

History of Vaccines

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Disclosures

- No financial conflict or interest with the manufacturer of any product named during this course.



Disclosures

- I will not present the use of any vaccine in a manner inconsistent with the label
- I will not present investigational new drugs



Disclosure

- I do NOT have a degree in HISTORY



The Early Years

- Early homeopathic attempts
- Vaccination
- Development of attenuation
- 1st Inactivated vaccines
- Theories of immunization

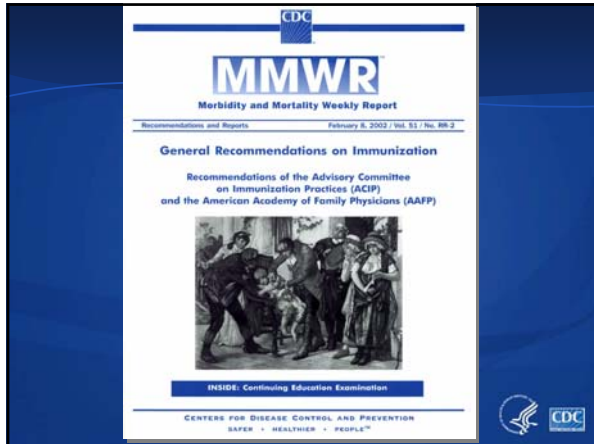


Variolation

- Introduction of variola virus in order to prevent variola (smallpox) infection
 - 16TH Century – India
 - 18th Century – China, Turkey

Lady Montagu, Charles Maitland, brought variolation to England





Smallpox Vaccination

- 1774 Benjamin Jesty, determined milkmaids were immune from smallpox due to cowpox
- Inoculated his wife and 2 children with cowpox
- First example of vaccination

Smallpox Vaccination

- Adopted slowly in North America in early 1800s
- Alternative progressive and regressive laws mandating vaccination
- Use increased when discovered that vaccine cowpox virus could be propagated in cows and not arm to arm

Attenuation

- The weakening of a microbe necessary to produce a live vaccine that will replicate but will not cause disease in the host

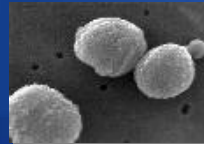
Louis Pasteur

- Left a vial of chicken cholera exposed to the air
- Found that the substance provided protection but did not cause disease



Louis Pasteur

- 1877 - Developed an animal anthrax vaccine
- 1880 - Isolated *Streptococcus pneumoniae*
- 1885 - Developed and tested a Rabies Vaccine



Live Attenuated Vaccines

- Discontinued
- Smallpox?
- Rabies
- Cholera
- Current
- Tuberculosis
- Yellow fever
- Polio
- MMR
- Typhoid
- Varicella
- Rotavirus
- LAIV
- Zoster



Development of Inactivated Vaccines

- Development of whole-inactivated vaccines
- Methods of inactivation
- Evolution of immunology
- Other methods of production

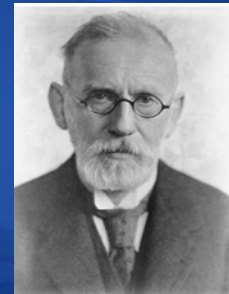
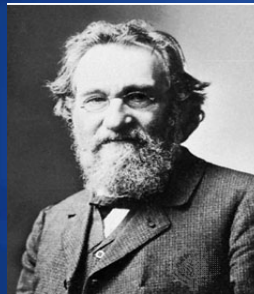


Whole Inactivated Vaccines

- Salmon and Smith – developed a Salmonella vaccine (heat killed)
- Vaccines to prevent typhoid fever, plague and cholera
- Methods of inactivation: heat, phenol, formalin



New (late 1800s) Theories of Immunity



Cellular Theory of Immunity

- Elie Metchnikoff
- Discovered body cells that ingested invading pathogens “Phagocytes”



Receptor theory

- Paul Ehrlich
- Toxin-antitoxin interactions
- Used to develop the theory of humoral immunity



Principles of Vaccination

Antigen

- A live or inactivated substance (e.g., protein, polysaccharide) capable of producing an immune response

Antibody

- Protein molecules (immunoglobulin) produced by B lymphocytes to help eliminate an antigen



Development of Diphtheria Antitoxin

- Emil Von Behring with Kitasato, developed passive antibody product Antitoxin



Principles of Vaccination

Passive Immunity

- Protection transferred from another person or animal as antibody

A2



Principles of Vaccination

Active Immunity

- Protection produced by a person's own immune system
- Usually permanent

A1



Other Methods of Inactivation

- Creation of toxoid
- 1923 Glenny and Hopkins, Ramon – diphtheria (formalin, heat)
- 1926 Zoeller(s) – tetanus toxoid



The Middle Years

- Development of new culture methods
- New risk-benefit balancing



New Culture Methods

- Development of Bacille Calmette-Guerin (BCG) vaccine
- 1906 – *Mycobacterium bovis* passaged 230 times in



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New Culture Methods

- Goodpasture – 1931 discovered that chorioallantoic membrane of a fertile hen's egg can be a medium for vaccine viral growth
 - Influenza vaccine
 - Yellow fever vaccine
 - Measles, mumps vaccine
 - Some rabies vaccine



Human Cell Culture Vaccines

- John Enders, Fredrick Robbins, Thomas Weller
- 1949 – Grew poliovirus in human fibroblasts from skin and muscle
- 1954 Won nobel prize
- 1954 Salk polio vaccine trials (over a million children)
- Polio eliminated from Western Hemisphere



Human Cell Culture Vaccines

- Rubella vaccine – human fibroblasts
- Wistar-RA27/3 strain – Stanley Plotkin
- Rubella eliminated from U.S. 2004



Vaccine Safety

- 1942 – Military vaccination with yellow fever vaccine
- Stabilized with human plasma from HepB sAg positive persons
- 50,000 cases of hepatitis, 62 deaths



Vaccine Safety

- Cutter incident - 1955
- 269 cases paralytic polio detected in vaccine recipients
- Result of incomplete inactivation/filtering



Recent Developments

- New technologies
- Eradication and elimination of disease



New Technologies

- Recombinant technology
 - Hepatitis B vaccine
 - Human Papillomavirus Vaccine
- Reassortant technology
 - LAIV vaccine
 - Pentavalent Rotavirus Vaccine



Polysaccharide Vaccines

- Linking a polysaccharide to a protein
- Pure polysaccharide vaccines
 - Pneumococcal– 1977
 - Meningococcal– 1978
 - Haemophilus 1985



Protein Conjugation Technology

- Pure polysaccharide conjugated to protein carrier
- Stimulates a T-dependent immune response
- Better boosting, longer duration of immunity, more effective at younger ages



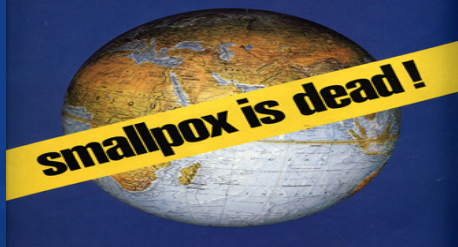
Conjugate Vaccines

- Hib – 1991
- Pneumococcal conjugate vaccine – 2000
- Meningococcal conjugate vaccine - 2005



WORLD HEALTH

THE MAGAZINE OF THE WORLD HEALTH ORGANIZATION · MAY 1980



Success of Vaccines

- Smallpox – eradicated 1980
- Polio – eliminated from Western Hemisphere – 1991
- Measles – eliminated from U.S. 2000
- Rubella – eliminated from U.S. 2004



Ten Most Important Discoveries in Vaccinology During the Last Two Decades*

- Acellular pertussis vaccine
- Combination vaccines
- Varicella vaccine
- Live influenza vaccine
- Rotavirus vaccine
- Protein conjugated bacterial polysaccharides
- Genetic engineering
- Attenuated vectors
- Transgenic plants and plant viruses
- Naked DNA

*Stanley Plotkin, in the Jordan Report



The Jordan Report 20th Anniversary

Accelerated Development of Vaccines 2002



Link to the *Jordan Report* from NIP website



