Vaccination
Past, Present and Future

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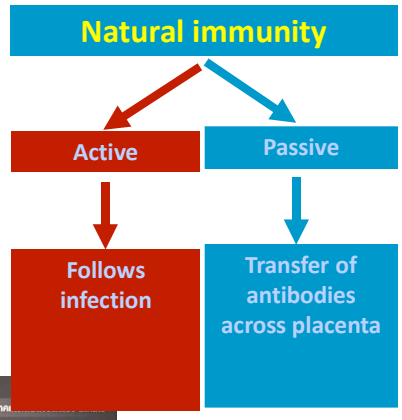
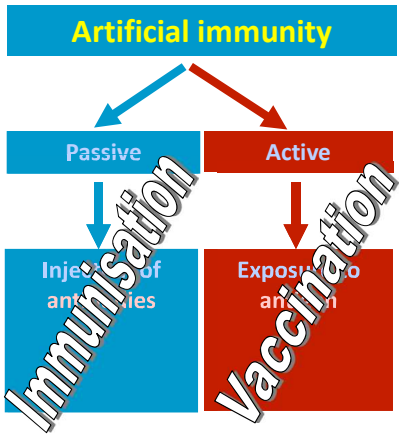
Prevention of Infectious Diseases

- Avoidance
- Personal hygiene
- Sanitation
- Vaccine
- Passive immunoprophylaxis
- Antimicrobial agent and antiseptic

Passive and active immunity





Outline of the Development of Human Vaccines

Live attenuate vaccine

- 18th Century
  - Smallpox vaccine 1798
- 19th Century
  - Rabies 1885
- Early 20th Century
  - BCG 1927
  - Yellow fever 1935

Outline of the Development of Human Vaccines

Killed whole cell vaccines Purified protein

- 19th Century
  - Typhoid 1896
  - Cholera 1896
  - Plague 1897
- Early 20th Century
  - Whole cell pertussis 1926 Diphtheria 1923
  - Influenza 1936 Tetanus 1927
  - Rickettsia 1938

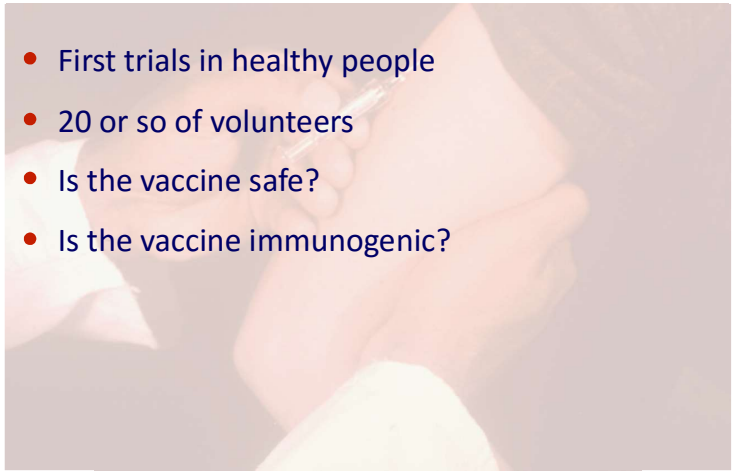
After World War II

- Live attenuated
  - Polio (Sabin)
  - Measles
  - Mumps
  - Rubella
  - Adenovirus
  - Typhoid Ty21a
  - Varicella
  - Rotavirus (Reassortment)
  - JE (Imojev)
  - Zoster
  - Dengue
  - Zigka
- Killed organisms
  - Polio (injected)
  - Rabies
  - Japanese encephalitis
  - Hepatitis A
  - Enterovirus 71

After World War II

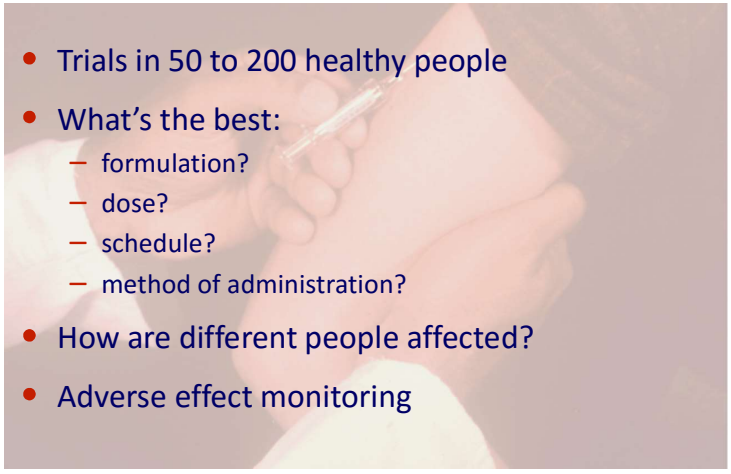
- Purified protein or Polysaccharide
  - Pneumococcus
  - Meningococcus
  - H.influemza b (PRP)
  - Hepatits B (plasma)
  - Tick-born enceph
  - Typhoid (Vi)
  - Acellular pertussis
- Genetically engineer
  - Hepatitis B recombinant
  - HPV vaccine
  - Pertussis toxoid

Clinical trials
Phase I trials



- First trials in healthy people
- 20 or so of volunteers
- Is the vaccine safe?
- Is the vaccine immunogenic?

Clinical trials
Phase II trials



- Trials in 50 to 200 healthy people
- What's the best:
  - formulation?
  - dose?
  - schedule?
  - method of administration?
- How are different people affected?
- Adverse effect monitoring

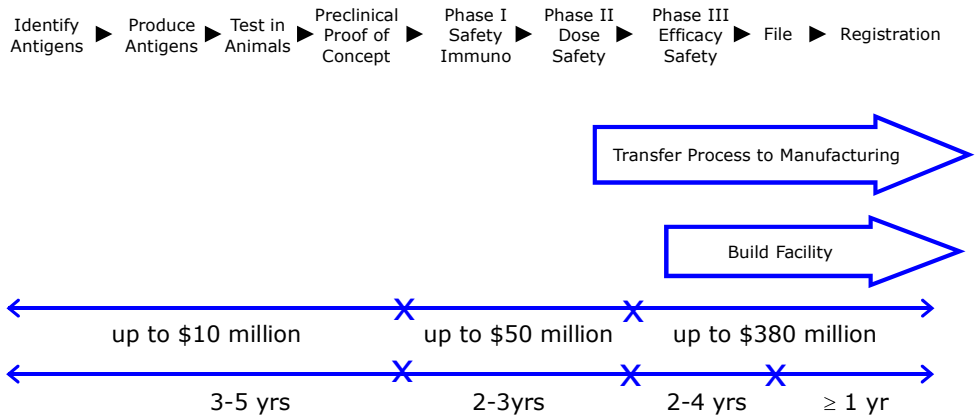
Clinical trials
Phase III trials

- Trials in 100s or 1000s of people
- Is the vaccine safe?
- Is the vaccine protective?
  - How does its immunogenicity compare with existing vaccines?
  - What's its protective efficacy?
- Do different production lots have similar effects?

Clinical trials
Phase IV trials

- Post-marketing trials
- Surveillance for adverse effects
- Additional data
  - New indications
  - Comparative trials
  - New schedules

Vaccine Development - long lead times and big investment required



The next 10 years in vaccinology

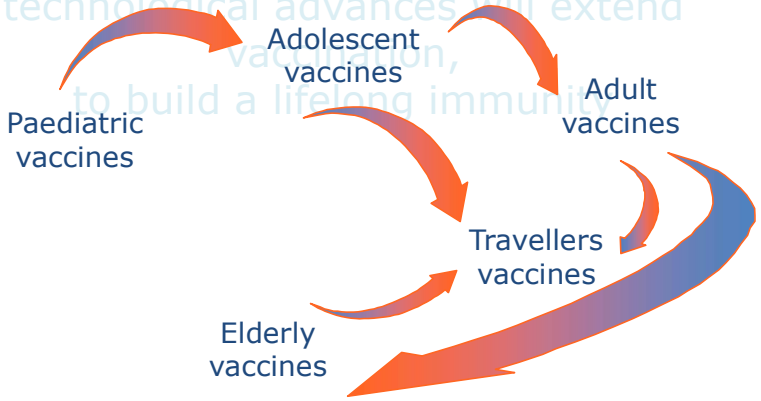
- Anti HIV vaccine will show partial efficiency
- Oral vaccine for enterotoxigenic E. coli and shigella for travellers
- Female adolescents will be immunized against some papilloma virus, CMV, herpes type 2
- Vaccine for high risk nosocomial infections
- Vaccine for prevention of chronic diseases
- Dengue vaccine for children less than 9 yrs old
- Malaria vaccine for travellers
- Ebola vaccine
- Zigka vaccine
- EV71 vaccine
- Cancer vaccines

The 10 most important discoveries in vaccinology during the last 2 decades

- Acellular pertussis vaccine
- Varicella vaccine
- Rotavirus vaccine
- Live influenza vaccine
- Protein-conjugated bacterial polysaccharide
- Genetic engineering
- Attenuated vector
- Combination vaccine
- Transgenic plant and plant virus
- Naked DNA

Vaccines for all life stages

Development of new vaccines, combinations of vaccines and technological advances will extend vaccination, to build a lifelong immunity



Current shifts in pediatric vaccination

- DTPw to DTPa vaccines
- OPV to IPV
- Separate to Combination
- Universal Hib vaccination
- Universal hepatitis B vaccination
- More new vaccines e.g. S pneu, Men C

Potential advantages of using combination vaccines

- number of injections
- compliance
- costs
- storage space
- complexity
- errors

Global Immunization

"Vaccines are one of the greatest achievements of biomedical science and public health"

Ref : MMWR; 1999, 48(12):243-248

"The greatest successes are those we cannot see; all the people who have not suffered or died from vaccine-preventable diseases"

Walter Orenstein, MD,
National Immunization Conference
April 29, 2002

But million lives still lost to vaccine-preventable diseases every year!

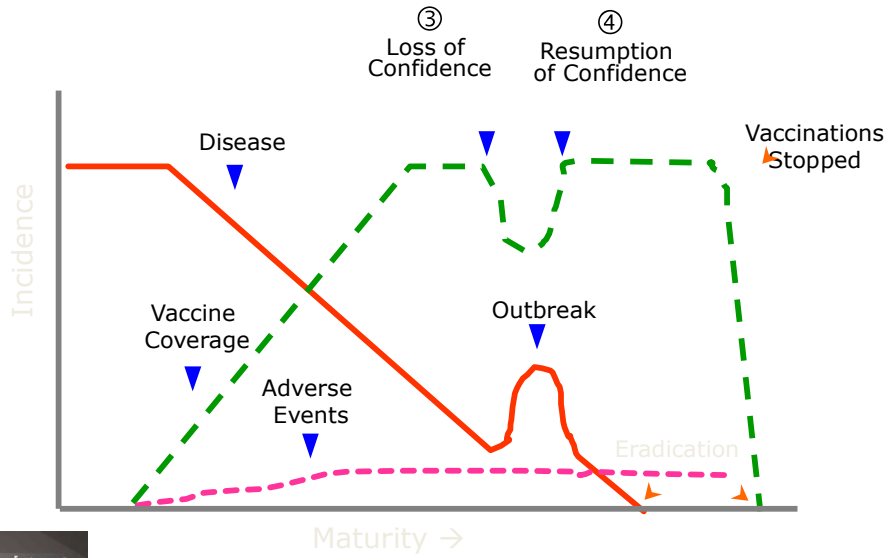
Prevention vs Therapy: a difficult task

Prevention	Therapy
→ Intervention in healthy people	→ Intervention in sick people
• compliance ↓	• compliance ↑
• willingness to pay	• willingness to pay
• acceptance of side effects	• acceptance of side effects
→ Long term benefit risk/cost assessment	→ Short term benefit
• epidemiology/vaccination strategy	

Features of postmodern society

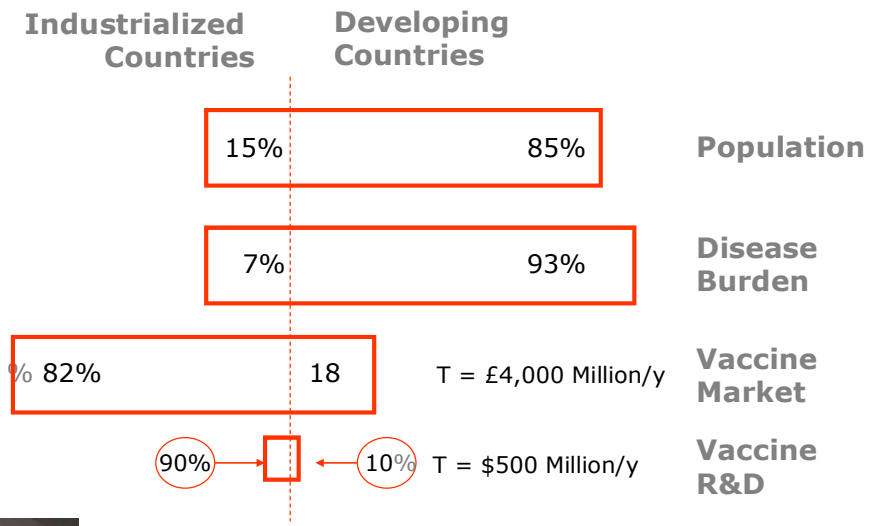
- Distrust of science
- Greater attention to risk
- Readiness to refer to the judiciary
- Better access to real-time information
- Physicians as knowledge managers rather than knowledge repositories

Natural History of Vaccination Programs



Robert Chen, CDC

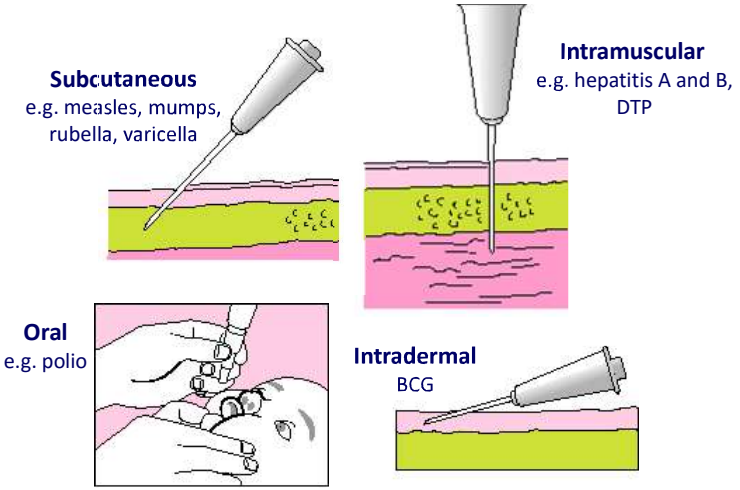
The world's vaccine market



*"An **ounce** of prevention is worth a **pound** of cure"*

Benjamin Franklin, 1706-1790

Methods of administration



Adverse reactions

- Local reactions
  - pain at injection site
  - redness
  - swelling
- Systemic reactions
  - fever
  - malaise
- Risk of infection (due to poor technique)

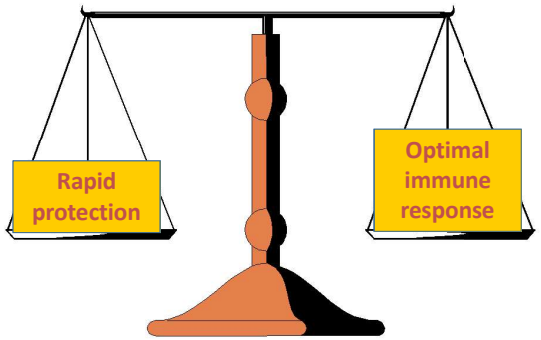
Contra-indications and precautions

- Hypersensitivity
  - adrenaline must be available
  - vaccinees should remain nearby for 30 minutes
- Acute febrile illness

Contra-indications and precautions

- Hypersensitivity
  - adrenaline must be available
  - vaccinees should remain nearby for 30 minutes
- Acute febrile illness
- Pregnancy
  - except for vaccination against tetanus
  - recently the ACIP has recommended flu vaccination in the 2nd and 3rd trimester

Vaccination policies
When to vaccinate?



Public health policy

The vaccination calendar of the future

Paediatric	Adolescent	Adult	Travellers	Elderly
OPV (eradication) MMR-V DTP-HBV-Hib-IPV + HAV + Rotavirus + Influenza + RSV + PIV + Otitis media + N. meningitidis + Lyme + TB	HBV-HAV + Herpes + Chlamydia + dTp booster + AIDS + CMV + Lyme + EBV + HPV + Dengue	HBV-HAV + Herpes + dTp booster + AIDS + Chlamydia + Lyme + TB + HPV	HBV-HAV + Typhoid + STDs + Shigella + Malaria + Yellow fever	Improved flu + RSV + S. pneumo. + Zoster

Stanley Plotkin