GENERAL PRINCIPLES OF VACCINATION

A. IMMUNITY

It is the ability of the body to tolerate the presence of material indigenous to the body (self) and to eliminate foreign material (non-self). This ability provides protection from infectious diseases, usually indicated by the presence of antibody. This is very specific to a single antigen.

TWO BASIC MECHANISMS FOR ACQUIRING IMMUNITY

1. Active Immunity
   - Protection produced by the person's own immune system
   - Permanent protection after infection (immunologic memory)
   - Also produced by vaccination
2. Passive Immunity
   - Protection transferred from another person or animal as antibody
   - Temporary protection
   - Sources: Transplacental - most important source in infancy
     Blood products
     Immune globulin
     Plasma products
     Antitoxin

Antigen

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

Antibody

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

B. CLASSIFICATION OF VACCINES

1. Live Attenuated Vaccines
   - attenuated (weakened) form of the " wild" virus or bacteria
   - must replicate to be effective

- immune response similar to natural infection
- usually effective with one dose
- severe reactions possible
- interference from circulating antibody
- heat labile

Viral: Measles, Mumps, Rubella, Varicella (Chicken pox and Herpes zoster), Yellow fever, Oral Polio, Influenza Nasal Spray, Rotavirus

Bacterial: BCG, Oral Typhoid

2. Inactivated Vaccines
   - **NOT** live and cannot replicate
   - minimal interference from circulating antibody
   - generally **NOT** as effective as live vaccines
   - generally requires multiple (3 to 5) doses
   - immune response mostly humoral
   - antibody titer falls over time requiring booster doses

Whole cell vaccines

- Viral: Influenza, Polio, Rabies, Hepatitis A, Japanese B Encephalitis
- Bacterial: Pertussis, Typhoid, Cholera

Fractional vaccines

- Subunit : Hepatitis B, Influenza, Acellular Pertussis, HPV, Typhoid Vi
- Toxoid : Diphtheria, Tetanus

Polysaccharide Vaccines

- Conjugate polysaccharide: *H. Influenzae* type b, Pneumococcal, Meningococcal
- Pure polysaccharide: Pneumococcal, Meningococcal, Typhoid Vi

Pure polysaccharide vaccines

- ➢ not immunogenic in children < 2 yrs. of age
- ➢ no booster response
- ➢ antibody with less functional activity
- ➢ immunogenicity improved by conjugation

Recombinant Vaccines

- ➢ Genetically engineered: Hepatitis B, Typhoid (TY 21 a), HPV, Influenza

C. TIMING AND SPACING OF VACCINES

1. There is **NO** contraindication to the simultaneous administration of any vaccine.
2. Inactivated vaccines are **NOT** substantially affected by circulating antibody, so that they can be administered before, after, or at the same time as blood products.
3. Live vaccines are substantially affected by circulating antibodies in blood products (e.g. immunoglobulin, plasma).
   - All live vaccines must replicate in order to cause an immune response, so that antibody contained in blood products against live injected vaccine antigen may interfere with replication.
   - If the live vaccine is given first, it is necessary to wait for AT LEAST 2 WEEKS before giving the antibody.
   - If the interval between the vaccine and antibody is less than 2 weeks, the recipient should be tested for immunity or the vaccine dose should be repeated after 3-6 months
   - If the blood product is given first, give the dose of MMR or varicella vaccine at least 3 months after.
   - Herpes Zoster and Yellow fever vaccines can be administered at any time before or after receiving an antibody-containing blood product.

Antibody and Live Vaccines

Product given first	Action
Vaccine	Give 2 weeks before giving antibody
Antibody	Wait 3 months or more before giving vaccine*

*Except Zoster and Yellow Fever vaccines

4. Spacing of vaccine combinations not given simultaneously

Combination	**Minimum Interval**
Two live injected	4 weeks
All other	None

- If two live parenteral vaccines are given < 4 weeks apart, the second vaccine should be repeated.
- Exception is yellow fever vaccine, which can be given < 4 weeks after measles vaccine.
- Interval between doses of the same vaccine

5. Interval between doses of the same vaccine
    - Vaccine doses should **NOT** be administered at intervals less than the recommended minimal intervals or earlier than the minimal ages
        - Exceptions: measles outbreak, impending travel
    - Increasing the interval between doses of a multi-dose vaccine does NOT diminish the effectiveness of the vaccine.
    - Decreasing the interval between doses of the multi-dose vaccine may interfere with antibody response and protection.
        - Vaccines given ≤4 days before the minimum interval or age may be considered valid
6. Extended Intervals
    - It is **NOT** necessary to restart the series of any vaccine due to extended intervals between doses
        - Except for oral typhoid vaccine: repeat the series if the four-dose series is extended to more than 3 weeks
7. Number of Doses
    - Inactivated and live vaccines generally require multiple doses and may require periodic boosting to maintain immunity.
8. Extra doses of vaccine antigen
    - Avoid giving the extra antigens contained in a combination vaccine if they are not necessary to limit expense and additional adverse events
    - May be administered if:
        - the extra antigen is not contraindicated
        - the product that contains only the needed antigen is not available
        - the potential benefits outweigh the potential risk for adverse reactions
    - Unless licensed for mixing, individual vaccines should **NOT** be mixed in the same syringe.

D. ADVERSE EVENT FOLLOWING VACCINATION

- Adverse event following immunization (AEFI) is any event that follows immunization that is "believed to be caused by the immunization".
- Can either be true vaccine reaction or coincidental event or due to human or program error.
- Providers should report serious adverse events (SAEs) to the National Adverse Effects Following Immunization (NAEFI) (Contact numbers: 6517800 loc 2930 or 7329057)
- Local reactions:
  - pain, swelling, redness at the site of injection
  - common with inactivated vaccines
  - usually mild or self-limited
- Systemic reactions:
  - fever, malaise, headache
  - nonspecific
  - may be unrelated to vaccine
- Allergic reactions:
  - due to vaccine or vaccine component
  - rare
  - risk minimized by screening

E. CONTRAINDICATIONS AND PRECAUTIONS TO VACCINATION

- A contraindication is a condition in a recipient which greatly increases the chance of a serious adverse reaction.
  - Example: administering influenza vaccine to a person with a true anaphylactic allergy to egg could cause serious illness or death in the recipient.
- A **precaution** is a condition in a recipient which may increase the chance or severity of an adverse event, or may compromise the ability of the vaccine to produce immunity.
  - Example: administering measles vaccine to a person with passive immunity to measles from a blood transfusion

Permanent Contraindications to Vaccination

- severe allergy to a prior dose of vaccine or to a vaccine component
- encephalopathy following pertussis vaccine

Contraindications and Precautions

Condition	Live	Inactivated
Allergy to vaccine	C	C
Encephalopathy	C	C
Pregnancy	C	V*
Immmunosuppresion	C	V
Severe Illness	P	P
Recent blood products	P**	V

C-contraindication P- precaution V- vaccinate if indicated
*except HPV ; administer Tdap preferably second or third trimester
**MMR and varicella-containing, except zoster and yellow fever vaccine

- Immunosuppression
  - Inactivated vaccines are safe to use but immunologic response may be decreased
  - Live vaccines should **NOT** be administered to:
    - severely immunosuppressed persons
    - Persons receiving large doses of corticosteroids (>20mg of prednisone per day or >2mg/kg per day of prednisone) for 14 days or longer
    - Persons with HIV/AIDS (see particular vaccine chapter)
  - Persons with isolated B-cell deficiency may receive varicella vaccine
  - Live vaccines can be given after chemotherapy has been discontinued for at least 3 months
  - Live vaccines are **NOT** contraindicated with steroids given via aerosols, topical, alternate day, short courses (less than 14 days)
  - Live vaccines may be given 1 month after discontinuation of systemic steroid treatment
- Recent Blood Products
  - Varicella and MMR vaccines should be given 14 days prior to the blood product, or delayed until the antibody has degraded.

- If MMR is given sooner than the minimum interval (3-7 months depending on the blood product and dose of IVIG) the recipient should be tested for immunity or the dose repeated after the appropriate interval.
- Household and close contacts of immunocompromised individuals should receive all age-appropriate vaccines

F. INVALID CONTRAINDICATIONS TO VACCINATION

- mild illness
- disease exposure or convalescence
- antibiotic therapy
- pregnancy in the household
- breastfeeding
- allergies to products in the vaccine
- premature birth
- family history unrelated to immunosuppression
- need for TB skin testing
- need for multiple vaccines
- minor illness- low grade fever, upper respiratory tract infection, otitis media
- mild diarrhea

G. SCREENING FOR CONTRAINDICATIONS AND PRECAUTIONS TO VACCINATION

Screening questions:

- Are you sick today?
- Do you have allergies to food or medications?
- Did you have any problems or serious reactions after the last shot?
- Do you have any problems with the immune system? (lung disease, heart disease, kidney disease, diabetes, blood disorder, malignancy, HIV/AIDS)
- Did you receive any blood products within the last 12 months?
- Are you taking any steroids or anti-cancer drugs or had x-ray treatments in the past 3 months?
- Are you pregnant or trying to be pregnant in the next 4 weeks?
- Did you receive vaccinations in the past 4 weeks?

H. HANDLING AND STORAGE

See sections on individual vaccines

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VACCINES

CHOLERA

The Disease

An acutely dehydrating, watery diarrheal disease that can cause massive loss of intravascular and extracellular fluids and electrolytes in the small intestine, leading to severe dehydration and shock. A case fatality rate of > 5% may occur with delayed or inappropriate treatment.

Etiologic Agent

- *Vibrio cholerae*
- >200 serogroups, of which O1 and O139 cause epidemic disease

V. cholerae has 2 biotypes

1. classical
2. El Tor

Each biotype has 2 distinct serotypes

1. Inaba
2. Ogawa

Immunity to *V. cholerae* infection is serogroup-specific, so that vaccines that target serogroup O1 do not protect from infection with serogroup O139.

Epidemiology

- disease of poverty
- endemic in developing countries where sanitation is poor
- outbreaks occur occasionally in the Philippines
- sporadic cases very rare
- death (mortality) rates – as high as 50%-60% during large outbreaks; can be reduced to about 1% if treated early
- global disease burden - 3–5 million cases and 100 000– 130 000 deaths per year
- new and more virulent variant strains of *V. cholerae* O1 El Tor are replacing the original El Tor in parts of Africa and Asia
- emergence of antibiotic-resistant *V. cholerae* strains

Transmission

- Fecal-oral route: consumption of contaminated food (fish and shellfish, produce, or not properly reheated leftover cooked grains) or drink

Clinical Features

- Incubation period: several hours to 5 days; usually 2 – 3 days
- acute, profuse watery diarrhea of one or a few days' duration
- Severe cholera – acute, profuse watery diarrhea (rice-water stools), copious projectile vomiting, leading to profound dehydration and electrolyte loss, hypovolemic shock and death
  - patients may become severely dehydrated within 3–4 hours
  - others: tachycardia, loss of skin turgor, dry mucous membranes, acidosis, hypotension (may occur in 4-12 H), thirst, muscle cramps
  - death may occur in 18 hours to several days

The Vaccine

General Description

- Killed oral cholera vaccine
  - provide high short-term protection in all age groups at 4-6 month following vaccination
  - mixture of four preparations of heat- or formalin-killed whole-cell V. cholerae O1, representing both serotypes (Inaba and Ogawa) and both biotypes (classical and El Tor), plus a purified recombinant cholera toxin B sub unit (CTB)
  - Added value protection against ETEC
  - Full protection is expected one week after the 2nd dose
  - Dosage:
    - For suspension (Shanchol): 1.5 ml given 2 doses at 2 weeks interval. Booster dose after 3 years
    - For capsule(Orovacs): 1 capsule on Days 0, 7 and 28. If booster is indicated, restart primary immunization

Indications

- Not routinely given
- For travelers visiting areas with on-goingepidemics/outbreaks
- Persons living in highly endemic areas in unsanitary conditions without access to medical care
- Persons with compromised gastric defense mechanisms (achlorydia, prior ulcer surgery, on antacid treatment) visiting cholera risk areas
- For refugees where cholera is known to be at risk

Special Situations

HIV-infected individuals

- Safety and immune response has not been clinically evaluated

Pregnancy

- Pregnant and lactating mothers should **NOT** receive the vaccine

Transplant recipients

- No data available

Side Effects

Gastrointestinal symptoms – upset stomach

Precautions and Contraindications

- Postpone vaccination in case of acute illness
- Avoid food and drink 2 hours before and 1 hour after vaccination.
- Avoid if with a history of severe systemic reaction or allergic response following a dose of cholera vaccine
- cannot be given to children below 2 years of age
- cannot be given to pregnant and to lactating mothers

Vaccine Storage and Handling

- Keep between 2° and 8°C (35° and 46°F)
- **DO NOT FREEZE.**
- After reconstitution, should be drunk in 2 hours

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HAEMOPHILUS INFLUENZAE

The Disease

Bacterial infection that is often severe especially in infants while it causes disease uncommonly in adults.

Etiologic Agent

- Small, nonmotile, non-sporeforming gram negative coccobacillus
- Found in the upper respiratory tract

Epidemiology

- *H. influenzae* disease occurs worldwide,
- Humans are the only known reservoir.
- It is recovered from the upper airway and rarely from the genital tract.
- Non typeable *H. influenzae* frequently colonizes the lower respiratory tract in the setting of chronic obstructive pulmonary disease and cysticfibrosis.

Transmission

- Airborne droplets
- Direct contact with secretions

Risk Factors

- Exposure Factors
  - Household crowding
  - Large household size
  - Childcare attendance
  - Low socioeconomic status
  - Low parental education levels
  - School-aged siblings
- Host Factors
  - Race/ethnicity (e.g.,African-American, Hispanics, Native Americans)
  - Sickle cell anemia
  - Antibody deficiency syndromes
  - Malignancies (esp. during chemotherapy)
  - Gender (higher risk for males)

Clinical Features

- Meningitis is the most serious acute manifestation of systemic infection caused by *H. influenza*.
- Antecedent symptoms of upper respiratory infection are common.
- Cases in adult are infrequent and often have a background of recent or remote head trauma, prior neurosurgery, paranasal sinusitis, otitis or cerebrospinal fluid leak.
- In children, the most common signs are fever, altered CNS function, seizure or coma as disease progresses.
- With appropriate management, overall mortality rate with *H. influenzae* meningitis is 3-5% however, permanent sequelae occur in many survivors.
- *H. influenzae* also causes epiglotitis, pneumonia and empyema, cellulitis, bacteremia without localized disease and septic arthritis

The Vaccine

General Description

- Polysaccharide conjugate vaccine
- Stimulates T-cell dependent immunity
- Enhanced antibody production especially in children
- Highly immunogenic with estimated clinical efficacy of 95-100%
- Illicit booster response
- Utilize different carrier proteins

Indications

- Routine immunization of Hib is indicated only for children less than 5 years of age.
- Previously unvaccinated persons older than 59 months of age with one of the high risk conditions below should be given at least one pediatric dose of any Hib conjugate vaccine.
- Functional or anatomic asplenia (e.g. Sickle cell disease, post-splenectomy)
- People living with HIV who acquire splenic dysfunction, whether or not they were immunized in infancy
- People living with HIV who have recovered from Hib disease and have risk factors for further disease, those with recurrent pulmonary infections or other risk factors for severe disease
- Immunodeficiency (e.g. IgG2 subclass deficiency)
- Immunosuppression from cancer chemotherapy
- Receipt of hematopoietic stem cell transplant

Dose and Schedule

- Single dose of0.5 mL intramuscular injection (or SC injection in persons with bleeding disorders), preferably in the deltoid

Special Situations

HIV-infected individuals and other persons with altered immune status

- Maybe given safely to people living with HIV regardless of CD4 T cell count considering the individual patient's risk of Hib disease and the effectiveness of the vaccine for these persons.
- Patients with Hodgkin's disease should be vaccinated at least 2 weeks before the initiation of chemotherapy or, if this is not possible, 3 months after the end of chemotherapy.

Pregnancy and Breastfeeding

- Recommended for pregnant women at increased risk of Hib disease (eg. hyposplenia, asplenia)
- Available clinical data suggest that it is unlikely that use of Hib vaccine in pregnant women would have any deleterious effects on the pregnancy.

Transplant Recipients

- *H. influenzae* type b vaccination is also known to be safe and effective in bone marrow recipients and solid organ recipients.
- Given 6-12 months post-HSCT

Side Effects And Adverse Events

Local

- Swelling, redness or pain at the injection site

Systemic

- Fever
- Irritability
- Serious adverse reactions are rare.

Precautions and Contraindications

- Severe allergic and life threatening reaction to a vaccine component or following a prior dose.
- Moderate to severe acute illnesses

Vaccine Storage and Handling

- Unreconstituted or liquid vaccine should be stored at 2-8°C.
- **DO NOT FREEZE**

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HEPATITIS A

The Disease

A common vaccine-preventable infection that is endemic in developing countries where it is frequently acquired during early childhood and manifests with mild symptoms. The risk for infection is highest for those who live in or visit rural areas, or frequently eat or drink in areas with poor sanitation.

Etiologic Agent

- Hepatitis A virus (HAV), a hepato-tropic picorna virus
- Stable at low pH (it can survive gastric acidity)

Epidemiology

- World-wide distribution
- Prevalence of previous infection is directly related to age, socio-economic status, and the general level of public sanitation.
- In the Philippines, Hepatitis A is highly endemic and is associated with urbanization, poor hygiene and lack of access to clean water. 90% of children in lower economic groups are seropositive.
- In 2011, out of the 500 reported cases in the Philippines, two patients died (case fatality rate 0.4%).

Transmission

- Direct person-to-person contact usually through fecal-oral route
- Through exposure to contaminated water, ice, or shellfish harvested from sewage-contaminated water;
- from fruits, vegetables, or other foods that are eaten uncooked or inadequately cooked and that were contaminated during harvesting or subsequent handling.

Clinical Features

- Incubation period: 28 days (range 2-6 weeks)
- Symptoms usually appear about 4 weeks after exposure
- Acute illness lasts from 1 to 3 weeks, followed by a period of prolonged convalescence
- Most common symptoms include fever, malaise, anorexia, nausea, and abdominal discomfort, followed within a few days by jaundice and dark urine

- Enzyme elevations may persist for weeks
- Chronic hepatitis does not follow the acute illness

The Vaccine

General Description

- Inactivated Hepatitis A virus formalin inactivated and adsorbed to aluminum hydroxide as adjuvant
- administered intramuscularly in the deltoid muscle

Indications

- Vaccinate any person seeking protection from hepatitis A virus (HAV) infection
- Men having sex with men (MSM)
- Users of injection drugs
- Persons who receive clotting factor concentrates or with clotting factor disorders (e.g. hemophiliacs)
- Persons traveling to or working in countries that have high or intermediate endemicity of hepatitis A
- Contacts of infected persons
- People with chronic liver disease (because of risk of fulminant hepatitis A)
- Persons for whom Hepatitis A is an occupational hazard (e.g. healthcare workers, some lab workers, food handlers)
- Persons employed in child care centers, health care institutions, institutions for persons with developmental disabilities, schools
- Persons exposed to sewage
- Armed forces
- Persons working with HAV-infected primates or with HAV in a research laboratory setting
- Travelers from nonendemic areas which include:
  - tourists
  - immigrants and their children returning to their country of origin to visit friends or relatives
  - military personnel
  - missionaries
  - others who work or study abroad in countries that have high or intermediate endemicity of Hepatitis A

Dose and Schedule

For monovalent Hepatitis A vaccine:

- Single dose of 1440 ELISA units/ml/vial
- Booster dose between 6 and 12 months after initiation of primary course

For combination Hep A and Hep B:

- 3 doses administered intramuscularly at 0, 1 and 6 months
- Dose: 720 ELISA units (Hep A) and 20μg/ml)
- Booster dose should be given at 1 year

*Serologic testing to assess response is not indicated.

Special Situations

HIV-infected individuals

- Maybe given safely if indicated regardless of CD4 T cell count
- Dose:
  - CD4 count of >300: two doses are given at either 0 and 6 through 12 months
  - CD4 count <300: three doses schedule over 6-12 months

Pregnancy and Breastfeeding

- Recommended for susceptible pregnant women who are at increased risk of exposure through lifestyle factors, or where severe outcomes may be expected (eg. pre-existing liver disease).
- The effect of HAV on fetal development has not been assessed. However, as with all inactivated viral vaccines, the risks to the fetus are considered to be negligible.
- Vaccine should be used with caution
- The effect of the vaccine on breastfed infants through its administration to their nursing mothers has not been evaluated in clinical studies

Other Immunocompromised Conditions

- No special precautions needed to be taken during vaccination.

Bleeding Disorders

- Vaccine should be administered with caution since bleeding may occur following an intramuscular injection.

Transplant recipient

- Vaccination is recommended for patients with end stage liver disease.
- HAV serologic response should be assessed 1–3 months after completionof the primary HAV vaccine series and a single HAV booster doses should be administered to nonresponders.

Side Effects

- Local adverse events include injection site soreness, induration, redness and swelling.
- Systemic adverse events reported include headache, malaise, fatigue, fever,nausea, & loss of appetite.

Precautions and Contraindications

- History of severe allergic reaction to a previous dose of Hepatitis A vaccine or a vaccine component (i.e. 2-phenoxyethanol, yeast)
- Severe febrile illness

Vaccine Storage and Handling

- Stored at 2-8˚C.
- **DO NOT FREEZE**

The Role of Passive Immunization

Hepatitis A Immunoglobulin

- May be indicated for health care personnel who are not immune and exposed to feces of infected persons during outbreaks
- In the case of travel within 4 weeks of vaccine administration, a dose of immunoglobulin (0.02 mL/kg) may be given alone or in addition to hepatitisA vaccine at a different site for optimal protection.

Recommended doses of immune globulin (IG)* for protection against Hepatitis A

SETTING	DURATION OF TRAVEL	DOSE (mL/kg)
Pre-exposure	Short-term (1–2 mos) Long-term (3–5 mos)	0.02 0.06
Post-exposure		0.02

*IG should be administered by intramuscular injection into the deltoid or gluteal muscle.

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HEPATITIS B

The Disease

A disease that causes a wide spectrum of illness ranging from asymptomatic to icteric including fulminant hepatitis. Chronic carrier state can lead to chronic liver disease, cirrhosis and liver cancer.

Etiologic Agent

- Hepatitis B virus, family *Hepadnaviridae*

Epidemiology

- Occurs throughout the world with highly variable prevalence
  Occurs very early in life in hyperendemic areas including the Philippine

Transmission

- Contact transmission in unprotected sex with an HBV-infected partner
- Percutaneous transmission in drug abusers
- Prolonged exposure to minute amounts of infected body fluids in non- intact skin
- Accidental needlestick injury or work exposure to blood/ body fluids
- Maternal-neonatal during labor or delivery
- Blood transfusion

Clinical Features

- Incubation period: 60-150 days (average 90 days)
- Phases of hepatitis:
  - Pre-icteric or prodromal phase
    - Insidious onset of malaise, anorexia, nausea, vomiting, right upper quadrant abdominal pain, fever, headache, myalgia, skin rashes, arthralgia, arthritis, dark urine
    - 3-10 days: from initial symptoms to onset of jaundice
  - Icteric phase
    - lasts from 1 to 3 weeks
    - characterized by jaundice, light or gray stools, hepatic tenderness and hepatomegaly

- Convalescence phase
  - malaise and fatigue persists for weeks to months
  - disappearance of other symptoms such as jaundice and anorexia
- Chronic carrier state
  - range from healthy asymptomatic stage to chronic liver disease, cirrhosis and liver cancer

The Vaccine

General Description

- Monovalent Hepatitis B vaccine uses recombinant DNA technology to express HBsAg in yeast, and purified from cells by biochemical and bio-physical separation techniques

Indications

Serologic Testing

- Prevaccination (Screen for HBsAg and Anti-HBs)
  - Recommended in those living in highly endemic areas like in the Philippines
- Post-vaccination (testing of Anti-HBs titer done 1 to 2 months after completion of series)
  - Not routinely recommended
  - Recommended only for:
    1. Healthcare workers
    2. Chronic hemodialysis patients
    3. Other immunocompromised patients
    4. Persons with HIV infection
    5. Sex partners of HBsAg+ persons
    6. Infants born to HBsAg+ women

Routine

- Universal immunization of all infants, adolescents and adults (with nonreactive HBsAg and Anti-HBs)
- Those seeking protection from Hepatitis B virus infection and who are not previously vaccinated
- Healthcare workers
- Sexually active persons who are not in a long-term mutually, monogamous relationship
  1. persons with more than one sex partner during the previous 6 months

    2. persons seeking evaluation or treatment for a sexually transmitted disease (STD)
    3. current or recent injection-drug users
    4. men who have sex with men
- IV drug users
- Diabetics
- Household contacts and sex partners of persons with chronic HBV infection or HBV carriers
- Patients receiving frequent blood transfusions or clotting factor concentrates
    1. thalassaemics
    2. sickle-cell anemic
    3. hemophiliacs
- Immigrants from areas of high HbsAg endemicity
- Travelers to countries with high or intermediate prevalence of chronic Hep B infection
- Persons with end stage renal disease including those receiving hemodialysis
- Chronic liver disease
- Clients and staff members of institutions for persons with disabilities
- Persons at risk for occupational exposure to HBV
    1. Police, brigade, and armed forces personnel
    2. Firefighters
    3. Household contacts of any of the above groups
- College entrants to healthcare associated courses
- Clients and staff members of institutions for persons with disabilities

<u>Dose and schedule</u>

For monovalent Hepatitis B vaccine:

- Two doses separated by no less than 4 weeks, and a third dose 4 to 6 months after the second dose
- Dose: 20ug/ml/vial (1 ml)
- Accelerated schedule: 0, 1, 2 and 12 months

For combination Hep B and Hep A:

- 0, 1 and 6 months
- Accelerated schedule: 0, 7, and 21–31 days and a booster dose 12 months after the first dose (not routinely recommended)

Booster/Revaccination:

- Not routinely recommended
- Recommended only for immunocompromised patients with Anti-HBs titers below10 IU.

Special Situations

HIV-infected individuals

- Routine vaccination regardless of CD4+ T cell count and those who belong to the high risk population
- Dose: 20 ug/ml/vial, administer 2 vials intramuscularly on a 3-dose schedule at day 0, 1 month and 6 months

Pregnancy

- Recommended for susceptible pregnant women for whom this vaccine would otherwise be recommended.
- Hepatitis B vaccine should only be given to pregnant women who are non-immune and where there is a clear indication. As for any inactivated viral vaccines, although data are limited, no adverse effects on the developing fetus are expected.

Transplant recipients

- Given to solid organ transplant recipients to prevent progression of hepatitis B infection and to prevent reactivation of latent disease while on immunosuppression.
- Give protection against infections from donors
- Dose: same with HIV patients
- For patients awaiting transplantation, the alternative schedule may be given, however this was noted to have lesser seroconversion titers.

Patients on hemodialysis

- Dose: 20 ug/ml/vial, administer 2 vials intramuscularly on a 3-dose schedule at day 0, 1 month and 6 months for <20 years of age and a 4-dose schedule at 0,1,2 and 6 months for ≥ 20 years old
- Accelerated dose: 0, 1, 2 and 6 months
- Hepatitis B surface antibody titers should be assessed 1–3 months after completion of the primary HBV vaccine series
- The need for Hepatitis B vaccine booster doses should be assessed

by annual testing for antibody to Hepatitis B surface antigen (anti-HBs)

- A booster dose should be administered when anti HBs levels decline to <10 mIU/mL.

Side Effects

- Local reactions are characterized by transient soreness erythema & induration
- Systemic early onset events temporally related to vaccination include:
  - fatigue, dizziness, syncope, hypotension, arthritis, arthralgia, lymphadenopathy, rash and urticaria
  - influenza-like symptoms, such as low-grade fever, malaise, headache and myalgia
  - gastrointestinal upsets, such as abdominal pain, diarrhea, vomiting, nausea and abnormal liver function tests

Precautions and Contraindications

- Hypersensitivity to any component of the vaccine, including baker's yeast
- Should not be administered to subjects with moderate or severe acute illness with or without fever
- Vaccination is not contraindicated in persons with a history of MS, GBS, autoimmune disease (e.g., systemic lupus erythematous or rheumatoid arthritis), or other chronic diseases
- The effect on breastfed infants of the administration of the vaccine to their mother has not been evaluated in clinical studies.

Vaccine Storage and Handling

- Vaccine must be stored at +2°C to +8°C.
- **DO NOT FREEZE.**

The Role of Passive Immunization

Hepatitis B Immunoglobulin

- Immunobiologics and schedules for which post-exposure prophylaxis may be indicated for HBVsusceptible health care personnel with percutaneous or mucous membrane exposure to blood known to be HbsAg seropositive or persons with IgA deficiency:
- One IM dose IG 0.02 ml/kg given within 2 weeks of exposure in large muscle mass (deltoid, gluteal)
- HBIG 0.06 ml/kg IM as soon as possible (and within 7 days) after

exposure (with dose 1 of hepatitis B vaccine given at different body site); if hepatitis B series has not been started, 2nd dose of HBIG should be given 1 month after 1st dose.

- If a live vaccine were given within 2 weeks prior to HBIG, repeat the dose of the vaccine after 3-6 months post-HBIG.

Post-exposure prophylaxis for healthcare workers

Management of healthcare workers (HCW) exposed to HBV either by needle-stick injury, bites or mucosal exposure depends on the HbsAg status of the source person; and the vaccination status and anti-HBs titer of the exposed HCW.

Table 1. Postexposure prophylaxis for occupational exposure to Hepatitis B virus

Vaccination and antibody status of exposed person		**Treatment**		
		Source HbsAg Positive	**Source HbsAg Negative**	**Source Unknown or not available for testing**
Unvaccinated (Check HbsAg and Anti-HBs)				
HbsAg positive		No treatment	No treatment	No treatment
HBsAg negative (Check Anti-HBs titer)	Anti-HBs ≥ 10 mlU/ml	No treatment	No treatment	No treatment
	Anti-HBs ≤ 10 mlU/ml	HBIG* x 1 dose then administer HepB vaccine series (3 doses) OR HBIG x 2 doses**	No treatment	If known high-risk source, treat as if source were HBsAg positive
Previously Vaccinated				
Check Anti-HBs titer	Anti-HBs ≥ 10 mlU/ml	No treatment	No treatment	No treatment
	Anti-HBs ≤ 10 mlU/ml	HBIG x 1 dose then administer HepB vaccine series (3 doses) OR HBIG x 2 doses**	No treatment	If known high-risk source, treat as if source were HBsAg positive

**HBIG 0.06 ml/kg intramuscularly (IM)*

***Give 1 dose of HBIG and reinitiate vaccine series for those who have not completed a second 3-dose series. Two doses of HBIG is preferred for those who have completed a second vaccine series but failed to respond.*

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HERPES ZOSTER

The Disease

Herpes Zoster, or shingles, is a reactivation of latent Varicella Zoster virus. It commonly presents with painful vesicular lesions occurring unilaterally in the distribution of the sensory nerve. In immunocompromised individuals, it may disseminate to involve the brain, lungs and liver. Factors associated with recurrent disease are aging, immunosuppression, intrauterine exposure to VZV and prior varicella infection.

Etiologic agent

- Varicella-Zoster virus

Epidemiology

- Worldwide
- Human disease
- Occurs throughout the year
- More common in adults than in children

Mode of Transmission

- Airborne
  - Most common
- Direct contact or Inhalation of aerosols from vesicular fluid of skin lesions

Clinical Features

- Painful vesicular lesion, unilaterally distributed along a sensory nerve.
- Pain and paresthesia are noted 48 to 72 hours prior to appearance of the lesions.
- In immunocompetent individuals, formation of lesions may take 3 to 5 days.
- Involvement of the eyelid (herpes zoster ophthalmicus) is a sight-threatening condition and is usually signaled by lesions at the tip of the nose.
- Pain in the area of occurrence (postherpetic neuralgia) is a common complication. Other complications include Ramsay Hunt syndrome, motor weakness, autonomic dysfunction, focal neurologic deficits, disseminated disease.

The Vaccine

General Description

- Lyophilized preparation of the Oka/Merck strain of live, attenuated VZV but with a much higher minimum potency
- It contains neomycin, and bovine calf serum; sucrose, hydrolyzed porcine gelatin, sodium chloride, monosodium L-glutamate, sodium phosphate dibasic, potassium phosphate monobasic, potassium chloride; residual components of MRC-5 cells (DNA and protein); neomycin and bovine calf serum.

Indication

- Adults ≥ 60 years old with or without a prior episode of Herpes Zoster
- Persons with history of zoster
- Persons with chronic medical conditions unless these conditions are contraindications to vaccinate
  - chronic renal failure
  - diabetes mellitus
  - rheumatoid arthritis
  - chronic pulmonary disease

Dose and Schedule

- Give as a single 0.65 mL SC in the deltoid area

Post-exposure Immunization

- Should **NOT** be used as post-exposure management

Special Situations

HIV-infected Individuals

- Contraindicated in those with CD4 count < 200 cells/uL

Pregnancy

- Contraindicated in pregnancy
- Pregnancy should be avoided for 4 weeks after receipt of zoster vaccine
- Should be given upon completion or termination of pregnancy to women who do not have evidence of varicella immunity

Stem cell transplant recipients

- Limited data
- If decision to vaccinate is made, should be administered at least 24 months after transplantation

Side Effects

- Injection site complaints (pain and erythema)
- Generalized rash
- Systemic reactions not common
- Adverse reactions similar to varicella vaccine

Precautions and Contraindications

- Moderate or severe acute illness
- Current treatment with an antiviral drug active against herpes virus
  - Drugs should be discontinued at least 24 hours before administration of the vaccine and the drugs should be avoided for at least 14 days after vaccination
- Recent receipt of a blood product is **NOT** a precaution
- Severe allergic reaction to prior dose or any vaccine component (gelatin and neomycin)
- Pregnancy or pregnancy within 4 weeks
- Immunosuppression:
  - Leukemia, lymphoma or other malignancy affecting the bone marrow or lymphatic system
  - Patients with leukemia or lymphoma in remission and those who have discontinued chemotherapy or radiation therapy for at least 3 months can be vaccinated
  - HIV/AIDS (CD4 < 200 cells/uL)
  - High-dose corticosteroid therapy (>20mg/day of prednisone or equivalent lasting >2 weeks)
  - May vaccinate at least 1 month after discontinuation of therapy
- Recombinant human immune mediators and immune modulators (e.g infliximab, rituximab)
  - Safety and efficacy of the vaccine is not known
  - Preferable to give zoster vaccine before treatment with these drugs
  - If vaccine is not given prior to treatment, immune status of recipient should be assessed to determine relevant risks

and benefits. Administer zoster vaccine at least 1 month after discontinuation of treatment.

Vaccine Storage and Handling

- Store in a continuously frozen state until administration, -15°C or colder
- Once reconstituted, use immediately or within 30 minutes of reconstitution.
- Transportation of the vaccine discouraged. If it must be transported, store at refrigerator temperatures between (2°C to 8°C) for not more than 72 hours prior to reconstitution.

**VACCINE CURRENTLY NOT LOCALLY AVAILABLE

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HUMAN PAPILLOMA VIRUS

The Disease

The most common sexually transmitted infection which infects the skin and mucous membranes of the genital areas of men and women. Forty types have been consistently associated with genital warts and cancer of the cervix, vulva, vagina, penis, anus, head, neck and respiratory tract.

Etiologic Agent

- Human papilloma virus
- More than 100 types have been identified based on the genetic sequence of the outer capsid protein L1
- 40 types infect the mucosal epithelium
- HPV types are categorized according to their epidemiologic association with cervical cancer
- Low-risk or non-oncogenic types: types 6 and 11 cause 90% ofbenign or low-grade cervical cell abnormalities, anogenitalwarts, and laryngeal papillomas
- High-risk or oncogenic types: types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 69, 73, 82, cause 99.7% of low-grade cervical cell abnormalities, high-grade cervical cell abnormalities that are precursors to cancer, and ano-genital cancers.
- Types 16 and 18 account for 70% of cervical cancers
- Types 6 and 11 cause 90% of anogenital warts
- HPV is responsible for 90% of anal cancers, 40% of vulvar, vaginal, or penile cancers, and 12% of oral and pharyngealcancers.
- High-risk types are detected in 99.7% of cervical cancers

Epidemiology

- Occurs worldwide.
- Humans are the only reservoir.
- The risk of acquiring HPV infection is 50% during one's lifetime.
- More than 80% of sexually active women will have been infected by age 50.
- Cancer of the cervix is the second most common cancer among women worldwide.
- Globally, there are 300 million asymptomatic infections, 30 million low-grade cervical lesions, 30 million genital warts,

10 million high grade precancerous lesions, and 0.4932 million cervical cancer in 2002.

- Risk factors: cigarette smoking, high parity, increased age, immune suppression, Long-term oral contraceptive use, co- infection with other sexually transmitted diseases (eg. HIV, gonorrhoea), other host factors (diet, genetics), endogenous hormones.
- In the Philippines
  - Cervical cancer incidence has remained unchanged from 1980 – 2005: 22/100,000 women and 56% die within 5 years.
  - 2/3 of cervical cancer are diagnosed in an advanced stage
  - Types 16, 18 and 45 are the most frequently isolated types in cervical cancer lesions
  - Genital warts prevalence is at 0.2%
  - primary goal of treatment is removal, however treatment does not eliminate the infection
  - if untreated, 40% spontaneously resolve
  - if treatment is performed, recurrence rate is 5%-65% within 3 months of successful treatment

Transmission

- Sexual Contact
  - genital-genital
  - manual-genital
  - oral-genital
- Nonsexual routes
  - Mother-to-infant

Clinical Features

- Most infections are transient and asymptomatic and result in no disease.
- Clinical manifestations of HPV infection include:
  - anogenital warts (condyloma)
  - anogenital cancers (eg. vaginal, vulvar, anal) and their precursor lesions
  - cervical cancer and cervical cancer precursors
  - recurrent respiratory papillomatosis
  - cancers of the head and neck

The Vaccine

General Description

- There are 2 available HPV vaccines
  1. Quadrivalent HPV vaccine
     - contains types 6, 11, 16, 18 L1 major capsid protein, self-assembled as intact, non-infectious virus-like particles (VLP's)
     - manufactured in yeast, *Saccharomyces cereviseae*
     - adjuvanted with proprietary amorphous aluminum hydroxyphosphate sulfate
     - schedule of vaccination: 0.5 ml each dose, given for 3 doses within 6 months at 0, 2, 6 months intervals IM (deltoid)
     - for the prevention of ano-genital warts, cervical, vulvar, vaginal and anal cancer and penile intraepithelial neoplasia
  2. Bivalent HPV vaccine
     - contains types 16 and 18 L1 major capsid protein, self-assembles as intact, non infectious virus-like particles (VLP's)
     - manufacture in insect cells, Baculovirus
     - adjuvanted with ASO4 -aluminum hydroxide plus monophosphoryl lipid A derived from *Salmonella Minnesota*
     - schedule of vaccination : 3 doses within 6 months at 0, 1, 6 months IM (deltoid)
     - for the prevention of cervical cancer

Minimum Dosing Intervals

- 4 weeks between doses 1 and 2
- 12 weeks between doses 2 and 3
- inadequate doses of quadrivalent HPV vaccine or vaccine doses received after a shorter-than-recommended dosing interval should be readministered
- Do not restart the series if the schedule is interrupted
- Administer at the same visit other age-appropriate vaccines

Routine Indications

- Quadrivalent (HPV4) vaccine
  - routinely given to females 10 to 45 years old and males 9 to 26 years old
  - may be given as early as 9 years old

- Bivalent (HPV2) vaccine
  - routinely given to females 10 to 55 years old

Catch-up Vaccination

- Quadrivalent (HPV4) vaccine for women 10 to 45 years old and males 9 to 26 years old
- Bivalent (HPV2) vaccine for women 19 to 55 years old
- Both vaccines do not require prior screening before administration. However, routine cervical screening should be continued even after vaccination as there are other types of HPV that can cause cervical cancer

Special Populations

Vaccines can be administered to:

- Women with equivocal or abnormal Pap smear
- Positive HPV DNA test
- Persons with a history or clinically evident genital warts
- Immunocompromised persons

HIV-infected individual

- Because HPV vaccine is not a live virus, it may be administered to HIV infected individuals regardless of immune status

Pregnancy

- HPV is **NOT** recommended for use during pregnancy
- If a woman is found pregnant after initiation of the vaccine series, remaining doses should be delayed until after delivery
- No adverse effects have been reported on women given inadvertently the vaccine during pregnancy
- May be given to lactating women

Transplant Recipient

- No published data of immunogenicity of the vaccine, however may still be given theoretically after transplantation following current recommendations for non-immunocompromised hosts

Side Effects And Adverse Events

- Local reactions- 84% mostly severe burning pain and swelling at the injection site
- Fever-10%
- Vasovagal syncope can occur among adolescents and adults after receiving HPV vaccine.
  - Patients should be observed for 15 minutes after receiving the vaccine
  - Recipients should always be seated during vaccine administration

Precautions and Contraindications

Precaution

- Moderate or severe acute illnesses (defer until symptoms improve)
- If a woman is found pregnant after initiation of the vaccine series, remaining doses should be delayed until after the pregnancy.

Contraindication

- persons with history of immediate hypersensitivity to yeast or to any vaccine component or following a prior dose

Vaccine Storage and Handling

- Store at refrigerator temperature (+2°C to +8°C)
- **DO NOT FREEZE.**
- Protect from light
- Administer immediately after removing from refrigeration

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INFLUENZA

The Disease

A disease characterized by upper respiratory tract symptoms and fever, which is caused by a constantly mutating virus, resulting in repeated episodes of the illness.

Etiologic Agent

- Influenza Virus
- 3 Virus Strains
  Type A – moderate to severe illness; affects all age groups
  Type B – milder illness; primarily affects children
  Type C – rare; no epidemics

Epidemiology

- Occurs worldwide
- In the Philippines, it occurs year-round, with peaks from July to October

Transmission

- Droplet inhalation
- Occasionally, through indirect contact (touching surfaces contaminated with influenza virus and then touching the eyes, nose or mouth and fomites)

Clinical Features

- Incubation Period: 2 days (range 1-4 days)
- Causes abrupt onset of fever, chills, myalgia, cough and sore throat
- Complications: pneumonia, myocarditis, encephalitis, Guillain-Barre syndrome and worsening of chronic bronchitis and co-morbid conditions which may lead to death.

The Vaccine

General Description

- Contains two strains of A and one strain of B
- 2 types of vaccine:
  1. Trivalent inactivated virus (TIV)

- Immunity is less than 1 year

2. Live attenuated virus (LAIV)
   - currently not available locally

- For the Philippines, current recommendations now state that the formulation for the Southern Hemisphere be used. If Southern Hemisphere is not available, the Northern Hemisphere formulation can be used.

Routine Indication

- Individuals ≥ 50 years of age
- Anyone who wants to reduce the chance of falling ill with influenza
- International travelers (must receive 2 weeks prior to departure)
- Persons providing essential services
- Students or other persons in institutional settings
- Healthcare workers and providers
- Persons at high risk for severe flu or its complications:
- Residents of chronic care facilities and nursing homes
- Those with chronic disorders: cardiovascular disorders, chronic pulmonary disease (including asthma), neuromuscular dysfunction, diabetes, renal dysfunction, hepatic disorder, other chronic metabolic diseases, hemoglobinopathies, immunosuppressed due to any cause

Special Situations

HIV-infected individuals

- Pre-exposure prophylaxis
  - Vaccination using the inactivated trivalent influenza vaccine is recommended annually for ALL HIV-infected individuals irrespective of immunologic status, viral load, age, and comorbidites
  - Intranasal live attenuated vaccine (LAIV) is not recommended for HIV-infected individuals. Immunocompromised HIV-infected individuals should avoid close contact with anyone who has received the LAIV within the previous 21 days
- Post-exposure prophylaxis
  - Post-exposure vaccination is not indicated but chemoprophylaxis may be given

Pregnancy

- No evidence that inactivated influenza vaccine caused damage to the fetus.
- Inactivated influenza vaccine can be administered to those who are pregnant in the 2nd or 3rd trimester or planning to be pregnant during the influenza season
- Live attenuated influenza vaccine should not be used in pregnancy.

Transplant recipients

- Life-long annual seasonal influenza vaccination, starting before hematopoietic stem cell transplant (HSCT) and restarting 6 months after HSCT
- Whole- or split virus influenza vaccine, 0.5 mL/dose IM or subcutaneously
- All family members and close or household contacts of HSCT recipients should continue tobe vaccinated annually as long as the HSCT recipient's immunocompromised state persists, even if beyond 24 months after HSCT.
- During outbreaks, all HSCT recipients who have not yet received a current influenza vaccination should be vaccinated against influenza immediately if it is more than 4 months after HSCT. Chemoprophylaxis should be used for 2 weeks after vaccination to allow sufficient time for immunologic response to influenza vaccine.

<u>Pre-exposure immunization</u>

- A single dose may be given intramuscularly or subcutaneously once every year for TIV
- A new TIV formulation is available for intradermal administration for ≥ 60 years old

<u>Side Effects</u>

- TIV
  - Most frequent: Soreness at the injection site lasting 1 to 2 days
  - Fever, malaise and muscle pain are very uncommon; allergic reactions may occur

Precautions and Contraindications

- TIV
  - Persons with a severe allergic reaction to a vaccine component (e.g. egg) or following a prior dose of vaccine
  - Moderate to severe illness with or without fever
  - History of Guillian-Barre Syndrome within 6 weeks following a previous dose of vaccine

Storage and Handling

- TIV
  - Store at refrigerator temperature (+2°C to +8°C).
  - **DO NOT FREEZE**.
  - Ship in insulated containers with coolant packs.

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JAPANESE ENCEPHALITIS

The Disease

A mosquito-borne disease which is symptomatic in less than 1% of cases, but the illness is usually severe encephalitis, leading frequently to coma and to a fatal outcome in 25% of cases.

Etiologic Agent

- JapaneseEncephalitis virus (JEV), a single-stranded RNA virus that belongs to the genus *Flavivirus*

Epidemiology

- Occurs throughout most Asia and parts of the western Pacific.
- Travel-associated JE can occur at any age among travelers from non endemic countries with an incidence of less than one case per 1 million.
- In endemic areas, JE is primarily a disease of childhood aged < 15 years old.
- In the Philippines, there has been no reported case of Japanese encephalitis in individuals above 15 years old. (Unpublished data).

Transmission

- Bites of infected mosquitoes
- Blood transfusion
- Organ transplantation
- Direct person to person spread of JEV does not occur except rarely through intrauterine transmission

Risk Factors

- Prolonged travel (>1 month) to endemic areas
- Recurrent traveling or traveling on brief trips with extensive outdoor or nighttime exposure in rural areas
- During travel, accommodations with no air conditioning, screens or bed nets
- Rural agricultural areas associated with rice production and flooding irrigation

Clinical Features

- Incubation period: 5-15 days
- Majority of human infections are asymptomatic; <1% of people infected with JEV develop clinical disease
- Illness begins with an acute onset of fever, headache and vomiting followed by mental status changes, focal neurologic deficits, generalized weakness and movement disorders over the next few days
- Seizures are common in children
- Classic description of Japanese Encephalitis (JE):
  - Parkinsonian syndrome with mask-like facies, tremors, cogwheel rigidity, and choreoathetoid movements
  - Acute encephalitis – most common clinical syndrome identified
  - Aseptic meningitis
  - Acute flaccid paralysis
  - Undifferentiated febrile illness – common in adults
- Common complications are:
  - Status epilepticus
  - Brain hypoxia
  - Increased ICP
  - Brainstem herniation
  - Aspiration pneumonia

The Vaccine

General Description

1. Inactivated mouse brain-derived vaccine (JE-VAX [JE-MB])
   - prepared by inoculating mice intracerebrally with the JEV Nakayama-NIH strain
   - contains thimerosal, gelatin, formaldehyde, Polysorbate 80, and mouse serum protein
   - licensed for use for persons aged ≥ 1 year old
2. Inactivated Vero cell culture-derived vaccine (IXIARO [JE-VC])
   - derived from the attenuated SA 14-14-2 JEV strain propagated in Vero cells
   - contains inactivated JEV proteins, and aluminum hydroxide as adjuvant
   - does not contain gelatin, antibiotics or thimerosal
   - approved for use for persons aged ≥ 17 years old

3. Cell Culture Derived Live SA-14-14-2 Vaccine
    - Based on a stable neuro-attenuated strain of JE virus (SA-14-14-2)
    - First license for use in People's Republic of China in 1988
    - It is also licensed in India, South Korea and Nepal
    - Available in 5-dose vials as a lyophilized powder that looks like a milky-white crisp cake which is rehydrated with 2.5 ml diluents
4. Novel recombinant chimeric virus vaccine (IMOJEV [JE-CV and previously known as Chimeri Vax™ JE])
    - Developed using the Yellow fever virus (YFV) vaccine vactor YFV17D by replacing the cDNA encoding the envelope proteins of YFV with that of attenuated JEV strains SA14-14-2
    - Found to be safe, higly immunogenic and capable of inducing long-lasting immunity in both preclinical and clinical trials
    - A single dose of IMOJEV was sufficient to induce protective immunity, which was similar to that induced in adults by three doses of JE-VAX
    - Phase III trials evaluating the immunogenicity and safety of the chimeric virus vaccine have been successfully completed in some JE-endemic countries thus this can be licensed for use in humans as an improved alternative to the currently licensed JE vaccines

<u>Indications</u>

Recommended for:

- People living in endemic areas
- Travelers to and residents of areas experiencing epidemic transmission
- Persons with extensive outdoor activities in rural areas
- Expatriates whose principal area of residence is an area where JEV is endemic or epidemic
- Laboratory workers with a potential for exposure to JE virus (JEV) through needlesticks and through mucosal or inhalational accidental exposures

Maybe considered in:

- Short-term travelers (<1 month) to endemic areas who plan to travel outside of an urban area and have an itinerary or activities that will increase their risk of JEV exposure such as the following:

- spending substantial time outdoors in rural or agricultural areas especially during the night
- participating in extensive outdoor activities (e.g., camping, hiking, farming, trekking, biking, fishing, hunting)
- staying in accommodations without air conditioning, screens, or bed nets
- Travelers to an area with an ongoing JE outbreak
- Travelers to endemic areas who are uncertain of specific destinations, activities, or duration of travel

Dose and Schedule

For inactivated mouse brain-derived vaccine:

- 3 doses within 30 days at 0, 7 and 30 days SC
- give 0.5 ml for children 1-2 years old and 1.0ml for persons aged ≥ 3 years old
- Accelerated schedule: days 0, 7, and 14
- booster dose
  - 1.0 ml (0.5 ml for children <3 years old) 2 years after the primary series when indicated for planned travel or possible laboratory exposure

For inactivated vero cell culture-derived vaccine:

- 0.5ml intramuscularly for 2 doses administered 28 days apart
- 2 dose-series should be completed at least 1 week before potential exposure to JEV

For cell culture derived live SA-14-14-2 Vaccine

- The dose Is 0.5 ml administered subcutaneously for all ages

Special Situations

HIV-infected individuals and other persons with altered immune states

- Maybe given to people living with HIV if indicated
- Dose: 3 doses deep SC route on days 0, 7-14 and 28
- For those aged >60 years, a 4th dose is recommended 1 month after completion of the initial course.
- A booster is recommended after 3 years for those at continued risk.

Pregnancy and Breastfeeding

- Vaccination should be deferred because of theoretical risk to the developing fetus

- If pregnant women must travel to a high risk area, they should be vaccinated if the benefits outweigh the risks of vaccination to the mother and the developing fetus
- Breastfeeding is not a contraindication to vaccination
- whether JE vaccines are excreted in human milk is not known; should use caution when considering JE vaccine

Transplant recipients

- JE vaccine maybe given if indicated however, vaccination should be avoided in the 6 months following transplantation when patients are usually receiving the highest doses of immunosuppressive drugs.

Side Effects

For inactivated mouse-brain derived vaccine

- Occur within 48 hours for the first dose but around 96 hours for the second
- Local
  - localized pain, erythema, tenderness and swelling at the injection site (JE-MB 20%; JE-VC ≤ 1 %)
- Systemic – usually mild
  - Fever
  - Chills
  - Headache
  - Rash
  - Myalgia
  - Fatigue
  - Influenza-like illness
  - Gastrointestinal symptoms
- Serious but rare reactions
  - Severe allergic reactions (e.g., generalized urticaria, angioedema of the extremities, face, and oropharynx, bronchospasm, respiratory distress, and hypotension)
  - Neurologic symptoms
  - Encephalitis, seizures, gait disturbances and parkinsonism
  - Acute Disseminated Encephalomyelitis (ADEM) – reported among children vaccinated with JE-MB in Japan and Korea
- recipients should be observed for a minimum of 30 minutes after vaccination and warned about the possibility of delayed allergic reactions therefore, they should remain in areas with access to medical care for 10 days after receiving each dose of JE-MB vaccine

For Vero cell culture-derived vaccine

- Local
  - Pain and tenderness in injection site (≤1%)
- Systemic – mild
  - Gastroenteritis
  - Headache
  - Myalgia
  - Fatigue
  - Influenza-like illness
  - Allergic dermatitis
  - Generalized urticaria
  - Neurologic adverse event – none reported in clinical trials (<5,000) adults but more monitoring surveillance needed

Precautions And Contraindications

Precaution

- History of previous allergic reactions or urticaria attributable to any cause (e.g., medications, other vaccinations, or insect bite)

Contraindication

- JE-MB Vaccine
  - History of an allergic reaction to a previous dose
  - Hypersensitivity to any vaccine component (e.g., thimerosal, gelatin)
  - Persons with proven or suspected hypersensitivity to proteins of rodent or neural origin
- JE-VC Vaccine
  - Severe allergic reaction (e.g., anaphylaxis) after a previous dose
  - Hypersensitivity to any vaccine component (e.g., protamine sulfate)

Vaccine Storage and Handling

- Stored at 2-8°C (35-46°F)
- **DO NOT FREEZE.**
- Protected from the light
- Should be reconstituted using the supplied diluents according to the package insert
- Reconstituted vaccine should be used within 8 hours.

**VACCINE CURRENTLY NOT LOCALLY AVAILABLE

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MEASLES, MUMPS, RUBELLA

Measles

The Disease

An acute exanthematous disease with high morbidity and mortality in children which can also affect young adults.

Etiologic Agent

- A paramyxovirus, genus Morbillivirus

Epidemiology

- Occurs worldwide
- Complications are more common among children <5 years and adults 20 years of age and older.
- In the Philippines, since 2005, there has been a markedly reduced incidence but several outbreaks have been occurring since 2010.

Transmission

- Person to person through large respiratory droplets
- Airborne transmission has been documented in closed areas for up to 2 hours after a person with measles occupied the area
- Highly communicable
- Period of communicability: from 4 days before to 4 days after onset of rash

Clinical Features

- Incubation period: 10-12 days from exposure to prodrome
- From exposure to onset of rash averages 14 days (range, 7-18 days)
- Fever, coryza, cough, conjunctivitis, Koplik spots, maculo-papular rash lasting 5-6 days appearing initially on the face proceeding downward and outward
- Complications: diarrhea, otitis media, pneumonia, encephalitis, seizure, death

Mumps

The Disease

Acute viral febrile illness often characterized by swelling of parotid and other salivary glands, and can also lead to epididymo-orchitis, meningitis and pancreatitis.

Etiologic Agent

- Mumps virus, a paramyxovirus

Epidemiology

- Occurs worldwide
- Most common among school-aged children and young adults

Transmission

- airborne or direct contact with infected droplet or saliva

Clinical Features

- Incubation period: 14-18 days
- Period of communicability: from 3 days before to the 4th day of active disease
- Prodomal symptoms are nonspecific and include: myalgia, anorexia, malaise, headache and low-grade fever
- Parotitis occurs in 30-40%, may be unilateral or bilateral, with single or multiple salivary glands affected
- Complications: aseptic meningitis, orchitis, oophoritis, deafness, encephalitis, pancreatitis

Rubella

The Disease

An acute febrile exanthematous disease characterized by cervical lymphadenopathy that can lead to congenital defects and fetal deaths if it occurs during pregnancy.

Etiologic Agent

- A togavirus, genus Rubivirus

Epidemiology

- Worldwide in distribution
- 10-20% of young adults are still susceptible

Transmission

- Person to person via airborne droplets from respiratory secretions of infected persons

Clinical Features

- Incubation period: varies from 12-23 days
- Period of communicability: one week before to one week after the onset of rash
- Symptoms are mild, up to 50% of infections may be subclinical or inapparent
- In older children and adults, it presents with a 1-5 day prodrome of low-grade fever, malaise, lymphadenopathy and upper respiratory symptoms preceding the rash
- Maculopapular rash 14-17 days after exposure, fainter than measles and does not coalesce
- Other manifestations include lymphadenopathy (postauricular, posterior cervical and suboccipital), athralgia, arthritis, conjunctivitis, testalgia or orchitis
- Infection during the first trimester of pregnancy may lead to Congenital Rubella Syndrome
- Complications: arthralgia, arthritis, encephalitis, thrombocytopenic purpura, neuritis, orchitis, syndrome of progressive panencephalitis

The Vaccine

General Description

- MMR vaccine contains live attenuated strains of measles, mumps and rubella.

Indications

Routine

- Given to adolescents and adults without documented evidence of measles, mumps and rubella immunity

- Adults who may be at increased risk for exposure to measles: post-high school educational institutions, persons working in medical facilities and international travelers.
- All healthcare workers without evidences of immunity should be given MMR vaccine, except those:
- With written documentation of vaccination with 2 doses of live measles, 1 dose of live rubella, 1 dose of live mumps or MMR vaccine administered at least 28 days apart
- With laboratory evidence of immunity
- With laboratory confirmation of disease, or born before 1957

Dose and route of administration

- Given subcutaneously 2 doses, 1 month apart

Special Situations

HIV-infected individuals

- Indicated for HIV-infected individuals who are asymptomatic and with a CD4+ T cell count of >200 cells/uL.
- The combined MMR vaccine is recommended for HIV-infected individuals who want to be protected against measles, mumps and rubella.
- HIV-infected women of childbearing age should also be screened for rubella IgG and the MMR vaccine offered to rubella IgG-seronegative women with CD4+ counts >200cells/uL
- Rubella IgG serology should be repeated after vaccination and a second MMR dose administered if the patients remains rubella IgG-seronegative

Pregnancy

- Pregnant patients should **NOT** receive MMR vaccine. Pregnancy should be avoided for 1 month following receipt of MMR vaccine.

Transplant recipients

- MMR is recommended to stable patients at least 2 years after bone marrow transplant and without evidence of graft-versus host disease.
- No large clinical trials of safety and efficacy in adult solid-organ recipients.

Post-exposure prophylaxis

- MMR vaccine may prevent measles if given within 72 hours of exposure.
- No effective post-exposure prophylaxis for rubella and mumps.

Side effects

- Adverse reactions following MMR vaccine (except allergic reactions) occur 5-12 days post-vaccination and only occur in persons who are susceptible to infection.
- No evidence of increased risk of adverse reactions following MMR vaccination in persons who are already immune to diseases
- Fever - most common occurring 7-12 days after vaccination
- Transient rash after 7-10 days
- Thrombocytopenia, parotitis, lymphadenopathy, arthalgias
- Allergic reactions are rare - wheal and flare or urticaria at the injection site.

Precautions and Contraindications

- Persons with severe allergy to gelatin or neomycin or who have had a severe allergic reaction to a prior dose of MMR
- Pregnancy
- Severely immunocompromised persons
- Persons receiving large daily doses of corticosteroids (>2mg/kg per day or >20 mg per day of prednisone) for 14 days or more
- Persons with moderate/severe acute illness
- Receipt of antibody-containing blood products (e.g., immune globulin, whole blood or packed red blood cells, intravenous immune globulin)

Vaccine Storage and Handling

- Must be shipped with refrigerant to maintain 10°C (50°F) or less at all times
- Refrigerated immediately and protected from light at all times
- Stored at refrigerator temperature +2°C to +8°C (3545°F), but may be frozen
- After reconstitution, store in a refrigerator and should be used immediately or discarded after 8 hours

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MENINGOCOCCAL DISEASE

The Disease

A severe acute bacterial infection that can cause meningitis, bacteremia, and other localized infections, such as pneumonia and arthritis. Symptoms develop and progress rapidly which may lead to death in 24-48 hours despite appropriate therapy.

Etiologic Agent

- Neisseria meningitidis, or meningococcus.
- There are 13 serogroups based on the structure of the polysaccharide capsule.
- All invasive disease is caused by one of five serogroups: A, B, C, Y, and W-135

Epidemiology

- Humans are the only natural reservoir.
- Occurs worldwide both in endemic and epidemic form.
- The distribution of serogroups varies by age, location and time.
- In the Philippines, all serogroups have been implicated with group A as the most prevalent serotype.
- Invasive disease is highest in infancy with second peak in adolescence.
- Case fatality rate ranges from 23-50% in all age groups, higher among adults and highest among the elderly

Transmission

- Asymptomatic colonization of the nasopharynx provides source for spread of the organism.
- Direct contact with respiratory droplet secretions through coughing, sneezing, kissing, mouth-to- mouth resuscitation
- Risk of secondary infection among close contacts, 500-¬800 times more than in the general population.
- Patients may still transmit the organism up to 24 hours after initiation of antimicrobial therapy.

Clinical Features

- Incubation period: average of 3-4 days, with a range of 2 to 10 days.
- Invasive infection usually results in meningococcal bacteremia, meningitis or both.

- Meningococcal bacteremia is characterized by sudden onset of fever, and a petechial or purpuric rash often presenting with shock, acute hemorrhage of the adrenals, and multi-organ failure.
- Meningitis signs and symptoms are indistinguishable from other forms of acute purulent meningitis.
- Less common presentations include pneumonia, arthritis, otitis media, and epiglotitis.
- Sequelae of hearing loss, neurologic disability, digit or limb amputation, and skin scarring occur in 11 - 20%.

The Vaccine

General Description

2 Types:

- Meningococcal Polysaccharide Vaccine (MPSV)
  - Available locally for children 2 years and above and adults
  - Meningococcal polysaccharide A and C
  - Meningococcal polysaccharide A, C, Y, and W-135
- Meningococcal Conjugate Vaccine (MCV4)
  - contains serogroups A, C, Y and W-135
  - Protective antibody is achieved within 7-10 days of vaccination.
  - In healthy adults, antibody levels decrease but are detectable as long as 10 years after vaccination.
  - MPSV is administered as a single dose 0.5ml and can be given concurrently with other vaccines but at different anatomic sites.
  - Little boost occurs following repeated vaccination.
  - Revaccination 5 years after receipt of the first dose if indications for vaccination still exist.

Routine Indication

- Not for routine use
- Give as a single intramuscular dose to high-risk groups except HIV-infected patients and patients with functional asplenia.
- Recommended for the following high-risk groups:
- with terminal complement component or properdin deficiencies
  - travelers to or reside in areas where N. meningitides is hyperendemic or endemic
  - for use in control of meningococcal outbreaks caused by vaccine-preventable serogroups (A,C,Y, and W-135)

- military recruits
- healthcare workers with direct patient care and exposure to secretions
- Clinical microbiologists and research microbiologists who might be exposed routinely to isolates of *N. meningitides*.

- Patients with persistent complement component deficiency (e.g., C5-C9, properidin, factor H or factor D deficiency) or asplenia must receive a 2-dose primary series of MCV administered 2 mos apart, and a booster every 5 years.
- functional or anatomic asplenia (2-dose primary series administered 2 months apart with a booster dose every 5 years)
- people who wish to decrease their risk of meningococcal infection may elect to receive the vaccine

Special Situations

HIV-infected individuals

- If indicated, MPSV4 should be administered preferably after ART-induced immunoreconstitution. Responses to the vaccine may be reduced in patients with CD4+ counts<200 cells/uL
- For those who are traveling to high risk areas

Pregnancy

- No data on the use of vaccine in pregnant woment.
- May be given only if clearly indicated following an assessment of healthcare professional

Transplant recipients

- Limited data on efficacy of MCV4 and MPSV4 in solid-organ transplant recipients
- Follow recommendations for general population since the vaccine is not a live vaccine
- Administer 6-12 months post-HSCT

Post-exposure prophylaxis

- No recommendations on the use of immuneglobulins
- Contacts of confirmed cases of meningococcal disease should be offered vaccination, as well as given chemoprophylaxis

Revaccination

- For MPSV
  - no revaccination

- For MCV
  - A booster dose is not recommended for healthy persons 22 years of age or older even if the first dose was administered at 11-15 years of age
  - Revaccinate a person every 5 years as long as he remains at increased risk.

Side effects

- Most common: pain and redness at site of injection
- Fever, headache and malaise within 7 days of vaccination

Precautions and Contraindications

- Severe allergic (anaphylactic) reaction to a vaccine component or following a prior dose
- Defer if moderate or severe acute illness exists

Storage and Handling

- Vaccine must be shipped in insulated containers.
- Should be stored at refrigerator temp (+2^{o}C to +8^{o}C).
- **DO NOT FREEZE.**
- Single dose vials must be used within 30 minutes of reconstitution.
- Multi-dose vials must be discarded after 10 days of reconstitution.

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PNEUMOCOCCAL DISEASE

The Disease

An acute bacterial illness affecting the upper (otitis media and sinusitis) and lower respiratory tract (pneumonia) and can cause invasive diseases such as meningitis, endocarditis and peritonitis via hematogenous spread.

Etiologic Agent

- *Streptococcus pneumoniae*

Epidemiology

- Occurs worldwide

Transmission

- Through droplet inhalation

Clinical Features

- Incubation Period: 1-3 days
- Upper respiratory tract infections: otitis media and sinusitis
- Pneumonia: acute, cough, fever, pleuritic chest pain, chills, tachypnea, dyspnea
- Invasive disease includes bacteremia, peritonitis, arthritis, meningitis and endocarditis
- Complications: empyema, pericarditis, endobronchial obstruction, lung abscess

The Vaccine

General Description

- 2 types of vaccines:
  - For adults and children above 2 years of age, the 23-valent polysaccharide vaccine is available (PPSV23). It contains serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F and 33F.
  - The pneumococcal conjugate vaccine (PCV13) can prevent pneumonia and invasive pneumococcal disease in adults aged >50 years old. It contains serotypes 1, 3, 4V, 5, 6A, 6B, 7, 9F, 14, 18, 19A, 19F and 23F. This vaccine is not approved for those between ages 6 – 49 years old.

- PCV10 is available but not licensed for adults. It contains serotypes 1, 4, 5, 6B, 7, 9F, 14, 18, 19F and 23F.

Indication

Routine

- Age 50 years and older
- Adults less than 50 years old with any the following diseases:
  - Chronic lung disease (COPD, emphysema, asthma)
  - Chronic cardiovascular diseases
  - Diabetes mellitus
  - Chronic liver disease (including cirrhosis)
  - Alcoholism
  - CSF fluid leaks
  - Immunocompromising conditions
  - Functional asplenia (sickle cell disease and other hemoglobinopathies, splenic dysfunction
  - Anatomic asplenia (congenital asplenia and splenectomy [if elective splenectomy is planned, vaccinate at least 2 weeks before surgery])
  - Generalized malignancy
  - Solid organ transplants
  - Multiple myeloma
  - Residents of nursing homes or long-term care facilities
  - Smokers
  - Patients with cochlear implant

Special Situations:

HIV-infected individuals

- Pneumococcal vaccine is recommended for all HIV-infected individuals regardless of age, CD4+ counts and co-morbid conditions
- The first dose may either be PPSV23 or PCV13, but PCV13 is strongly recommended.
- The duration of the protective effect of primary pneumococcal vaccination is unknown
- Revaccination can be considered for persons who were initially immunized when their CD4+ counts were <200 cells/uL and whose CD4+ counts have increase to >200 cells/uL in response to cART.
  - If PCV13 is given first, give PPSV23 after 2 months.
    - Revaccination every 5 years may be considered

- If PPSV23 is given first, give PCV13 at least after 1 year.
  - Revaccinate with PPSV23 after 2 months of the PCV13.

Pregnancy

- Immunization with PPSV23 can be given during pregnancy although its safety during the first trimester of pregnancy has not been evaluated, no adverse consequences have been reported among newborns whose mothers were inadvertently vaccinated during pregnancy
- No data on PCV13 in pregnancy.

Transplant recipients

- In solid organ recipients, PPSV23 should be started before transplantation and repeated booster doses should be administered at 2-5 years interval
- In hematopoietic stem cell transplant recipients, 3-4 doses of PCV13, first dose to be given on the 6th month post-transplant, second dose on the 8th month and the third dose on 10th month post-transplant. For patients with chronic GVHD, a fourth dose of PCV13 is recommended 2 months from the last dose.

Immunization Schedule

- PPSV23 and PCV13: A single 0.5 ml dose given IM or subcutaneous
- Immunocompromised adults who have not received any pneumococcal vaccine, should receive a dose of PCV13 FIRST then PPSV23 after 2 months
  - For subsequent doses of PPSV23, follow the recommended revaccination schedule
- Immunocompromised adults, who have received previous PPSV23, give PCV13 after 1 year or more. If the patient is still at risk, give PPSV23 after 2 months of the PCV13.
- Revaccination of immunocompetent persons is not recommended.
- Revaccination may be given to the following:
  - Those ≥ 50 years who received their first dose more than 5 years ago and before they reached age 50.
  - Persons less than 50 years old who received the vaccine more than 5 years ago and who have the following:
  - Functional or anatomic asplenia
  - HIV, Leukemia, Lymphoma, Generalized Malignancy, Multiple Myeloma

- Chronic renal failure or nephrotic syndrome
- Receiving immunosuppressive therapy, including corticosteroids
- Received solid organ or bone marrow transplant

Side Effects

- Most common: Soreness, swelling and redness at injection site
- Fever, malaise and muscle pain are very uncommon
- Allergic reactions may occur

Precautions and Contraindications

- An immediate anaphylactic reaction to a previous dose of pneumococcal vaccine
- Allergy to a vaccine component: anaphylaxis to phenol or thimerosal
- Moderate to severe illness with or without a fever

Vaccine Storage & Handling

- Store at refrigerator temperature (+2°C to +8°C).
- **DO NOT FREEZE.**
- Ship in insulated containers with coolant packs

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RABIES

The Disease

Rabies is a preventable, zoonotic viral infection of the central venous system (acute encephalitis), with a fatal outcome, and no effective cure.

Etiologic Agent

- Rabies Virus, RNA Rhabdovirus, genus *Lyssavirus*

Epidemiology

- Worldwide zoonotic disease
- Endemic in the Philippines
- Incidence of 6-8/million population 300-500 cases/year
- Domestic dog transmits 83% of human rabies cases
- Cats and other domestic animals transmit 17% of human rabies
- Rats and bats do not transmit rabies to humans in the Philippines.
- About 55, 000 deaths from rabies occur every year, 99% of which are due to dog bites
- Of these 55, 000 deaths, 31,000 are estimated to occur in Asia (20,000 in India alone) and 24,000 in Africa
- Annual global incidence of animal bites - 100-200 bites per 100,000 population
- In 2011, DOH reported 209 documented cases of rabies.

Transmission

- Most common mode of transmission -bites of rabid animals
- Less common mode of transmission
  - scratches from animals with contaminated claws
  - licks of mucus membranes or abraded skin with infected saliva or with infected body materials
- Rare modes of transmission
  - airborne route such as exposure in caves populated by bats
  - corneal transplantation

Clinical Features

- Four stages namely:
  - Incubation period: usually 20-90 days but can range from days to years; patients have no symptoms except those related to local wound healing

- Prodrome: 2-3 days (sometimes only a few hours); changes in attitude/behavior/temperament such as unusual shyness or aggressiveness, dilated pupils, nonspecific symptoms of fever, headache, malaise, body aches, pain, itching, or paresthesia at bite site.
- Acute neurologic phase: 2-7 days encephalitis or furious rabies in 80% of cases, with hydrophobia and aerophobia; paralytic or dumb rabies in 20% of cases
- Coma: 4-10 days, complications start to appear followed by death due to respiratory paralysis.

The Vaccine

General Description

- First known human rabies vaccines utilized nerve tissue (brain, spiral cord) of animals like goat, sheep, and rabbits. **NO LONGER AVAILABLE**. These vaccines produced SERIOUS neurologic adverse reactions.
- Cell Culture Rabies Vaccines – These are modern day vaccines prepared from rabies virus grown on tissue culture, free of neuronal tissues, inactivated by ß- Propiolactone and purified by ultracentrifugation
  - Human Diploid Cell Vaccine (HDCV) – gold standard of human rabies vaccines
  - Purified Vero Cell Rabies Vaccine (PVRV)
  - Purified Chick Embryo Cell Vaccine (PCECV)
  - Purified Duck Embryo Vaccine – **not locally available**

Rabies Pre-Exposure Prophylaxis

Indications

- Health care workers in hospitals that handle dog bites and rabies cases
- Rabies research and diagnostic lab workers
- Rabies biologic production workers
- Veterinarians and Veterinary students
- Animal control, wildlife and animal handlers
- Spelunkers
- Field workers (bill collectors, mailman, delivery man)

Dose and schedule (any of the following):

- Three doses 1.0-mL of HDCV or PCECV administered IM (deltoid area), one injection per day on days 0, 7, and 21 or 28
- Three doses of 0.5 mL of PVRV administered IM, one injection per day on days 0, 7, and 21 or 28
- Three doses of 0.1mL of PVRV, HDCV or PCECV Intradermal (ID), one injection per day on days 0, 7 and 21 or 28.

Post-exposure Prophylaxis for Previously Vaccinated Persons (any of the following)*

- Two IM doses (1.0 mL each of HDCV or PCECV in the deltoid, or 0.5 mL of PVRV) on days 0 and 3, regardless of the interval from the last dose
- Two Intradermal (0.1mL on each side of the deltoid) of HDCV, PCECV, PVRV on days 0 and 3

*No RIG required.

Post-exposure prophylaxis

Indicated only:

- when the person is bitten by a rabid person or animal
- when the saliva or other potentially infectious material such as neural tissue has contaminated an open wound or mucous membrane
- All persons exposed to rabid or suspect rabid animals or persons
  - Categorized as follows:
    Category I* touching or feeding of animals or persons, licks on intact skin
    Category II** nibbling of uncovered skin, minor scratches or abrasion without bleeding, licks on broken skin
    Category III** – Single or multiple transversal bites or scratches, contamination of mucous membranes with saliva, All Category II exposures in the head, face or neck

  ** Pre-exposure prophylaxis may be recommended*

  *** Post-exposure treatment MUST be administered*
- If post-exposure prophylaxis has been initiated and appropriate laboratory diagnostic testing (i.e., the direct fluorescent antibody test) indicates that the animal that caused the exposure was not rabid, post-exposure prophylaxis may be discontinued. HOWEVER, it is encouraged to complete the course to serve as a pre-exposure prophylaxis.

- If post-exposure prophylaxis has been initiated and the animal is still alive after 14 days of observation, post-exposure prophylaxis may be discontinued. HOWEVER, completion of the full course may serve as a pre-exposure prophylaxis.
- Post-exposure prophylaxis may be delayed for Category II exposures provided that the following conditions must be satisfied:
  - Animal is healthy and available for observation for 14 days
  - Animal was vaccinated against rabies for the past 2 years:
    - Animal must have a certificate from a duly licensed veterinarian that it was vaccinated for the last 2 years
    - The last vaccination must be within the past 12 months.
- Post-exposure prophylaxis schedule for persons without previous rabies vaccination:
  - Any of the following:
    Intramuscular administration:
    - 1 mL PCEC or 0.5 ml PVRV: Days 0,3,7,14 and 28
    - 1 ml PCEC or 0.5 ml PVRV: 2 doses on Day 0, 1 dose on days 7 and 21
  - Intradermal administration:
    - 2 injections of 0.1 ml on Days 0,3,7 and 28

Rabies Immunoglobulin (RIG):

- provides an immediate supply of virus neutralizing antibodies to bridge the gap until the production of active immunity in response to vaccine administration
- provides a rapid, passive immunity that persists for a short time (half-life of approximately 21 days)
- two types:
  1. Human IgG (HRIG)
  2. Highly purified equine IgG (ERIG)

RIG Use (HRIG and ERIG)

- RIG is administered once to previously unvaccinated persons to provide rabies virus-neutralizing antibody coverage until the patient responds to vaccination by actively producing virus-neutralizing antibodies
- Administered once on day 0 at the time post-exposure prophylaxis is initiated.

- If not administered on day 0, RIG is **NOT** recommended beyond 7 days.
- RIG is infiltrated around and into any wounds and remaining volume is injected IM at deltoid area. HRIG should **NOT** be administered in the same syringe nor at the same anatomic site as the vaccine.
- The dose administered should **NOT** exceed the recommended dose because HRIG can partially suppress active production of antibody
- Recommended dose of HRIG is 20 IU/kg; ERIG dose is 40 IU/kg
- All patients with Category III exposure
- All Category II exposure patients who are immunocompromised

Special Situations

Immunosuppressed patients

- Rabies post-exposure prophylaxis should be administered using a 5-dose vaccine regimen (i.e., 1 dose of vaccine on days 0, 3, 7, 14, and 28) for patients on corticosteroids, other immunosuppressive agents and antimalarial drugs
- Immunosuppressive agents should **NOT** be administered during rabies post-exposure prophylaxis unless essential for the treatment of other conditions.
- Ideally, immunosuppressed patients should postpone pre-exposure vaccinations if possible.
- Check antibody titers after completing the pre-exposure series.

HIV-infected Individuals

- Should receive RIG for the same indications and in the same doses as immunocompetent patients
- RIG is indicated for Category III contact along with rabies vaccine series
- **NOT** necessary for people vaccinated against rabies who have demonstrated neutralizing antibodytitres of at least 0.5 IU/ml

Pregnancy

- Pregnancy is **NOT** a contraindication to post-exposure prophylaxis.

Transplant Recipients

- Give rabies vaccine 12 months after HSCT
- Pre-exposure: 3 doses
  - Should be delayed 12 – 24 months after HSCT and given only to those considered high-risk (e.g., occupational exposure to potentially rabid animals).
  - Must be given intramuscularly: 1.0 mL on days 0, 7, 21 or 28
  - Immunity screening is recommended 1 month after last dose of series and every 2 years if risk continues.
  - Provide booster if indicated.
- Post-exposure: 5 doses
- Rabies prophylaxis can be administered at any time following transplant if indicated (i.e., if bitten by potentially rabid animal). Schedule for vaccine: days 0, 3, 7, 14, 28.
- Immunity screening is recommended two weeks after completion of series.

Post-Vaccination Serologic Testing

- **NO** testing is needed to document seroconversion **UNLESS** the person is immunosuppressed
- All healthy persons tested 2-4 weeks after completion of pre-exposure and post-exposure rabies prophylaxis demonstrate adequate antibody response to rabies

Adverse Events

Vaccines

- Hypersensitivity reactions (urticaria, pruritic rash, and angioedema)
- Local reactions (pain at the injection site, redness, swelling, and induration)
- Mild systemic reactions (fever, headache, dizziness, and gastrointestinal symptoms)
- Neurologic illness resembling Guillain-Barré syndrome

RIG

- Local reactions:
  - pain/tenderness (100% conventional HRIG, 50% heat-treated HRIG)
  - erythema (63% conventional, 25% heat-treated)
  - induration (50% conventional, 31% heat-treated)
- Headache - most commonly reported

Precaution

- Moderate and severe acute illnesses
- Allergic reaction to any vaccine component or who had an immediate anaphylactic reaction to a previous dose of rabies vaccine
- Always inject IM vaccines on the deltoid – NEVER IN THE BUTTOCKS (administration of vaccine in this area might result in a diminished immunologic response); In infants and neonates – inject at the anterolateral thigh
- For persons on corticosteroids, other immunosuppressive agents, or antimalarial prophylaxis agents, give vaccine only by IM route
- For persons with bleeding disorders, consider intradermal route

Vaccine Storage and Handling

- Ideal storage conditions are +2°C to +8°C
- Vaccine remains stable for at least 3-5 years

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TETANUS, DIPHTHERIA, PERTUSSIS

TETANUS

The Disease

A disease of the nervous system characterized by persistent tonic spasm, with violent brief exacerbations.

Etiologic Agent

- *Clostridium tetani*

Epidemiology

- Worldwide
- Incidence highest in densely populated regions with warm, damp climate and rich organic soil

Transmission

- Spread by direct contamination of spores in a traumatized site
- Other causes: elective surgery, burns, deep puncture and crush wounds, diabetic foot, ear infections, dental infection, animal bites, abortion, and pregnancy
- Neonatal tetanus is mainly due to contamination of umbilical stump

Clinical Feature

- Incubation period: typically 7 -10 days, can range from few days to several months.
- Shorter incubation period is associated with more severe disease
- Progressive stiffness, rigidity and spasm of the jaw, neck, abdomen and back causing trismus, risussardonicusandopisthotonus.
- Three clinical forms:
  - Local(uncommon)
  - cephalic (rare)
  - generalized (most common)
- Complications: Laryngospasm, fractures, hypertension, nosocomial infections, pulmonary embolism, aspiration pneumonia, death

DIPHTHERIA

The Disease

A nasopharyngeal and skin infection with pseudomembrane due to a protein toxin that causes systemic toxicity, myocarditis and polyneuropathy.

Etiologic Agent
- *Corynebacterium diphtheriae*

Epidemiology
- Worldwide
- Humans are the principal reservoir for *C. diphtheriae*

Transmission
- Airborne respiratory droplet
- Contact with exudates from infected skin lesion
- Occasionally by fomites

Clinical features
- Incubation period: 1-10 days
- Fever
- Pseudomembrane in the pharynx is the hallmark of the disease
- May involve any mucous membrane (anterior nasal, pharyngeal and tonsillar, laryngeal, cutaneous, ocular, genital)
- Complications: obstruction of the respiratory tract, paralysis of the soft palate, eye muscles, limbs and diaphragm, otitis media, myocarditis, polyneuritis, pneumonia, death

PERTUSSIS

The Disease

A highly contagious acute infection of the respiratory tract characterized bypersistent, paroxysmal coughing which can last more than 21 days. In adults, post-tussive vomiting is strongly suggestive of Pertussis.

Etiologic Agent

- *Bordetella pertussis*

Epidemiology

- Worldwide
- Human as reservoir
- Significant cause of morbidity and mortality in the non-immunized and insufficiently immunized persons.
- Occurs most notably among adolescents and adults.
- Immunity from childhood pertussis vaccination wanes after several years and most adolescents and adults are again susceptible to pertussis.

Transmission

- Predominantly by aerosol droplet with higher rate of transmission from a coughing patient
- Transmission can still occur from an asymptomatic individuals

Clinical Features

- Incubation period: 7-10 days up to 3 weeks.
- Catarrhal phase (1-2 weeks): rhinorrhea, lacrimation, mild conjunctival injection, malaise, low grade fever followed by dry non-productive cough.
- Paroxysmal phase (1 to 6 weeks): series of short expiratory bursts, followed by an inspiratory gap
- Convalescence phase (weeks to months): cough is less paroxysmal
- Complications: difficulty sleeping, school or work disruption, urinary incontinence, ribs fracture, epistaxis, pneumonia, CNS abnormalities, subconjunctival and scleral hemorrhages.

The Vaccine

General Description

- Tetanus: Inactivated fractional adsorbed tetanus toxoid
- Diphtheria: Purified inactivated adsorbed diphtheria toxoid
- Pertussis: subunit fractional inactivated vaccine formulated to contain 5Lf of tetanus toxoid, 2Lf diphtheria toxoid, 2.5Lf ug detoxified pertussis toxoid
- Vaccine is available as:
  - Tetanus-diphtheria-acellular pertussis vaccine (Tdap)

- Adult tetanus-diphtheria (Td)
- Tetanus toxoid is available as a single-antigen preparation (TT)

Routine Indications

- All susceptible adults who have not completed the primary series or have not received any dose, should receive Tdap dose
- Healthcare workers and providers
- Adults ≥ 65 years who have or who anticipate close contact with an infant (< 12 months old) and who have not previously received Tdap should receive a single dose of Tdap
- Persons recovering from any of the above mentioned diseases
- Part of wound care management
- Those who wish to receive the vaccine as long as there are no contraindications to any of the vaccine component

Vaccination Schedule

For unvaccinated persons 7 years and older (including those without documented prior vaccination)

- Administer three doses (1 Tdap + 2 Td) at 0, 1-2 months, 6-12 months schedule for a primary series
- Tdap should be administered regardless of interval since the last tetanus- or diphtheria-toxoid containing vaccine.
- Booster dose of Td every 10 years

Wound Management of an Immunocompetent individual

Characteristic	Clean, minor wounds		All other wounds	
History of Tetanus toxoid/Doses	Tdap or Td	TIG	Tdap or Td	TIG
Unknown or < 3 doses	Yes	No	Yes	No
3 or more doses	No (yes, if >10 years since last Td)	No	No (yes, if >10 years since last Td)	No

Special Situations

HIV- Infected Individuals

- Tetanus/diphtheria/acellular pertussis (Tdap)
  - Tdap is recommended in all HIV infected individuals regardless of CD4+ cell count
  - HIV infected individuals without prior immunization or undocumented immunization require five doses (1Tdap + 4 Td) at 0, 1 month, 2 months, 5 years and 10 years. Booster dose every 10 years with Td
  - Those who have received a full primary course (three doses) as infants and a booster at preschool age (total of four doses) require a single booster dose Tetanus/diphtheria (Td)
  - Tetanus/diphtheria (Td)
  - Td can be used if Tdap is not available

Wound management of an HIV-infected individual

History of tetanus toxoid/ Number of doses	Clean, minor wounds		All other wounds	
	Tdap or Td[1]	TIG	Tdap or Td[1]	TIG[2]
Unknown or <3 doses	yes	No	yes	yes
3 or more doses	Yes (1 dose) if > 10 years from last dose	No	Yes (1 dose) if > 10 years from last dose or CD4+ count < 200 cells/uL	Yes[3]

[1]Tetanus vaccine is recommended in all HIV infected individuals following a possible exposure.

[2]TIG should be given by intramuscular injection in the deltoid within 24h of possible exposure. When tetanus vaccine and TIG are given concurrently, separate syringes and separate sites should be used

[3]TIG is not usually indicated for persons who have received at least three vaccine doses including a dose within the previous 10 years. However, individuals with a high-risk wound who are severely immunosuppressed should receive TIG even if fully vaccinated in the past and where the last vaccine dose occurred within the last 10 years

Pregnancy

- For pregnant individual who has NOT received any tetanus – diphtheria- pertussis containing vaccine within the past 10 years, vaccinate during pregnancy (second or third trimester) as follows:
  - 3 doses (1Tdap + 2Td) at 0, 1 month, and 6-12 months schedule. (The 3rd dose given at least 2 weeks before delivery)
- For pregnant individual has received the last Td vaccination within the past 10 years, Tdap should be given during pregnancy (second or third trimester) or immediately postpartum or before discharge

Transplant-Recipient

- Transplant recipients should be considered as ''never vaccinated'' and be given the primary series (1Tdap +2Td) within 6-12 months post-transplant

Side Effects

- Local reactions (pain at injection site)
- Exaggerated local reactions (Arthus-type)
- Fever
- Headache
- Generalized body aches
- Tiredness

Precautions and Contraindications

- Moderate to severe allergic reaction to vaccine component like Thimerosal or following prior dose
- Moderate or severe acute illness
- History of Guillain-Barré syndrome within 6 weeks after a previous dose of tetanus toxoid containing vaccine
- Active neurologic disorder
- Thrombocytopenia, hemophilia and other coagulation disorders
- Encephalopathy occurring within 7 days after vaccination with a pertussis-containing vaccine

Vaccine Storage and Handling

- All tetanus-toxoid-containing vaccines should be stored at 2°–8°C (Refrigerator temperature)
- **DO NOT FREEZE**

The Role of Passive Immunization

Tetanus Immuneglobulin

2 types:

Human Immuneglobulin: 250-500 IU, IM

Equine Immuneglobulin: 1500-5000 IU, IM

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TYPHOID FEVER

The Disease

Acute, generalized infection of the reticuloendothelial, system, the intestinal lymphoid tissue and gall bladder.

Etiologic agent

- *Salmonella typhi*

Epidemiology

- Disease of developing countries, with poor sanitation and untreated water supplies
- Endemic in the Philippines
- Risk of typhoid fever is highest for travelers to southern Asia (6–30x higher than for all other destinations)
- Occurs in all places, all year round, all ages
- about 22 million cases of typhoid fever and 200,000 related deaths occur each year worldwide
- risk of typhoid fever is highest for travelers to southern Asia (6–30 x higher)
- In the latest Philippine 2011 survey, there were 415 confirmed typhoid fever cases, with 2 reported deaths (case fatality rate 0.5%).
- Case-fatality rates is about 1%-4% with appropriate antibiotic therapy
- After the 1994 outbreak of MDR typhoid, it was noted that there was a decrease in incidence of MDR typhoid
- In 2011, ARSP reported no significant resistance to the following antibiotics: ampicillin, ceftriaxone, chloramphenicol, ciprofloxacin, and cotrimoxazole

Mode of transmission:

- fecal-oral route: by ingestion of dairy products or water contaminated by excreta from patients or chronic carriers or handled by infected persons, shellfish taken from sewage-contaminated beds, vegetables fertilized with night-soil and eaten raw

Clinical Presentation

- Incubation period: 6–30 days
- Onset of illness - insidious, with gradually increasing fatigue and increasing fever from low-grade to as high as 38°C–40°C by the 3rd and 4th day of illness
- Clinical Manifestations
  - Fever (classic step ladder pattern): commonly lowest in the morning, reaching a peak in late afternoon or evening
  - Headache (more than 70% of cases), malaise, anorexia, abdominal pains, constipation or diarrhea, vomiting, muscle aches, weakness, loss of appetite, hepatosplenomegaly, transient, macular rash of rose-colored spots occasionally seen on the trunk,
  - Confusion or agitation, mental dullness, stupor, delirium and shock
- Complications: occur after 2–3 weeks of illness; intestinal hemorrhage or perforation

The Vaccine

Two vaccines:

1. Parenteral vaccine (intramuscular route) - a subunit (Vi PS) vaccine
2. Oral vaccine - live attenuated S typhi strain (Ty21a); **NOT LOCALLY AVAILABLE**

- The Vi polysaccharide (ViPS) vaccine
  - Vi capsular polysaccharide vaccine
  - given either SC or IM in a single dose
  - re-vaccination is recommended every 3 years for travelers
- The live attenuated Ty21a vaccine
  - Oral live, attenuated vaccine
  - first live oral typhoid fever vaccine
  - enteric-coated capsules to be swallowed every other day for one week
  - provide protection for at least 5-7 years

Indications

Routine

- Hospital personnel involved in food handling
- Microbiology lab technicians
- Persons with intimate exposure to a documented *S.typhi* carrier/ patient
- Any person who wants to get protected
- People in refugee camps, evacuation and disaster areas

Dosage and schedule

- Vi Capsular Polysaccharide Vaccine (Typhim Vi)
  - 1 dose should be given ≥2 weeks before expected exposure
  - **Primary dose** (≥2 years old)

Dose – 1 dose, 0.50 mL,IM

  - Booster dose– 1 dose, 0.50 mL, IM, every 2 years
  - **Adverse reactions:** injection-site reactions (7%); resolves within 48 hours, fever, swollen glands, rash or itching, joint pains, tremors or shaking; headache (16%–20%), nausea, diarrhea, stomach pain; weakness

Special Situations

HIV

- Vaccination with the Vi polysaccharide vaccine is recommended for all HIV-infected people
- 1 dose of the vaccine should be given at least 2 weeks before the expected exposure
- Booster dose is recommended every 2-3 years in those who remain at risk; interval might be reduced to 2 years, if CD4 count is <200 cells/mm^3

Pregnant women

- No data have been reported on the use of any of the typhoid vaccines among pregnant women.

Stem cell transplant patients

- Give TYVI 12 months after HSCT

Precautions and Contraindications

ViCPS vaccine (parenteral)

- should **NOT** be administered intradermally
- bleeding disorders and taking anticoagulants
- moderate or severe acute illness
- history of any adverse reaction to a previous dose of vaccine

Precautions while traveling:

- Avoid eating raw, unpeeled fruits or vegetables, or any street foods; drinks with ice, or frozen treats, flavored ice that may have been made with contaminated water; unbottled or unboiled water
- Eat well cooked foods prepared with properly washed utensils on clean surfaces
- Drink only bottled or boiled water

Vaccine Storage and Handling

- Store vaccines in refrigerator between +2^{o}C to +8^{o}C
- **DO NOT FREEZE.**

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VARICELLA

The Disease

It is an acute, generalized viral illness commonly presenting as sudden onset of fever and the appearance of skin rashes varying from maculopapular rashes to vesicles to granular scabs. These stages are seen in one anatomical area. While it is a common childhood illness with mild manifestations, adults can suffer from severe illness or serious complications.

Etiologic Agent

- Varicella-Zoster virus

Epidemiology

- Highly infectious with incubation period of 14-16 days
- Incubation period may be longer in immunocompromised hosts and those who have received post-exposure vaccination
- Progressively affects more adolescents than children
- Generalized disease more common in neonates, in children with acute leukemia, and in pregnant women who get ill at or near delivery
- High secondary attack rates within a household
- Results typically in lifetime immunity

Transmission

- Airborne – most common
- Direct contact with lesions

Clinical Features

- Highly contagious
- Commonly with fever, mild constitutional symptoms and successive appearance of pruritic maculopapular, vesicular rashes and crusted lesions or scabs in centripetal distribution
- Period of communicability is from 1 to 2 days before the appearance of rash through the first 4 to 5 days, or until all lesions have crusted
- Complications: pneumonia, secondary bacterial infections of the lesions, hemorrhagic manifestations and encephalitis. Rarely, myocarditis, glomerulonephritis, arthritis, orchitis, uveitis and hepatitis.

- Groups at increased risk of complications are those younger than 1 year and older than 15 years, immunocompromised hosts, and newborns born to women with maternal varicella
- Some vaccinated persons may develop modified disease with a typical presentation
- Post-vaccination breakthrough varicella presents with mild disease accompanied by maculopapular rashes

The Vaccine

General Description

- Live attenuated Varicella virus vaccine
- Propagated in human (or guinea-pig) cells
- Lyophilized and to be reconstituted when used
- Contains hydrolyzed gelatin, neomycin, fetal bovine serum, sucrose, human-diploid cells (MRC-5) and egg protein (in combination MMR vaccine)
- Does not contain known preservatives

Routine Indications

- Recommended for all adolescents and adults without evidence of immunity
- Healthcare workers
- Live or work in settings where there varicella transmission is likely (schools, child care centers, institutional settings, colleges, prisons, military)
- Non-pregnant women of childbearing age
- Live in households with children
- International travelers
- Two doses, given at least 4 weeks apart

Catch-up

- Second dose recommended for all persons who received one dose previously provided at least 4-8 weeks interval from the first dose

Post-exposure Immunization

- Give within 3-5 days of exposure
- Two doses subcutaneously, given 4-8 weeks apart

Special Situations

HIV Infected Individuals

- Limited data on the efficacy of vaccination among HIV infected individuals
- May be considered for HIV+ individuals with CD4 count >200 cell/uL with the following conditions:
  - VZV IgG negative
  - uncertain history of varicella infection
  - at risk of exposure
- Administer two doses of varicella vaccine 0.5 mL SC (deltoid) at 3-month interval
- Post-exposure prophylaxis:
  - Should be based on the patient's clinical status
  - Asymptomatic HIV infected individuals with CD4+ count >400 cells/uL (with or without ART):
    - varicella vaccine should be given within 3 days of exposure, followed by second dose after 3 months
  - Symptomatic HIV infected individuals with CD4+ count < 400 cells/uL (with or without ART):
    - VZVIG must be given as soon as possible (or within 7 days; not later than 10 days)

Pregnant women

- Pregnant individuals should NOT receive the vaccine
- If given, avoid pregnancy for 4 weeks
- Give vaccine postpartum, if susceptible. Two doses at least 4 weeks apart.

Hematopoietic cell transplant recipients

- Limited data
- If clinician decides to vaccinate, it should be given at least 24 months after transplantation if the patient is presumed to be immunocompetent

Side Effects

- Injection site complaints (pain, erythema, swelling)
- Generalized rash
- Systemic reactions not common

Precautions and Contraindications

Precautions

- Acute severe illness
- Untreated tuberculosis
- Thrombocytopenia
- Recent administration of blood, plasma, or immune globulin
- Use of salicylates

Contraindications

- History of anaphylactic reaction to any vaccine component, including neomycin and gelatin.
- Pregnancy
- Malignant condition affecting bone marrow or lymphatic system
- Primary or acquired immunodeficiency including HIV+ (if combination MMR)
- Family history of congenital or hereditary immunodeficiency in first degree relatives
- Untreated active tuberculosis
- Recent (3 to 11 months) blood transfusion (including fresh frozen plasma, platelets, cryoprecipitate) or antibody-containing products (IVIG)
- Administration of another live attenuated vaccine within the past 4 weeks
- High dose immunosuppressive therapy or any low-dose steroid therapy exceeding two weeks duration
    - Person, whose steroid therapy has been discontinued for 1 month, or 3 months for chemotherapy, may be vaccinated.

Vaccine Storage and Handling

- Stored in a continuously frozen state (-15°C or colder). Store only in stand-alone freezers or the freezer compartment of refrigerator-freezer combinations, provided that the freezer compartment has its own separate, sealed, and insulated exterior door
- Use immediately or within 30 minutes of reconstitution or within 72 hours upon removal from freezer
- Do not refreeze.
- Transportation of the vaccine discouraged. If it must be transported, store at refrigerator temperatures between (2°C to 8°C) for not more than 72 hours prior to reconstitution.

- For field vaccination, may be transported using dry ice or frozen packs
- Combination MMR may not be transported at any time

The Role of Passive Immunization

Passive Immunization with Varicella Zoster Immune Globulin (not locally available)

- Indication:
  - Patients without evidence of immunity to varicella who are at high risk for severe disease complication who:
  - Have been exposed to varicella or herpes zoster
  - Are not eligible for varicella vaccine (pregnant, immunocompromised patients)
- Given IM as soon as possible or within 10 days after exposure
- Do not use to treat Varicella, Herpes Zoster, or postherpetic neuralgia
- Do not use if person is on regular immune globulin treatment

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YELLOW FEVER

The Disease

Febrile illness endemic in South America and sub-Saharan Africa depicted with undifferentiated symptoms to severe manifestation with bleeding and jaundice.

Etiologic Agent

- Yellow Fever Virus, a Flavivirus
- 1 Virus Strain, with 3 genotypes
  - East African
  - West African
  - New World

Epidemiology

- Occurs in sub-Saharan Africa and tropical South America
- Has never been documented in Asia

Transmission

- Transmitted by the *Aedes aegypti* mosquito

Clinical Features

- Incubation period: 3 to 6 days
- Period of infection: fever, chills, myalgia, with conjunctival injection, relative bradycardia, then resolves
- Period of intoxication: may follow period of infection from a few hours to several days, with renewed fever, headache, abdominal pain, somnolence, later with icteric hepatitis, hemorrhagic diathesis with GI bleeding
- With hemorrhage: up to 50% mortality rate
- 5-50% of cases are asymptomatic

The Vaccine

Yellow Fever is the only disease for which the WHO requires an International Certificate of Vaccination for travelers. Some countries require a certificate for all travelers, while other countries require it only from travelers coming from endemic areas. The Philippines requires a vaccination certificate from all travelers over 1 year of age coming from endemic countries. Filipinos traveling to endemic areas

can get the vaccine and the certificate from the Bureau of Quarantine, Port Area, Manila, at telephone number: (632) 527-4678.

General Description

- A live attenuated virus vaccine

Indication

- Routine
  - Not indicated for routine use
  - Given to 9 months or older travelling to or living in areas of South America or Africa where yellow fever is endemic.
  - Pre-exposure immunization: A single 0.5 ml dose is given SC
  - Booster: Given every 10 years

Special Population

HIV-infected individuals

- contraindicated
- if travel cannot be avoided, a medical waiver should be provided and counseling to prevent mosquito bites must be emphasized

Pregnant women

- limited data regarding safety and immunogenicity
- contraindicated
- should also be avoided in breastfeeding individuals

Transplant recipients

- contraindicated to patients within 2 years of transplantation
- contraindicated to patients who underwent transplant more than 2 years ago but are still taking immunosuppressive drugs
- if travelling cannot be avoided, counsel on mosquito bites prevention

Side Effects

- Most common: Fever, headache and muscle ache may occur from 5-14 days after immunization
- Rare cases of encephalitis reported in young infants
- Allergic reactions rarely occur.

Precautions and Contraindications

- Not given to immunocompromised individuals.
- Infants < 9 months, travel to endemic areas should be avoided due to high risk of adverse events with the vaccine
- For adults ≥ 60 years old, vaccine is a precaution due to increased risk for serious adverse events
- An immediate anaphylactic reaction to a previous dose of yellow vaccine
- Anaphylactic reaction to a vaccine component
- Moderate to severe illness with or without a fever
- History of anaphylaxis or sensitivity to eggs or egg protein

Vaccine Storage & Handling

- Store at a temperature between +2°C to +8°C (refrigerator temperature)
- **DO NOT FREEZE.**

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SPECIAL SITUATIONS: GENERAL PRINCIPLES AND RECOMMENDATIONS

General Principles

- Inactivated vaccines are safe to use but immunologic response may be decreased.
- Vaccinating an immunocompromised individual and achieve a less-than-optimal response is acceptable than not vaccinating and obtain no response.
- Live vaccines should **NOT** be administered to:
  - severely immunosuppressed persons;
  - Persons receiving large doses of corticosteroids (>20mg of prednisone per day or >2mg/kg per day of prednisone) for 14 days or longer;
  - Persons with HIV/AIDS (see particular vaccine chapter).
- Individuals who are on immunomodulators and biologicals such as infliximab and etanercept should be treated like patients on corticosteroids.
- Household and close contacts of immunocompromised individuals should receive all age-appropriate vaccines.
  - Inactivated formulation of vaccines is preferred to reduce the risk of transmitting the attenuated vaccine to the immunocompromised household member.

1. **HIV/AIDS**
   - Vaccines that **MUST** be given to all HIV/AIDS patients regardless of CD4 + T cell count
     - Hepatitis B
     - Influenza
     - Pneumococcal
   - Vaccines that **MAY BE** given safely to HIV/AIDS patients if indicated, regardless of CD4 + T cell count
     - Cholera
     - Haemophilus influenza B
     - Hepatitis A
     - Human Papilloma virus
     - Japanese Encephalitis virus
     - Meningococcus
     - Rabies
     - Tetanus, Diphtheria, Pertussis
     - Typhoid fever

- Vaccines that **CAN BE** given safely to HIV/AIDS patients if indicated, and if they are asymptomatic, with a CD4+ T cell count of >200 cells/µl
  - MMR
  - Varicella
  - Yellow Fever

2. Pregnancy

- Live vaccines should not be given to pregnant women.
- Inactivated vaccines may be given to pregnant women for whom they are indicated.
- Defer HPV vaccine during pregnancy.
- Tdap vaccine may be given to pregnant women.

3. Hematopoietic cell transplant recipients and other individuals with altered immunocompetence state

- If post-HCT patients are not revaccinated, antibodies against vaccine preventable diseases decline after 1-10 years post-transplant. This relevance may not be clinically apparent however it still poses a risk, hence, post-HCT patients should be routinely revaccinated.
- Revaccinate with inactivated vaccines 6-12 months after HCT.
- Post-HCT individuals should have clinically acceptable immunity for proper vaccine response:
  - B lymphocytes are recovered after 3 months of transplant
  - T lymphocytes recover after 6-12 months post-transplant.
- Household contacts of immunocompromised persons are advised to have immunization.
- Live vaccines are generally considered as precautions to HCT recipients.
- Influenza vaccine can be given 6 months after the HCT, then annually thereafter.
- Three doses (2 Td + 1Tdap), followed by a Td booster every 10 years.
- MMR and varicella vaccines should be given 24 months after transplantation if the patient is presumed to be immunocompetent.
- All live vaccines are contraindicated to persons with primary T-lymphocyte (cell-mediated and humoral) deficiency.

- Live bacterial vaccines are contraindicated to individuals with primary phagocytic function deficiency (e.g. chronic granulomatous diseae).
- Persons with isolated B-cell deficiency may receive varicella vaccine.
- Live vaccines can be given after chemotherapy has been discontinued for at least 3 months.
- Live vaccines are **NOT** contraindicated with steroids given via aerosols, topical, alternate day, short courses (less than 14 days).
- Live vaccines may be given 1 month after discontinuation of systemic steroid treatment.

C. INVALID CONTRAINDICATIONS TO VACCINATION

- mild illness
- disease exposure or convalescence
- antibiotic therapy
- pregnancy in the household
- breastfeeding
- allergies to products in the vaccine
- premature birth
- family history unrelated to immunosuppression
- need for TB skin testing
- need for multiple vaccines
- minor illness- low grade fever, upper respiratory tract infection, otitis media
- mild diarrhea

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SUMMARY OF RECOMMENDATION FOR SPECIAL SITUATIONS – HIV*

Table 1. Vaccines that MUST be given to all PLHIV REGARDLESS of CD4+ T CELL COUNT

Vaccine	Dose	Route	Schedule of Immunization	Adverse reactions	Remarks
Hepatitis B	20 ug/ml vial, administer 2 vials on a 3-dose schedule	Intramuscular (IM) IM (or by deep subcutaneous injection- SC in case of bleeding disorde SC or IM injection, preferably into the deltoid	Day 0,1 month and 6 months Annually First dose may be either PPSV23 or PCV13, but PCV13 is strongly recommended.	Common: transient soreness, erythema and induration at injection site Uncommon systemic early onset events temporally related to vaccination include: - fatigue, dizziness, syncope, hypotension, arthritis, arthralgia, lymphadenopathy, rash and urticaria - influenza-like symptoms, such as low-grade fever, malaise, headache, myalgia - gastrointestinal upsets, such as abdominal pain, diarrhea, vomiting, nausea and abnormal liver function tests - neurological manifestations include rarely paresthesia and extremely rarely paralysis,	

				neuropathy, and neuritis (including Guillain-Barre syndrome, multiple sclerosis and optic neuritis) - severe skin disorders such as erythema multiforme	
Influenza	0.5 mL Single dose	IM (or by deep subcutaneous injection- SC in case of bleeding disorde	Annually	Most frequent: soreness at the injection site Rare: fever, malaise, muscle pain, arthralgia (beginning 6-12 hrs after immunization and lasting up to 48 hrs) - Allergic reactions may occur most likely due to hypersensitivity to residual egg protein - Guillain-Barre syndrome has been reported but causal relationship with the vaccine has not been established	
Pneumococcal	0.5 ml single dose of the 23 polyvalent polysaccharide vaccine	SC or IM injection, preferably into the deltoid	First dose may be either PPSV23 or PCV13, but PCV13 is strongly recommended.	Most frequent: soreness, swelling and redness at injection site; resolves within 48 hrs Rare: fever, malaise and muscle Pain	• PLHIV who have not received any pneumococcal vaccine, should

				Allergic reactions may occur Local reactions reported more frequently following a second dose of PPV-23 than after the first dose, especially if < 3 years interval from the first injection	receive a dose of PCV13 FIRST then PPSV23 after 2 months ➢ For subsequent doses of PPSV23, give PPSV23 every 5 years • PLHIV who have received previous PPSV23, give PCV13 after 1 year or more. If the patient is still at risk, give PPSV23 after 2 months of the PCV13 and every 5 years thereafter.

Table 2. Vaccines that MAY BE GIVEN safely to PLHIV IF INDICATED, REGARDLESS OF CD4++ T - CELL COUNT

Vaccine	Dose	Route	Schedule of Immunization	Adverse reactions	Remarks
Cholera	- Dissolve buffer in 1 glass water. Add 1 vial vaccine. Mix well and drink	Oral vaccine (against cholera and enterotoxigenic *E coli*- ETEC)	2 doses at 10 - 14 days interval If > 6 weeks has elapsed between doses, repeat course Booster after 2 years if continuous protection is required	- Common: upset stomach, nausea, vomiting loss of appetite - Rare: fever, malaise, dizziness, runny nose, cough, dizziness - Very rare: fatigue, joint pains, sweating, sore throat, rash, severe diarrhea, itching, swelling of lymph glands	
Haemophilus influenzae type B	0.5 mL	IM injection (or SC injection in persons with bleeding disorders), preferably in the deltoid	Single dose	- Fever, restlessness, prolonged crying, loss of appetite, vomiting and diarrhea - Redness and pain at injection site - Potentially fatal: Anaphylaxis	

Hepatitis A	1 mL CD4+ count >300: 2 doses CD4+ count <300: 3 doses	IM route (deltoid)	CD4+ count > 300: 2- dose at either 0 and 6 through 12 months CD4+ count < 300: 3-dose IM route schedule over 6-12 Months - For travelers to endemic areas, vaccine should be given at least 2 weeks before travel	- Common adverse events: injection site reactions such as soreness, induration, redness and swelling - Less common: headache, malaise, fatigue, fever, nausea, & loss of appetite - Rare: serious allergic reactions	
Human papilloma virus	Quadrivalent vaccine – 3 doses Bivalent HPV vaccine – 3 doses	IM (deltoid)	Quadrivalent vaccine within 6 months at 0, 2, 6 months Bivalent HPV vaccine within 6 months at 0, 1, 6 months	Local reactions: mostly pain and swelling - Fever - Syncope (fainting) may follow any vaccination, especially in adolescents and young adults. Syncope, sometimes associated with falling, has occurred after vaccination with quadrivalent	

			Minimum intervals for both vaccines are: 4 weeks between doses 1 and 2 12 weeks between doses 2 and 3	HPV recombinant vaccine. Therefore, vaccinees should be carefully observed for approximately 15 minutes after administration of quadrivalent HPV recombinant vaccine	
Japanese B encephalitis	Three doses	Deep SC route	Days 0, 7–14 and 28 - Last dose should be administered at least 10 days before the commencement of travel to ensure an adequate immune response and access to medical care in the event of delayed adverse reactions.	Adverse reactions tend to occur within 48 hours for the first dose but around 96 hours for the second. The hypersensitivity reaction may occur as late as 10 to14 days after the last dose - Common: Tenderness, redness, swelling, and other local effects - Less common: fever, headache, malaise, rash, and other reactions such as chills, dizziness, myalgia, nausea, vomiting, and abdominal pain - Rare: severe hypersensitivity, including angioedema or urticaria	

			- For those aged >60 years, a 4th dose is recommended 1 month after completion of the initial course. - A booster is recommended after 3 years for those at continued risk.		
Meningococcal	Meningococcal polysaccharide vaccine Single dose 0.5ml.	Deep SC or IM injection preferably in the deltoid	Boosters are recommended after 5 years for those at continuous risk	- Very common: Transient local pain with associated swelling or redness and fever - Common: headache, vomiting, irritability, fatigue and loss of appetite - Rare: serious (neurological) complications or anaphylaxis	

Rabies	Pre-exposure prophylaxis - 3 doses Post exposure prophylaxis 1 dose each on Days 0, 3, 7, 14, 28 or 30 OR 2 doses on Day 0, and 1 IM dose each on Day 7 and Day 21	IM (deltoids) IM	Pre-exposure prophylaxis: Days 0, 7, and 28 Post exposure prophylaxis: 1 dose each on Days 0, 3, 7, 14, 28 or 30 OR 2 doses on Day 0, and 1 IM dose each on Day 7 and Day 21 If currently asymptomatic, with CD4+ >400cells/mm, with completed pre-exposure prophylaxis: 1 IM dose on Day 0, and 1 IM dose on Day 3 Serologic testing like rapid	- Soreness, swelling or itching, induration at injection site - Headache, dizziness, nausea, abdominal pain - Rare: neurologic reactions reported, resolved spontaneously	

			focus flourescent inhibition test (RFFIT), if available, should be done between day 14 and 28. If the antibody response is <0.5 IU/ml, a further booster dose of rabies vaccine should be administered - 2 doses of Td at 4 to 8 weeks apart followed by 3rd dose, tetanus diphtheria pertussis (Tdap) to be given 6 to 12 months later	- Local: Pain at the injection site - Systemic: Headache, generalized body aches, tiredness, fever - Rare: severe systemic reactions such as generalized urticaria, anaphylaxis or neurological complications- Rare: severe systemic reactions such as generalized urticaria, anaphylaxis or neurological complications	

			Booster every 10 years with Tdap - Partially immunized pregnant women should complete the 3 series. In pregnancy 3rd dose given at least two weeks before delivery - Adults who have received a full primary course (3 doses) as infants and a booster at pre-school age (total of 4 doses) require a single booster dose, then every 10 years		

Typhoid Vi polysaccharide (Parenteral)	25 mcg (0.5 ml) - Single dose	IM (preferably in the deltoid) or SC in persons with bleeding disorders)	- At least 2 weeks before expected exposure - Booster recommended every 3 years in those who remain at risk. Interval might be reduced to 2 years if the CD4+ count is < 200 cells/mL	Mild reactions: Fever, headache, redness or swelling at the site of the injection - Very rare: severe allergic reactions	

Table 3. Vaccines that CAN BE GIVEN SAFELY to PLHIV if INDICATED, and if they are ASYMPTOMATIC, with a CD4+ T cell count of > 200 cells/mm3

Vaccine	Dose	Route	Schedule of Immunization	Adverse reactions	Remarks
Measles, mumps, rubella	Two doses	Deep SC or IM injection preferably in the deltoid	Second dose given at any time but at least one month after the first	- PLHIV who wants to be protected and immune against measles, mumps and rubella infections - Rubella IgGseronegative women with CD4+ counts >200cells/uL - Second MMR dose if the patient remains rubella IgGseronegative - Measles, mumps and rubella susceptible and healthy close contacts of HIV infected individuals should receive two doses of MMR vaccine	- Fever and rash occur usually 7-12 days after vaccination and lasting 1-2 days. These are usually attributable to the measles component - Arthalgia and / or arthritis are reported in up to 25% of vaccinated women and are usually mild and transient. - Transient lymphade-nopathy sometimes occurs and is associated with rubella vaccination. - Parotitis and deafness occur rarely and are attributable to the mumps component

Varicella	0.5 mL two doses	SC injection, preferably in the deltoid	3 months interval between doses if HIV (+)	- VZV IgG negative, - PLHIV with uncertain history of varicella infection - PLHIV who are at risk of exposure (e.g. HCW)	- Rash, localized at the site of injection or generalized, within one month of immunization - Fever
Yellow fever	0.5 ml - Single dose	SC injection, preferably in the deltoid	Booster after 10 years for those at risk, provided that the CD4+ count is >200 cells/uL - Other live-virus vaccines may be given concurrently; alternatively subsequent live vaccinations should given only after 4 weeks		- Most common: Injection site reactions - An influenza-like illness, characterized by fever, headache and muscle ache, occurs in 2-10% of vaccine recipients 5-14 days after immunization. - Severe: risk of encephalitis to PLHIV - Rare: Hypersensitivity or anaphylaxis, neurotropic disease and viscerotropic disease

Adapted from the Philippine Guideline for Immunization of HIV 2010 with modifications.

SUMMARY OF RECOMMENDATION FOR SPECIAL SITUATIONS - PREGNANCY

ANTIGEN	DOSE AND ROUTE	SCHEDULE OF IMMUNIZATION	COMMENTS
Cholera	CONTRAINDICATED		
Haemophilus influenza type B	• 0.5 ml IM or SC	• Single dose	• Recommended for those at increased risk of Hib disease
Hepatitis A	• Monovalent 1440 ELISA units/ml/vial Via IM • Combination Hep A and Hep B Dose: 720 ELISA units and 20ug/ml Via IM	• Single dose • Booster dose between 6 and 12 months after initiation of primary course • 3 doses at 0,1 and 6 months • Booster dose should be given at 1 yr	• Effect of HAV on fetal development has not been assessed. • Vaccine should be used with caution. • The effect of vaccine on breastfed infants through its administration to their nursing mother has not been evaluated in clinical studies.
Hepatitis B			• Serologic testing for HBsAg and Anti-HBs must be done prior to immunization

Herpes Zoster	• CONTRAINDICATED		
Human Papilloma virus	• CONTRAINDICATED		• If woman is found pregnant after initiation of the vaccine series, remaining doses should be delayed until after the delivery
Influenza	• 0.5 ml IM	• Single dose annually	• Inactivated vaccine can be administered to those who are pregnant in the 2nd or 3rd trimester or planning to be pregnant during the influenza season
Japanese Encephalitis	• CONTRAINDICATED in pregnancy • Can be given to breastfeeding women		• If pregnant women must travel to high risk area, they should be vaccinated if the benefits outweigh the risks.
Measles, Mumps and Rubella	• CONTRAINDICATED		• Avoid pregnancy one month after receipt of MMR vaccine.
Meningococcal Disease	• 0.5 ml	• Single dose	• Contacts of confirmed cases of meningococcal disease should be offered vaccination, as well as given prophylaxis.

Pneumococcal Disease	• 0.5 ml PPV23	• Single dose	• Immunization can be given during pregnancy although safety during the first trimester has not been evaluated.
	• PCV13 –INSUFFICIENT DATA		
Rabies			• May be given post-exposure prophylaxis
Tetanus, Diptheria, Pertussis	• 0.5 ml IM	• For pregnant individuals who has not received any tdap vaccine within the past 10 years, vaccinate during pregnancy (second or third trimester) as follows: 3 doses (1Tdap+2Td) at 0,1, 6-12 months (the 3rd dose given at least 2 weeks before delivery)	• For pregnant individual who has received the last Td vaccination within the past 10 years, give Tdap during 2nd or 3rd trimester or immediately postpartum or before discharge.
Typhoid Fever	• INSUFFICIENT DATA		

Varicella	• CONTRAINDICATED		• May give postpartum if susceptible
Yellow Fever	• CONTRAINDICATED		• If pregnant women must travel to high risk area, they should be vaccinated if the benefits outweigh the risks.

SUMMARY OF RECOMMENDATION FOR SPECIAL SITUATIONS –TRANSPLANT RECIPIENTS

ANTIGEN	RECOMMENDED FOR USE	SCHEDULE OF IMMUNIZATION	COMMENTS
Cholera	INSUFFICIENT DATA		
Haemophilus influenza type B	• RECOMMENDED • 0.5 ml IM or SC (in persons with bleeding disorders)	HSCT • 6-12 months post HSCT • Single dose Solid organt recipient • No data on timing	Known to be safe and effective in bone marrow and recipients and solid organ recipients
Hepatitis A	• OPTIONAL • Monovalent 1440 ELISA units/ml/vial Via IM	• Given before and after transplantation	
	• Combination Hep A and Hep B Dose: 720 ELISA units and 20ug/ml Via IM		
Hepatitis B	RECOMMENDED Administer 2 vials of 20ug/ml IM	HSCT • Give 6-12 months post HCT • 0, 1, 2 and 6 months	

		Solid Organ • 3 months post-transplant	
Herpes Zoster	INSUFFICIENT DATA	May be given at least 24 months post HSCT	
Human Papilloma virus	INSUFFICIENT DATA		
Influenza	RECOMMENDED 0.5ml IM or SC	Life-long annual seasonal influenza vaccination, starting before hematopoietic stem cell transplant (HSCT) and restarting 6 months after HSCT	Give inactivated vaccine Double dose Give also to household members before and after solid organ transplant During outbreaks, all HSCT recipients who have not yet received a current influenza vaccination should be vaccinated against influenza immediately if it is more than 4 months after HSCT. Chemoprophylaxis should be used for 2 weeks after vaccination to allow sufficient time for immunologic response to influenza vaccine

Japanese Encephalitis	OPTIONAL		Vaccination should be avoided in the 6 months following transplantation
Measles, Mumps and Rubella	RECOMMENDED 0.5 ml SC	HSCT • Give at least 2 yrs after months post HSCT and without evidence of GVHD Solid organ • No data on solid organ transplant	
Meningococcal Disease	0.5 ml IM	HSCT • Single dose • Give 6-12 months post-HSCT Solid organ • Limited data	Follow recommendations for general population since the vaccine is not a live vaccine.
Pneumococcal Disease	RECOMMEND For solid organ recipients: 0.5 ml PPV23 For HSCT: 0.5 ml PCV13	HSCT • Give 3-6 months post-HSCT of PCV13 in 3-4 doses Solid organ • PPV23 should be started before transplantation and	Immunity screening is recommended 1 month after last dose of series and every 2 years if risk continues Immunity screening is recommended two weeks after completion of series

		repeated booster doses should be administered at 2-5 yrs interval	
Rabies	Pre-exposure: delay Postexposure prophylaxis: 5-dose vaccine regimen	• Pre-exposure immunization should be delayed until 12-24 months post transplant • Give 1 mL on days 0,7,21 Give 1 ml IM on days 0, 3, 7, 14, and 28	Immunity screening is recommended 1 month after last dose of series and every 2 years if risk continues Immunity screening is recommended two weeks after completion of series
Tetanus, Diptheria, Pertussis	0.5 ml IM	Transplant recipients should be considered as "never vaccinated" and be given the primary series (1Tdap +2Td) within 6-12 months post-transplant	
Typhoid Fever	OPTIONAL	HSCT • Give 12 months after HSCT Solid organ • No data	Limited data

Varicella	CONTRAINDICATED		should be given at least 24 months after transplantation if the patient is presumed to be immunocompetent
Yellow Fever	CONTRAINDICATED		If travelling cannot be avoided, counsel on mosquito bites.

SUMMARY TABLE FOR IMMUNIZATION OF HEALTHCARE WORKERS

CATEGORY	VACCINE TYPE	ROUTE	SCHEDULE	CONTRAINDICATIONS/PRECAUTIONS
Strongly Recommended	Tetanus, Diphtheria, acellular Pertussis Vaccine (Tdap)	IM	3 doses (1Tdap + 2 Td): 0, 1, 6-12 months Booster every 10 years with Td	Severe allergic reactions to vaccine components or following prior dose; Moderate to severe illness
	Hepatitis B vaccine	IM	3 doses: 0, 1, 6 months Alternate: 4 doses : 0, 1, 2, 12 months Booster is not routinely recommended (After anti-Hbs screening)	Severe allergic reactions to vaccine components or following prior dose
	Influenza vaccine	IM	1 dose annually (preferably from January to July)	Severe allergic reactions to vaccine components or following prior dose; Moderate to severe acute illness; History of severe acute illness; GuillainBarre Syndrome

	Varicella Vaccine	SC	2 doses at 4 weeks interval • Indicated for first line healthcare worker	Severe allergic reactions to vaccine components or following prior dose; Pregnancy; Immmunosuppression; Recently received a blood product; Untreated active TB; Adolescents on aspirin therapy
	Measles, Mumps, Rubella Vaccine	SC	2doses at 4 weeks interval • Indicated for first line healthcare worker	Severe allergic reactions to vaccine components or following prior dose; Moderate to severe acute illness; Recently received a blood product; Thrombocytopenia/ITP
Recommmended	Pneumococcal Polysaccharide Vaccine	IM	Single dose	Severe allergic reactions to vaccine components or following prior dose; Moderate to severe acute illness; Pregnancy (safety unknown, if indicated, give before pregnancy)
	Rabies Vaccine	IM/ID	Primary: 3-dose series (IM/ID) at Days 0, 7 and 21 or 28 Booster: single dose IM or ID every 5 years	Severe allergic reactions to vaccine components or following prior dose; Moderate to severe acute illness

Recommended for Selected HCW	Meningococccal Vaccine	IM	Single dose	Severe allergic reactions to vaccine components or following prior dose; Moderate to severe acute illness; GuillianBarre Syndrome
	Typhoid Vaccine	IM	Single dose Booster every 2-3 years	Severe allergic reactions to vaccine components or following prior dose; Bleeding disorder
	Hepatitis A vaccine	IM	2 doses : 0, 6-12 months	Severe allergic reactions to vaccine components or following prior dose

SUMMARY TABLE OF IMMUNIZATION FOR TRAVELERS

CATEGORY	VACCINE TYPE	ROUTE	SCHEDULE	REMARKS
Recommended	Tetanus, Diphtheria, acellular Pertussis Vaccine (Tdap)	IM	3 doses (1Tdap + 2 Td): 0, 1, 6-12 months Booster every 10 years with Td	• Adult travelers should have their diphtheria- pertussis-tetanus immunization up to date.
	Hepatitis A	Monovalent 1 ml IM Combination Hep A and Hep B, 1 ml IM	Monovalent • 2 doses, giving the second dose 6–12 months (Havrix) or 6–18 months (Vaqta) after the first Combination (Twinrix) • 3 doses if primary immunization (0,1,6 months) Accelerated Schedule (Twinrix) • 0, 7, 21-30 days and 12 months after last dose	• For adults aged > 40 years, immunocompromised hosts, and people with chronic medical conditions departing in less than 2 weeks, the initial dose of the vaccine and IG (0.02 mL/kg) should be given simultaneously at separate anatomic site of injection.

	Hepatitis B	1.0 mL IM	• 3 doses (0,1,6 months) or 4 doses (0,1,2 and 12 months for Engerix-B) • An accelerated vaccination schedule with combined hepatitis A and hepatitis B vaccine can also be used (doses at 0, 7, and 21–30 days) for travelling to endemic areas with short notice ➢ a booster dose should be given at 12 months to promote long-term immunity	• People who engage in practices that place them at risk for HBV infection during travel should receive the vaccine, regardless of the destination. • Vaccination should begin 6 months before travel.
	Influenza	0.5 ml IM or SC	Single dose annually	• Risk of exposure to influenza during travel depends on the destination and the time of year. • Northern Hemisphere flu season: October to May • Temperate regions of the Southern Hemisphere: April to September • Tropical countries: all throughout the year

	Japanese Encephalitis	0.5ml IM/SC	Inactivated mouse-derived vaccine: • 3 doses within 30 days at 0, 7, and 30 days SC Inactivated vero cell culture-derived vaccine: • 2 doses IM administered 28 days apart For cell culture derived live SA-14-12-2 vaccine • 0.5 SC for all ages	• JEV transmission activity varies within countries and from year to year • Vaccine should be completed at least 1 week before scheduled visit. • NOT LOCALLY AVAILABLE
	MMR	0.5 ml SC	2 doses 1 month apart	• Vaccination against mumps is not a requirement for entry into any country however leaving abroad should ensure they are immune to mumps. • Before international travel, travelers should be immune to rubella.
	Meningococcal disease	0.5 ml IM	Single dose See text for specific situations.	• Travelers to Haji must show proof of vaccination in the previous 3 years

VACCINE UNDER DEVELOPMENT
DENGUE

The Disease

It isa vector-borne systemic and dynamic disease with a wide clinical spectrum that includes both severe and non-severe clinical manifestations.

Etiologic Agent

- Dengue virus (DEN) - a small single-stranded RNA virus comprising 4distinct serotypes
- (DEN-1 to -4); belong to the genus Flavivirus, family Flaviviridae.

Vectors

- Aedes mosquitoes (primarily Ae. Aegypti; Aedes albopictus, Aedes polynesiensis and several species of the Aedes scutellaris complex)
- Once infected with the dengue virus, the mosquito remains infective for the rest of its life.
- *Ae. aegypti*: one of the most efficient vectors for arboviruses because it is highly anthropophilic, frequently bites several times before completing oogenesis, and thrives in close proximity to humans.
- eggs can remain viable for many months in the absence of water

Epidemiology

- 50 million dengue infections occur annually
- 1998-last major pandemic in Western Pacific Region
- 2001 – 2008 – 1,020, 333 cases were reported in Cambodia, Malaysia, Philippines, and Viet Nam -- the four countries in the Western Pacific Region with the highest numbers of cases and deaths; 4798 combined death toll for these countries
- number of cases and deaths remained highest in Cambodia and the Philippines in 2008

Transmission

- enters when an infected mosquito is taking a bloodmeal from the skin
- incubation period: 4-10 days, infection by any of the 4 virus serotypes

Clinical Features

- Dengue can produce a wide spectrum of illness (thrombocytopenia, plasma leakage, haemoconcentration and derangement of the haemocoagulation system)
- Primary infection – thought to induce lifelong protective immunity to the infecting serotype
- Infected individuals are protected from clinical illness with a different serotype within 2-3 months of the primary infection but with no long-term cross-protective immunity.
- Individual risk factors determine the severity of disease:
    - secondary infection
    - age
    - ethnicity
    - chronic diseases (bronchial asthma, sickle cell anaemia and diabetes mellitus)

The Vaccine

General Description

- Two types of vaccine
    1. Live attenuated virus
    2. Non-live attenuated dengue vaccine
- PRODUCT UNDER PHASE 3 CLINICAL TRIAL.

Reference

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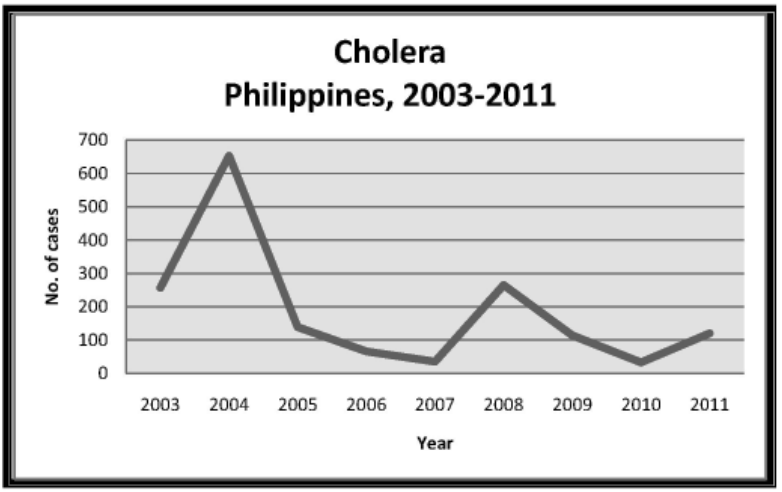
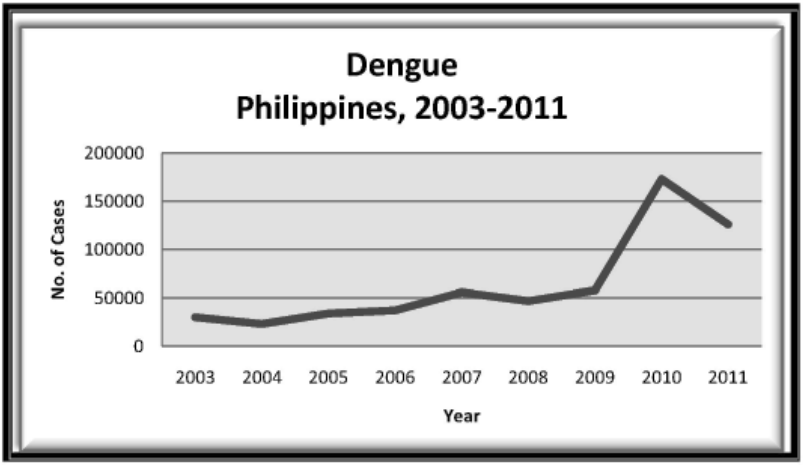
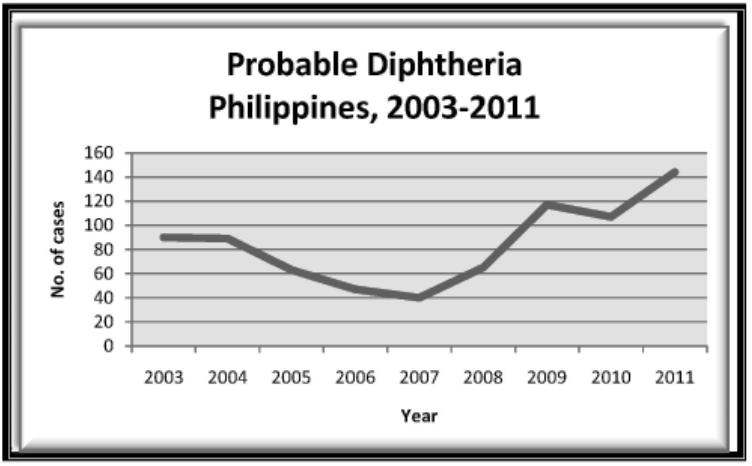
APPENDICES

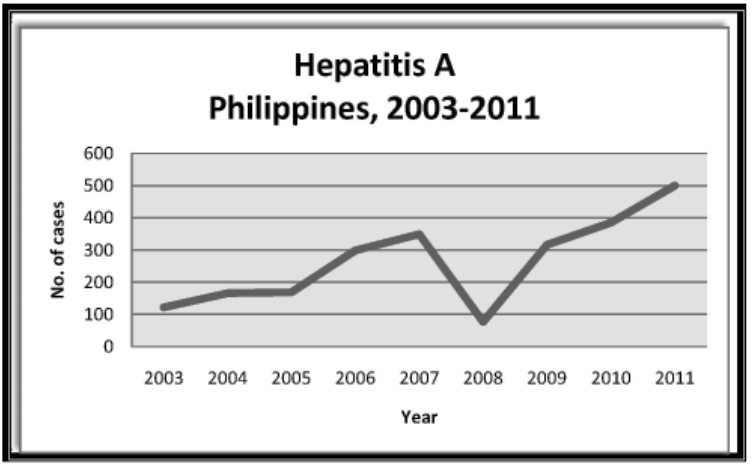
APPENDIX A

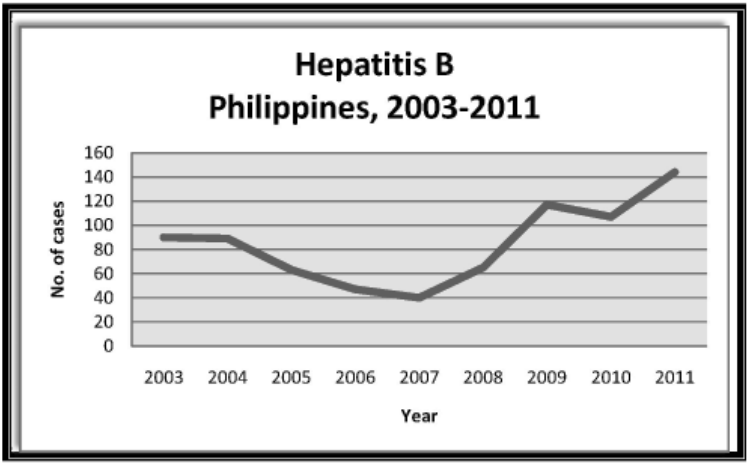
All information from Field Health Service Information System and Philippine Integrated Disease Surveillance and Response (Annual Report 2011), National Epidemiology Center, Department of Health

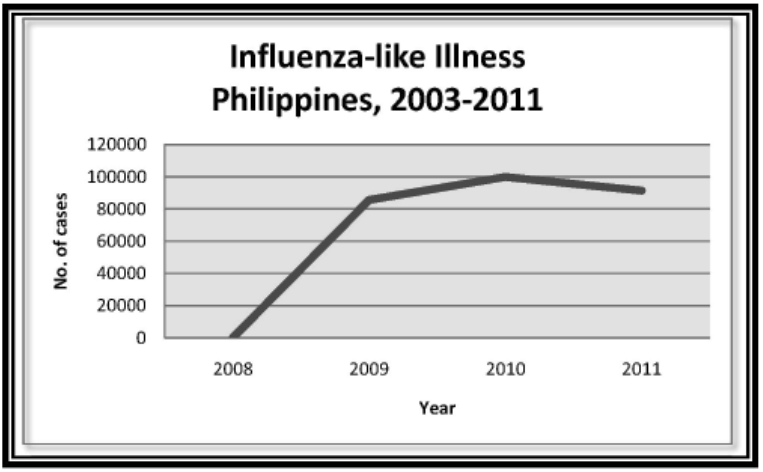





Probable Diphtheria
Philippines, 2003-2011
No. of cases
160
140
120
100
80
60
40
20
0
2003
2004
2005
2006
2007
2008
2009
2010
2011
Year


Hepatitis A
Philippines, 2003-2011
No. of cases
600
500
400
300
200
100
0
2003
2004
2005
2006
2007
2008
2009
2010
2011
Year


Hepatitis B
Philippines, 2003-2011
No. of cases
160
140
120
100
80
60
40
20
0
2003
2004
2005
2006
2007
2008
2009
2010
2011
Year


Influenza-like Illness
Philippines, 2003-2011
No. of cases
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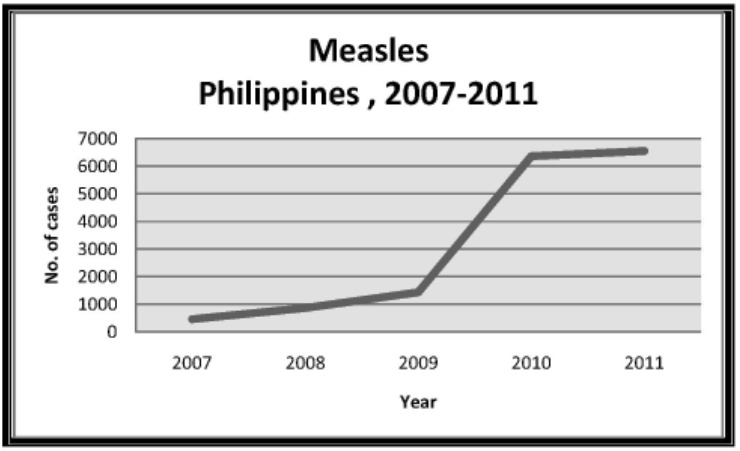
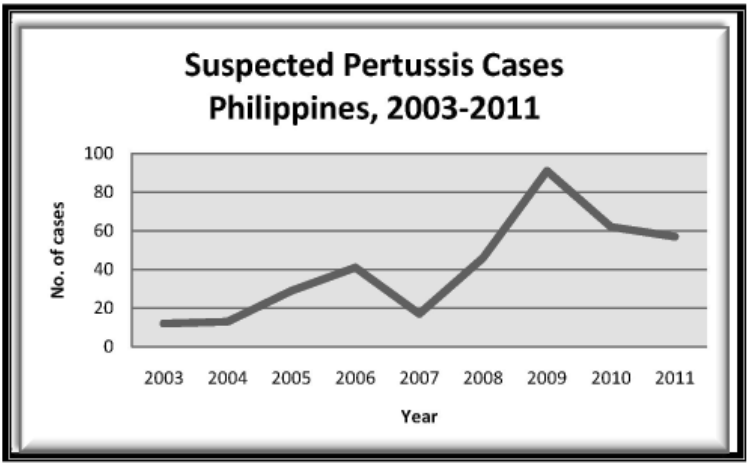
100000
80000
60000
40000
20000
0
2008
2009
2010
2011
Year


Measles
Philippines , 2007-2011
No. of cases
7000
6000
5000
4000
3000
2000
1000
0
2007
2008
2009
2010
2011
Year


Suspected Meningococcal Cases
Philippines, 2003-2011
No. of cases
500
400
300
200
100
0
2003
2004
2005
2006
2007
2008
2009
2010
2011
Year


Suspected Pertussis Cases
Philippines, 2003-2011
No. of cases
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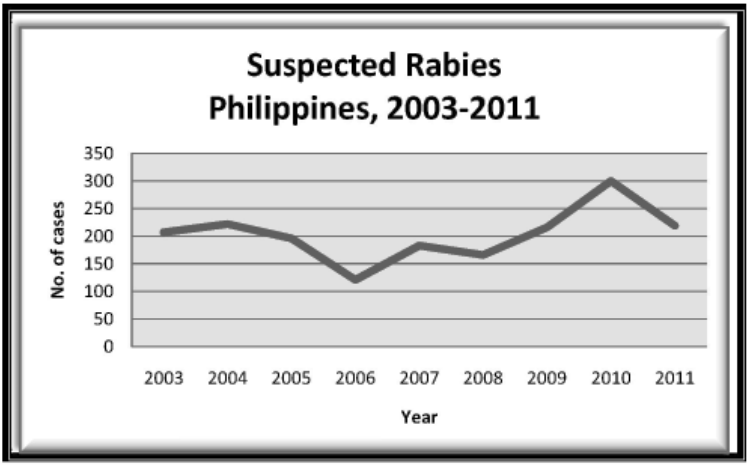
80
60
40
20
0
2003
2004
2005
2006
2007
2008
2009
2010
2011
Year


Suspected Rabies
Philippines, 2003-2011
No. of cases
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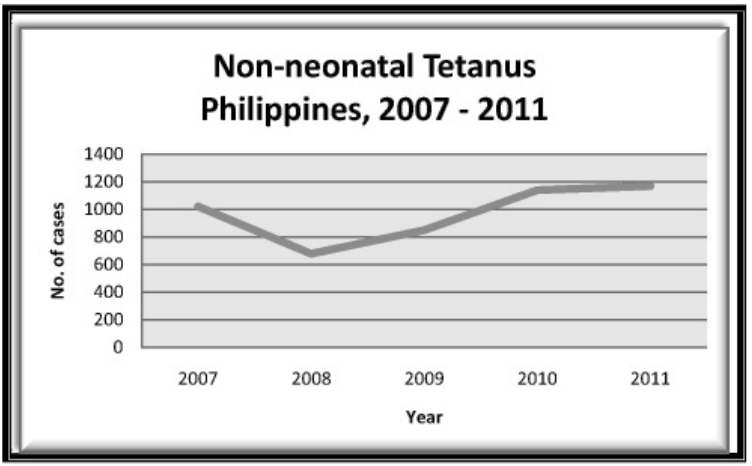
300
250
200
150
100
50
0
2003
2004
2005
2006
2007
2008
2009
2010
2011
Year


Non-neonatal Tetanus
Philippines, 2007 - 2011
No. of cases
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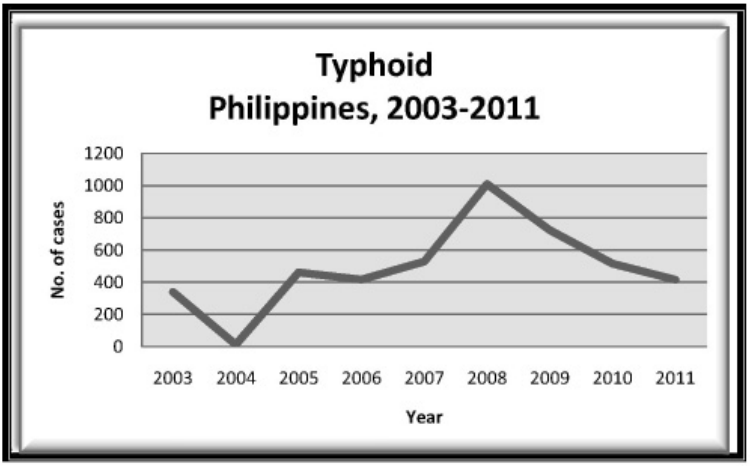
1200
1000
800
600
400
200
0
2007
2008
2009
2010
2011
Year


Typhoid
Philippines, 2003-2011
No. of cases
1200
1000
800
600
400
200
0
2003
2004
2005
2006
2007
2008
2009
2010
2011
Year

APPENDIX B

LOCALLY AVAILABLE VACCINES

VACCINE TYPE	BRAND NAME	DOSAGE	REMARKS
CHOLERA			
Oral cholera vaccine	Shanchol(killed bivalent (01 and 0139) Whole Cell Oral Cholera Vaccine 1.5 ml	2 doses of suspension at 2 weeks interval	Booster after 3 years
	Oravacs(inactivated whole cell vaccine with B subunit cholera toxin) (Unilab)	Take 1 capsule on Days 0, 7 and 28	Recommend first dose 2 weeks before travel. Booster dose: Take 1 capsule on Days 0, 7 and 28 before prevalent season.
HAEMOPHILUS INFLUENZA TYPE B			
Haemophilusinfluenzae type B	ActHIB (Sanofi Pasteur) Hiberix (GlaxoSmithKline) Vaxem HIB (Novartis)	1 dose	
HEPATITIS A			
Hepatitis A	Havrix 720 (GlaxoSmithKline)	1 ml IM (deltoid) – 2 doses 1 month apart	Booster dose between 6 & 12 months after initiation of primary course is recommended to ensure long term antibody titers.
	Havrix 1440 (GlaxoSmithKline) Avaxim (Sanofi Pasteur)	1 single dose	
Combined Hepatitis A & B	Twinrix: Combined Hepatitis A (720 ELISA Units) &Hepatitis B (20 ug/ml recombinant)	3 doses at 0,1,6 months	Post-vaccination testing to assess serologic response or antibody levels is not indicated for Hepatitis A.
		Accelerated schedule: Doses at days 0, 7, and 21 for travelers	A booster dose of the combined vaccine should be given at 1 year if accelerated schedule was given. Post-vaccination testing to assess serologic response or antibody levels is not indicated for Hepatitis A.

HEPATITIS B			
Recombinant Hepatitis B Vaccine	Engerix B Adult 20 ug/ml (GlaxoSmithKline) Boryung Hepatitis B Vaccine 20 ug/ml (BoryungBiopharmaMarketlink) Euvax-B 20 ug/ml (Sanofi Pasteur)	3 doses of 1 ml IM at 0,1,6 months	
Hepatitis Immuneglobulin	HepaBIg 0.5 and 1 ml (Greencross Corp)	One IM dose IG 0.02 ml/kg given within 2 weeks of exposure in large muscle mass (deltoid, gluteal) HBIG 0.06 ml/kg IM as soon as possible (and within 7 days) after exposure (with dose 1 of hepatitis B vaccine given at different body site)	If hepatitis B series has not been started, 2nd dose of HBIG should be given 1 month after 1st dose.
HERPES ZOSTER*			
Herpes zoster	Zostavax (MSD)	SC	Licensed for age 50 and older
HUMAN PAPILLOMA VIRUS			
Quadrivalent HPV Types 6,11,16 &18	Gardsil (MSD)	0.5 ml IM 0,2, 6 months	For Cervical Ca and anogenital warts. Routine use for 10 to 18 years old adolescents. Catch up immunization for women 19-55 years old
Bivalent HPV types 16 & 18	Cervarix (GlaxoSmithKline)	0.5 ml IM 0,1, 6 months	For cervical ca Routine use for 10 to 18 years old adolescents. Catch up immunization for women 19-55 years old

INFLUENZA			
Split type	Vaxigrip (Sanofi Pasteur) Fluarix (GlaxoSmithKline)	Single IM 0.5 ml; given annually	
Inactivated influenza	Agrippal S1 (Novartis) Influvac (Solvay Pharma)	Single IM 0.5 ml; given annually	
Split virion inactivated	Intanza (Sanofi)	15 ugin a prefilled syringe, ID	Indicated only for patients ≥ 60 years old
MEASLES, MUMPS AND RUBELLA			
MMR	Trimovax (Sanofi Pasteur) Priorix (GlaxoSmithKline)	Single 0.5 ml SC	2 doses, 1 month apart
MENINGOCOCCAL DISEASE			
Purified polysaccharides types A+C	Meningococcal polysaccharide vaccine A+C (Sanofi Pasteur)	Single dose 0.5 ml SC or IM	Not for routine use. May be given in special situations. For outbreak control may be given to infants 3 months and above
Purified polysaccharides types A,C,Y, W-135	Mencevac (GSK) Menomune (Sanofi Pasteur)	Single dose 0.5 ml SC or IM Single dose 0.5 ml SC ONLY	
Polysaccharide conjugated vaccine (diphtheria toxoid carrier, serogroups A,C,Y, W135)	Menactra (Sanofi Pasteur)	Single dose 0.5 ml IM ONLY	Not recommended for: • Immunosuppressed patients • Pregnancy and lactatioin • < 2 or > 55 years old
PNEUMOCOCCAL DISEASE			
23-valent, polysaccharide vaccine	Pneumo 23 (Sanofi Pasteur) Pneumovax 23 (MSD)	Single IM or SC 0.5 ml dose	>2 yrs and above
13-valent Polysaccharide conjugate	Prevenar 13 (Pfizer)	Single dose 0.5 ml IM	
pneumococcal vaccine			

RABIES			
Purified vero cell rabies vaccine (PVRV)	VERORAB (Sanofi Pasteur)	0.5 ml IM OR 0.1 ml ID	See text for pre-exposure and post-exposure dose and schedule
Purified chick embryo cell vaccine (PCECV)	Rabipur (Novartis)	1.0 ml IM OR 0.1 ml ID	See text for pre-exposure and post-exposure dose and schedule
Human Rabies Immunoglobulin (HRIG)	Berirab P(Sanofi Pasteur)	20 IU/kg body weight	½ to almost total dose to be infiltrated around the wound, and the remaining dose to be injected IM on the anterolateral aspect of the thigh.
Fractionated Equine Rabies Immune Globulin	FAVIRAB (Sanofi Pasteur)	40 IU/kg body weight	
Equine Rabies Immune Globulin (ERIG)	Equirab (Bharat Serums and vaccines)		
TETANUS, DIPTHERIA, PERTUSSIS			
Adsorbed Tetanus toxoid	Anatetall (Novartis) Tetliv (Instituto Finlay) TeanatoxalBerna (bernal/Swiss Serum) Tetavax (Sanofi Pasteur)	0.5 ml given IM at 0, 1, 6 mos	Booster dose of 0.5 ml given every 5-10 years
Purified Diptheria and Tetanus toxoid	Td pur (Novartis)	3 doses 0.5 ml given at 6-8 weeks interval	
Adsorbed tetanus diphtheria acellular pertussis vaccine (Tdap)	Adacel (Sanofi Pasteur) Boostrix (GSK)	0.5 ml IM	Given as booster; can replace one dose of the primary series
Human Tetanus Immuneglobulin	Tetagam P (Sanofi Pasteur) Baxter Human tetanus immuneglobulin (Baxter Healthcare)	250 IU, IM for minor wounds 500 IU, IM for severe wounds and burn	
Equine Tetanus Immuneglobulin	Tetanea 1500 IU/ml (Sanofi Pasteur) Antiten 1500 IU Antiten 3000 IU Antitet 5000 IU (SinochemMingho)	1500-3000 IU IM 1500-5000 IU IM	Do skin testing before administration. **Give Equine Immuneglobulin ONLY ONCE in a lifetime.**

TYPHOID FEVER			
Polysaccharide Vi capsular vaccine	Typhim Vi (Sanofi Pasteur) Typherix (GSK)	Single IM dose 0.5 ml	Booster: Same dose after 2 years
VARICELLA			
Live-attenuated	Okavax (Sanofi Pasteur) Varilrix (GSK) V-Z-Vax (VizcarraPharma)	2 doses SC, 4 weeks apart but 3 months apart if HIV+	
YELLOW FEVER			
Live attenuated	Stamaril (Sanofi Pasteur)	Single 0.5 ml given SC Primary: 1 dose Booster: Every 10 years	Available only at the Bureau of Quarantine

*Soon to be available.

APPENDIX C

Version 2011

Philippine Integrated Disease Surveillance and Response

Case Investigation Form

Adverse Event Following Immunization

Name of DRU: **Address:**	**Type**: ☐RHU ☐CHO ☐Gov't Hospital ☐Private Hospital ☐Clinic ☐Gov't Laboratory ☐Private Laboratory ☐Airport/Seaport

I. PATIENT INFORMATION: Patient Number: | Patient's First Name | Middle Name | Last Name

Complete Address:		Sex: ☐Male ☐Female	Date of Birth:	MM	DD	YYYY	Age:	☐Days ☐Months ☐Years
District:	ILHZ:							
Patient Admitted? ☐ Yes ☐No ☐Unknown	Date Admitted/ Seen/ Consult	MM	DD	YYYY	Name of hospital/health facility:			
Address of hospital/health facility:			Date onset of illness	MM	DD	YYYY	TIME (hh:min:sec) ___:___:___ AM / PM	
Date next higher level notified:	MM	DD	YYYY	TIME (hh:min:sec) ___:___:___ AM/PM	Interval from onset of illness to notification: _____days _____hours			
Date of Investigation:	MM	DD	YYYY	TIME (hh:min:sec) ___:___:___ AM/PM	Interval from notification to investigation: _____days _____hours			
Name of Investigator:			Contact Nos.:					

II. TYPE OF SERIOUS AEFI (See back page for descriptions): check all that apply

1. LOCAL	*2. CENTRAL NERVOUS SYSTEM*	*3. OTHER ADVERSE EVENTS*	
☐ Injection site abscess	☐ Acute paralysis	☐ Anaphylactoid reaction	☐ Osteitis/osteomyelitis
☐ Lymphadenitis	☐ Encephalopathy	☐ Anaphylactic shock	☐ Persistent screaming (inconsolable continuous crying lasting at least 3 hours)
☐ Severe local reaction (redness and/or swelling centered at the site of injection)	☐ Seizures	☐ Neuritis	☐ Sepsis
		☐ Disseminated BCG infections	☐ Thrombocytopenia
		☐ Hypotensive-hyporesponsive episode (shock collapse)	☐ Toxic shock syndrome

4. OTHER SEVERE and UNUSUAL EVENTS OCCURRING WITHIN 4 WEEKS AFTER IMMUNIZATION AND NOT COVERED UNDER ITEM NOS. 1, 2 or 3

☐ Any death of a vaccine recipient temporarily linked (within 4 weeks) to immunization, where no other clear cause of death can be established.
☐ Other severe/unusual event (specify):_____

III. MOST RECENT VACCINATION HISTORY:

SUSPECTED VACCINE/S	DETAILS OF VACCINE				DETAILS OF DILUENT IF USED			
(BCG, DPT, OPV, Measles, HBV, others)	Dose Number/vial	Lot/Batch number	Manufacturer	Expiry date	Dose Number/ vial	Lot/Batch number	Manufacturer	Expiry date

Date of vaccination:____/____/____ Time of vaccination: ____:____: ____ ☐ AM ☐ PM
Name of vaccinator:_____ Profession of vaccinator: ☐ Physician ☐ Nurse ☐ Midwife ☐ Other_____
Place of vaccination: ☐ Health center ☐ BHS ☐ Public hospital
☐ Outreach ☐ Private clinic ☐ Private hospital ☐ Other (specify):_____

Did the patient receive any vaccination within 4 weeks prior to this adverse event? ☐ Y ☐ N (If YES, complete the information below).

VACCINE/S	DETAILS OF VACCINE				
(BCG, DPT, OPV, Measles, HBV, others)	Dose number (single/multiple)	Lot/Batch number	Manufacturer	Expiry date	Date given

IV. MEDICAL HISTORY:

Did the patient take other medications at the time of vaccination?
☐ Y ☐ N If YES, what were these medications?
_____
Does the patient had history of similar reaction? ☐ Y ☐ N
Does the patient had history of allergy? ☐ Y ☐ N
If YES, what are these allergies?_____

Birth defects: ☐ Y ☐ N
Family history of similar event? ☐ Y ☐ N
Is the patient suffering from other medical conditions?
☐ Y ☐ N
If YES, what are these conditions? _____
_____

Case Investigation Form

Adverse Event Following Immunization

V. CAUSALITY ASSESSMENT:

What is the cause of AEFI?

☐ Coincidental ☐ Vaccine reaction

☐ Injection Reaction ☐ Program related adverse event

Final diagnosis:_____

_____

If program-related adverse event, was it due to :

☐ non-sterile injection ☐ vaccine prepared incorrectly

☐ improper vaccine transport or storage ☐ wrong administration technique

☐ Other, specify_____

_____

VI. CAUSALITY ASSESSMENT LEVEL

☐ National ☐ Regional

☐ Provincial ☐ City/Municipal

VII. OUTCOME:

☐ Alive Patient sustained disability? ☐ Yes ☐No

If YES, specify type of disability:_____

☐ Died Date died: ____/____/____

CASE DEFINITION:

***Suspected AEFI case*:** Any individual that experience a serious condition any time after he or she received an immunization and is considered

DEFINITION OF TERMS:

- An ***adverse*** event following immunization (AEFI) is defined as a medical incident that takes place after an immunization, causes concern, and is believed to be caused by immunization.
- A cluster of AEFI is defined as two or more cases of the same adverse event related in time, place or vaccine administered.
- Serious medical condition is defined as those that are life-threatening and those that result in hospitalization (or prolonged hospitalization), disability (or have the potential to result in disability) or death.

LOCAL ADVERSE EVENTS:

- ***Injection-Site Abscess:*** Occurrence of a fluctuant or draining fluid-filled lesion at the site of injection with or without fever.
- ***Lymphadenitis (includes suppurative lymphadenitis):*** Occurrence of either: at least one lymph node, 1.5 cm in size (one adult finger width) or larger; or a draining sinus over a lymph node. Almost exclusively caused by BCG and then occurring within 2 to 6 months after receipt of BCG vaccine, on the same side as inoculation (mostly axillary).
- ***Severe local reaction:*** Redness and/or swelling centered at the site of injection and one or more of the following: swelling beyond the nearest joint; pain, redness and swelling of more than 3 days duration; or requires hospitalization.

CENTRAL NERVOUS SYSTEM ADVERSE EVENTS:

- ***Acute Paralysis***
  - Acute onset of flaccid paralysis within 4 to 30 days of receipt of oral polio-virus vaccine (OPV), or within 4 -75 days after contact with a vaccine recipient, with neurological deficits remaining 60 days after onset, or death.
  - Guillain-Barré Syndrome (GBS): Acute onset of rapidly progressive, ascending, symmetrical flaccid paralysis, without fever at onset of paralysis and with sensory loss. Cases are diagnosed by cerebrospinal fluid (CSF) investigation showing dissociation between cellular count and protein content. GBS occurring within 30 days after immunization should be reported.
- ***Encephalopathy:*** Encephalopathy is an acute onset of major illness temporally linked with immunization and characterized by any two of the following three conditions: Seizures; Severe alteration in level of consciousness lasting for one day or more; and Distinct change in behavior lasting one day or more. Cases occurring within 72 hours after vaccination should be reported.
- ***Encephalitis:*** Encephalitis is characterized by encephalopathy and signs of cerebral inflammation and, in many cases, CSF pleocytosis and/or virus isolation. Any encephalitis occurring within 1 to 4 weeks following immunization should be reported.
- ***Meningitis:*** Acute onset of major illness with fever, neck stiffness/positive meningeal signs (Kernig, Brudzinski). Symptoms may be subtle to similar to those of encephalitis. CSF examination is the most important diagnostic measure: CSF pleocytosis and/or detection of microorganism (Gram stain or isolation).
- ***Seizures:*** Seizures lasting from several minutes to more than 15 minutes and not accompanied by focal neurological signs or symptoms. Febrile Seizures or Afebrile Seizures. Onset is usually 0 to 2 days.

OTHER ADVERSE EVENTS:

- ***Anaphylactoid Reaction (acute hypersensitivity reaction):*** Exaggerated acute reaction, occurring within 2 hours after immunization, characterized by one or more of the following: (1) wheezing and shortness of breath due to bronchospasm; (2) laryngospasm/laryngeal edema; (3) one or more skin manifestations, e.g. hives, facial edema, or generalized edema.
- ***Anaphylactic Shock:*** Circulatory failure (e.g. alteration of the level of consciousness, low arterial blood pressure, weakness or absence of peripheral pulses, cold extremities secondary to reduced peripheral circulation, flushed face and increased perspiration) with or without bronchospasm and/or laryngospasm/laryngeal edema leading to respiratory distress occurring immediately (0 to1 hr) after immunization.
- ***Neuritis:*** Dysfunction of nerves supplying the arm/shoulder/gluteal area without other involvement of nervous system. A deep steady, often severe aching pain in the shoulder and upper arm or gluteal area followed in days or weakness by weakness and wasting in arm/shoulder/gluteal muscles. Sensory loss may be present, but is less prominent. May present on the same or the opposite side to the injection and sometimes affects both arms or gluteal area. Onset is usually 2 to 28 days.
- ***Disseminated BCG infection:*** Disseminated infection occurring within 1 to 12 months after BCG vaccination and confirmed by isolation of Mycobacterium bovis BCG strain.
- ***Hypotensive-Hyporesponsive Episode (shock collapse):*** Sudden onset of paleness, decreased level or loss of responsiveness, decreased level or loss of muscle tone (occurring within 24 hours of vaccination). The episode is transient and self-limiting.
- ***Osteitis/Osteomyelitis:*** Inflammation of the bone either due to BCG immunization (occurring within 8 to 16 months after immunization) or caused by other bacterial infection.
- ***Persistent Screaming:*** Inconsolable continuous crying lasting at least 3 hours accompanied by high-pitched screaming. Onset 0 to 24 hrs.
- ***Sepsis:*** Acute onset of severe generalized illness due to bacterial infection and confirmed by positive blood culture.
- ***Thrombocytopenia:*** Platelet count of 100,000 cells or less per mm3. Onset is 15 to 35 days.
- ***Toxic-Shock Syndrome:*** Abrupt onset of fever, vomiting and watery diarrhea within a few hours of immunization, often leading to death within 24-48 hours.

APPENDIX D

List of Abbreviations

ACIP	Advisory Committee On Immunization Practices
ADEM	Acute Disseminated Encephalomyelitis
AEFI	Adverse Event Following Immunization
AIDS	Acquired Immune Deficiency Syndrome
BCG	Bacillus Calmette-Guêrin
CNS	Central Nervous System
CSF	Cerebrospinal Fluid
CTB	Cholera Toxin B Subunit
DOH	Department Of Health
ERIG	Equine Rabies Immuneglobulin
HAV	Hepatitis A Virus
HBsAg	Hepatitis B Surface Antigen
HBV	Hepatitis B Virus
HCW	Healthcare Workers
HDCV	Human Diploid Cell Vaccine
Hib	Haemophilus Influenza Type B
HIV	Human Immunodeficiency Virus
HPV	Human Papilloma Virus
HPV2	Bivalent Hepatitis B Virus
HPV4	Quadrivalent Hepatitis B Virus
HRIG	Human Rabis Immuneglobulin
HSCT	Hematopoeitic Stem Cell Transplant
ID	Intradermal
IM	Intramuscular
IVIG	Intravenous Immuneglobulin
JE-CV	Japanese Encephalitis Chimeric Virus
JE-MB	Japanese Encephalitis Mouse Brain
LAIV	Live Attenuated Virus
MCV	Meningococcal Conjugate Vaccine
MDR	Multi Drug Resistant
MMR	Measles Mumps Rubella
MPSV	Meningococcal Polysaccharide Vaccine
MSM	Men Having Sex With Men
NAEFI	National Adverse Effects Following Immunization
PCECV	Purified Chick Embryo Cell Vaccine
PCV13	13-Valent Pneumococcal Conjugate Vaccine
PPSV23	23-Valent Polysaccharide Vaccine
PVRV	Purified Vero Cell Rabies Vaccine
RIG	Rabies Immunoglobulin
RNA	Ribonucleic Acid
SAE	Serious Adverse Events
SC	Subcutaneous
STD	Sexually Transmitted Disease
Td	Tetanus-Diptheria
Tdap	Tetanus-Diptheria-Acellular Pertussis
TIV	Trivalent Inactivated Influenza Virus
TIG	Tetanus Immuneglobulin
TT	Tetanus Toxoid
TY 21 a	Oral Ty21a Typhoid Vaccine, containing live attenuated S. Typhi Ty21a “strain”
ViPS	Vi Polysaccharide
VLP	Virus-Like Particles
VZV	Varicella-Zoster Virus
YFV	Yellow Fever Virus