INFECTIOUS DISEASES
Definitions

• **Fever**
  Controlled increase in body temperature over normal values for an individual.

  **Temp. regulation** –
  *Thermosensitive neurons* in preoptic / anterior hypothalamus
  (neural connections with cold & warm recep in skin/ muscles )

  **Thermoregulatory responses**
  **Diurnal variation**
Pathogenesis of fever

Exogenous pyrogens (microbes, toxins etc.)

Endogenous pyrogens (IL-1, IL-6, TNF-α, IFN- β & -γ, PGs)

Thermostat set at higher temperature

*Fever is an adaptive response, should be treated in special circumstances only.*
Etiology Of Fever

- Infections
- Vaccines
- Biologic products
- Tissue injury
- Malignancy
- Drugs
- Immunological - Rheumatological disorder
- Inflammatory disorders
- Granulamatous disorders
- Endocrine disorders
- Metabolic disorders
- Genetic disorders
- Unidentified etiology
- Factitious Fever
Effects of Fever
(Increased heat production)

• ↑ oxygen consumption (Pulmonary diseases)
• ↑ Carbon dioxide production
• ↑ Cardiac output (cardiac diseases)
• Metabolic instability (eg. In diabetics)
• Febrile seizures /in epileptics

In above circumstances, treatment of fever is necessary.
Patterns of Fever

- Continuous
- Intermittent fever
- Remittent
- Relapsing

- Hyperpyrexia  Temp $> 41^\circ C$
• Fever without focus

• Fever of unknown origin-

Fever documented by a health care provider & for which cause could not be identified after 3 weeks of OPD & 1 week of IPD evaluation
• **Bacteremia** Recovery of bacteria in blood culture

• **Sepsis** Systemic response to infection with bacteria/ viruses/ fungi/ protozoa/ rickettsiae

• **Severe sepsis** Sepsis with organ dysfunction/ hypoperfusion/ hypotension

• **Septic shock** Severe sepsis with persistent hypotension despite adequate fluid resuscitation

• **Systemic inflammatory response syndrome** Response to a wide variety of clinical insults, characterized by Hyper or hypothermia; Tachycardia; Tachypnea; ↑/↓WBC

• **Multiple organ dysfunction syndrome**
Investigations in infectious diseases

Based on

1. Direct exam of specimens- culture/ antigens
2. Isolation in culture
3. Serological testing for antibodies
4. Molecular genetic detection- PCR
Viral Infections
Measles

• Also known as Rubeola

• Caused by RNA virus (Paramyxoviridae)
Measles

• Transmission

Highly contagious (90% household contacts acquire ds)

Droplet infection (prodromal period, for short pd after rash appearance)

Before 6 months rare (trasplacentally acquired maternal antibodies)

*Infants of mothers with vaccine induced immunity lose passive antibodies earlier.*

Infants of susceptible mothers may contract the ds simultaneously with the mother.
Pathogenesis

• Essential lesion: Perivascular serous exuates with proliferation of mononuclear & PMN cells
• Found in Skin, Mucous membranes of nasopharynx/ bronchi/ intestinal tract
• Hyperplasia of lymphoid tissue (eg. Appendix)
• Interstitial pneumonia: **Hecht Giant Cell Pneumonia**
• Encephalomyelitis: Perivascular demyelination
• SSPE: Degeneration of cortex & white matter (intracytoplasmic inclusion bodies)
Clinical Picture

- **Incubation stage**: 10 -12 days
- **Prodromal stage**: 3 -5 days
- Low/ moderate grade fever, URI sx, conjunctivitis, red mottling over hard/ soft palate
  
  *Koplik spots*: grayish white spots opposite lower molars
  
  :Can be found over lower lip/ palate/lacrimal caruncle
  
  :Appear /disappear within 12 -18 hours.

- Occasionally, high grade fever/ convulsions/ pneumonia
Measles Rash

Koplik spots

Conjunctival congestion
Exanthematous stage:

- High grade fever up to this stage
- Starts from face & neck spreads to arms, trunk & lower limbs within 24-48 hours.
- Rash can be – Macular /Maculopapular /Hemorrhagic (Petechiae / ecchymotic)/urticarial
- **Black measles**: Hemorrhagic measles, bleeding from nose, mouth, bowel etc.
- Complete absence of rash: IVIg; HIV infection; <9 months of age
- **Branny desquamation** & brownish discoloration during fading.
**RES involvement:**
- Lymph node enlargement –Cervical/ mesenteric
- Splenomegaly

**Other sx** Bronchopneumonia/ otitis media/ diarrhea/ vomiting etc.

**Atypical measles:**
- In patients who received killed measles virus vaccine before 1967.
- Atypical rash: distribution /morphology .
- Systemic features : severe headache / vomiting/ pain abdomen / pneumonia etc.
Diagnosis

- Clinical picture
- Measles IgM antibodies
- In prodromal stage: multinucleated giant cells in nasal mucosa smears
- TLC – Low, Relative Lymphocytosis
- In measles encephalitis: ↑ proteins, ↑ lymphocytes, glucose normal.
Differential diagnosis

- Rubella/ adenoviral/ enteroviral: Milder degree of rash / fever
- Roseola infantum (Human herpes virus 6): rash appears after subsidence of fever
- Rickettsial infections: rash spares the face
- Meningococcemia: cough/ conjunctivitis -nt.
- Scarlet fever
- Kawasaki disease
- Serum sickness
- Drug rash
Treatment

Supportive only

• Fever control
• Adequate fluid intake
• Bacterial infections: antibiotics
• Watch for complications
• **Vitamin A**
  Reduces mortality & morbidity.
  6 months -2 years. Single dose of 100,000 units
  > 2 years : Single dose of 200,000 units .
  Children with ophthalmological evidence of vit A deficiency : 3 doses ,on day 1 ,2 & 28.
Complications

- Otitis media
- Respiratory:
  - Interstitial pneumonia (Viral).
  - Bacterial superinfection
  - Laryngitis, Tracheitis, Bronchitis
- Cardiac: Myocarditis
- Purpura fulminans
- DIC
- Noma of cheeks
Complication (contd.)

- **Neurological:**
  - Encephalitis: In pre eruptive stage/ 2 -5 days after rash. Direct viral invasion / Demyelination.
  - LGBS
  - Cerebral thrombophlebitis
  - Retrobulbar neuritis
  - Hemiplegia
  - SSPE

- **Flaring of tuberculosis**
- **Malnutrition**
Prognosis

• Poor in presence of concomitant malnutrition
Prevention

1. Vaccination:
   9 months f/b MMR at 15 months, repeated at 4-6 years or 11-12 years.

   **Live vaccine Contraindications:**
   pregnant women
   primary immunodeficiency
   untreated TB
   On immunosuppressive therapy
   HIV infected with severe immunosuppression
2. Isolation precautions
   From 7\textsuperscript{th} d after exposure to 5\textsuperscript{th} d posteruptive phase

Postexposure prophylaxis
   Passive immunization with immunoglobulin within 6 days of exposure
   Pregnant women
   Immunocompromised persons
   Infants of nonimmune mothers < 6 month of age

Vaccination
   Children between 6 -12 months of age (Vaccine + IVIg);
   > 12 months Vaccine alone
   For pregnant women & Immunocompromised persons
   IVIg alone
Rubella
• Also known as German measles/ Three day measles
• Caused by RNA virus
• Humans only natural hosts
• Transmission: droplet/ transplacental
• Age group: 5-14 years, teenagers/ young adults
• Incubation period: 14 -21 days
• 2/ 3 rd cases subclinical
Clinical Manifestations

Prodromal phase: mild catarrhal symptoms
• **Lymphadenopathy**: 24 hours prior to rash to 1 wk after
  Markedly tender enlargement of L.N.
  Retroauricular/ posterior cervical/ postoccipital
• **Enanthem**: Forchheimer spots (rose coloured spots on
  soft palate)

Exanthem:
  Maculopapular
  Rapid evolution
  Starts from face & spreads to entire body within 24
  hours, clears by 3rd day.
Rubella
• **Polyarthritis:**
  Seen in adolescent girls & women
  Can involve any joint
  Subsides within 2 weeks but can persist for several months also.
  No residual damage.

• **Congenital Rubella Syndrome**
Diagnosis
  Clinical Picture
  Serology
  Viral culture

Differential Diagnosis
  Measles (mild) (*Unlike measles, children with rubella often don't have a fever and the rash is fainter than the rash of measles.*)
  Scarlet fever
  Roseola infantum
  Infectious mononucleosis
  Drug rash
• **Treatment**: No specific Tt.

• **Complications**:  
  Encephalitis: mortality 20%  
  TTP  
  Congenital Rubella syndrome  
  Progressive Rubella Panencephalitis

• **Reinfection**:  
  With natural infection: 3-10%  
  After vaccination: 14-18%  
  Maternal reinfection: CRS
Congenital Rubella Syndrome

- Microcephaly
- Fetal Death
- Cataracts
Congenital Rubella Syndrome

• Most common complication of rubella in pregnant women.

• Risk of defects:
  Greatest with primary maternal infection
  Before 11th week of pregnancy > 90%
  b/w 11th -13th week 10-20%
  After 16th week very low risk

• Affects all organ systems.
Clinical Features

- IUGR
- Global development delay
- Microcephaly
- Eye defects: Cataracts (u/l or b/l), Microphthalmia
- Cardiac defects: PDA, Pulmonary artery stenosis; Myocarditis
- Sensorineural hearing loss
- Meningoencephalitis
- Blueberry muffin skin lesions
- Pneumonia
- Hepatitis
- Bone lucencies
- TTP, Anemia
Congenital Rubella Syndrome

Newborn with CRS

Congenital cataract
Diagnosis

**In infant:** Rubella specific IgM Ab
Culture from nasopharynx/ urine/ tissues

**Prenatal:** Rubella specific IgM from cord blood

**Treatment:** No specific therapy

**Prognosis of CRS**
Poor prognosis: with complete spectrum of disease
With encephalitis: only 30% escape sequelae
Prevention

- **Vaccine:**
  - Live vaccine
  - Derived from RA 27/3 strain

  **Dosing schedule**
  - 1\(^{st}\) dose 12-15 months of age
  - 2\(^{nd}\) dose 4-6 years / 11-12 years

- **Contraindications:**
  - Pregnancy (should avoid becoming pregnant for 3 months)
  - Immunodeficiency
  - Recent IVIg administration

**Symptoms following Vaccine:**
- Fever/ Rash/ LN enlargement / Arthralgias or Arthritis/ Peripheral parasthesias
Varicella- Zoster Virus
• **VZV**: Neurotropic human herpes virus
• 3 types of infection
  - **Primary Infection**: Chickenpox
  - **Latent**: sensory ganglion neurons
  - **Recurrent**: Herpes Zoster
Chickenpox
Varicella

- **Transmission**: 65-86% in household subjects.
- Susceptible persons acquire ds after contact with herpes zoster case.
- **Period of infectivity**: 24-48 hours before appearance of rash till crusting of vesicles.
- **Airborne/ direct spread through respiratory secretions / Vesicular fluid / Transplacental**
- **Incubation period**: 10-21 days.
- Infection limitation by host immune responses
- **More severe in adolescents & adults.**
- Primary infection leads to latent infection in sensory ganglia cells.
Clinical Features

• Subclinical varicella rare.
• Patients are most contagious 1 -2 days before appearance of rash to shortly after onset of rash.
• **Prodromal symptoms**: Fever, malaise, anorexia, pain abdomen
Rash:
• Centripetal in origin.
• Starts as pruritic maculopapular rash, then evolves into vesicular stage, after 24-48 hours clouding, umblication & crusting.
• Several stages can be seen simultaneously.
• Exantheme more extensive in skin disorders.
• Ulcerative lesions in oropharynx, vagina, eyelids & conjunctiva

• Breakthrough varicella: after vaccination. Milder illness, atypical rash.
Chickenpox Rash
Diagnostic Tests

- Tissue culture
- PCR
- Direct fluorescent antibody
- Enzyme immunoassay (for assaying immune status in healthy persons after natural infection)
- Latex agglutination

TLC: Leukopenia
CSF: Mild lymphocytic pleocytosis, ↑/ n protein, glucose- n
LFT: mildly deranged
Complications

- **In healthy individuals**: rare, mild hepatitis, mild thrombocytopenia
- **In Immunocompromised**: complications are common

**Bacterial infections**: Esp by grp A streptococcus
**Skin**: impetigo, cellulitis, subcutaneous abscess, necrotizing fascitis
**Bacterial sepsis**
**Pneumonia**
**Arthritis**
**Osteomyelitis**
**TSS**
Complications (contd.)

Neurological:
  Cerebellar ataxia
  Encephalitis
  LGBS

Reye Syndrome

Hemorrhage: Hemorrhagic vesicles, GI bleed, Hematuria

Renal: HUS, Nephritis, Nephrotic syndrome

Cardiac: myocarditis, pericarditis

Pancreatitis

Orchitis
Progressive varicella

• Severe complication, high chances of mortality
• Characterized by:
  
  **Continued lesions (for weeks to months)** - may be hemorrhagic

  **Visceral involvement**

  **Coagulopathy** - severe hemorrhage

• At risk: Immunocompromised patients
  1. Congenital cellular immunodeficiency
  2. Malignancy: risk is more if CT given in incubation period
  3. Organ transplant recipients
  4. High dose corticosteroids, even inhaled steroids
  5. Newborn
Maternal varicella:

1. < 20 weeks – Fetal death/ Embryopathy
2. >20 weeks- Inapparent varicella , H. zoster early in life
3. During last week of pregnancy- Neonatal Varicella
Neonatal chickenpox

• Can develop in a neonate:
  1. If mother develops varicella 5 days before to 2 days after delivery.
  2. Neonate of a nonimmune mother comes in contact with a c/o varicella
• Severity of disease is modified by transplacental transfer of VZV specific maternal IgG.
• Complications: Pneumonia, Hepatitis, Encephalitis
• Mortality is very high
• Prevention:
  VZVIG / IVIG within 96 hours of delivery.
• Treatment: I.V. Acyclovir
Congenital varicella syndrome:

Upto 2% fetuses of infected mothers
Most of the stigmata are related to virus induced nervous system injury
Stigmata involve : Skin, Extremities , eyes, brain
**Skin:** Cicatrical skin lesions
**Eyes:** Microphthalmia, cataracts, chorioretinitis, optic atrophy
**Brain:** Microcephaly, hydrocephalus, calcifications, aplasia of brain
**Spinal Cord:** Limb hypoplasia, motor & sensory deficits, anisocoria, Horner syndrome, sphincter disturbances
Congenital varicella syndrome (contd.)

**Diagnosis:**
- Clinical
- PCR for viral DNA

**Treatment:**
- Mother- VZIG & Acyclovir – Safety & efficacy in prevention not known.
- Neonate – Antiviral treatment not indicated
Treatment of Chickenpox

- **In immunocompetent hosts**: Viral replication stops by 24 hours after onset of rash
  - Children < 12 years: No treatment
  - Adults: Oral Acyclovir 20mg/kg/dose, 4 doses/day, max. 800mg/dose for 5 days

- **Immunocompetent hosts (at increased risk)** (oral acyclovir)
  - Chronic skin disorders
  - Chronic pulmonary conditions
  - On long term salicylate therapy
  - On steroids (short, intermittent, aerosolized)
Treatment

• **Pregnant women:** Oral acyclovir; if seriously ill IV acyclovir

• **In immunocompromised patients:**
  
  **IV Acyclovir** (poor bioavailability of oral acyclovir) should be initiated early in the course.

  For resistant infections: **Foscarnet Sodium**

  **For disseminated varicella:** IV acyclovir 500 mg/m² 8 hourly for 7 days/ no new lesions for 48 hours
Prevention

• Primary prophylaxis:
  Vaccination: Live attenuated vaccine, s.c. route
    1- 12 years- 1 dose
    A >12 year- 2 doses at least 4 weeks apart

Contraindications:
  1. Serious intercurrent illness
  2. Immunocompromised persons
  3. Pregnancy/ Lactation
  4. On Salicylates
Postexposure prophylaxis:

**Vaccination:** For all susceptible persons >12 months of age within 72-120 hours (if no contraindication to vaccination)

**Passive immunization:**
1. Immunocompromised children
2. Susceptible pregnant women
3. Newborns whose mother had chickenpox within 5 days before delivery or within 48 hours after delivery
4. Hospitalized PT (>28 wks), susceptible mother
5. Hosp. PT (<28 wks), regardless of maternal immunity status

**Control Measures** School absenteeism: till crusting of lesions
Herpes Zoster

- Reactivation of varicella virus in nerve roots
- **C/P:**
  - Vesicular lesions clustered within one/two dermatomes
  - Localized pain, hyperesthesia, pruritis, low grade fever
  - Resolution within 1-2 wks
  - Post herpetic neuralgia (uncommon).
  - Recurrent attacks can occur (4%).

- **Complications:**
  - Transverse myelitis
  - In Immunocompromised:
    - Disseminated disease
    - Retinitis
    - CNS disease
Herpes zoster contd.

• **Treatment:**
  In adults: Acyclovir/ Famciclovir/ valacyclovir
  In healthy children: no treatment
  In Immunocompromised children: I.V. acyclovir
Herpes Zoster
Mumps

- **Etiology**: Paramyxovirus
- Transmission: Airborne droplets/ direct contact/ fomites contaminated by saliva/ ? Urine
- More common in late winter & spring
- Incubation period: 14- 24 days
- In 30 -40% cases subclinical infection
- Prodromal symptoms: fever, ms pain, headache
- **Salivary gland swelling:**
Parotid gland involvement
**Salivary gland involvement**

- Involves **parotid** (most common), submandibular (in 10-15%), sublingual glands
- In 1/3rd cases no swelling, primarily respiratory involvement
- May manifest as earache before appearance of swelling
- **Parotid swelling**: filling of space between mandible & mastoid, erythema & swelling of overlying skin & soft tissue. Swelling may extend over manubrium sterni & upper chest wall.
- Stenson duct opening is red & swollen.
- Pain on tasting sour liquids.
- Swelling subsides in 3-7 days.
Diagnosis

• Clinical
• Lab Ix.:
  Serology
  Viral culture

  S. Amylase – elevated
CSF- Pleocytosis
Differential Diagnosis

- Viral infections:
  - HIV
  - Influenza
  - Parainfluenza 1 & 3
  - CMV
  - Cytomegalovirus
- Staph aureus
- Salivary calculus
- Preauricular lymphadenitis
Treatment

No specific antiviral treatment

Supportive:
Antipyretics
Orchitis: local support, bed rest
Arthritis: NSAIDS/ Steroids
Complications

- Orchitis (uncommon before puberty)
- **CNS involvement:**
  - Encephalitis
  - Cerebellar ataxia
  - LGBS
  - Polyradiculitis
  - Transverse myelitis
- Thyroiditis
- Pancreatitis

- **Cardiac:** Myocarditis, Endocardial fibroelastosis
- Arthritis
- Mastitis
- Hearing impairment
- Optic neuritis
- Lacrimal gland swelling
Prevention

• **Primary prophylaxis:**
  **Vaccination:**
  Live attenuated vaccine
  1\textsuperscript{st} dose- 12- 15 months of age
  2\textsuperscript{nd} dose- 4- 6 years/ 11- 12 years of age

**Contraindications:**
Immunodeficiency( Primary / Acquired)
Recent IVIG treatment
Moderate/ severe acute illness

• **Secondary prophylaxis**
  **Vaccination**
  Isolation : 9 days
Japanese Encephalitis
Distribution of JE in Asia
Japenese Encephalitis

- Leading cause of childhood encephalitis
- Major outbreaks in India since 1995
- Highly endemic areas: AP, TN, Karnataka, UP
- In Northern India: epidemics from May to October
- In Southern India: from July to December
Life cycle of JE virus

Infected Mosquito

Infected bird

Mosquito

Pig

Human
• Causative organism: Flavivirus, RNA virus
• Vector: Mosquito – **Culex tritaenorrhynchus, Culex vishnui**
• **Transmission**: Zoonotic cycle among mosquitoes & vertebrate- amplifying hosts, chiefly pigs & wading birds
• Man to man transmission is not known.
Pathophysiology

Mosquito bite

Virus multiplication in regional lymph nodes

Transient viremia

CNS invasion

Viral replication in neuronal secretory system

Destruction of neurons
Clinical picture

- Age group (In endemic areas): <15 years
- Asymptomatic: symptomatic infection 1:250
- Incubation period- 1- 14 days
- Onset: abrupt/ acute/ subacute/ gradual
- **Stages:**
  - **Prodromal stage:**
    - Fever (high grade)
    - Headache
    - Nausea/ vomiting
    - Malaise
• **Encephalitis stage:**
  - Starts from $3^{rd}$ to $5^{th}$ day

**Symptoms**
- Altered sensorium
- Seizures
- Abnormal posturing

**Signs:**
- Abn doll’s eye reflex, hemiparesis, decorticate/decerebrate posturing

**Gastric bleeding**

**Death occurs most commonly in this stage**
• Late stage:
  Stage of recovery/ neurological sequelae
  Slow regaining of neurological functions in survived
  Sequelae: Paresis/ Speech defects/ intellectual/ cognitive dysfunctions
  Secondary infections: Pneumonia/ UTI/ Bed sores

Atypical presentations of JE:
  AFP like illness
  Short period of altered sensorium/ altered behaviour
Lab Diagnosis

• TLC -↑
• CSF: Lymphocytic pleocytosis/ proteins- mildly raised/ normal glucose
• CT head: Involvement of thalamus/ basal ganglia/ midbrain/ pons/ medulla
• MRI: more informative
• EEG: nonspecific changes
• **Definitive tests:**
  
  S. antibody titre > 4 fold rise
  
  Virus detection: PCR/ immunechemistry
  
  JE virus specific IgM in CSF
Differential Diagnosis

- Viral infections
- Pyo meningitis
- Enteric fever
- ICSOL
- SLE
- CVA
Management

• No specific treatment
• **Supportive:**
  ABC
  BBB care
  Temperature control
  Fluids/ electrolytes/ blood sugar management
  Seizure control
  Management of raised ICP
  Respiratory support
  Prevention & management of nosocomial infections
  Physiotherapy( in late stage)
Prognosis

• Mortality: 8.5% - 72%
Prevention

- Control of mosquito vectors
- Prevention of mosquito from biting humans
- Control/ protection of reservoirs
- Vaccination
Vaccination:

- Most cost effective method of prevention
- Three types: Inactivated mouse brain
  - Inactivated primary hamster kidney cells – P3
  - Live attenuated primary hamster kidney cells
    - SA 14 -14 -2
- In India, live attenuated vaccine is being used
  2 doses schedule -6- 8 weeks apart
  s.c. administration
Adverse effects: fever/ headache/ dizziness
Dengue & Dengue hemorrhagic fever
Introduction

• It is a mosquito born viral illness caused by RNA flavivirus: 4 distinct antigenic types.
• Female mosquitoes of the genus *Aedes aegypti* are the vectors, reside in pools of rainwater/man-made pools of water, bites during daytime.
• Humans are the primary reservoir for the virus, although some scientists have hypothesized that monkeys can also serve as reservoirs.
• Potentially lethal complication called dengue hemorrhagic fever.
• Global incidence of dengue has grown dramatically in recent decades.
• About two fifths of the world's population are now at risk.
• Dengue is found in tropical and sub-tropical climates worldwide, mostly in urban and semi-urban areas.
• Epidemics are common.
• India, Srilanka & Myamar are hyper endemic.
• As A. aegypti has a limited range, spread of epidemic occurs mainly through viremic human beings.
• Once the virus enters a human, it circulates in the bloodstream for two to seven days, during which time the virus can be spread to other blood-feeding Aedes mosquitoes.
• **Infected humans are the main carriers and multipliers of the virus**, serving as a source of the virus for uninfected mosquitoes.
• > 90% children with severe disease are < 15 years of age.
• About 25,000 deaths reported each year.
Dengue infection

Antibody formation

Reinfection

Augmentation of viral multiplication

Increased vascular permeability

Plasma leakage

Hypovolemia

Shock

Death

Reduced platelets

Coagulopathy

DIC

Severe bleeding

PATHOPHYSIOLOGY
Pathogenesis

• Antibody dependent enhancement of virus multiplication in macrophages by heterotypic antibodies which were formed during previous dengue infection
• Circulating dengue antigen-antibody complexes, activation of complement, and release of vasoactive amines cause increased vascular permeability, bleeding, and possible DIC.
• In the process of immune elimination of infected cells, proteases and lymphokines may be released and activate complement coagulation cascades and vascular permeability factors.
Clinical Spectrum

Dengue infection

Asymptomatic

Symptomatic

Undifferentiated fever

DF

Without hemorrhage

With Hemorrhage

DHF

Without shock

DSS
Box 10
The Spectrum of Dengue Haemorrhagic Fever

Dengue Infection

- Fever
- Positive tourniquet test
- Increased vascular permeability
- Hepatomegaly
- Thrombocytopenia

Other haemorrhagic manifestations
- Rising haematocrit
- Hypoproteinaemia
- Serous effusion

Leakage of plasma

Hypovolaemia

Shock

- Coagulopathy
- Disseminated intravascular coagulation

Severe bleeding

Death

Grade I
Grade II
Grade III
Grade IV

Source: Dengue haemorrhagic fever - Diagnosis, treatment, prevention and control, 2nd edition. World Health Organization, Geneva
**Dengue Fever**

- In primary/ secondary infection
- **Biphasic illness**
  - High grade fever- lasts for 2- 7 days
  - Severe headache (esp. retro- orbital)
  - Arthralgia/ myalgia
  - Anorexia/ abdominal discomfort
  - Maculopapular rash/ Flushing
  - In younger children: Coryza/ rash/ diarrhea/ seizure
  - Hemorrhagic manifestations rare.
- DHF/DSS: DF =1:150/ 200
• Signs to help assess severity/ need for admission:
  1. Vitals
  2. **Tourniquet Test**: Keep inflated BP cuff midway b/w SP & DP for 5 minutes.
     >20 petechiae in 2.5 cm² area below elbow.
  3. Rash
  4. Bleeding
  5. ↓ Air entry
  6. H.splenomealy
  7. Ascitis/ ileus
  8. Altered sensorium
DHF

- Usually occurs in 2nd infection, but can occur in infants d/t maternally acquired antibodies.
- Intermittent high fever
- Severe headache
- Flushing
- Arthralgia/ myalgia
- Anorexia/ abdominal discomfort
- **Bleeding manifestations**
- **Features of plasma leakage:**
  Circulatory disturbances/ Periserositis

**Complications:**
- Encephalopathy/ Encephalitis
- Hepatic failure
- Myocarditis
- DIC
WHO case definition of DHF

- Acute sudden onset high grade fever for 2-7 days
- Hemorrhagic manifestations
- Platelet count < 1 lac/ cmm.
- Hemoconcentration (rise in PCV > 20%)/ other evidence of plasma leakage
Grading of DHF

- Grade I: No shock- only positive tourniquet test
- Grade II: No shock- spontaneous bleeding
- Grade III: Shock
- Grade IV: Profound shock with unmeasurable BP/Pulse

(Gr. III & IV : DSS)
Investigations

- **Serology:**
  - IgM: for short period in 1*/2* infection
  - IgG: fourfold rise in paired sera ( >5 d after infection)
- PCR: for detection of viral DNA
- Hemogram
- LFT
- SERFT
- Coagulogram
- ABG
- CXR
- ECG
Differential Diagnosis

Febrile illness:
Malaria/ Leptospirosis/ other viral illness

DHF:
Dengue like illnesses: Chickengunya/ Onyong- nyong
Meningococcemia
Rickettsial diseases
Yellow fever
Other viral hemorrhagic fevers
Management

Dengue Fever:
Antipyretics ( aspirin/ ibuprofen contraindicated)
Oral fluids
H2 blockers( if bleeding)
Domperidone
Antibiotics not indicated
**DHF/ DSS:**
Vitals monitoring

**Shock**

**IVF**
If PCV increase > 20% / Pulse pressure <10mm Hg: Normal saline 10ml/kg/hour
Colloids/plasma/ blood (if e/o hemorrhage)
Ionotropic support
Overhydration should be avoided
During recovery: Fluid returns to IV space, overhydration can occur
IVF: given with caution
Diuretics/ digoxin
Management contd.

**Bleeding**
PRP
FFP (in c/o DIC)
Whole blood : in c/o shock
Anti Rho immunoglobulin
IVIG ?
Invasive procedures X

**Management of complications**
Causes of death in DHF

- Prolonged shock
- Massive bleeding
- Fluid overload
- Acute hepatic failure
- Poor medical care
Prognosis

**DSS:**

Early & intensive care can reduce mortality to 1% in good centres, otherwise 40-50% mortality.
Prevention

• Prevention of mosquito breeding
• Personal protection
• Vaccine: not yet developed
Rotavirus
Leading cause of diarrhoea in infants
• RNA virus
• Infects & destroy villus tip cells in small intestine

Clinical Picture:
• Incubation period- <48 hours
• Mild/ moderate fever
• Vomiting
• Diarrhoea: continues for 5 -7 days
• Dehydration
• Severe illness in malnourished/ immunocompromised children
Investigations:
   Enzyme immunoassays
Stool examination: normal

Differential Diagnosis:
Viral: Norwalk/ Astrovirus/ Enteric adenovirus
Bacterial: blood in stools/ high grade fever
Treatment:
Avoidance / treatment of dehydration
No role of antiviral/ antibiotics
Probiotics ?
Prevention:
Vaccination- Live vaccine
Poliomyelitis
Poliomyelitis

- Poliovirus belongs to genus Enterovirus.
- 3 types: 1, 2, 3
- Inactivated by heat, chlorine, UV rays
- Found only in human beings, no animal reservoir
- **Transmission**: Feco-oral route (virus multiplies in intestine)
- Virus is intermittently excreted for ≈2 months, maximum excretion just before paralysis & during first 2 weeks after paralysis.
- Highly communicable disease,
Immunity:

- All unimmunized persons are susceptible.
- Infants of immune mothers protected for few weeks
- Natural infection/ immunization: Humoral/ local intestinal cellular responses
Clinical picture

- Incubation period: 7-10 days
- **Inapparent infection**: only 5-10% symptomatic

**Abortive polio-**
- 4-8%
- Minor illness: low grade fever, vomiting, abdominal pain, malaise
- Rapid recovery, no paralysis
- Similar to other viral infections
Nonparalytic Poliomyelitis-

- 1- 2%
- Headache/neck stiffness/ backache/ leg stiffness for several days
- May reach imminent paralysis, but reverts back
- Tripod sign/ signs of meningeal irritation
- DTR/ superficial reflexes- normal
- Changes in reflexes ↑/↓ may precede weakness by 12 - 24 hours
Paralytic Polio

• 0.5 -1% infections
• Biphasic illness
• **Minor illness:** similar to abortive polio
• Asymptomatic period
• **Major illness:** Begins with Muscle pain/spasms / return of fever
  Followed by rapid onset of AFP which is complete in 72 hours
• 3 types
• Involves **anterior horn cells**
Anterior Horn Cells
Spinal paralytic polio:

- Severe headache
- Fever
- Severe muscle pain
- Paralysis: asymmetric flaccid paralysis
- Proximal ms involvement more common
- Weakness of some muscles of neck/ abdomen / trunk ±
- No Sensory involvement
- Complete weakness appear within 72 hours
- Bladder/ bowel involvement can occur
- **Provocation paralysis: after IM injection**
Recovery of paralysis:
• Usually within first 6 months
• In permanent weakness: Atrophy of muscles/ deformity/ asymmetry of limbs seen
Bulbar polio

- Without apparent involvement of spinal cord
- Dysfunction of cranial nerves & medullary centers

Clinical finding
- Respiratory difficulty
- Paralysis of extraocular, facial, masticatory muscles.
- Nasal twang to the voice/cry
- Inability to swallow smoothly
- Accumulated pharyngeal secretions leading to irregular respiration
- Absence of effective coughing
• Nasal regurgitation of saliva / fluids
• Deviation of palate uvula, tongue
• Vocal cord paralysis one or both (hoarseness, aphonia, asphyxia)
• **Rope sign** - Acute angulation between the chin and larynx due to weakness of hyoid muscles

• Involvement of vital centers (irregularities in rate, depth, rhythm of respiration, BP changes, arrhythmias, body temperature changes).

• Uncommonly bulbar disease may culminate in an ascending paralysis (Landry type)
Course

Variable

1. Some die due to involvement of vital centers
2. Other recover partially but require ongoing respiratory support
3. Others recover completely.

Cranial nerve involvement is seldom permanent
Polioencephalitis

- Rare form
- Higher centers of brain severely involved
- Manifest as seizure, coma, spastic paralysis with brisk reflexes, irritability, disorientation, drowsiness, coarse tremors, peripheral/cranial nerve paralysis may coexist.
- D/D: Any other Viral encephalitis
- **Diagnosis:**
  1. specific viral diagnosis
  2. If accompanied by flaccid paralysis
Respiratory insufficiency in Polio

Spinal Polio:
Paralysis of Diaphragmatic/ accessory muscles

Bulbar Polio:
1. Paralysis of Pharyngeal/ Laryngeal muscles
2. Respiratory centre involvement

Bulbospinal Polio:
Both mechanisms
F/O impending respiratory failure

- Anxiety/ Restlessness
- Breathless sentences
- Increased respiratory rate
- Inability to cough/ sniff full depth
- Deltoid weakness
- Paradoxical abdominal movements
- Relative immobility tof the intercostal spaces
Diagnosis

Clinical:
Should be considered in any unimmunized/ partially immunized child with nonspecific febrile illness/ aseptic meningitis/paralytic disease.

1. Wild virus associated paralytic polio
2. Vaccine associated paralytic polio : 7-14 days after receiving OPV
Lab Diagnosis

Stool specimens:

• For isolation & identification of polio virus

• **Adequate stool sample:** 2 stool specimens collected within 14 days of paralysis onset & at least 24 hours apart; each specimen must be of adequate volume (8-10 gms) & arrive at a WHO- accredited laboratory in good condition (i.e. no dessication or leakage, with adequate documentation & evidence that the cold chain was maintained)

• If child is constipated: rectal tube specimen (less preferred).
Transportation of specimen

Reverse cold chain:
The process of keeping the specimen in the desired temperature of 2-8°C after collection from the child to the time of reaching the lab.
Specimen should reach lab within 72 hours of dispatch.
If not possible freeze at -20°C & ship in frozen state.

Contact stool specimen: If adequate stool samples can't be collected from the patient.
Dx (contd.)

• **CSF analysis:** Pleocytosis b/w 20-300 cells/ cmm (PMN/Mononuclear cells), Protein N/ slightly ↑

• **Serological testing:** Fourfold or greater rise in antibody titres in paired sera
Acute Flaccid Paralysis (AFP)

AFP is defined as sudden onset of weakness & floppiness in any part of body in a child <15 years of age or paralysis in a person of any age in whom polio is suspected.

Common causes of AFP (other than polio): LGBS/ Tr myelitis/ traumatic neuritis/ nonpolio enterovirus
AFP surveillance

Helps to detect reliably areas where polio transmission is occurring, thus identifying areas of priority for immunisation.

**Background rate of AFP:** 1 case/ 100000 children detected by active surveillance (collection & analysis of data for action)

**All cases of AFP should be reported irrespective of diagnosis within 6 months of onset.**

Stool samples should be collected up to 60 days after onset of paralysis.
AFP case classification

- Wild polio virus
  - Confirm
  - Compatible
    - Residual weakness, Died/lost to FU
      - Expert review
      - Discard (non polio AFP)
    - Inadequate ss
      - No residual weakness
      - No wild polio virus
      - AFP
      - 2 adequate ss

- No wild polio virus
  - Inadequate ss
Treatment

Abortive polio: Temperature control/ analgesics/ bed rest
Nonparalytic polio: Analgesics/ hot packs/ firm bed
Paralytic polio:
Hospitalization
Complete physical rest for 2-3 weeks
Suitable body alignment: neutral position with feet at right angle to legs, knees slightly flexed, hips & spine straight
Moist hot packs
Sedation
Bladder paresis: parasym. Stimulant (bethanechol)
Treatment (contd.)

Bulbar polio:
ABC
Strict vitals monitoring
Tracheostomy
Respiratory support
Complications

Melena
Acute gastric dilatation
Hypertension
Acute pulmonary edema
Hypercalcemia (d/t immobilization)
Bed sores
Prognosis

Abortive / nonparalytic: good prognosis

Severe bulbar variety: 60% mortality

Less severe bulbar/ spinal: 5-10% mortality
Paralysis

Beyond 6 months paralysis is permanent
Common in male children/ pregnant women

Factors increasing risk:
Tonsillectomy/ IMI – bulbar/ localised ds
Physical activity/ fatigue in early phase
Type 1 virus- natural ds; Type 3- VAPP
Post polio syndrome

In persons with paralytic polio, 30-40 yrs later on acute exacerbation of weakness/ appearance of new weakness/ muscle pain
Vaccination

**OPV**
1. serum IgG titres +
2. Mucosal IgA immunity (limits viral replication in oropharynx/ gut)
3. Limits viral transmission by fecal route
4. Affected by maternal Ab
5. Risk of VAPP(1/6.2 million)
6. Can’t be given to immunodeficient persons

**IPV**
1. S IgG ++
2. --
3. --
4. Not affected
5. No risk of VAPP
6. Can be given
Polio Eradication

1. Routine immunization
2. Polio surveillance
3. National immunization days
4. Mopping up immunization
Influenza Viruses
• RNA viruses/ orthomyxoviridae
• 3 types: A,B,C
• No cross immunity
<table>
<thead>
<tr>
<th>Type A</th>
<th>Type B</th>
<th>Type C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Causes significant disease (Epidemics/pandemics)</td>
<td>Significant disease: epidemics</td>
<td>Insignificant disease</td>
</tr>
<tr>
<td><strong>Infected humans &amp; other species</strong></td>
<td>Limited to humans</td>
<td>Limited to humans</td>
</tr>
<tr>
<td>Frequent antigenic variation</td>
<td>Infrequent antigenic variation</td>
<td>Antigenically stable</td>
</tr>
</tbody>
</table>
Influenza A

- 2 surface antigens:
  - **Hemagglutinin**: 1-16 (resp for attachment of virus to cells)
    - Swine: H1,3,9; Avian: all 16
  - **Neuraminidase**: 1-9 (resp for release of virus from infected cells)
    - Swine: N1,2; Avian: all 9
  Different combinations can occur.

- Involves animal hosts which serve as reservoir for diverse strains with potential to infect human population.
- Reassortment b/w human & animal virus can lead to formation of new strains.
• **Antigenic Drift:**
  Gradual antigenic change over a period. Point mutations, can cause epidemics

• **Antigenic shift:**
  Sudden complete/ major change
  Genetic recombination of human with animal/ avian virus
  Can cause pandemics

H1N1, H2N2, H3N2
Pandemic Influenza:

Worldwide surge in influenza cases d/t introduction of new type A surface protein (antigenic shift).
Can affect all age groups.
Usually occur at interval of 10-15 years.
Higher attack rate during pandemic (50%).
Pandemic Phases

Prepandemic phases:
  Phase 1: No avian virus poses a risk to humans
  Phase 2: New avian virus a risk for humans

Pandemic alert period:
  Phase 3: No human to human transmission
  Phase 4: Limited H-H
  Phase 5: H-H in large clusters but localized

Pandemic period:
  Phase 6: Sustained transmission, global spread
• Annually new strains emerge d/t variation in antigenic composition of surface proteins, as no immunity for new strain, capacity to cause excessive morbidity & mortality is high.
• When a virus with serologically distinct H/N enters the population, potential for causing pandemic is there.

• Epidemics occur in winters.
• Sporadic cases any time.
• Overcrowding enhances transmission.
Pathogenesis

Virus causes lytic infection of respiratory epithelium l/t:
1. Loss of ciliary function
2. Decreased mucus production
3. Desquamation of epithelial layer
All of the above will lead to 2* bacterial infection

Antibodies against influenza do not persist for long, reinfection can occur.
Disease transmission

- Airborne: Droplet infection
- Through direct contact
- Fomites

**Human influenza (H5N1):**

Poultry handling

Consuming raw /undercooked poultry products
Clinical Manifestations

- Incubation period: 18-72 hours
- A & B primarily cause respiratory illness.
- High grade fever (due to cytokine production by the respiratory epithelium) (2-4 days)
- Myalgias/ malaise/ headache
- URTI: Coryza, croup
- LRTI: Bronchiolitis, Pneumonia
- Myocarditis (A/B)
- Myositis (A)
- Reye’s syndrome (with use of salicylate ingestion)
• Respiratory failure
• Encephalopathy
• Bleeding
• MODS
Diagnosis

• Depends upon epidemiological & clinical considerations.

**Lab confirmation:**
• Virus isolation from nasopharynx
• Serological assays
• CBC: leukopenia
• CXR: Pneumonia
Treatment

Supportive:
• Fluids
• Rest
• Fever control
• Management of complications
Antivirals: To be given only during 1\textsuperscript{st} 48 hours of illness

1. **Neuraminidase inhibitors:** (effective against A/B)
   - Zanamavir (inhalation)
   - Oseltamivir (oral)

2. Amantidine
   - Rimantidine

For type A only
Not to be given below 1 year of age
Complications

- Otitis media
- Pneumonia (hemorrhagic pneumonia)
  Viral/ bacterial
- Myocarditis
- Myositis
- TSS
- In immunocompromised/underlying cardiopulmonary disease: severe
Prognosis

• Usually good
• In pandemics: can cause several complications
Prevention

• **Vaccination:**
  Children (>6 months of age)
  High risk patients
  2 doses 1 month apart
• **Chemoprophylaxis:**
  Oseltamivir
Pandemic Interventions

- Personal Protective equipment
- Antiviral chemoprophylaxis
- Influenza vaccine
- Behavioral interventions
Human Immunodeficiency Virus Infection
• Retrovirus: Lentivirus
• RNA virus
• HIV-1, HIV-2 (> common in West Africa)
• Humans only known reservoirs (related viruses found in chimpanzees & monkeys)
HIV: Structure

HIV particles:

- viral envelope/membrane: coat of fatty material
- Spikes: Projecting from envelope (72 in no.) formed from proteins gp120, gp41
- Matrix: Just below the viral envelope - protein p17.
Viral core: (or capsid)

- Bullet-shaped
- Made from **protein p24**
- 3 Enzymes: inside the core, required for HIV replication called **reverse transcriptase, integrase and protease**
- **Genetic material:** consists of two identical strands of RNA.
Genes:

- 9 genes
- **gag, pol and env**: contain information needed to make structural proteins for new virus particles
- Other six genes, known as **tat, rev, nef, vif, vpr and vpu**, code for proteins that control the ability of HIV to infect a cell, produce new copies of virus, or cause disease.
- At either end of each strand of RNA is a sequence called the **long terminal repeat**, which helps to control HIV replication.
HIV→CD4 cell  
Virus envelop fuses with cell membrane  
|  
|  
|  
|  
|  
Viral contents released in cell  
|  
|  
Reverse trans forms DNA from RNA  
(Compatible with human genetic material)  
|  
|  
Transported to nucleus  
|  
|  
Integrated into human DNA  
(by enzyme integrase)  
|  
|  
Provirus  

Viral Entry/ Reverse transcription/ Provirus formation
Activated cells

Messenger RNA formation → Genetic material formation

Transported outside nucleus

Produces new viral proteins/ enzymes

New viral particles

Released from cell

Infect other cells

Assembly/ Budding/ Maturation
Epidemiology

• Worldwide almost 40 million individuals infected with HIV, 90% in developing countries.
• Children: 4.4 million, deaths- 3.2 million.
• 1800 children/day (the vast majority newborns) get infected with HIV.
• HIV-1 is the most common cause of HIV infection in the America, Europe, Asia, and Africa.
• HIV type 2 (HIV-2) has caused epidemics in West Africa.
Sub-Saharan Africa

- Approximately 7% population infected with HIV
- Represent 64% of the world's HIV-infected population.
- 76% of all women infected with HIV live in this region.
Eastern Europe /Central Asia:

- 1.6 million in 2005 (an increase of almost 20-fold in less than 10 years)
- Majority of these people living with HIV are young (75% of infections reported between 2000 and 2004 were in people younger than 30 years). In Western Europe, the corresponding percentage was 33%.
Asia

- Although national HIV infection levels are low in Asia compared with other continents (notably Africa), the populations of many Asian nations are so large that even low prevalence reflect large numbers of people are living with HIV.
- Seroprevalence rate in pregnant women -2%
- Vertical transmission rate- 24% (without breastfeeding).
- Indian mothers infected with HIV routinely breastfeed and have transmission rates as high as 48%.
• Perinatal transmission rates relatively low in Europe and high in Africa, independent of treatment.

• Untreated women infect 13% and 40% of children in Europe and Africa, respectively.

• Rate of postnatal transmission in Africa and other developing countries is elevated because of the need to breastfeed.
Modes of transmission

1. **Sexual contact**: (Vaginal/ anal/ orogenital)
2. **Percutaneous**: (needles/ sharps/ mucous membrane exposure to body fluids)
3. **Contaminated blood/ blood products**
4. **Mother to child transmission**:
   a. **In utero**: (30- 40%)
   b. **Intrapartum**: (60-70%)
   c. **Postpartum** (breastfeeding) in dev countries: 40%

> Common in mothers who acquire infection postnatally, b/c of high viral load
Factors influencing rate of vertical transmission

- Preterm delivery < 34 weeks
- Low maternal antenatal CD4 counts
- Use of recreational drugs during pregnancy
- PROM > 4 hours
Pathogenesis

Mucosal entry

- Bind to dendritic cells

Lymph node

- CD4 cells (Helper T lym) Antigen driven Migration of CD4 cells
- Gen. lymphadenopathy

2-4 months

Intense viremia

3-6 weeks

Establishment Of cellular/humoral response

Lower viral load

Viral replication ↓ CD4 counts

Deterioration of Immune system

Lack of symptoms, CD4 counts normal

Long latent period

Symptoms of AIDS
In Pediatric Patients

1. Rapid disease course:

- 15-25% cases (in developing countries > 85%)
- Onset of AIDS in 1st few months of life
- Untreated median survival: 6-9 months
- Occurs in cases where fetal infection coincides with the period of rapid expansion of CD4 cells thus effectively infecting body’s immunocompetent cells, therefore infection is established before normal ontogenic development of immune system causing severe impairment of immunity.
- Positive HIV-1 culture in 1st 48 hours of life.
2. Slow progressors (60-80%)
   - Infected intrapartum
   - Negative viral culture/ PCR in 1st week of life
   - Median survival time: 6 years
   - Viral load rapidly increases after 2-3 months then slowly decline over a period of 24 months (in contrast to sharp decline in adults possibly d/t immaturity of immune system)

3. Long term survivors: (<5%)
   - Minimal / no progression of ds / normal CD4 counts / low viral loads for >8 years
Distinct features of HIV Infection in Children

- After initial infection: **persistence of high viral loads** for longer durations, slow decline (b/c of immaturity of immune system)
- **Less dramatic ↓ in CD4 counts** (despite severe immunosuppression) b/c of relative lymphocytosis.
- **Hypergammaglobulinemia**: b/c of B-cell activation (acts as surrogate marker of HIV infection in symptomatic children when PCR etc. are not easily available)
- **CNS involvement > common in children** (developing brain > prone to invasion by HIV)
Clinical Picture

At birth: most of NB normal
Initial symptoms:
  • FTT
  • Chronic/ recurrent diarrhoea
  • Interstitial Pneumonia
  • Oral thrush
  • Lymphadenopathy/ HSM
> Common than adults

- Recurrent bacterial infections
- Chronic parotid swelling
- LIP
- Progressive neurological deterioration
CDC Pediatric HIV Classification System

• **Clinical status:**
  Category A, B, C

• **Immunological impairment:**
  Absolute CD4 counts/ CD4%
  Age adjustment of counts necessary
<table>
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<tr>
<th>Immune categories</th>
<th>&lt;12 months</th>
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<th>1- 5years</th>
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<td></td>
<td>Cells /µL</td>
<td>%</td>
<td>Cells /µL</td>
<td>%</td>
<td>Cells /µL</td>
<td>%</td>
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<tr>
<td>No evidence of suppression</td>
<td>&gt;1500</td>
<td>&gt;25</td>
<td>&gt;1000</td>
<td>&gt;25</td>
<td>&gt;500</td>
<td>&gt;25</td>
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<tr>
<td>Moderate suppression</td>
<td>750-1499</td>
<td>15- 24</td>
<td>500-999</td>
<td>15- 24</td>
<td>200-499</td>
<td>15- 24</td>
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<tr>
<td>Sever suppression</td>
<td>&lt;750</td>
<td>&lt; 15</td>
<td>&lt;500</td>
<td>&lt; 15</td>
<td>&lt;200</td>
<td>&lt; 15</td>
</tr>
</tbody>
</table>
Clinical Categories

Category A: (2 mild symptoms)
Lymphadenopathy
Parotitis
Hepatomegaly/ Splenomegaly
Dermatitis
R/C / persistent URI /Sinusitis or Otitis media
Category **B**: (moderate symptoms)

- Anemia/Neutropenia/thrombocytopenia lasting > 30 days
- Bacterial meningitis/pneumonia/sepsis (single episode)
- CMV infection with onset before 1 month of age
- Toxoplasmosis with onset before 1 month of age
- HSV bronchitis/pneumonitis/esophagitis with onset before 1 month of age
- LIP
- H zoster at least 2 distinct episodes or involving > one dermatome
- Leimyosarcoma
- Nocardiosis
Oropharyngeal thrush > 2 months
R/C / chronic diarrhoea
Persistent fever > 2 months
Hepatitis
R/C H. simplex stomatitis/ oesophagitis/ pneumonitis
Disseminated varicella
Cardiomyopathy
Nephropathy
Category C: (severe symptoms)
2 serious bacterial infections in a 2 year period (sepsis/meningitis/pneumonia)
Oesophageal/Lower resp tract candidiasis
Disseminated Coccidiomycosis, cryptococcosis
Cryptosporidiosis (> 1 month)
HSV infection
Disseminated histoplasmosis
Encehalopathy
Malignancies
Disseminated mycobacterial infection
• Pneumocystis jiroveci Pneumonia
• Cerebral toxoplasmosis (onset after 1 month of age)
• Progressive multifocal encephalopathy
• Recurrent salmonella (nontyphoidal) septicemia
• Wasting syndrome in the absence of concurrent illness other than HIV plus chronic diarrhoea > 30 days or documented fever > 30 days
Lab diagnosis

**ELISA:**
Highly sensitive & specific
Not useful in <18 months of age

**Western Blot test:**
Highly specific for > 18 months old

**PCR DNA:**
Useful in children <18 months of age
In neonates infected in utero, it can be positive within first 48 hours also

**PCR RNA:**
Not recommended for routine testing for <18 months of age
(negative result does not rule out infection)

**Viral culture:**
Not useful, takes 4 weeks

**HIV p24Ag:**
Less sensitive
• CD4 counts: decreased

• CD8 counts: might be ↑ initially, later on↓

• Hypergammaglobulinemia( IgG & IgA)/Panhypogammaglobulinemia( <10% cases)
• Informed consent for HIV testing
• Pre test/ Post test counselling
• Confidentiality
Treatment

6-12 months of age:
ART as soon as infection is confirmed, regardless of clinical/ immunological/ virological parameters

>1 year:
All except slow progressors

Adolescents:
Adult guidelines

In resource poor setting:
<18 months: CD4 % < 20%
Older children: CD4 % < 15%
• **Combination therapy**
  • At least 3 AR drugs- 2 RT inhibitor + 1 Protease inhibitor/Nonnucleoside RT inhibitor

  **Desired Goal:** undetectable concentration of virus in body

• **Immunoglobulin therapy:**
  - For Hypogammaglobulinemia
  - R/C, serious bacterial infection in 1 year period

• **Early diagnosis & aggressive management of opportunistic infections**

• **PCP Prophylaxis for HIV exposed children:**
  - Septran- beginning at 4-6 weeks of age & continued for first year of life unless HIV infection is excluded, thereafter determined on basis of CD4 counts
HAART

**NRTI:**
Thymidine analogues- stavudine, Zidovudine
Nonthymidine analogues-Didanosine, lamivudine, dideoxycytidine

**NNRTI:**
Nevirapine, efavirenz

**Protease inhibitors:**
Ritonavir, Nelfinavir, saquinavir
Control measures

Decrease in MTCT:

- **ART** before labor, before rupture of membranes: Zidovudine beginning at 14-34 weeks of gestation, continuing throughout pregnancy, IV during Intrapartum period, oral administration to infants till 6 weeks of life.

- In resource poor countries:
  Zidovudine to mother in 3rd trimester as soon as possible +1 dose of Nevirapine to mother & baby

- Complete avoidance of breastfeeding
Postexposure prophylaxis (occupational)

Risk after -percutaneous exposure: 0.3%
- Mucous membrane exposure: 0.09%

Postexposure:
- Baseline HIV testing
- Repeat testing at 4, 6, 12 weeks & 6 months after exposure (most will seroconvert after 3 months)
- HIV class 1: 2 drugs
- HIV class 2/ HIVclass1+ large volume: 2 drugs
- HIV class 2+ large volume: > 3 drugs

4 week PEP should be completed, monitoring for adverse reactions should be done.
Immunization Recommendations

- If not severely immunocompromised, live vaccines can be given according to age
- Inactivated vaccines can be given at any time