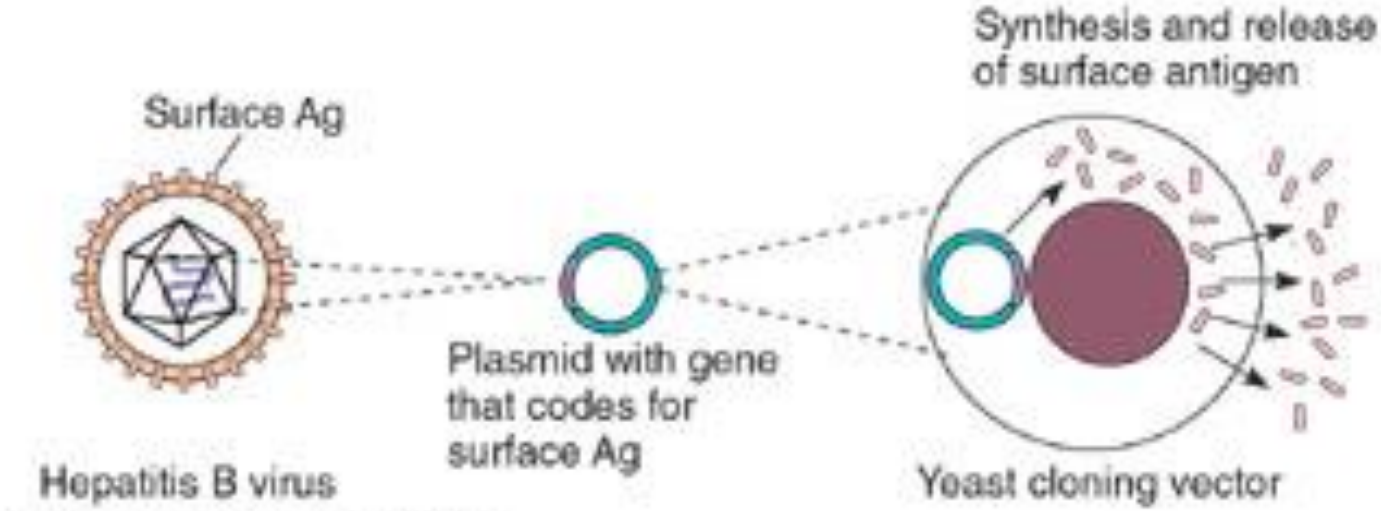
March 3, 1985 The New York Times



(a) **Whole Cell Vaccines**

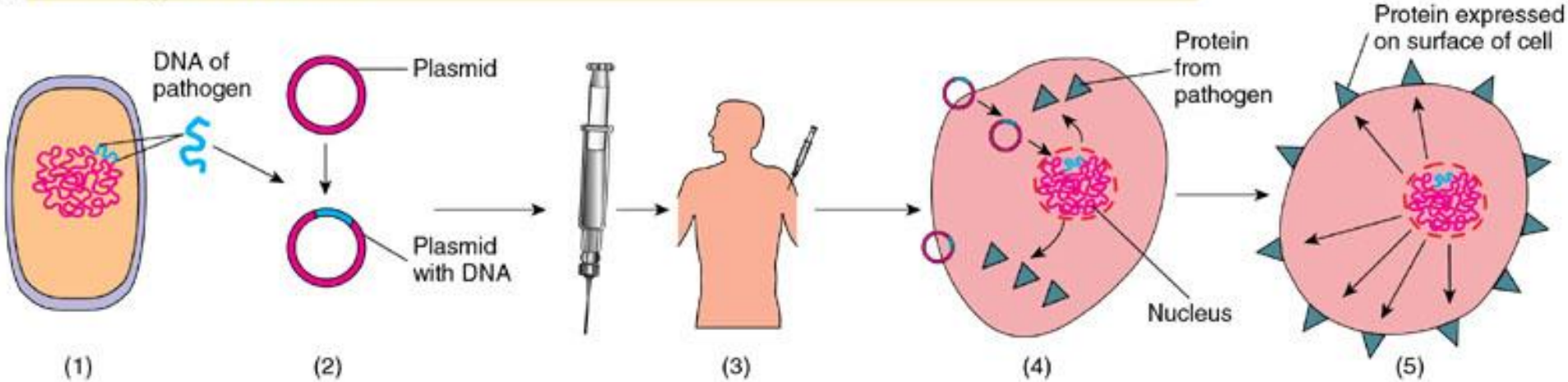


(b) **Vaccines from Microbe Parts**



(c) **Recombinant Vaccine**

(a) **Technology for DNA vaccines**



(1) DNA that codes for protein antigen extracted from pathogen genome.

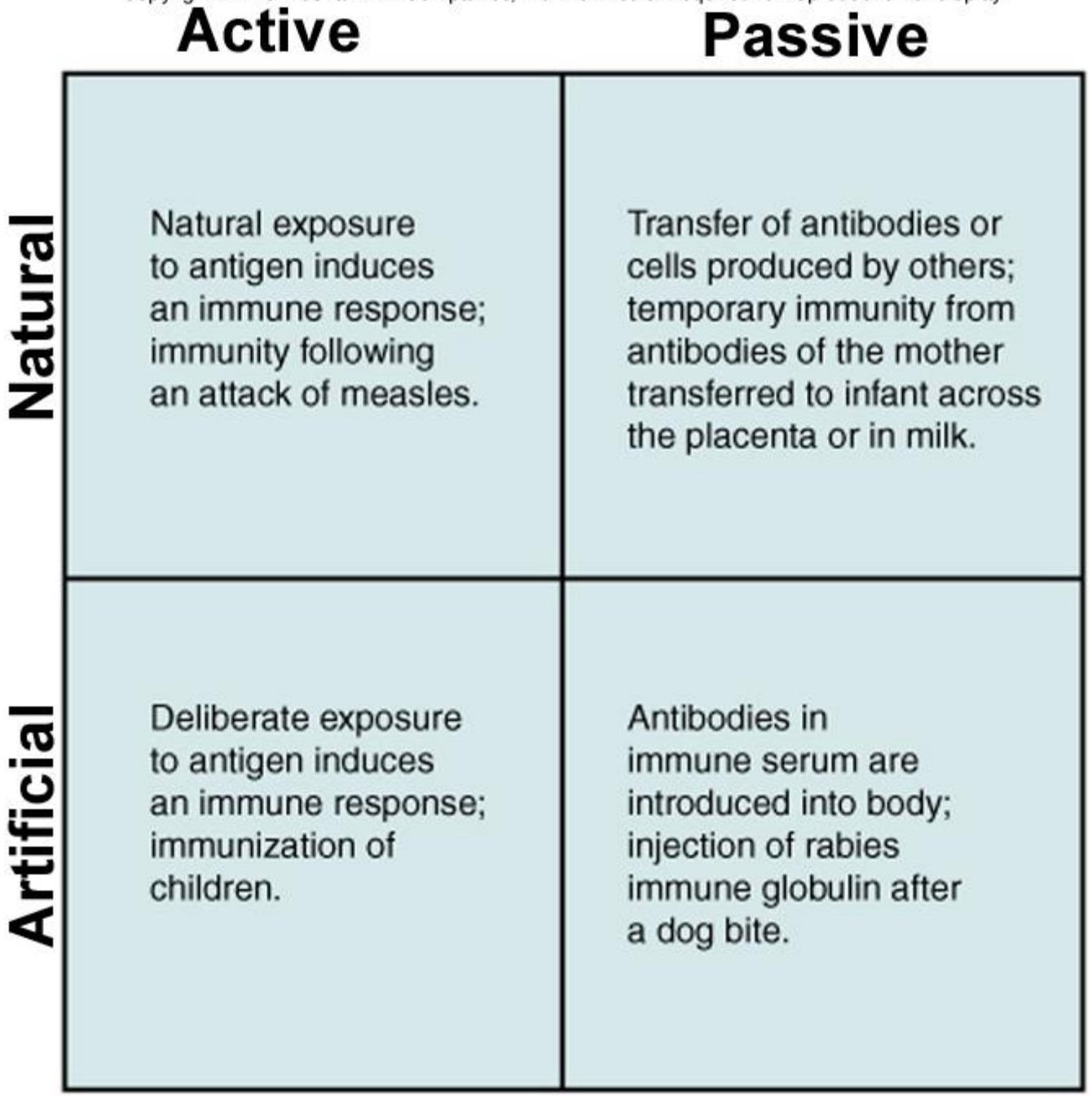
(2) Genomic DNA inserted into plasmid vector; plasmid is amplified and prepared as vaccine.

(3) DNA vaccine injected into subject.

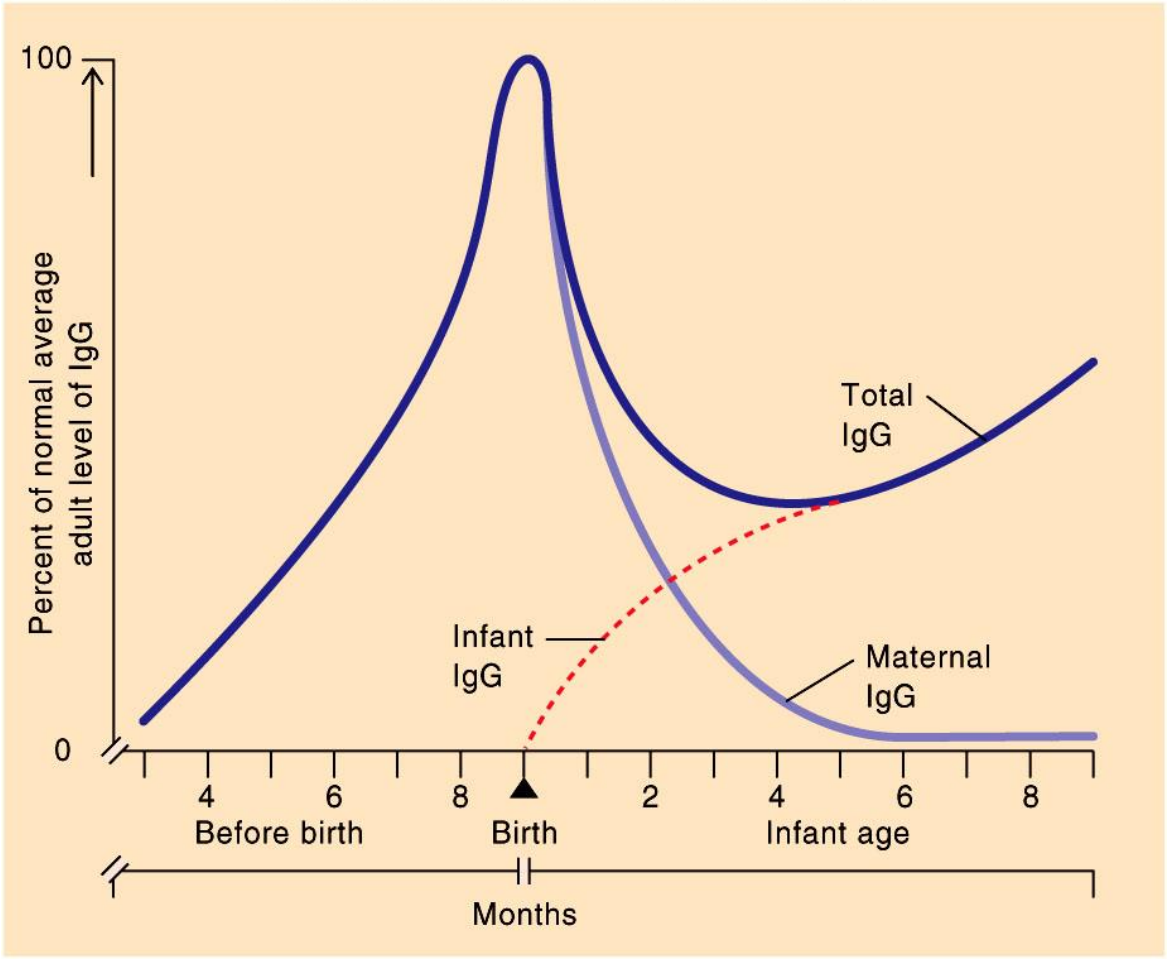
(4) Cells of subject accept plasmid with pathogen's DNA. DNA is transcribed and translated into various proteins.

(5) Foreign protein of pathogen is inserted into cell membrane, where it will stimulate immune response.

Applications of Principles of Immunity



IgG levels in fetus vs infant



What is passive and what is active?

Principles of Immunization

- Natural or artificial
- Passive or active
- Natural passive , e.g. IgG across the placenta
- Artificial passive, use of immune serum globulin e.g. IgG fraction of donor blood.
- Active involves lymphocytes and confers lasting protection due to memory

Can you put the types of vaccines listed into categories?

Table 17.1 Some Important Immunizing Agents for Humans

Disease	Type of Vaccine	Persons Who Should Receive the Vaccine
Mumps	Attenuated virus	Same as measles
Pertussis (whooping cough)	Acellular vaccine given together with diphtheria and tetanus toxoids (DTaP)	Children
Pneumococcal infection	Two forms—purified polysaccharide (PPV) and polysaccharide-protein conjugate (PCV)	Children should receive PCV; adults over 65, people with certain chronic infections, and others in high-risk groups should receive PPV
Rabies	Inactivated virus grown in human or rhesus monkey cells	People exposed to the virus, people at high risk for exposure, such as veterinarians and other animal handlers
Rubella (German measles)	Attenuated virus	Children, adults (particularly women) who are susceptible, health care workers who are at high risk of exposure
Tetanus	Toxoid	Children; adults receive a booster every 10 years
Tuberculosis	Attenuated BCG strain of tuberculosis bacteria	Used only in special circumstances in the United States; widely used in other countries
Typhoid fever	Two forms—attenuated bacteria (taken orally) and purified polysaccharide	People traveling to certain parts of the world
Varicella-zoster (chickenpox)	Attenuated virus	Children; may also be given to susceptible adults
Yellow fever	Attenuated virus	Travelers to affected areas

Table 17.1 Some Important Immunizing Agents for Humans

Disease	Type of Vaccine	Persons Who Should Receive the Vaccine
Anthrax	Acellular	People in occupations that put them at risk of exposure, such as military personnel
Diphtheria	Toxoid	Children; adults receive a booster every 10 years
Haemophilus influenzae type b infections	Polysaccharide-protein conjugate	Children
Hepatitis A	Inactivated virus	Children who live in selected regions, people traveling to certain parts of the world
Hepatitis B	Protein subunit is produced by genetically engineered *Saccharomyces cereviseae* and purified	Children, adults in high-risk groups such as IV drug abusers, health care workers who might be exposed to infected blood, and contacts of infected people, homosexual men, and people who have multiple sexual partners
Influenza	Inactivated virus, usually given by injection in the United States, but as a nasal spray in parts of Europe	Adults over age 50, medical personnel, and people at increased risk for complications; given yearly, as the antigens of the virus change frequently
Measles	Attenuated virus	Children, people entering college, adults born after 1956 who have not been immunized, travelers to foreign countries, and HIV-infected people without severe immunosuppression
Meningococcal disease	Purified polysaccharide (4 serotypes)	Children and adults with certain conditions that put them at greater risk (for example, those without a spleen or who have certain complement system defects); people traveling to sub-Saharan Africa

Vaccines

- Induce artificial active immunity
- Preparation of living or inactivated microbe or virus or their components.
- Adjuvants help to induce better response
- Effective vaccines should be safe, few side effects, lasting protection, low cost, stable, easy to administer
- Should induce appropriate specific response

Attenuated immunizing vaccines

- Use modified live microbe/virus
- Induce infection & mild disease and solid long lasting immunity.
- Single dose can induce immunity
- Potential for spread to other people helps to develop HERD IMMUNITY
- Disadvantages: may cause disease, cannot use in pregnancy, require refrigeration
- Examples: measles, mumps, rubella, Sabin polio vaccine, (Vaccinia (for smallpox))

Inactivated Immunization

- Inactivated by chemical treatment but still antigenic
- Cannot cause infection
- Disadvantages: require several boosters, may cause side effects

- Whole agent--Use inactivated bacteria or virus
  - Examples : Salk polio vaccine, diphtheria & tetanus toxoids

Inactivated Immunization: Subunit vaccines

- Use isolated antigens or antigen fragments: a subunit of the total agent
  - bacterial toxin (toxoid), protein subunit, polysaccharide
  - e.g vaccines against meningococci, pneumococci, pertussis, *H. influenza*
  - Recombinant vaccine, e.g. Hepatitis B. Require several doses.

TABLE 17.2 The Effectiveness of Universal Immunization of Children in the United States During the Twentieth Century

Disease	Cases per Year Before Immunization	Decrease After Immunization
Smallpox	48,164 (1900–1904)	100%
Diphtheria	175,885 (1920–1922)	100%
Pertussis (whooping cough)	147,271 (1922–1925)	95.7%
Tetanus	1,314 (1922–1926)	100%
Paralytic poliomyelitis	16,316 (1951–1954)	100%
Measles	503,282 (1958–1962)	100%
Mumps	152,209 (1968)	99.6%
Rubella (congenital syndrome)	823 (estimated)	99.4%
Haemophilus influenzae type b infections	20,000 (estimated)	99.7%

TABLE 17.3 Recommended Childhood Immunization Schedule in the United States (2000)

Vaccine	Birth	1 mo	2 mo	4 mo	6 mo	12 mo	15 mo	18 mo	4–6 yrs	11–12 yrs	14–16 yrs
Hepatitis B	First dose	Second dose			Third dose						
Diphtheria, tetanus (Td) acellular pertussis (DTaP)			DTaP	DTaP	DTaP		DTaP	Subsequent doses		Td	
Haemophilus infuenzae type b (Hib)			First dose	Second dose	Third dose	Subsequent doses					
Poliovirus (IPV-inactivated polio vaccine)			First dose	Second dose	Third dose					Subsequent doses	
Measles-mumps-rubella (MMR)						First dose			Second dose	To be assessed and given if necessary	
Varicella (chickenpox-Var)						First dose				To be assessed and given if necessary	

Range of acceptable ages for vaccination indicated by colors:

First dose | Second dose | Third dose | Subsequent doses | To be assessed and given if necessary

Future developments & information

- HIV/AIDS, Malaria, cancer
- Use of DNA alone
- Further information: www.immunizationinfo.org

  vaccine.chop.edu (Children's Hospital of Philadelphia)
- Developing New Smallpox Vaccines, in EID, vol7, #6, 2001. On line at www.cdc.gov/eid

Serology

- Testing for the presence of a specific antigen using specific antibody (antiserum)
- Examples: ELISA blood test for HIV,

  home pregnancy test

http://www.sumanasinc.com/webcontent/animations/content/ELISA.html

Types of antibodies used for diagnostic purposes

- Polyclonal antibodies: Animals repeatedly immunized to develop very high antibody levels (the protein can be the organism of interest, a protein from its wall or human antibodies)

- Monoclonal antibodies developed when animal spleen cells are fused with malignant myeloma cells. These cells are then selected for those that produce only one kind of antibody in very high (and pure) amount.

Thanks