

# VACCINOLOGY AND EPI VACCINES

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# Overview of Immunity

- Immunity: ability of the body to protect itself against disease causing organisms
- Natural history of diseases
  - Colonization and infection
  - Incubation period
  - Outcome: recovery, chronic infection, disability (blindness, paralysis), death (childhood killers-measles, Hib infection, neonatal tetanus)

# Disease causing agents

- Micro-organisms: bacteria (Tb, Hib), parasites (malaria), fungi (candida), viruses (HBV, polio, yellow fever), prions (CJD)
- Specificity and sub-types
- Method of contact:
  - Inhalation: Tb, diphtheria, measles, whooping cough
  - Ingestion: poliomyelitis, hepatitis A
  - Skin: HBV, tetanus

# Types of immunity

- Non-specific (innate): first line defense, does not require prior exposure
- Specific (adaptive): requires prior exposure, hallmarks (memory, specificity, recognition of self and non-self), antigen-antibody
- Immune response: T & B lymphocytes, tolerance, hypersensitivity, immunodeficiency

# Acquisition of Immunity<sup>1</sup>

- **Natural immunity**: from infection with the microbe in nature, e.g. measles resulting in protection from future exposure (note notion of prior exposure)
- **Artificial immunity**: vaccine or immunoglobulin administration
  - **Vaccine**: organism or toxin, either killed or live but attenuated (organism) or inactivated (toxin). Live vaccines (BCG, polio, measles); killed vaccines (pertussis, polio), toxoids (tetanus, diphtheria), subunit (hep B).
- **Passive immunity**: from mother or Ig infusions

# Immunization

- Administration of vaccine: potent immune response in a few weeks, several injections for some (DPT), some one shot (measles). Booster doses may be necessary (hep. B).
- Vaccines are safe, side effects (AEFI) rarer than complications of disease prevented. Vaccines are fragile (storage).
- AEFI: hypersensitivity, human errors (poor or absent training, or level).

# What is a vaccine

- Dictionary (Dorland's 29th 2000)

Attenuated or killed microorganisms or proteins

derived from them, administered for the prevention, treatment, or amelioration of infectious diseases

Practical (2004)

- Product administered to induce an immune response for prevention or treatment of disease

# Similarities between vaccines and other drugs

- Vaccines are also medicines
- Potential for adverse effects
- Multiple ingredients
- Potential for interaction with disease and other medicines
- Also need to comply with standards of safety, efficacy and quality

# The Principles of Immunization

- To prime recipient's immune response
- To generate B and T memory cells
- To heighten immune response (humoral and cell mediated) to pathogens
- Vaccine(s) should
  - have minimal adverse effects
  - prevent/reduce severity of infectious diseases (effectiveness)
  - be of assured quality and available for general use

# The ideal vaccine

- Immunogenic
- Long lasting immunity
- Safe
- Stable in field conditions
- Combined
- Single dose
- Affordable (and accessible) to all

# Categorization of current vaccines

- **Live attenuated**: viruses (oral polio, measles, mumps, rubella, yellow fever), bacteria (BCG, cholera)- long lasting immunity, very fragile (cold chain), mutation to pathogenicity
- **Killed vaccines**: viruses (hep. A, Salk polio), bacteria (pertussis, cholera)- intermediate immunity, several doses may be required
- **Sub-unit vaccines incl. toxoids**: tetanus, hep. B, acellular vaccines, conjugate polysaccharide vaccines linked with suitable carrier proteins (Hib). Also single or polyvalent vaccines.

# Methods to enhance immunity

- Conjugation e.g. Hib vaccine
- Adjuvants e.g. aluminium salts

**Why are adjuvants used?**

**What adverse reactions are associated with aluminium as an adjuvant?**

# ROUTE OF ADMINISTRATION

- Route: elicit IR with minimal risk
- Deep IM for vaccines with adjuvants (depot effect, less granuloma formation)
- ID - better for live vaccines, e.g. BCG
- Intranasal influenza vaccine - increased risk of Bell's Palsy reported
- New routes may have other safety risks

# Adverse effect following immunization AEFI?

A medical incident that takes place after an immunization, causes concern, and is believed to be caused by immunization

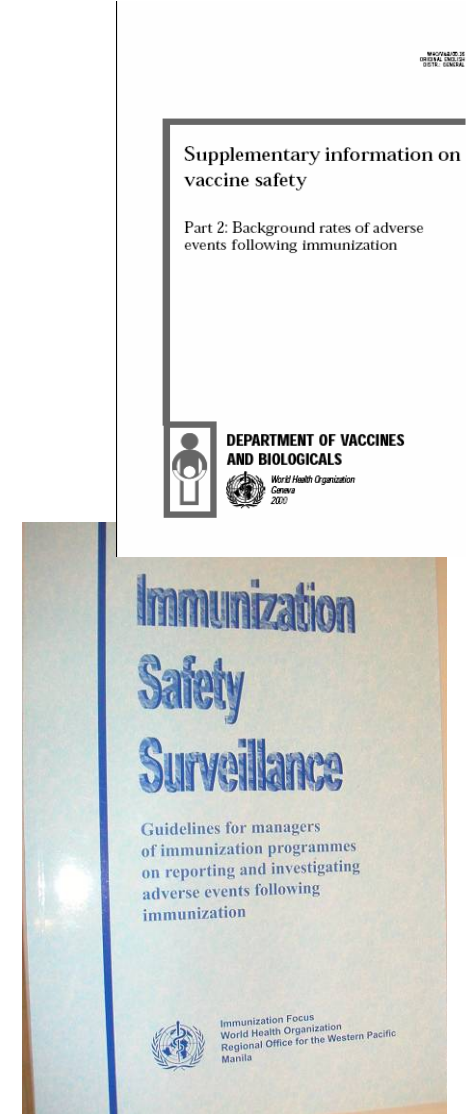
- ◆ **Vaccine reaction** - caused by vaccine's inherent properties
- ◆ **Programme error** - caused by error in vaccine preparation, handling, or administration
- ◆ **Coincidental** - happens after immunization but not caused by the vaccine or vaccination process (a chance association)
- ◆ **Injection reaction** - anxiety about or pain caused by the injection not vaccine/vaccination
- ◆ **Unknown** - cause cannot be determined

# VACCINE REACTIONS

- Common, minor reactions
  - Part of immune response to vaccine, Settle on their own
  - Warn parents and advise how to manage
  - e.g. fever, malaise etc.
- Rare, more severe reactions
  - Usually require clinical management, e.g., severe allergic reaction (such as anaphylaxis), Vaccine specific reactions (e.g. BCG osteitis)

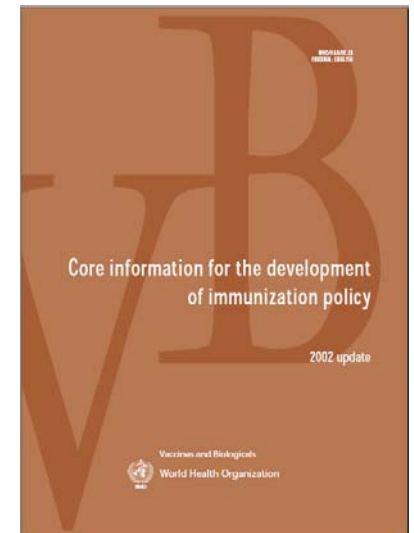
# Rates of Rare Reactions

- Can be used to assess extent of underreporting or to identify trends of concern (e.g. higher than expected rates reported in system)
  - Consider product quality
  - Special risks in local population
- Time to onset of events useful to investigate and verify validity of the case



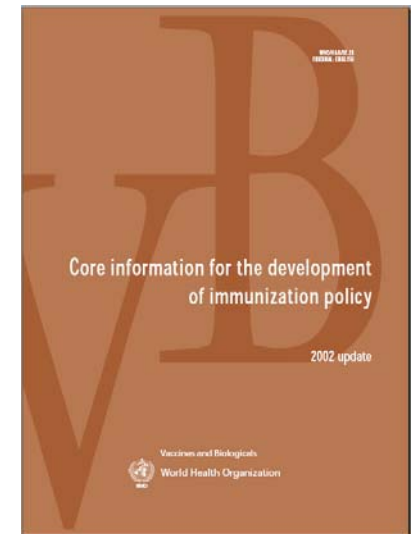
# Immunizing special populations: pregnant women

- Safety concerns: potential teratogenicity and induction of abortion, vaccination generally deferred to 3<sup>rd</sup> trimester
- Vaccinate only if indicated
- Live viral vaccines usually not recommended
- Birth defect unrelated to the vaccine may be falsely attributed to the vaccine
- Newer vaccines/regimens may have unknown effects - use with caution
- Women (especially adolescents) may not be aware of or disclose pregnancy , screen?



# Immunizing the immunocompromised

- Patients may be immunocompromised due to
  - HIV , congenital immune deficiencies, immuno-suppression, e.g. steroids, chemotherapy, etc., malnutrition
- May not respond adequately to vaccination
- Risk of disseminated infection from live attenuated vaccines
- In some cases, recommended to weigh risk of exposure to disease (e.g., BCG in asym HIV +ve children)



# CONTRAINDICATIONS

## True contraindications are rare

- Current serious febrile illness: delay vaccine
- History of severe reaction after previous dose (e.g. anaphylactic reaction)
- Evolving neurological disease (e.g. uncontrolled epilepsy)- avoid whole cell pertussis vaccine
- Type 1 hypersensitivity to egg - avoid yellow fever & influenza, can use vaccines made in chick fibroblasts
- Symptomatic HIV
  - avoid BCG and yellow fever, consider withholding measles vaccine in severely IC (monitor immune status), measles not recommended if person is seriously ill

# Importance of contra- indications

- Ignoring contraindications can lead to avoidable vaccine reactions
  - train vaccination staff on instructions, proper use of vaccine, and management of reactions
- Too many contraindications (not evidence-based) can decrease coverage and reduce public confidence in safety of vaccine
  - e.g., precautions stated in product labelling can sometimes be inappropriately used as absolute contraindications

# ANAPHYLAXIS

- Reported less from developing countries
  - Less sensitization?, Less reporting?
- Anaphylaxis is rare (1/1 000 000 vaccinats)
- Fainting is common and untrained staff may misdiagnose fainting/dizziness for anaphylaxis or vice versa
- Administration of adrenaline during a faint may be dangerous
  - PROMPT MANAGEMENT IS VITAL!

# Examples of real safety issues

- Rare "disasters" due to faulty production; risk drastically reduced by better production controls and better science
  - Lubeck incident (1929-30): occurrence of TB following vaccination
  - Cutter (inactivated) polio incident (1955)
- True **vaccine reactions**
  - Vaccine-associated paralytic polio
  - Mumps vaccine-associated aseptic meningitis
  - Rotavirus and intussusception
  - Bell's palsy following intranasal flu
  - Influenza vaccine and oculorespiratory syndrome

# Unproven associations and public concern.

- Influenza vaccine and Guillain Barré Syndrome
- MMR and autism, Crohn's disease
- Polio and HIV
- Hepatitis B and multiple sclerosis
- DTP and permanent brain damage
- DTP and increased risk of mortality
- Aluminium and macrophagic myofasciitis
- Bovine spongiform encephalopathy (BSE)
- Thimerosal and autism, neurodevelopmental problems
- Multiple vaccines given simultaneously

# Can vaccines overload the immune system?

- Giving multiple vaccines at the same time is safe
- People are exposed daily to hundreds of antigens
- Multiple vaccines work with the immune system to boost it
- Simultaneous vaccination protects against several diseases quickly
- Combo vaccines reduce discomfort and costs



# Steps in vaccine development

- Thousands of individual steps but most will be omitted for simplicity

- Recognize the disease as a distinct entity



- Identify etiologic agent
- Grow agent in laboratory
- Establish an animal model for disease
- Identify an immunologic correlate for immunity to the disease- Usually a serum antibody

- Inactivate or attenuate the agent in the laboratory—or choose antigens
- Prepare candidate vaccine following Good Manufacturing Procedures
- Evaluate candidate vaccine(s) for ability to protect animals

- Prepare protocol(s) for human studies
- Apply to MCC for Investigational New Drug (IND) approval
- Phase I human trials- Safety and immunogenicity, dose-response
- Phase II trials- Safety and immunogenicity
- Phase III trial(s)- Efficacy

- Submit Product Licensure Application MCC approval
- Advisory Committees review and make recommendations
- Marketing Post-licensure surveillance for safety and effectiveness (Phase IV)
- Long and complicated process
  - Usually takes 10-15 years
  - Many vaccine candidates fail for every success
  - Costs: \$100-\$700 million per successful vaccine

# Conclusion

- Immune response: antigen, antibody, cells-competent host
- Dysfunction: hypersensitivity reactions, auto-immunity, immunodeficiency
- Nature of vaccine important in scheduling
- Vaccine is a medicine but is different from other drugs because of its promotion and other

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**THANK YOU**