SAFE VACCINATION

MODULE IV

Technical Aspects - ESAVI

Pan American Health Organization

ESAVI Definition

- **Events supposedly attributable to vaccination or immunization (ESAVI)**

- **A set of symptoms that occur after a vaccination has been given, which causes concern and is supposedly attributable to vaccination or immunization.**

Pathogenesis

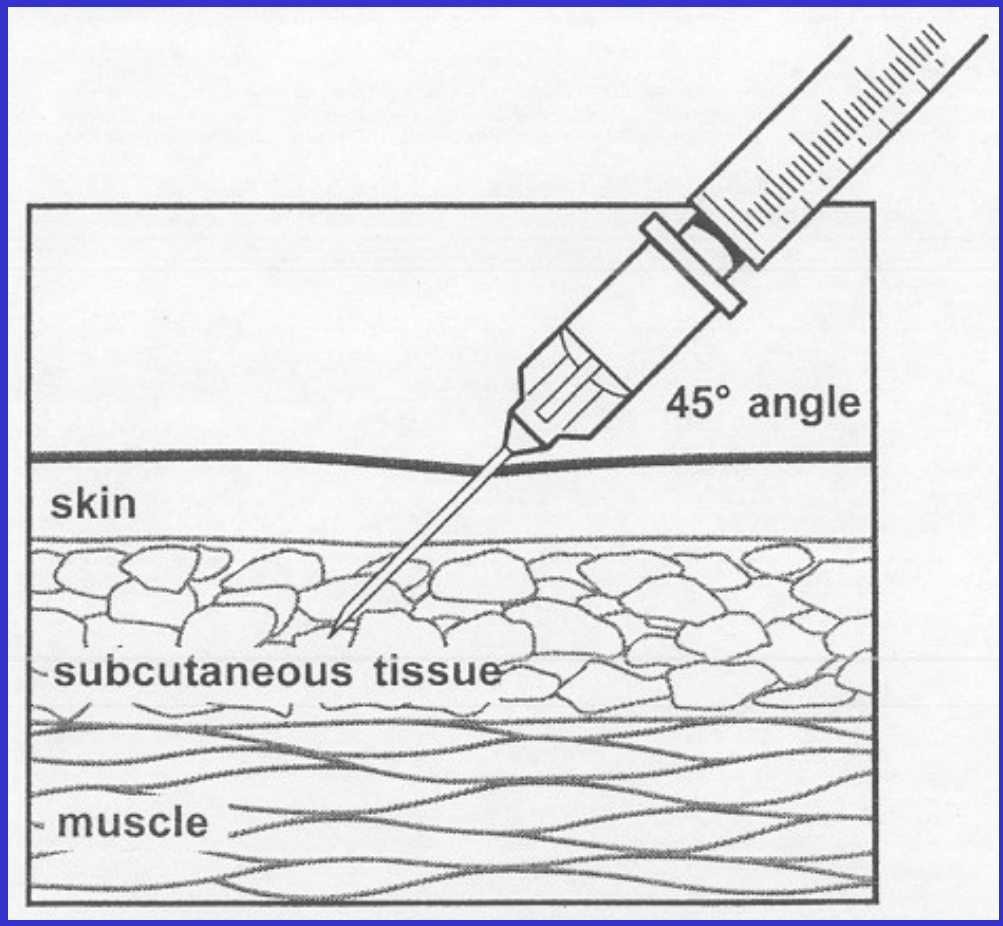
- Type of vaccine
- Administration route
- Composition of immunobiological products
- Type of host

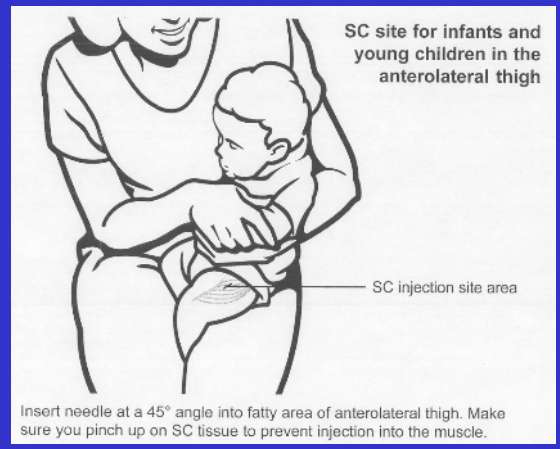
Type of vaccines

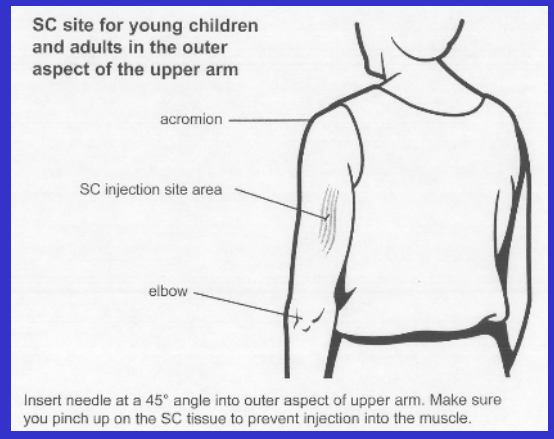
- **Life attenuated vaccines**
  - viral
  - bacterial

- **Inactivated**
  - viral
  - bacterial
  - toxoids
  - polysaccharides
  - antigen subunits

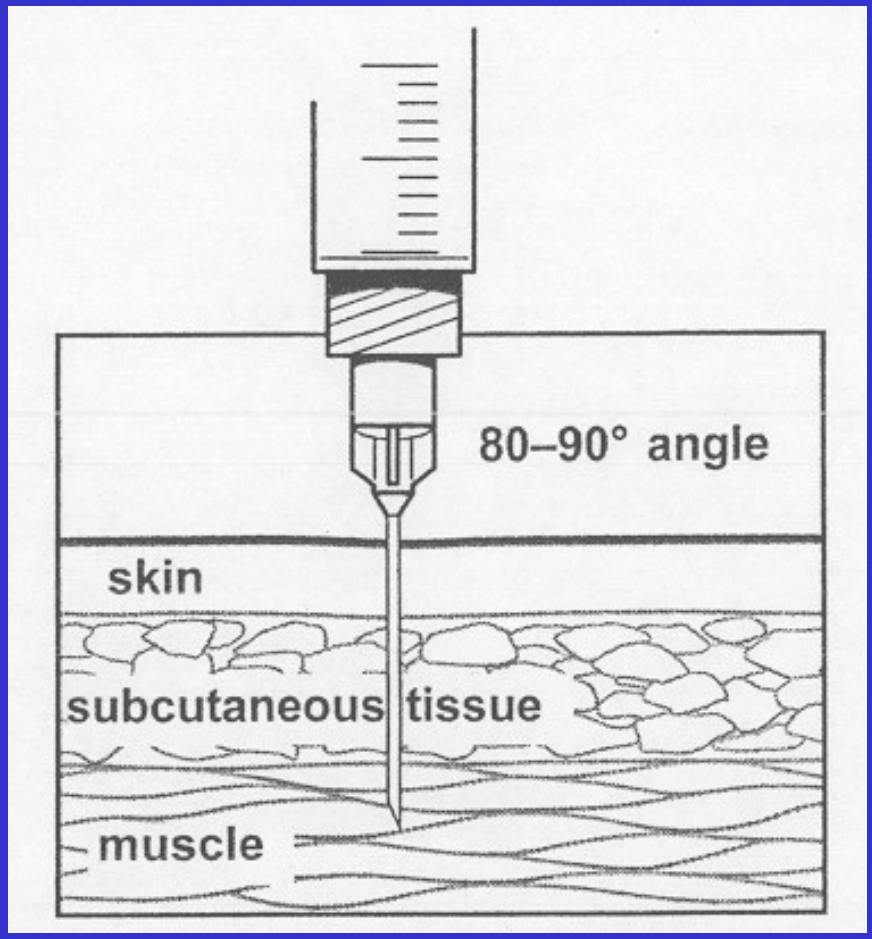
Administration (SC)

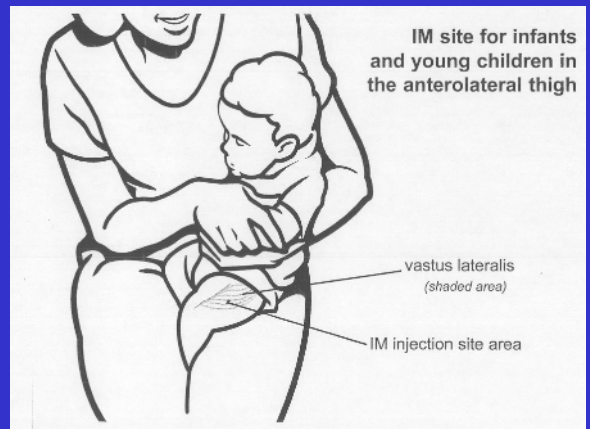




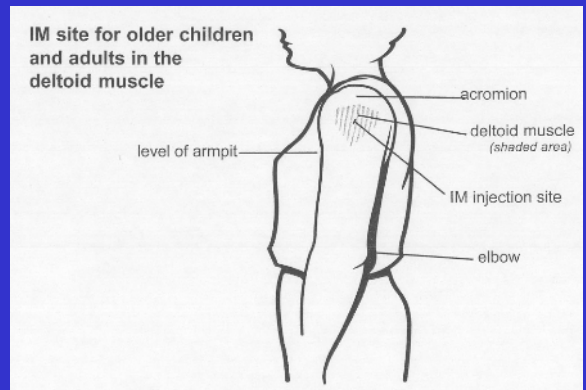


Administration (IM)





Insert needle at an 80–90° angle into vastus lateralis muscle in the anterolateral aspect of middle or upper thigh.



Insert needle at an 80–90° angle into densest portion of deltoid muscle—above the level of armpit and below the acromion.

Composition of immunobiological products

- Suspension liquid
- Preservatives, stabilizers and antibiotics
- Adjuvant

Type of Host
Special Situations

- Immunocompromised
  - Baseline disease
  - Medication
- HIV patients
- Pregnancy
  - Increased risk in the use of life attenuated vaccines
  - They may not respond adequately to vaccination

Immunization of special populations

WHO/ UNICEF Recommendations for vaccinating HIV patients and pregnant women

Vaccine	Asymptomatic	Symptomatic	Optimal time
BCG	Yes	No	Birth
DTP	Yes	Yes	2, 3, 4 months
OPV	Yes	No, IPV is available	2, 3, 4 months
Measles.	Yes	Yes (risk - benefit)	12 months
Hep B	Yes	Yes	0, 1, 6 months
Yellow Fever	Yes	No (needs more studies)	
Tet tox	Yes	Yes	5 doses

Immunization of pregnant women

- Potential teratogenicity and induction of abortion.
- Vaccination only if indicated.
- Life attenuated vaccines are not recommended.
- Birth defects can be falsely attributed to the vaccine.
- New vaccines / regimes should be used with caution.
- Pregnancy among adolescents: should it be screened before vaccination?

Types of adverse effects

1. Coincidental events

2. Programmatic errors

3. Reactions related to the inherent properties of the vaccine

Types of adverse effects

1. Coincidental events

Often misinterpreted as caused by vaccination because during the first years of their life children are more vulnerable to diseases and it coincides with the period during which most vaccines are given.

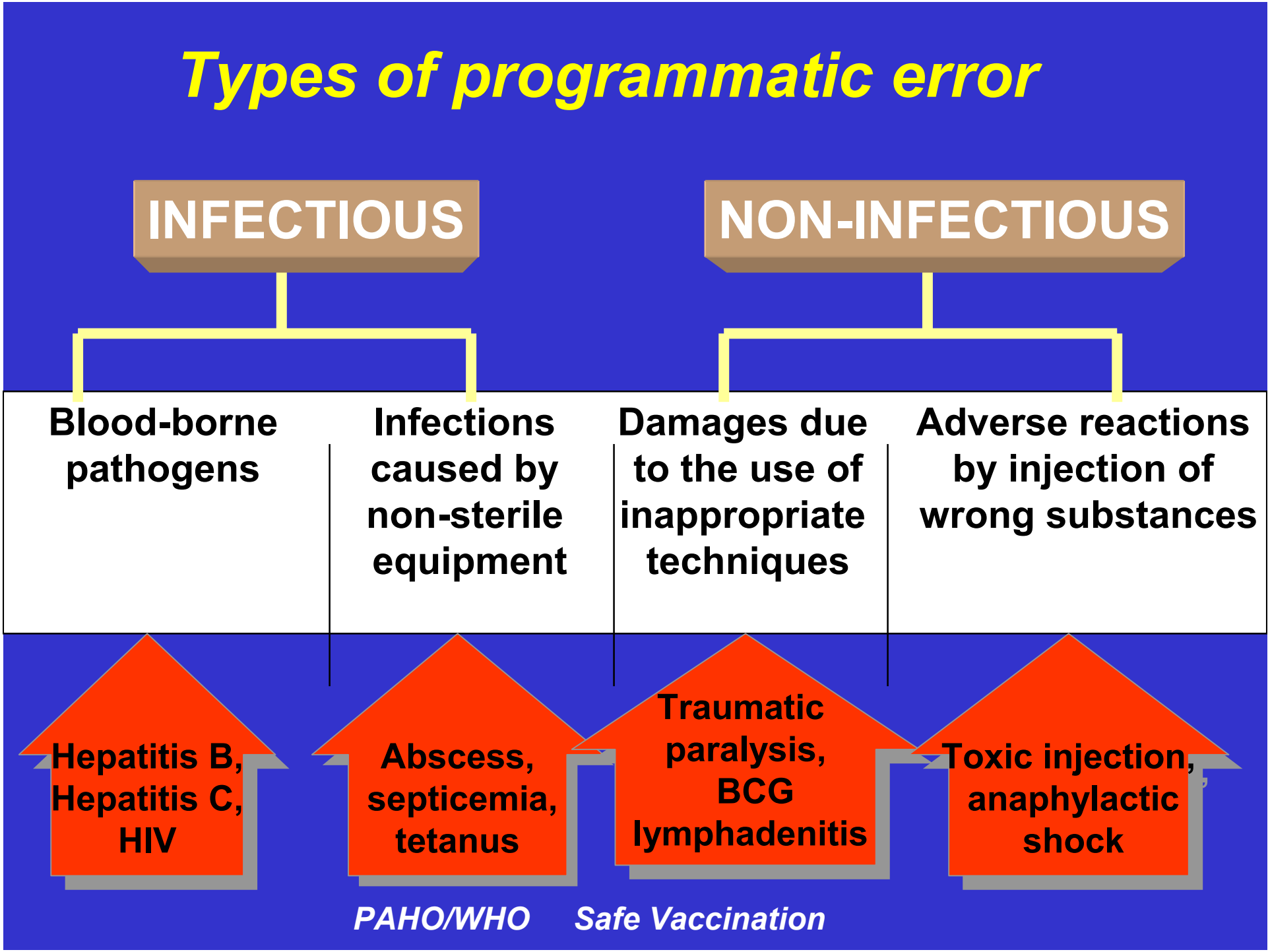
Types of adverse effects

2. Programmatic errors

Due to an error in the preparation, handling or administration of the vaccine.

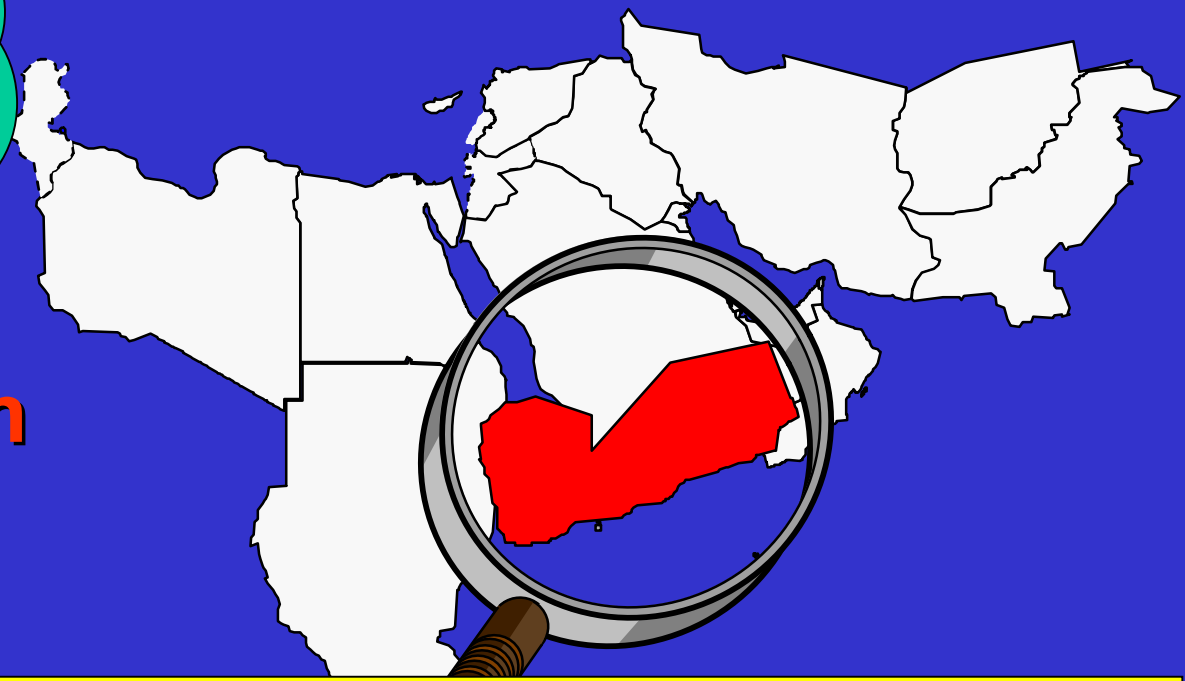
Corrective measures need to be implemented immediately and should include logistic, training and supervision aspects.

Types of programmatic error



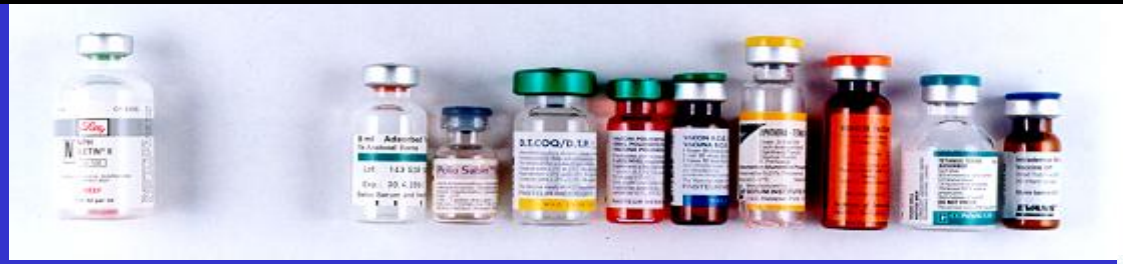
Programmatic error

Yemen 1997



Insulin given to 70 infants instead of DPT vaccine caused 21 deaths

Insulin vial



Vaccine vials

Medical incidents attributed to vaccination

- ✓ **Guatemala:** 1 infant died, suspicion of using a neuromuscular blocker (succinylcholine) as diluent for the measles vaccine, 1999

- ✓ **Cuba:** 3 infants died after receiving the measles vaccine. Revision indicates toxic shock syndrome, 2002

Operational program error	Predicted event
Non-sterile injection • Reuse of a disposable syringe or needle • Use of syringes that do not ensure adequate sterility • Contaminated vaccine o diluent • Use of freeze-dried vaccines for a period longer than indicated.	• Infection such as abscess localized in the injection area, sepsis, toxic shock syndrome or death. • Blood-borne infection such as hepatitis or HIV.
Reconstitution error • Reconstitution with the wrong diluent • Replacement of the vaccine or diluent with a drug.	• Local abscess by improper agitation • Adverse effect of a drug; for instance, insulin • Severe preventable reaction.

Operational error of the program	Predicted event
Injection in the wrong place • BCG applied subcutaneously • Very superficial administration of the DPT/DT/TT vaccine • Injection in the buttock.	• Local reaction or abscess • Local reaction or abscess • Possible damage to the sciatic nerve among infants.
Incorrect transport / storage	• Local reaction by frozen vaccine • Ineffective vaccine
Take no notice of contraindications	• Severe predictable reaction

Types of adverse events

3. Reactions related to the inherent properties of the vaccine

Classification of vaccine-related events

- Minor and more common
- Severe and less frequent

Reactions that may be attributed to vaccines

Vaccine	Local reaction (pain, swelling, redness)	Fever >38 C	Irritability, malaise & non-specific symptoms
BCG	90 - 95%	-	-
Hib	5 - 15%	2 - 10%	-
HepB	Adults: 15%; Child: 5%	-	1 - 6%
Measles MMR	~10%	5 - 15%	5% rash
Polio (OPV)	-	<1%	<1%**
Tetanus	~10%*	~10%	~25%
DPT	Up to 50%	Up to 50%	Up to 55%

* Rate of local reactions likely to increase with booster doses, up to 50-85%.

**Symptoms include diarrhea, headache and/or muscle pain.

Vaccine	Event	Onset interval	Rates per 1.000.000 doses
BCG	•Suppurative lymphadenitis •BCG osteitis •Disseminated BCG	2-6 months 1-12 months 1-12 months	100-1000 1-700 2
Hib	Nil known	-	-
Hepatitis B	•Anaphylaxis •Guillain-Barré Syndrome (vaccine obtained from plasma)*	0-1 hour 0-6 weeks	1-2 5
Measles /MMR[a)]	•Febrile seizures •Thrombocytopenia (low platelet count) •Anaphylaxis	5-12 days 15-35 days 0-1 hour	333 33 1-50

Vaccine	Reaction	Onset interval	Rates per 1.000.000 doses
OPV	Vaccine-associated paralytic poliomyelitis (VAPP)	4-30 days 20 -28 days	< 1 [b)] (-
Tetanus	•Brachial neuritis •Anaphylaxis •Sterile abscess	l hour 1-6 weeks -0-24 hours	5-10 1-6 6-10
DPT	•Persistent (>3 hours) inconsolable screaming •Seizures •Hypotonic, hypotensive episode (HHE) •Anaphylaxis •Encephalopathy	00-2 days 0-24 hours 00-1 hours 0-3 days	1.000-60.000 570 [c)] 570 20 0-1
Yellow fever	•Post-vaccination encephalitis •Allergic reaction/anaphylaxis	7-21 days 0-1 hour	500-4.000 in inf < 6 months 5-20

Clinical Management

Case definition

Actions to be taken in case of an event:

- Treatment
- Notification and Investigation
- Contraindication for a subsequent dose
- Health Care Center

Clinical management

- Local signs
- BCG Lymphadenitis
- Fever
- Inconsolable screaming
- Seizures
- Shock syndrome
- Hypersensitivity reactions

Clinical management

- Encephalopathy and encephalitis
- Exanthema
- Thrombocytopenic purpura
- Vaccine-associated paralysis
- Disseminated BCG
- Peripheral neuritis (brachial and sciatica)
- Toxic shock and septicemia

Anaphylaxis

- Type 1 hypersensitivity reaction
- Circulatory failure
- Bronchospasm +/- laryngospasm / laryngeal edema

  → Respiratory distress
- It may include itching, blushing, angioedema, edema, seizures, vomits, abdominal cramps or incontinence.
- It affects previously-sensitized patients.

Anaphylaxis

- Less reports in developing countries:
  - Less awareness?
  - Less reports?
- Anaphylaxis is not common (1 / 1 000 000 vaccinees)
- Faints are common
- Untrained personnel may confuse faint and dizziness with anaphylaxis or vice versa
- Administration of adrenaline in a blackout can be dangerous.
  - ***Rapid treatment is vital!***

Seizures

- Particularly associated with measles and the pertussis component of DPT vaccination
  - Febrile seizures: Temp > 38 C
  - Afebrile seizures: Normal temp.
- Febrile seizures are more common with pertussis.
- Association with non-febrile seizures has NOT been demonstrated.

Adverse reactions to BCG

Disseminated BCG:

- **Widespread infection: 1 to 12 months after BCG .**
- **Usually in immunocompromised patients.**
- **Confirmed by isolation of *Mycobacterium bovis* strains**
- **Treatment: anti-TB drug including rifampicin or izoniacid.**

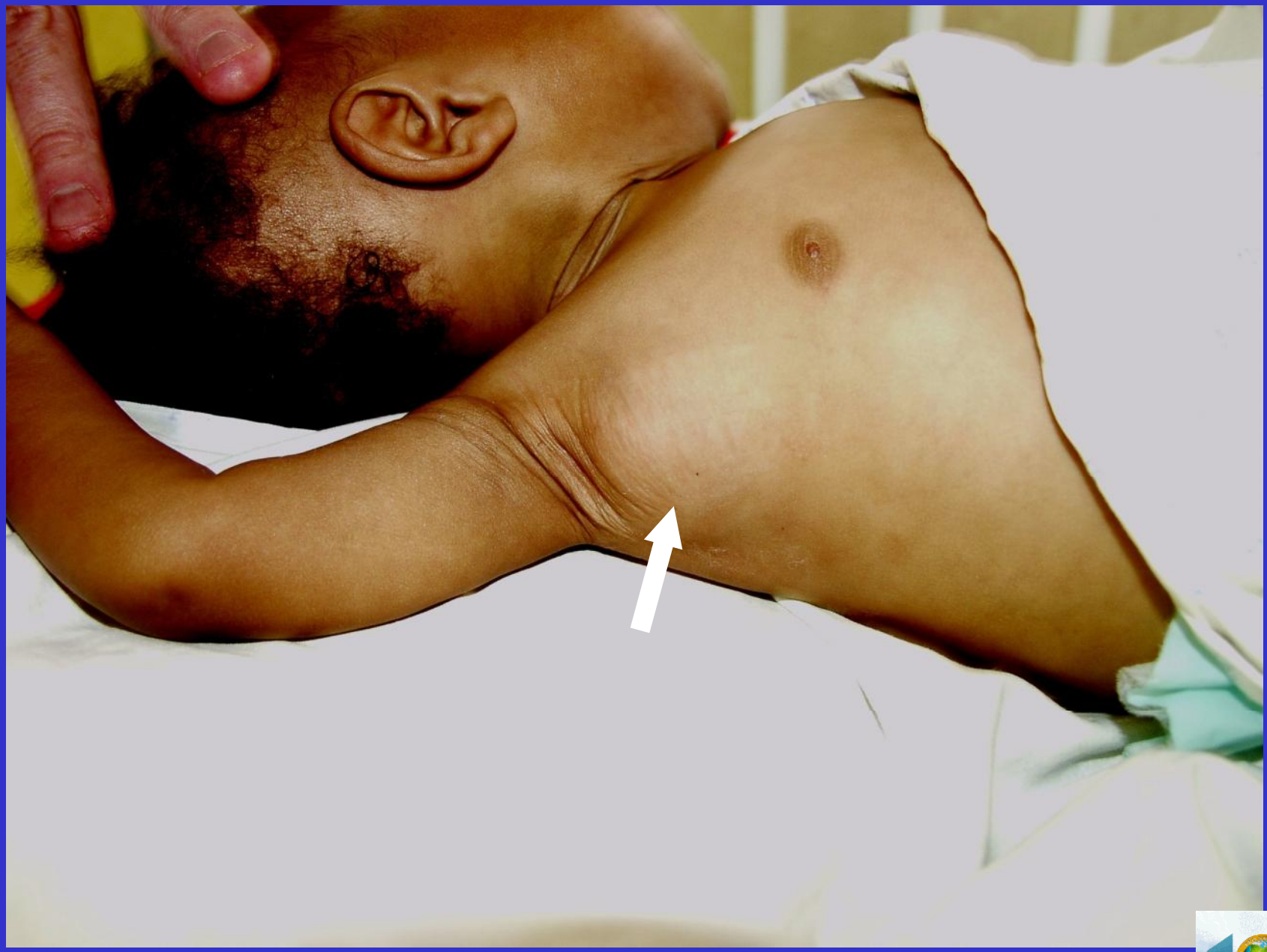
Osteitis / Osteomyelitis:

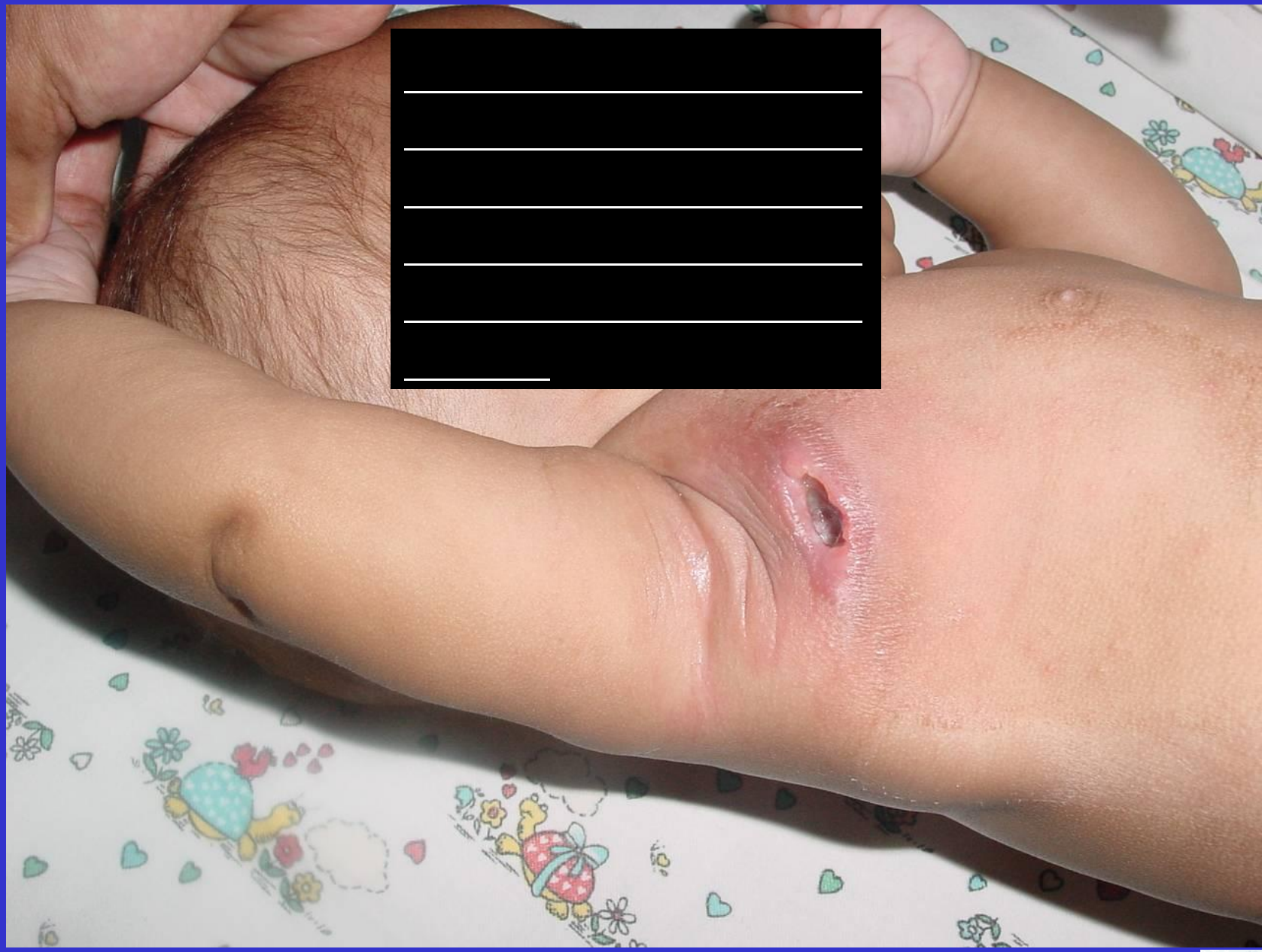
- **Infection of the bone with *M bovis* BCG strain**
- **Treatment: as with disseminated BCG patients**

Adverse reactions to BCG

Suppurative lymphadenitis:

- This occurs within 2-6 months of BCG vaccination.
- Case definition:
  - 1 lymph node > 1.5 cm in size / draining sinus over a lymph node
- Usually occurs in the armpit, on the same side as inoculation.
- Management:
  - The lesion will heal spontaneously over months
  - Manage only if the involve nodes stick to skin or form draining sinuses.
  - Surgical drainage?
  - Systemic treatment is ineffective.





Tetanus vaccine

Braquial Neuritis

- This presents with pain shoulder and upper arm.
- Weakness and wasting of arm and shoulder muscles.
- Sensory loss: not prominent.
- Occurs 2-28 days after vaccination.
- It is possibly a manifestation of immune complex disease.
- Management is symptomatic.

Encephalopathy and encephalitis

- Possibly associated with measles and pertussis vaccine.

- **Case definition of encephalopathy:**
  - **2 out of 3:**
    - **Seizures**
    - **Alteration of consciousness for one day or more.**
    - **Change in behavior for one day or more.**
- **Temporal relationship**
  - **Within 48 hrs with DTP**
  - **Within 7-12 days after measles or MMR**

Encephalitis and measles vaccination

- 8-9 days after vaccination (Wetbel 1998, Duclos 1998)
- This supports, but does not prove the possibility that measles vaccine was causative.
- Risk is less than 1 case per million

Hypotonic hypotensive episode (HHE or shock-collapse)

- Mainly associated with DTP
  - Case definition: an event of sudden onset occurring within 48 (usually less than 12) hours of vaccination and lasting from one minute to several hours.
- Age: < 10 years of age
- ALL of the following must be present
  - Hypotonic
  - Reduced responsiveness to stimulus
  - Pallor or cyanosis
- Transient, self limiting, IT IS NOT a contraindication to further vaccination.

Vaccine-Associated Paralytic Poliomyelitis (Oral Polio)

Occurs between:

- **4-30 days after receiving the oral polio vaccine or**

- **4-75 days after being in contact with a vaccinee.**

Yellow Fever Vaccine

Encephalitis

- ✓ **In infants under 6 months of age.**
- ✓ **Onset is 7-21 days after vaccination.**
- ✓ **There is no significant risk in older children and adults.**
- ✓ **Insufficient data on safety in symptomatic HIV+ patients: vaccine should be avoided in such patients**
- ✓ **Contraindicated in pregnancy (unless significant risk exists)**

Contraindications

Contraindications are uncommon

Severe febrile disease

- **postpone the administration of the vaccine.**

- **History of a severe ESAVI with a previous dose.**
- **Uncontrolled acute or chronic neurological compromise:**
  - **avoid the pertussis vaccine to whole cells (e.g. uncontrolled epilepsy)**
- **Egg Anaphylaxis (Type I Hypersensitivity)**
  - **Avoid yellow fever and influenza vaccination but vaccines made in chicken fibroblasts may be used.**
- **Symptomatic HIV**
  - **avoid BCG and yellow fever vaccination**

WHO Immunisation Policy 1996

PAHO/WHO Safe Vaccination

Contraindications

Vaccine	Contraindication
All vaccines	Anaphylactic reaction to the vaccine or its constituents. Severe febrile illness.
DTP	Encephalopathy within 7 days of administration.
OPV	Immunodeficiency, contact with immunodeficient patients*.
IPV	Anaphylactic reaction to neomycin, polymyxin B or streptomycin.

* Evaluate risk-benefit when administering HIV+ patients.

Adapted from Plotkin pg 66-67

Contraindications

Vaccine	Contraindication
MMR	Anaphylaxis, Pregnancy, Immunodeficiency.*
Hib	None
Hepatitis B	Anaphylaxis to some components.
Yellow Fever	Egg anaphylaxis, immunodeficiency.

* Evaluate risk-benefit when administering HIV+ patients..

Adapted from Plotkin pg 66-67

Conclusions

- It is important to understand the safety profile of the most common vaccines.
- The safety profile of vaccines depends on the risk factors of the person to be vaccinated.
- The ESAVI record system should identify priority events to be reported.
- It is important to understand the possible mechanisms, treatment and preventive measures of vaccine reactions.

THANK YOU VERY MUCH!!!