A Short Historical Perspective on Immunization Philip LaRussa, MD June 1, 2020

Course Number PB-VI01P: Development of a Vaccine During a Pandemic Course Directors: Philip LaRussa, MD and Lawrence Stanberry MD, PhD

Readings

- Plotkin's Vaccines
 - Plotkin, Orenstein, Offit, Edwards, 7th edition, Elsevier, 2017
- Immunology
 - D. Male & S. Peebles & V. Male, 9th edition, Elsevier, 2020
- Posted articles

- "Ancient Times", the Balochi people
 - encouraged children with wounds on their hands to touch skin lesions of cow and camelpox
- "Centuries ago" Variolation in India & China?
 - inoculation of fluid or scabs from smallpox lesions into skin or intranasally of smallpox-susceptibles
 - usually mild illness, occasionally severe disease with spread to others
- 11th century, Iran
 - applied dried liver/ rabid dog on wound of bitten person



1721, Lady Mary Montague: observed variolation in Turkey & promoted its use in Europe



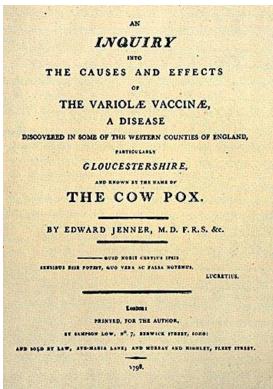
1774, Benjamin Jesty's tombstone: To the Memory OF Benj.in. Jesty (of Downshay) who departed this Life, April 16th 1816 aged 79 Years. He was born at Yetminster in this County, and was an upright honest Man: particularly noted for having been the first Person (known) that Introduced the Cow

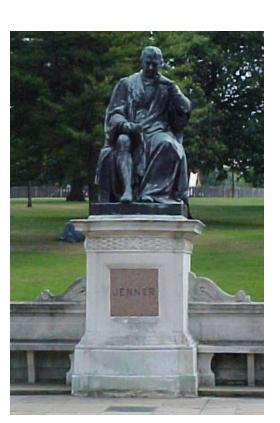
Pox by Inoculation, and who from his great strength of mind made the Experiment from the (Cow) on his Wife and two Sons in the Year 1774

1796, Sir Edward Jenner

- milkmaids who had cowpox (vaccinia?) were immune to smallpox
- inoculated fluid from cowpox lesions into the skin of smallpox susceptible people (calf lymph-derived vaccinia virus)
 - "1st" documented use of a less virulent related species to protect against an exclusively human pathogen



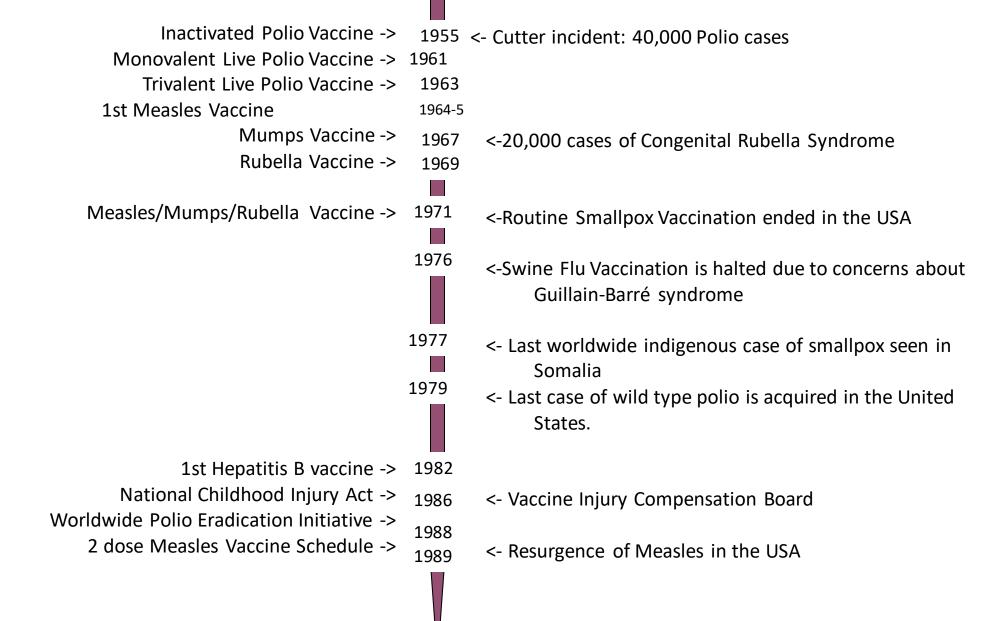




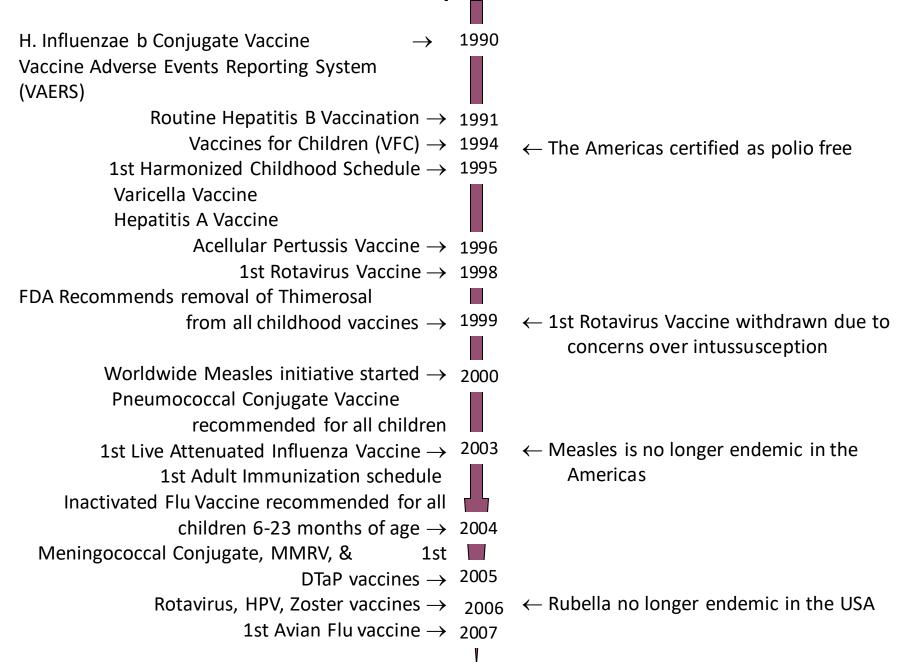
- 1886, Salmon/Smith: killed hog cholera "virus" vaccine (salmonella)
 - led to killed vaccines for typhoid, cholera & plague
- 1909, Smith: inactivated diphtheria toxin (toxoid) protects guinea pigs
 - led to diphtheria & tetanus toxoid vaccines for humans
- 1927, Bacillus of Calmette & Guerin (BCG)
 - attenuated by passage in beef bile over 13 years of Mycobacterium bovis
- 1931, Goodpasture: chorioallantoic membrane/hen's egg
 - safe, reliable method for growing viruses for vaccines
- 1937, Live attenuated yellow fever vaccine
 - passage in mouse brain & chorioallantoic membrane/hen's egg (17D strain)
- 1955, Salk: formalin-inactivated polio vaccine (IPV)
- 1962, Sabin: Live attenuated polio vaccine (OPV, TOPV)

- 1885: Louis Pasteur vaccinates Joseph Meister with rabies vaccine
 - Air-dried infected rabbit spinal cord:
 - started with avirulent virus, then proceeded with a series of more virulent strains
 - Coins "vaccination" in honor of Jenner
- 1955, Jonas Salk, senior:
 - formalin-inactivated polio vaccine (IPV)
- 1962, Albert Sabin:
 - live attenuated polio vaccine (OPV, TOPV)

Modern Vaccine Development Timeline: 1955 - 1989



Modern Vaccine Development Timeline: 1990-2007



Modern Vaccine Development Timeline: 2008-Present

2008: DTaP-IPV

• 2009: HPV-2 (Human Papilloma Virus 16 & 18 Vaccine)

• 2010:

- MCV4 (Menveo: meningococcal groups A, C, Y, W-135 oligosaccharides-Diphtheria CRM197 Conjugate Vaccine)
- PCV13 (Pneumococcal Conjugate Vaccine, 13 serotypes)

• 2014: HPV-9