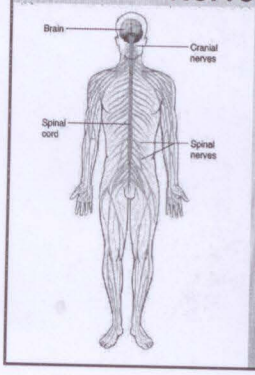
Viral Infections of the Central Nervous System

Nervous System



- CNS: brain and spinal cord
- PNS: peripheral nerves

Cells are called neuron

NERVOUS SYSTEM DISEASES

- Meningitis: inflammation of the meninges = membranes surrounding the brain and spinal cord
- Encephalitis: inflammation of the brain

INTRODUCTION

* Central nervous system infections are usually:

1- Blood-borne invasion; most common
(e.g. polioviruses or *Neisseria meningitidis)*

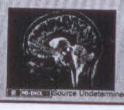
2- Invasion via peripheral nerves; less common
(e.g. herpes simplex, varicella-zoster, rabies)

COMMON CHARACTERISTICS OF CNS VIRUS INFECTIONS

- Clinical presentation
  - Typically acute onset
  - Healthy hosts are often afflicted
  - Frequently occurs as meningoencephalitis
    - Meningitis – fever, headache, stiff neck
    - Encephalitis – meningitis with mental status changes (seizures, decreased consciousness, confusion)

CNS VIRUS PATHOGENESIS

	Pathogenic event
Exposure	Epithelial layer disruption Local replication
Dissemination	Viremia Secondary amplification
CNS Entry	Blood-brain barrier disruption Axonal transport
Inflammation	Direct and indirect cell damage
Clinical Disease	**Target cells (neurons, glial cells, endothelial cells)**



CAUSES OF VIRAL ENCEPHALITIS

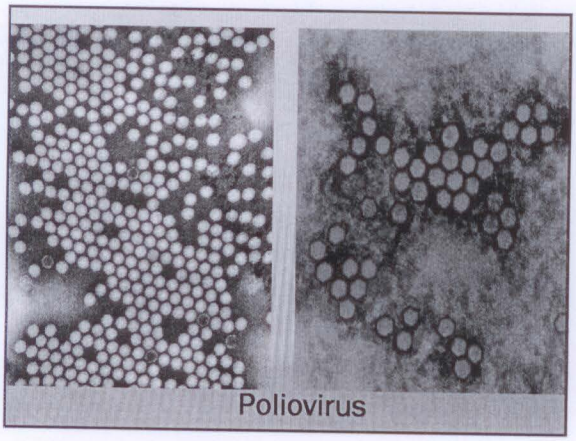
- Herpes viruses: HSV-1, HSV-2, VZV, CMV, EBV, HHV-6
- Adenoviruses
- Enteroviruses, poliovirus
- Measles, mumps, and rubella viruses
- Rabies
- Arboviruses: Japanese encephalitis; St. Louis encephalitis virus; West Nile encephalitis virus
- Reoviruses: Colorado tick fever virus
- Arenaviruses: lymphocytic choriomeningitis virus

POLIO VIRUS

Family: *Picornaviridae*

Gender: *Enterovirus*

Species: ***Poliovirus***



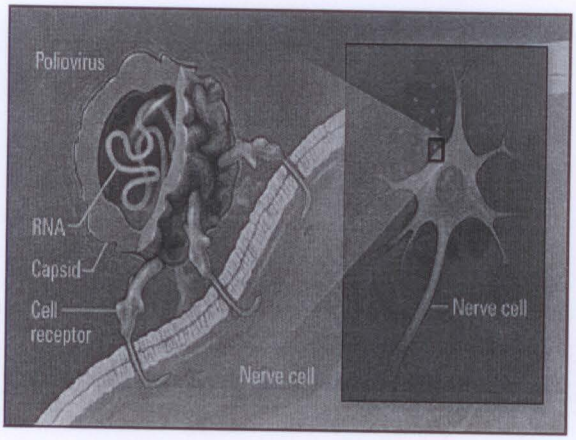
Poliovirus

POLIOMYELITIS

polio= gray matter

Myelitis= inflammation of the spinal cord

Virus localized in the anterior horn cells of the spinal cord and certain brain steam motor nuclei.



POLIOVIRUS

- Enterovirus single stranded(RNA), naked
- Human only natural host
- Three serotypes: 1, 2, 3
- Minimal heterotypic immunity between serotypes

- The poliovirus is a member of a larger family known as Picornaviruses, which also includes rhinoviruses (such as influenza) and the hepatitis A virus.

- Polio belongs to the enterovirus subgroup, made up of over 70 viruses that infect the intestines

- It is one of the smallest RNA viruses, measuring around 25 nm in diameter

- the most commonly associated with paralysis
- PV infects and causes disease in humans alone
- Individuals exposed to PV(infection or vaccination) develop immunity to PV
- Three serotypes of poliovirus have been identified—poliovirus type 1 (PV1), type 2 (PV2), and type 3 (PV3)—each with a slightly different capsid protein
- All three are extremely virulent and produce the same disease symptoms
- PV1 is the most commonly encountered form, and the one most closely associated with paralysis

MODES OF TRANSMISSION

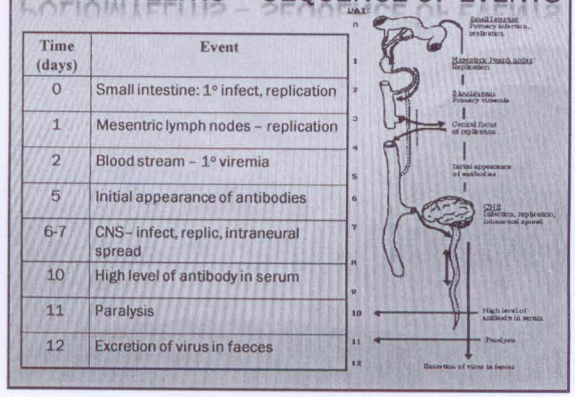
1: *Oral-oral infection*: Direct droplet infection

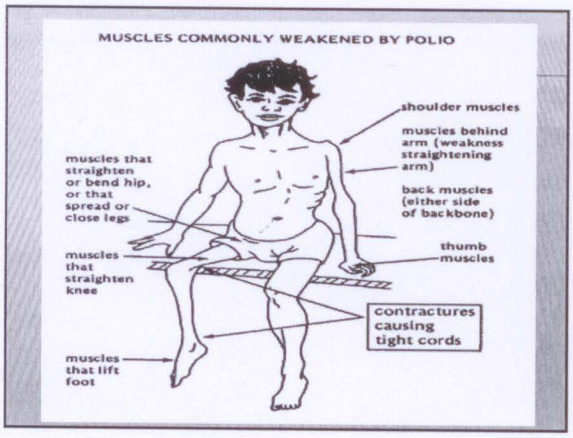
2: *Faeco-oral infection*:

- Food-borne (ingestion) infection through the ingestion of contaminated foods. Vehicles include milk, water.
- Hand to mouth infection.

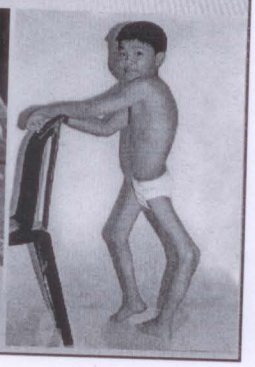
POLIOMYELITIS – SEQUENCE OF EVENTS

Time (days)	Event
0	Small intestine: 1° infect, replication
1	Mesentric lymph nodes – replication
2	Blood stream – 1° viremia
5	Initial appearance of antibodies
6-7	CNS – infect, replic, intraneural spread
10	High level of antibody in serum
11	Paralysis
12	Excretion of virus in faeces





Poliomyelitis in Children



VIRUS ISOLATION- CONTINUES

- poliovirus can be readily isolated from throat swabs, faeces, and rectal swabs.
- Requires molecular techniques to differentiate between the wild type and the vaccine type.

- *Serologic testing*

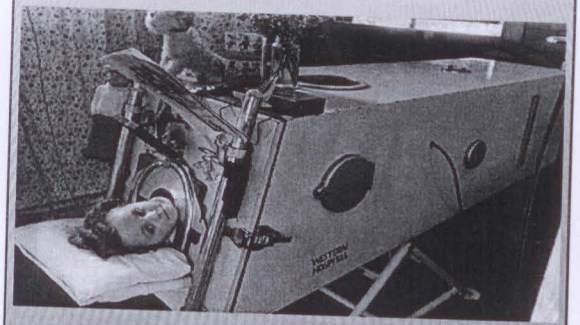
A four-fold titer rise between the acute and convalescent specimens suggests poliovirus infection.

- *Cerebrospinal fluid (CSF) analysis*

The cerebrospinal fluid usually contains an increased number of leukocytes—from 10 to 200 cells/mm3 (primarily lymphocytes) and a mildly elevated protein, from 40 to 50 mg/100 ml.

TREATMENT IN THE ACUTE STAGE

- close monitoring of respiratory and cardiovascular functioning is essential along with fever control and pain relievers for muscle spasms
- Mechanical ventilation, respiratory therapy may be needed depending of the severity of patients



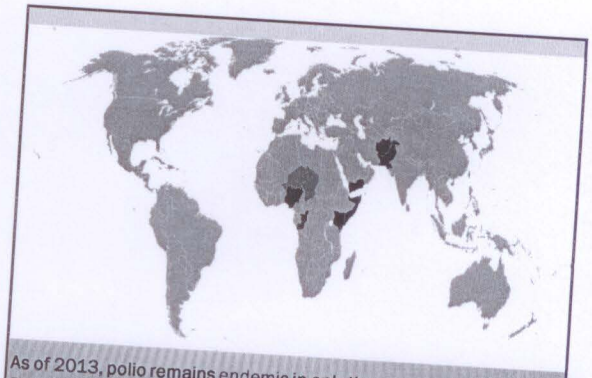
CHRONIC STAGE

24 months after the active illness:

The goals of treatment include correcting any significant muscle imbalance and preventing or correcting soft tissue or bony deformities.

POLIO VIRUS -EPIDEMIOLOGY

- The availability of immunization and the poliovirus eradication campaign has eradicated poliovirus in most regions of the world except in the Indian Subcontinent and Africa



As of 2013, polio remains endemic in only three countries: Nigeria, Pakistan, and Afghanistan

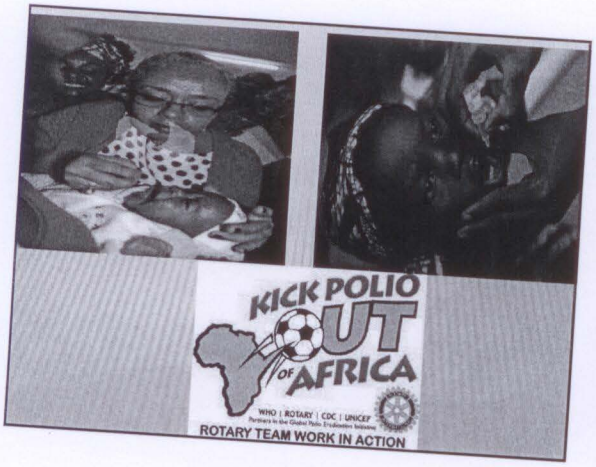
POLIOMYELITIS IN KENYA

- The first recorded poliomyelitis epidemic in Kenya occurred in 1921-1922
- The last case of confirmed poliomyelitis in Kenya was in 1984 and was isolated on stool culture to have been due to poliovirus Type II.
- 15.3 million children under five years in 86 high risk districts vaccination campaigns will kick off mid July to run until November 2013
- 29 August 2013, Kenya confirmed a dozen cases of circulating Vaccine Derived Polio Virus (cVDPV)in Dadaab refugee camps

PREVENTION

General prevention:

- Health promotion through environmental sanitation.
- Health education (modes of spread, protective value of vaccination).



PREVENTION-VACCINATION

Active immunization:

- Salk vaccine (intramuscular polio trivalent killed vaccine)
- Sabin vaccine (oral polio trivalent live attenuated vaccine)

ORAL POLIO VACCINE

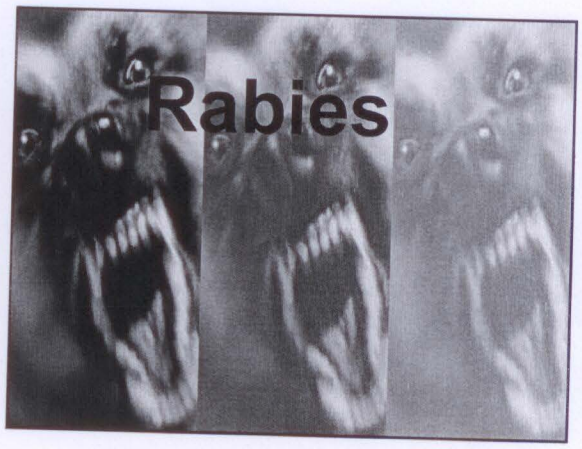
- Contains 3 serotypes of vaccine virus
- Shed in stool for up to 6 weeks following vaccination
- Highly effective in producing immunity to poliovirus
- 50% immune after 1 dose
- >95% immune after 3 doses
- Immunity probably lifelong

ADVANTAGES AND DISADVANTAGES OF OPV

- Advantages
  - Lifelong immunity
  - Induction of secretory antibody response similar to that of natural infection
  - Possibility of attenuated virus circulating in community by spread to contacts (indirect immunization)(herd immunity)
  - Ease of administration
  - Lack of need for repeated boosters
- Disadvantages
  - Risk of vaccine-associated poliomyelites in vaccine recipients or contacts
  - Spread of vaccine to contacts without their consent
  - Unsafe administration for immunodeficient patients

ADVANTAGES AND DISADVANTAGES OF IPV

- Advantages
  - Effectiveness
  - Good stability during transport and in storage
  - Safe administration in immunodeficient patients
  - No risk of vaccine-related disease
- Disadvantages
  - Lack of induction of local (gut) immunity
  - Need for booster vacine for lifelong immunity
  - Fact that injection is more painful than oral administration
  - Fact that higher cominity immunization levels are needed than with live vaccine



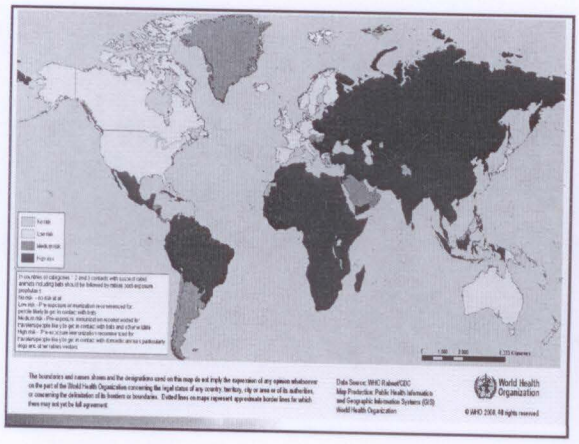
Introduction

- Rabies is a **preventable viral disease** of mammals most often transmitted through the bite of a rabid animal
- Rabies is primarily a disease of terrestrial and airborne **mammals**
- The **dog** has been, and still is, the main **reservoir of rabies** in Kenya.[1]

1. Karugah AK. Rabies in Kenya. Department of Veterinary Services, Kabete, Nairobi, Kenya

ETIOLOGY

- Rabies is caused by RNA viruses in the family *Rhabdoviridae*, genus *Lyssavirus*
- The type species of the genus is Rabies Virus
- At least other 6 other lyssavirus species or genotypes cause rabies



RABIES HOSTS

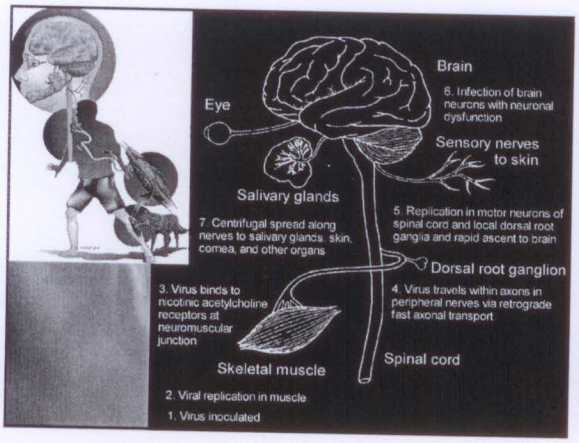
- All warm-blooded vertebrates are susceptible to experimental infection
- Mammals are the natural hosts of rabies
- Reservoirs consist of the *Carnivora* (canids, skunks, raccoons, mongoose, etc.) and *Chiroptera* (bats)

BURDEN

- More than ~55,000 human rabies deaths per year
- Most occur in developing countries
- Millions of human exposures per year
- The domestic dog is the single most important animal reservoir
- Wildlife important, especially in developed countries

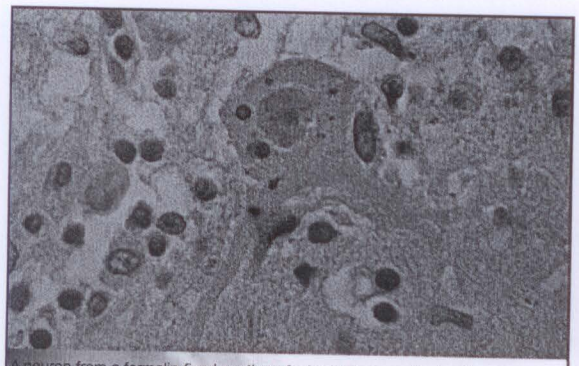
RABIES PATHOGENESIS

- Virus is transmitted via bite
- Multiplies in the Salivary glands
- Enter peripheral nerves
- travel by retrograde axon flow in axoplasm of nerves to CNS
- Once it reaches this stage, immunisation not effective
- Replicate in brain
- Centrifugal flow to innervated organs, including the portal of exit, the salivary glands
- Viral excretion in saliva



RABIES DIAGNOSIS

- Based upon history of animal exposure and typical neurological clinical signs
- Postmortem demonstration of viral antigen in CNS is gold standard
- In humans, antemortem detection of virus or viral amplicons, antibodies, or antigens (sera, csf, saliva, nuchal biopsy)

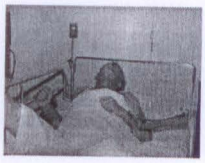


A neuron from a formalin-fixed section of a brain from a patient with rabies, showing reddish-brown viral inclusions in the cytoplasm. Processed by immunohistochemistry.

Rupprecht CE. The Lancet Infectious Diseases Vol 2, June 2002

CLINICAL STAGES

- Incubation Period (range = ~<7 days to >6 years; average is ~4-6 weeks)
- Prodromal Phase (Non-specific signs)
- Acute Neurological Phase
- Coma
- Death (recovery from rabies?)



PROPHYLAXIS

- **Pre-exposure Vaccination**
- **Postexposure Prophylaxis (PEP)**

PRE-EXPOSURE VACCINATION

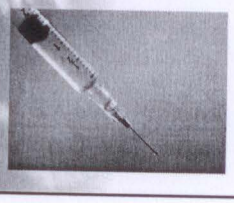
- Provided to subjects at risk before occupational or vocational exposure to rabies
- Subjects include diagnosticians, laboratory & vaccine workers, veterinarians, cavers, etc.
- Simplifies postexposure management

POSTEXPOSURE PROPHYLAXIS

- **Provided to subjects after rabies exposure**
- **Consists of wound care, rabies immune globulin, and vaccine**
- **If prompt and proper, survival virtually assured**

RABIES BIOLOGICALS

- **Rabies Vaccines (for pre- and PEP)**
- **Rabies immune globulin (only in PEP)**



RABIES IMMUNE GLOBULIN

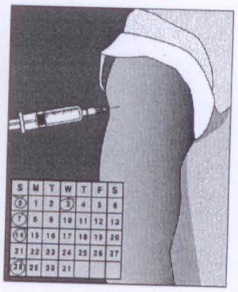
- Two Human Rabies Immune Globulins :
  - HyperRabTM S/D
  - Imogam® Rabies-HT
- Both supplied in vials at ~ 150 IU/ml

Human rabies immune globulin (HRIG) is administered only once, at the beginning of anti-rabies prophylaxis, to previously unvaccinated persons.

This will provide immediate antibodies until the body can respond to the vaccine by actively producing antibodies of its own.

POSTEXPOSURE PROPHYLAXIS

- **Wash lesions well with soap and water (tetanus booster ad hoc)**
- **Infiltrate rabies immune globulin (20 IU/kg) into and around the margin of the bites**
- **Administer vaccine on days 0,3,7,14, and 28**



Microbiology, A clinical Approach -Danielle Moszyk-Strelkauskas-Garland Science 2010

Shortage of anti-rabies vaccine:2012-09-28 The Ministry of Public Health and Sanitation has disclosed that there is a shortage of anti-rabies vaccines

MICROBIOLOGY 5TH EDITION, Prescott, Harley and Klein (2002)