# SEMINAR ON RABIES

**MODERATOR:**

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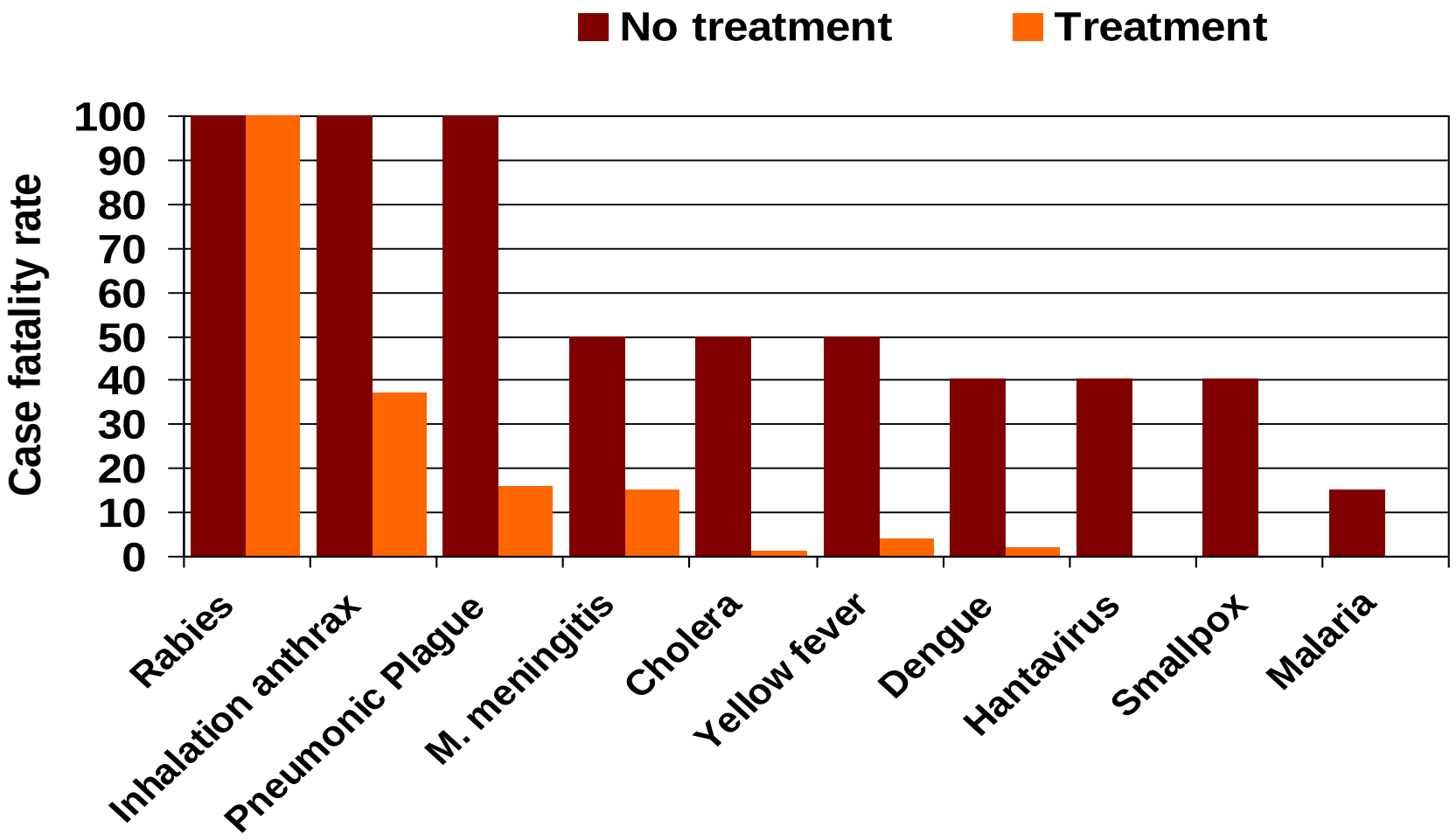
# CONTENTS

# INTRODUCTION

- Rabies is one of the oldest recognized diseases affecting humans and one of the most important zoonotic diseases
- Discovered and named by Girolamo Fracastoro in 15$^{th}$ century
- Acute, highly infectious and fatal disease of the CNS
- Caused by Lyssavirus type 1
- Zoonotic disease of warm blooded animals
- Transmitted by bites of rabid animal
- Long and variable IP with short period of illness
- Virtually 100% fatal but 100% preventable




CASE FATALITY RATE OF DIFFERENT DISEASES

# HISTORICAL PERSPECTIVE

- The word "*Rabies*" has been derived from the Sanskrit word "*Rabhas*" which means "*To do violence*"
- Another belief is that, the word has originated from the Latin word "*Rebere*" which means "*To rave*", meaning talking irrelevantly (delirium)
- Also known as "*Jalasanthra*", which means agony caused by water
- Shushrutha emphasized that the antecedent cause of this condition in human being was the bite of a mad dog and it was fatal

- Because of its potentially violent nature, rabies has been known since 2200 B.C.
- The first written record of rabies is in the Mesopotamian Codex of Eshnunna (1930 BC), which dictates that the owner of a dog showing symptoms of rabies should take preventive measure against bites
- If another person was bitten by a rabid dog and later died, the owner was heavily fined

Painting of a rabid dog biting a man
Arabic
A.D. 1224
Baghdad school, by Abdallah ibn al-Fadl

Picture courtesy of Smithonian Institution, Washington D.C.

- Rabies was considered a scourge for its prevalence in the 19th century
- In France and Belgium, where Saint Hubert was venerated, the "St Hubert's Key" was heated and applied to cauterize the wound; by an application of magical thinking, dogs were branded with the key in hopes of protecting them from rabies
- 6th July 1885- Sir Louis Pasteur for the first time successfully treated a 9 yr. old boy (Joseph Meister) with his vaccine

- 1903- Negri, an Italian scientist, demonstrated inclusion bodies in the neurons of rabid animal, which are named after him as “Negri Bodies”
- 1911- David Semple developed Semple vaccine or BPL vaccine
- 1964- Witkor and Kaprowski, developed tissue culture vaccine by culturing the virus in human diploid cell
- 6$^{th}$ July is celebrated as world zoonoses day or world Rabies free day

# VACCINES - HISTORY

APCRI - 2006

| | |
|---|---|
| 1885 Louis Pasteur | - 1st Human Antirabies vaccine, France. |
| 1911 Sir David Semple | - Sheep Brain Vaccine, CRI Kasauli, India. |
| 1955 Fuenzalida et al | - Suckling Mouse Brain vaccine, Chile. |
| 1958 Peck et al | - Duck Embryo Vaccine, USA. |
| 1960 CRI Kasauli | - Introduction of BPL inactivated NTV |
| 1965 Wiktor & Koprowsky | - Human Diploid Cell Vaccine, USA. |
| 1985 Gluk et al | - Purified Duck Embryo Vaccine, Switzerland. |
| 1985 Barth et al | - Purified Chick Embryo Cell Vaccine, Germany. |
| 1988 Montegnan et al | - Purified Vero Cell Rabies Vaccine, France. |
| 2004 December | - Neural Tissue Vaccine (NTV) Production stopped in India |

# Immunoglobulins – History

APCRI - 2006

| | |
|---|---|
| 1890 Babes & Cerchez | – Whole blood of vaccinated humans used for treating people severely bitten by rabid wolf. |
| 1945 Habel et al | – usefulness of RIGs clearly demonstrated by animal experiments. |
| 1954 Habel & Koprowsky | – RIGs and vaccine was used as PEP in Wolf bite cases in Iran. |
| 1959 Hosty et al | – production of ERIGs. |
| 1963 Atanasiu | – clinical trials with ERIG & optimal dose was determined. |
| 1966 WHO | – guidelines on standard guidelines on the combined use of RIGs & Vaccine for PEP |
| 1971 Cabasso et al | – Standardized production of HRIG, determined the optimal dosage. |
| 1972 CRI (Kasauli) | - Purified ERIG production. |

# EPIDEMIOLOGY

# PROBLEM STATEMENT

- Enzoonotic as well as epizoonotic disease
- Occurs in more than 100 countries and territories
- Potential threat to more than 3 billion people
- **Incidence** -- 35,000-50,000 deaths/Year (WHO)

  30,000 deaths/yr in India

  24,000 deaths/yr in Africa
- **15 million** people receive rabies prophylaxis annually with majority males

# INDIA

- 20,000 Deaths, 17.4 million animal bite case annually.
- India accounts for 36% of the Global and 65% of the Asian human rabies deaths.
- In India rabies is reported from all states except In India rabies is reported from all states except Lakshadweep and the Andaman & Nicobar Islands.
- No age or sex predilections (higher incidence of animal bites and rabies deaths among children and adult males)
- 96 % of human rabies cases are due to bites


Worldwide risk of rabies (WHO-2009)

# Rabies free areas

Continents: Australia and Antarctica

Asia: Japan, Malaysia, Oman and Qatar

Europe: Great Britain, Scandinavian countries, Spain and Portugal

America: Guyana, Uruguay and Jamaica

Oceania: Fiji and Papua New Guinea

India: Andaman & Nicobar and Lakshadweep Islands

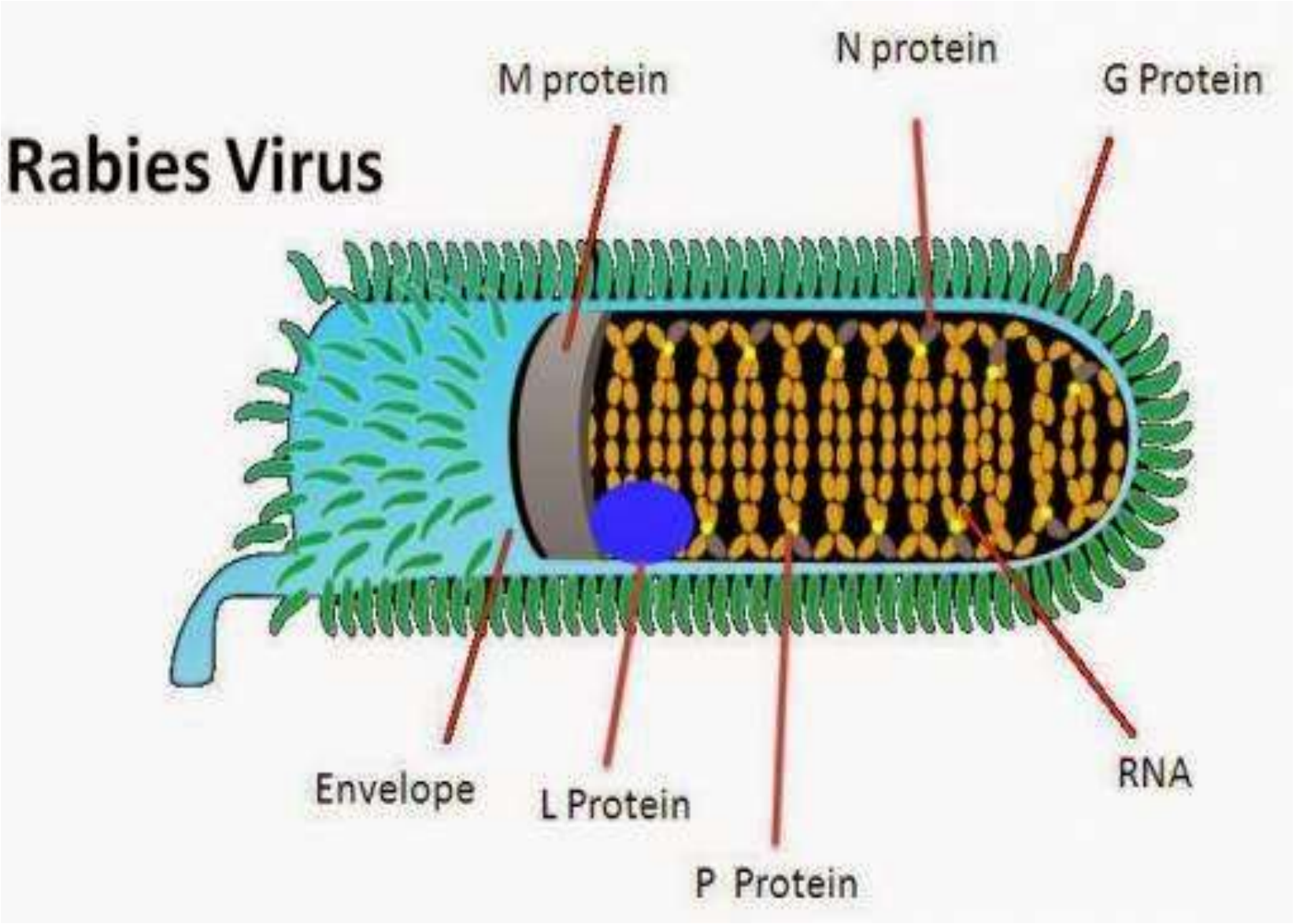
# AGENT- RABIES VIRUS

- Rhabdovirus
- Lyssa virus -type 1
- Bullet shaped virus
- Size is 180 x 75 nm
- Has Lipoprotein envelope
- Knob like spikes /Glycoprotein G (Antigenic substance)
- M protein layer
- Genome-unsegmented,Linear, negative sense

# AGENT-RABIES VIRUS

**Taxonomy:**

- Family: Rhabdoviridae
- Genus: *Lyssavirus type 1*
- Species: Rabies virus
- Bullet-shaped
- Has lipoprotein envelope
- Knob like spikes /Glycoprotein G substance)
- ~180 nm long and ~75 nm wide
- Single-stranded
- Negative sense RNA


Rabies Virus
M protein
N protein
G Protein
Envelope
L Protein
P Protein
RNA

# TYPES OF RABIES VIRUS

## STREET VIRUS

**Definition**: The virus recovered from naturally occurring cases of rabies is called “street virus”

**Sources**: It is naturally occurring virus. It is found in saliva of infected animal

## FIXED VIRUS

**Definition**: the virus which has a short, fixed and reproducible incubation period is called “fixed Virus”

**Sources**: It is prepared by repeated culture in brain of rabbit such that its I.P. is reduced & fixed

| **Features** | **Features** |
| --- | --- |
| • It produces Negri bodies | • It does not form Negri bodies |
| • Incubation period is long i.e. 3 weeks to 3 months | • Incubation period is constant between 5-6 days |
| • It is pathogenic for all mammals | • It can be pathogenic for humans under certain conditions |
| • Cannot be used for preparation of vaccine | • Is used for preparation of antirabies vaccine |

# RESERVOIR OF INFECTION

**URBAN RABIES**:

- From Dogs and cats.
- 99% cases in India
- A single infected dog is capable of transmitting over an area of 40km

## WILDLIFE RABIES

- SYLVATIC RABIES
- Unidentified reservoir of infection
- Foxes, jackals, hynas, skunks etc
- Enzootic in South America by Mongoose
- Transmit infection among themselves and to dogs and man

## BAT RABIES

- Latin American Countries, USA
- Vampire bats-feed on blood of man and animals
- Found from Mexico to Northern Argentina
- Cause havoc to cattle
- Not reported in India
- Constant source of infection to man and animals
- Transmission by bites and aerosols

# ANIMALS TRANSMITTING RABIES IN INDIA

APCRI - 2006

| Domestic | Peridomestic | Wild | Not reported |
|---|---|---|---|
| Dogs & Cats | Cows & Buffaloes | Foxes & Jackals | Bats * |
| | Sheep & Goats | Monkeys | Rodents * |
| | Pigs | Mongoose | Birds |
| | Donkeys | Bears | Squirrel |
| | Horses | | |
| | Camels | | |

**Note:**

All exposures in wild are considered as category III exposures.

* Bite by Bats or Rodents do not ordinarily necessitate rabies vaccination. However, bites by Bats or rodents in unusual circumstances may be considered for vaccination in consultation with an expert in the field of rabies.

# INFECTIVE MATERIAL

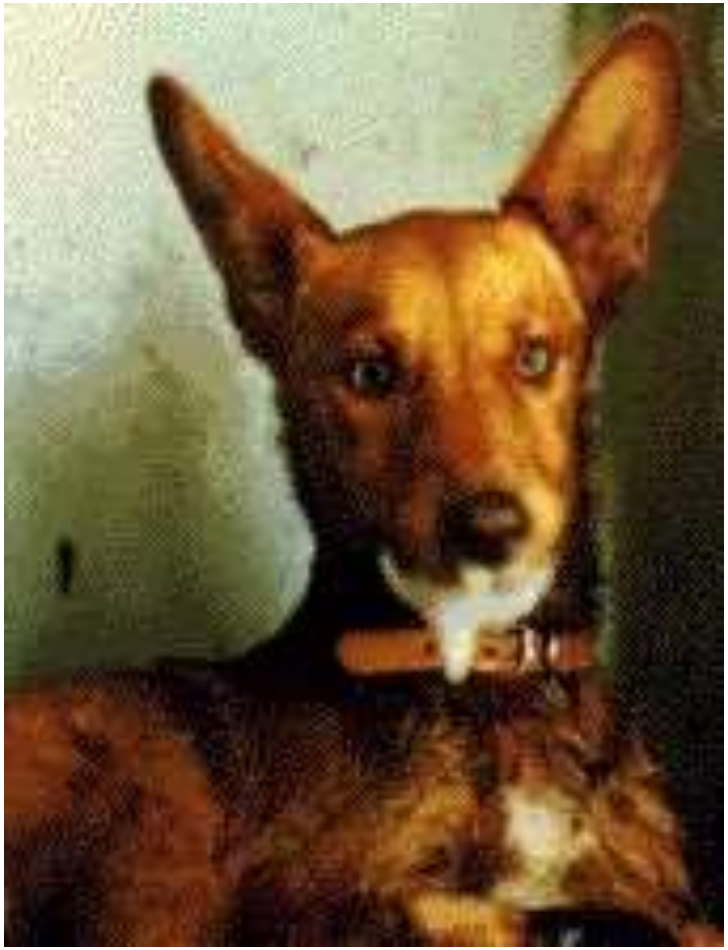
- Rabid animals- saliva, serum, urine and milk
- Human cases- saliva, sweat, semen and tears

# PERIOD OF INFECTIVITY

- The rabid dog is infectious during last 3-5 days of incubation period and during the entire period of illness, 8-10 days

# SOURCE OF INFECTION

- Saliva of Rabid animal
- Dogs and cats-virus in saliva 3-4 days before clinical symptoms
- Variable in quantity



# MODES OF TRANSMISSION

## Bites from infected animals

Licks on Broken Skin or Mucous Membrane

Scratches

Inhalation

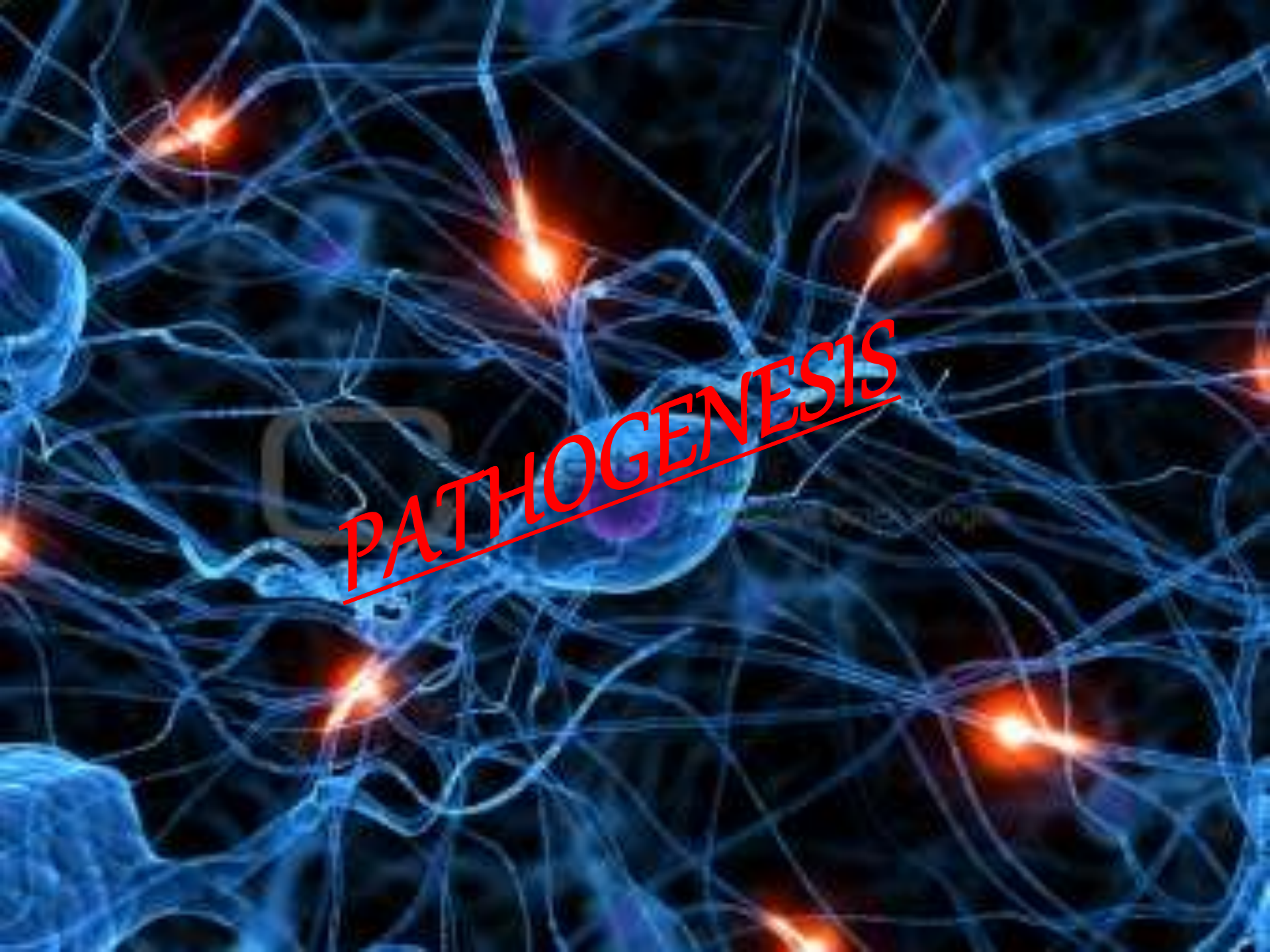
Organ transplantation

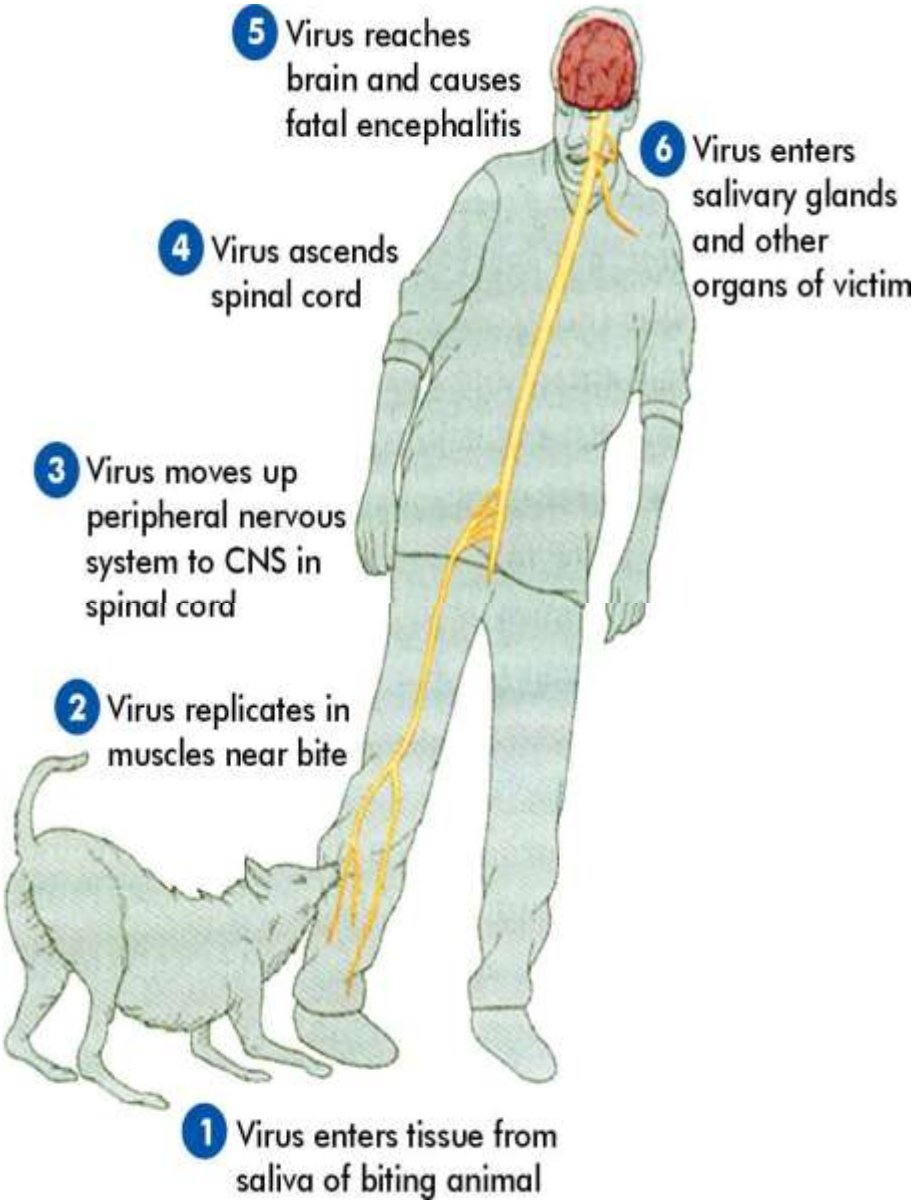
# Host Factors

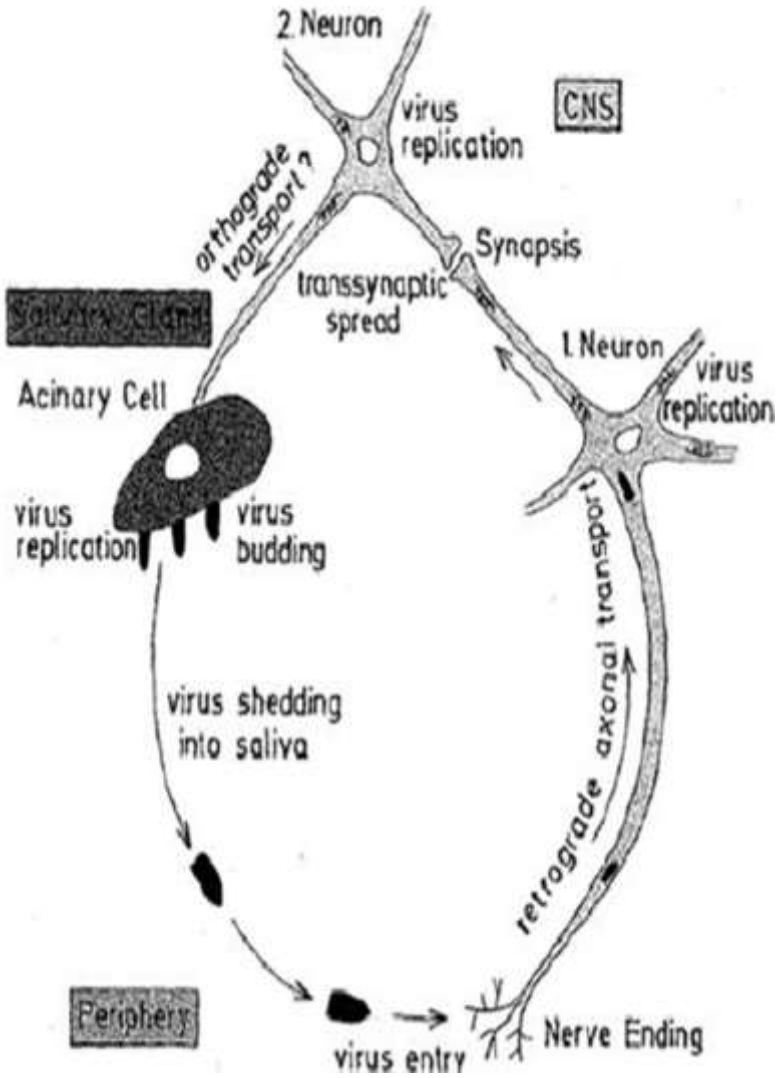
- All warm blooded animals including man
- Rabies in man is a dead-end infection
- People at risk-lab workers, veterinarians, dog handlers, hunters, etc

# INCUBATION PERIOD:

- Normally 3 weeks – 3 months
- May be short that is 15 days or may be prolonged for years.
- Depends on
  - site of bite
  - Severity of bite
  - Richness of nerve supply
  - Amount of saliva deposited
  - Species of biting animal
  - Protection provided by clothing


PATHOGENESIS



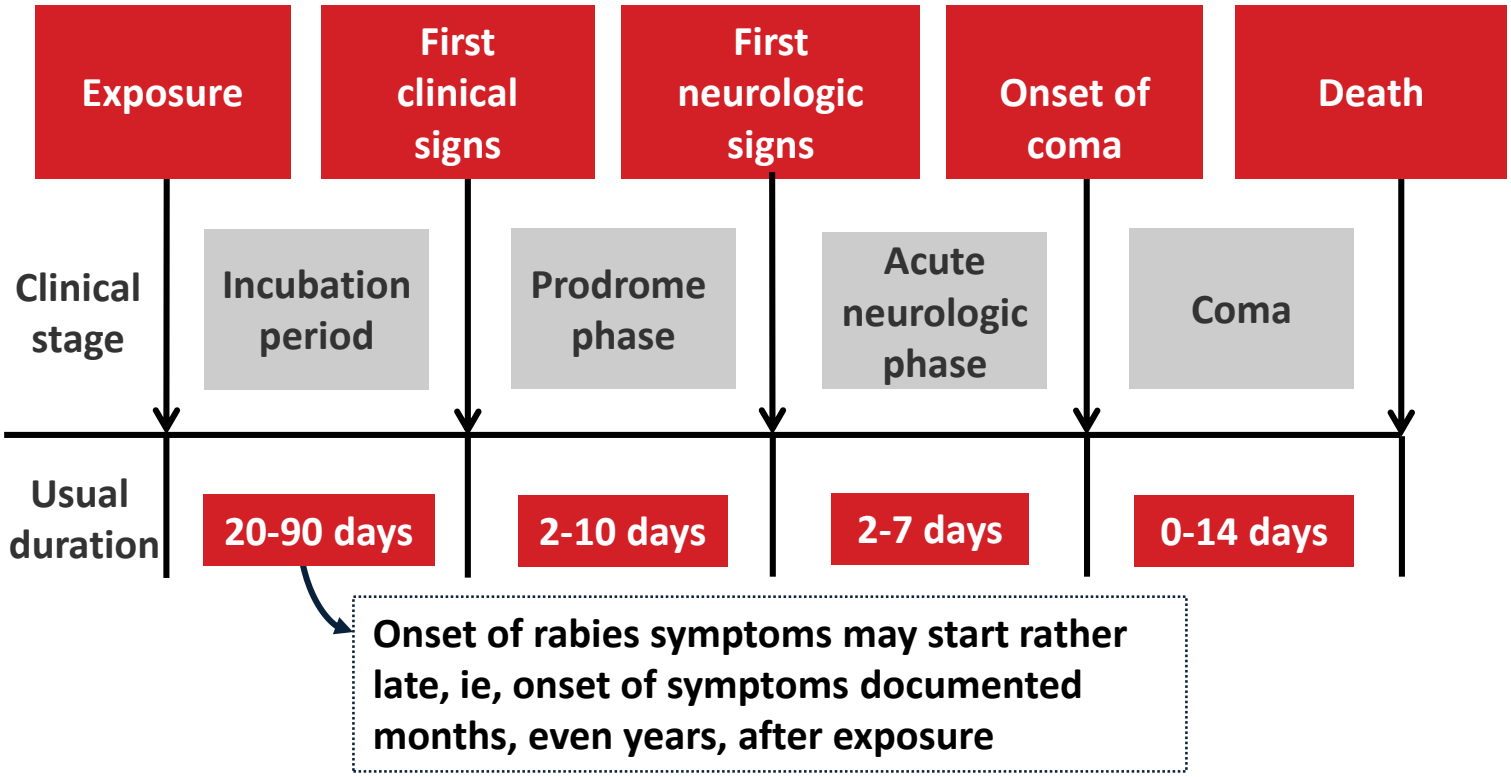

# PATHOGENESIS OF RABIES

# PATHOLOGY

- Despite 100% fatal nature of the disease there are only minimal pathological changes
- Grossly - Brain is oedematous, congested
- Histopathology -Perivascular cuffing, Gliosis
- Minimal Neuronal Damage – necrosis
- Presence of Negri bodies is Pathognomonic

# CLINICAL MANIFESTATIONS

# Human rabies: Clinical stages




**Death usually occurs within a few days after the appearance of clinical symptoms**

# Clinical Rabies in Humans

## CLASSICAL HYDROPHOBIA: (80-90% of cases)

### Prodromal stage:

- First clinical symptoms: non-specific, i.e., malaise, fever,headache, tingling and numbness at the site of bite

### Stage of excitement:

- CNS is affected in the following order- sensory, motor and sympathetic system

### Stage of paralysis

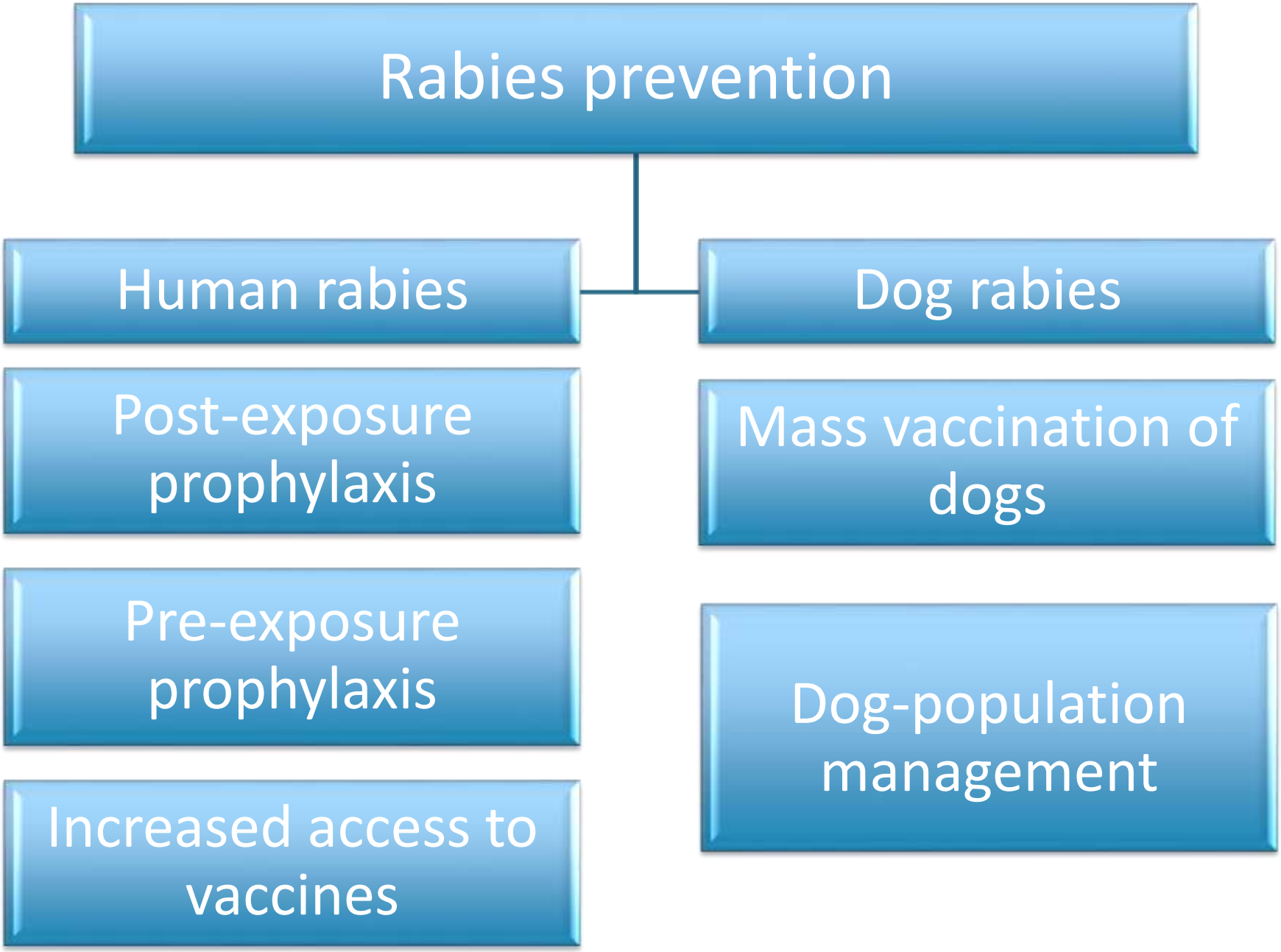
## DUMB/PARALYTIC RABIES: (10-20% of cases)

- Seen among partially immunized persons
- Common clinical features include
  - Gradual ascending paralysis
  - Constipation and urinary retention
  - Stupor, coma and death within 1-2 weeks
- Hydrophobia is usually absent

# Clinical rabies in Dogs

- **Two forms of rabies are distinguished:**
- Furious or Frank Rabies (75-80%) (encephalitic; three-forth of all cases):
  - Rabies transmitted from dogs is usually furious
- Paralytic (20-25%) (dumb; one-fourth of all cases)

# RABIES SURVEIILANCE


Rabies prevention
Human rabies
Post-exposure prophylaxis
Pre-exposure prophylaxis
Increased access to vaccines
Dog rabies
Mass vaccination of dogs
Dog-population management

# Rabies surveillance

Essential to detect high-risk areas and outbreaks quickly and to monitor the use of vaccine

- ***In Human populations***

☑ Surveillance of human exposure to rabies

☑ Surveillance of cases of human rabies

☑ Rapid exchange of information with services in charge of animal rabies surveillance and control is required

☑ Epidemiological investigation of outbreaks

- ***In animal populations***

☑ Surveillance in endemic areas for similar illness in both wild & domestic species likely to be reserviors

☑ Laboratory based- on human exposure

☑ Suspected domestic animals- kept under observation for 10 days

☑ Rapid exchange of information

☑ Where samples can not be collected, cases to be recorded as suspected animal rabies & data sharing

**Prevention**

- Immunize all dogs and cats owned by an individual or by the community
- Reduce the size of the ownerless dog population by reproduction control, reduction of the carrying capacity of the environment and law inforcement when needed

**Epidemics**

- Intensive vaccination of dogs in combination with dog-
- population control and movement restriction to be implemented immediately

- History
- Signs and symptoms
- Clinical examination

# Ante-mortem Diagnosis

- ☑ Samples-saliva, serum, spinal fluid, and skin biopsies of hair follicles at the nape of the neck
- ☑ Saliva-virus isolation or reverse transcription followed by polymerase chain reaction (RT-PCR)
- ☑ Serum and spinal fluid-antibodies to rabies virus
- ☑ Skin biopsy specimens are examined for rabies antigen in the cutaneous nerves at the base of hair follicles.

# Diagnostic tests

- ☑ Histopathology & Electron Microscopy
- ☑ Detection of antigen by taking skin biopsy using Direct fluorescent antibody test (DFA)
- ☑ Virus isolation from saliva & other secretions
- ☑ CSF analysis and CT scan
- ☑ ELISA
- ☑ RT-PCR- saliva & skin biopsy
- ☑ Negri bodies

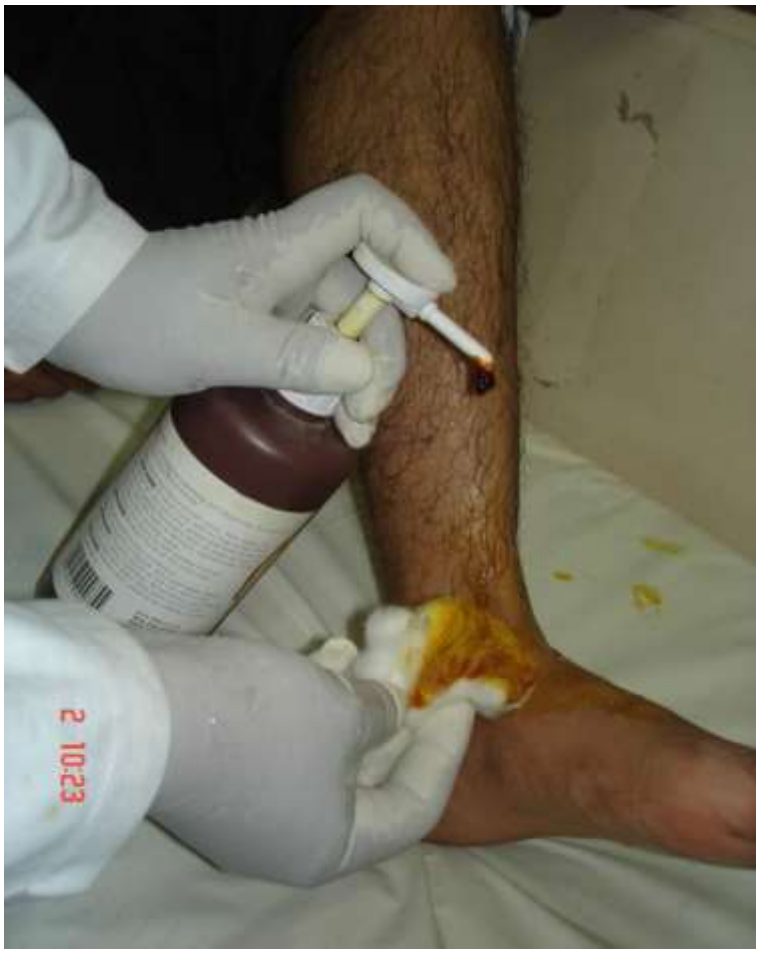
# Post-exposure prophylaxis

- Management of animal bite wound(s)
- Passive immunization with Rabies Immunoglobulin (RIG)
- Active immunization with Anti-Rabies Vaccines (ARV)

# Management of animal bite wound(s)

## Wound(s) toilet

Mechanical removal of virus from the wound(s)



Inactivation of the virus

Neutralization of the virus

- Application of antiseptics
- Local infiltration of rabies immunoglobulin
- Suturing
- Cauterization
- Tetanus prophylaxis

# Prevention of human rabies

*The 5 Important Things*

Magico-Religious Practices *(e.g. witchcraft, turmeric powder etc.) DO NOT HELP*

Wash the wound thoroughly with plenty of water and soap

Apply an antiseptic (povidone iodine) or even alcohol

Do not cover or Suture the wound

Vaccinate Immediately *e.g. Raibipur 1 mL IM*

# Category of bites (WHO)

| | |
|---|---|
| Category I | • Touching or feeding of animals<br>• Licks on intact skin<br>• Contact of intact skin with secretions/ excretions of rabid animal/human case |
| Category II | • Nibbling of uncovered skin<br>• Minor scratches or abrasions without bleeding |
| Category III | • Licks on mucous membrane<br>• Single or multipe transdermal bites or scratches, licks on broken skin |

# Recommended Treatment

| | |
|---|---|
| Category I | • None |
| Category II | • Local Rx of wounds<br>• Anti rabies vaccine |
| Category III | • Local Rx of wounds<br>• Anti rabies vaccine<br>• Rabies immunoglobulin |

# Rabies Immunoglobulin (RIG)

- Ready-made anti-rabies antibodies, to tide over the initial phase of the infection
- Binds with the rabies virus resulting in neutralization and thus loss of infectivity
- Infiltrated locally at the site of wound/bite

  Two types are available:

  Equine Rabies Immunoglobulin (ERIG)

  Human Rabies Immunoglobulin (HRIG)
- Indicated to i. all category III exposures

  ii. both category II and III exposures in immuno-compromised patients

# Equine Rabies Immunoglobulin

- Heterologous, produced by hyperimmunisation of equines
- Highly purified Fab 2’ fragments
- Small risk of anaphylactic reaction
- Dose of ERIG is 40 IU per kg body weight of patient
- Preparations contain 300 IU of immunoglobulin per ml

# Currently available equine rabies immunoglobulin in India

| Brand | Product | Pharmaceutical |
|---|---|---|
| Anti-Rabies Serum (ARS) | Purified equine RIGs, 5 ml vial (300 IU/ml, 1500 IU potency) | Central Research Institute, Kasauli, Himachal Pradesh |
| Equirab | Purified Equine RIGs, 5ml vial (300 IU/ml, 1500 IU potency) | Bharat Serums and Vaccines Limited, Mumbai |
| Vinrig | Purified Equine RIGs, 5ml vial (300 IU/ml, 1500 IU potency) | VINS Biopharma, Hyderabad |
| Abhayrig | Purified Equine RIGs, 5 ml vial (300 IU/ml, 1500 IU potency) | Human Biologicals Institute, Hyderabad |

# Human Rabies Immunoglobulin

- Homologous origin; relatively free from the side effects
- Expensive and is imported from other countries
- Longer half-life-given at half the dose of equine anti-rabies serum
- Dose of the HRIG is 20 IU per kg body weight
- HRIG preparation is available in concentration of 150 IU per ml

# Currently available human rabies immunoglobulin in India

| Brand | Product | Pharmaceutical |
|---|---|---|
| Berirab-P | Human Rabies Immunoglobulin, 150IU/ml; 2 ml (300 IU) ampoule & 5 ml (750 IU) ampoule | ZLB Behring AG,Marburg, Germany/Bharat Serums and Vaccines Ltd., Mumbai. |
| Imogamrab | Human Rabies Immunoglobulin, 150IU/ml; 2 ml (300 IU) ampoule & 5 ml (750 IU) ampoule | Sanofi Pasteur, France |
| Kamrab | Human Rabies Immunoglobulin, 150 IU/ml; 2 ml (300 IU) vial and 5 ml (750 IU) vial | Kamada Ltd.,Beit-Kama, Israel /Synergy Diagnostics Pvt. Ltd.,Thane,Maharashtra |

# Administration of RIG
# Do's

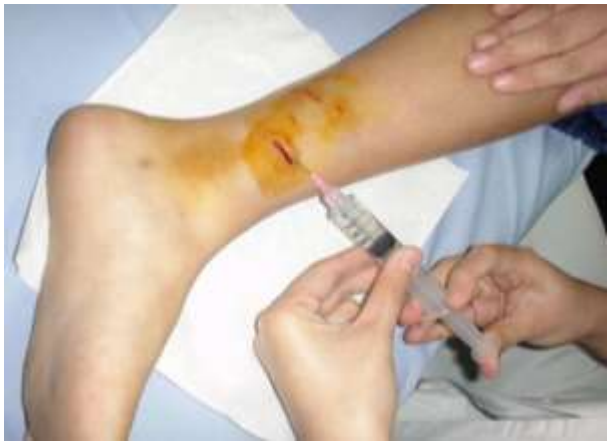
- Should be brought to room temperature before administration
- As much of the dose is anatomically feasible should be infiltrated into and around the wound
- Remaining dose to be administered by deep IM at a site distant from the vaccine injection site
- If multiple wounds present, calculated volume to be diluted in sterile normal saline to a volume sufficient to infiltrate all the wounds

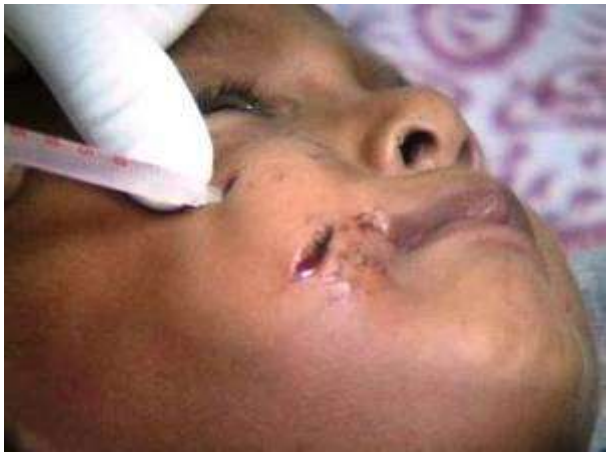
- Can be administered up to the seventh day after the first dose of ARV
- Tip of finger/s and toe/s, ear lobe/s or bites on nose or around the eye should be carefully infiltrated without excessive pressure
- Patient kept under observation for at least half–an–hour after administration of ERIG

## Don’t’s

- Multiple needle injections into the wound/s should be avoided

- Total recommended dose of RIG must not be exceeded⟶ suppress antibody production
- Should never be administered in the same syringe or at the same anatomical site as vaccine





# Anti-Rabies vaccines

- Nerve tissue vaccines used previously
- Reactogenic and less immunogenic
- Production was stopped in December, 2004
- Cell culture vaccines (CCVs) and Purified Duck Embryo vaccines (PDEV) are now used for active immunization
- Given as one single intramuscular dose with potency of > 2.5IU per IM dose
- CCVs approved for intradermal could be given ID
- Adverse events following immunization (AEFI) very minimal with CCVs & PDEVs

# Vaccines

1. **Cell Culture Vaccines**

- Human Diploid Cell Vaccine (HDCV), Liquid (Adsorbed), 1ml: Produced locally in private sector
- Purified Chick Embryo Cell Vaccine (PCECV), 1ml: Produced locally in private sector
- Purified Vero Cell Rabies Vaccine (PVRV), 0.5ml and 1ml: Imported and also produced locally in public & private sectors

2. **Purified Duck Embryo Vaccine (PDEV**), 1ml: Produced locally in private sector

# Currently available anti-rabies vaccines in India

| Brand | Product | Pharmaceutical |
|---|---|---|
| Abhayrab* | Purified Vero cell Rabies Vaccines (PVRV) | Human Biologicals Institute, Hyderabad |
| Indirab* | Chromatographically purified (PVRV) | Bharat Biotech International Ltd, Hyderabad |
| PVRV | Purified Vero cell Rabies Vaccine (PVRV) | Pasteur Institute of India, Coonoor, Tamilnadu |
| Rabipur* | Purified Chick Embryo Cell Vaccine (PCECV) | Novartis Vaccines, Mumbai |
| Rabivax | Human Diploid Cell Culture Vaccine (HDCV) (Liquid) | Serum Institute of India, Pune |
| Vaxirab | Purified Duck Embryo Vaccine (PDEV) | Zydus Health Care ltd., Ahmedabad |
| Vaxirab-N* | Purified Chick Embryo Cell Vaccine (PCECV) | Zydus Health Care Ltd, Ahmedabad |
| Verorab* | Purified Vero cell Rabies Vaccines (PVRV) | Sanofi Pasteur/ Zuventus Health Care, Mumbai |

# Storage, Transport & Reconstitution

- Most CCVs and PDEV are stored and marketed in freeze dried (lyophilized) form
- But vaccines should be kept and transported at a temperature range of 2-8ºC and protected from sunlight
- Reconstituted with the diluent prior to use
- IM dose to be given immediately after reconstitution
- Should not be used after 8 hours of reconstitution
- For ID administration, vaccine vial should be stored at 2-8ºC after reconstitution and total content should be used at the most within 8 hours

# Immunity & antibody titre

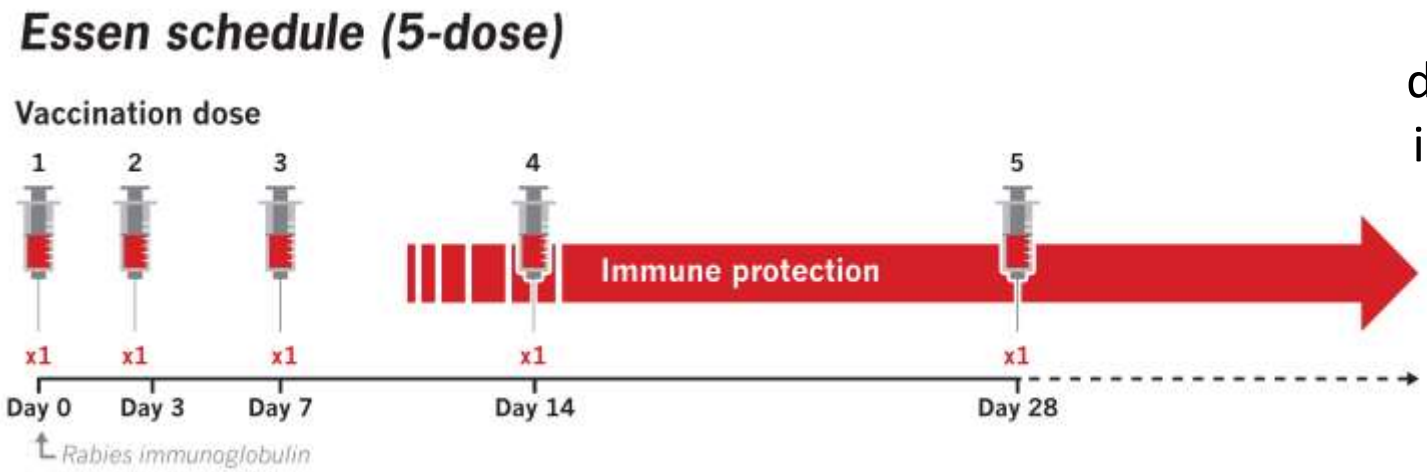
- Lasting immunological memory with CCVs & PDEVs
- Good anamnestic responses for booster vaccination in those who received primary series 5-21 years back
- No difference in response with route of vaccination
- Anti-rabies neutralizing antibody titre of 0.5 IU/ml or more in serum is considered as protective
- Achieved in most healthy individuals by day 14 of a post-exposure regimen

# Common PEP regimens

| Regimen | Doses in the regimen | Site of injection | Amp used | Dose (ml) |
|---|---|---|---|---|
| Essen (IM) | 1-1-1-1-1 | Deltoid<br>Ant Lat Thigh | 5 | 0.5 or 1 |
| Abbreviated Multisite IM (Zagreb) | 2-0-1-0-1 | Rt arm$^0$, Left arm$^0$<br>Deltoid | 4 | 0.5 or 1 |
| 8-site ID | 8-0-4-0-1-1 | Deltoid, thigh, Supx, lower ant abd | <2 | 0.1 |
| Thai Red Cross (ID) | 2-2-2-0-1-1 | Both Deltoid | <2 | 0.1 |
| Updated Thai Red Cross (ID) | 2-2-2-0-2 | Both Deltoid | <2 | 0.1 |

# Post-exposure prophylaxis IM administration:
*Essen regimen*

**One IM dose of vaccine on Days 0, 3, 7, 14, and 28**




1 mL (IM) into deltoid (adults) or into anterolateral area of thigh (children)

5 doses – 5 visits

RIG is always recommended for transdermal wounds

1. WHO 2004; 2. WHO 2007

# Post-exposure prophylaxis IM administration:
*Updated Thai Red Cross (2-2-2-0-2)*

Days 0, 3, 7, and 28 – two 0.1 mL doses


left deltoid

8 doses – 4 visits

RIG is always recommended for transdermal wounds

1. WHO 2004; 2. WHO 2007

# ID injection technique

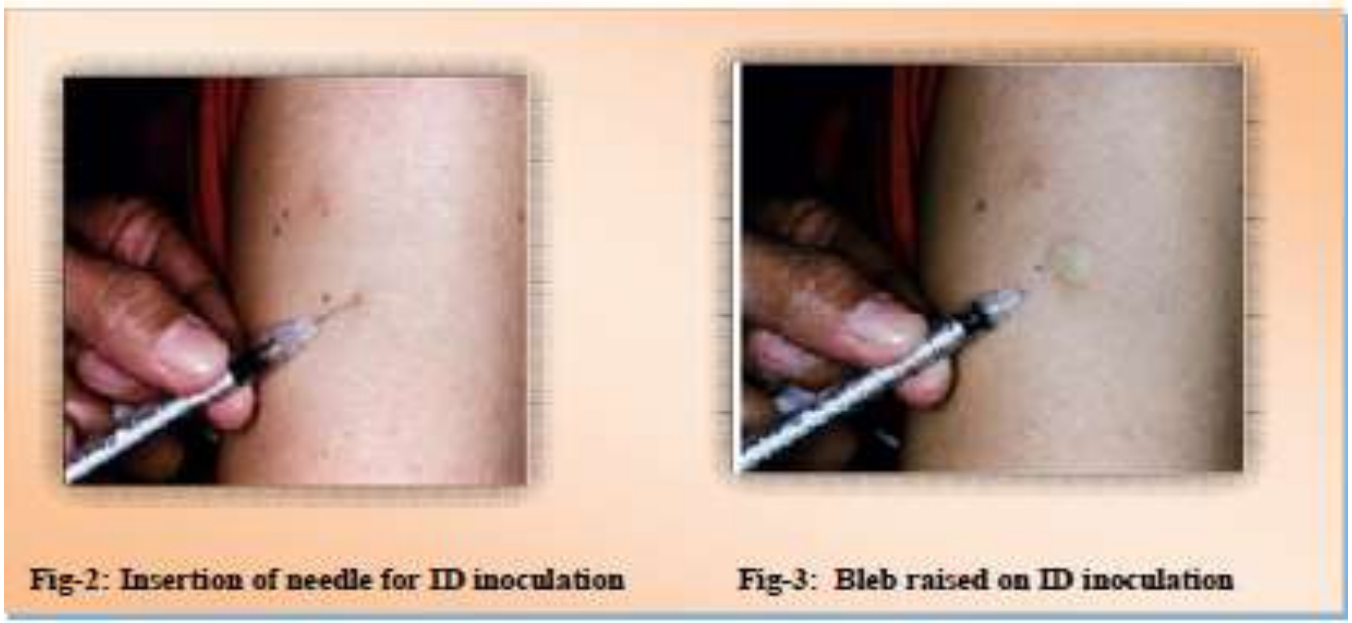


Fig-2: Insertion of needle for ID inoculation

Fig-3: Bleb raised on ID inoculation

- The needle should be almost parallel with the skin surface and the bevel of the needle facing upwards
- Inserted approximately 2 mm into the superficial layers of the dermis
- Intradermal injections reduce the volume of vaccine required and vaccine cost by 60% to 80%

# DCGI recommended post-exposure IM and ID regimens: Summary

| Regimen | Day 0 | Day 3 | Day 7 | Day 14 | Day 21 | Day 28 | Day 90 | Vials | Visits |
|---|---|---|---|---|---|---|---|---|---|
| Essen | 1.0 mL | 1.0 mL | 1.0 mL | 1.0 mL | – | 1.0 mL | – | 5 | 5 |

| Regimen | Day 0 | Day 3 | Day 7 | Day 14 | Day 21 | Day 28 | Day 90 | mL | Visits |
|---|---|---|---|---|---|---|---|---|---|
| Thai Red Cross (updated) | 2 x 0.1 mL | 2 x 0.1 mL | 2 x 0.1 mL | – | – | 2 x 0.1 mL | – | <1 | 4 |

National Guidelines for Rabies Prophylaxis and Intra-dermal Administration of Cell Culture Rabies Vaccines, 2007

# Management of re-exposure in previously vaccinated individuals

- Priming of immune system and the development of immunological memory→ long lasting immunity
- Anamnestic response to one or more booster doses in persons previously receiving complete PrEP or PEP
- Two booster doses IM (0.5ml/1ml) or CCVs ID (0.1 ml at 1 site) on days 0 and 3
- Proper wound toilet should be done
- Treatment with RIG not required
- Persons previously receiving NTV or vaccines of unknown efficacy should be treated as fresh case & given full regimen

# Pre-Exposure Prophylaxis (PrEP)

- ☑ ***Full IM dose or 0.1 ml ID dose to be given on days 0, 7 and either day 21 or 28***
- ☑ Laboratory staff handling the virus and infected material
- ☑ Clinicians, Persons attending to human rabies cases
- ☑ Veterinarians, Animal handlers and catchers
- ☑ Wildlife wardens
- ☑ Quarantine officers and travelers from rabies free areas to rabies endemic areas
- ☑ Antibody titres checked every 6 months during the initial two years period after the primary vaccination
- ☑ If it is less than 0.5 IU/ml a booster dose of vaccine should be given.
- ☑ Subsequently, sero-monitoring is recommended every two years.

# Treatment

☑There is no specific treatment for rabies; it is invariably fatal

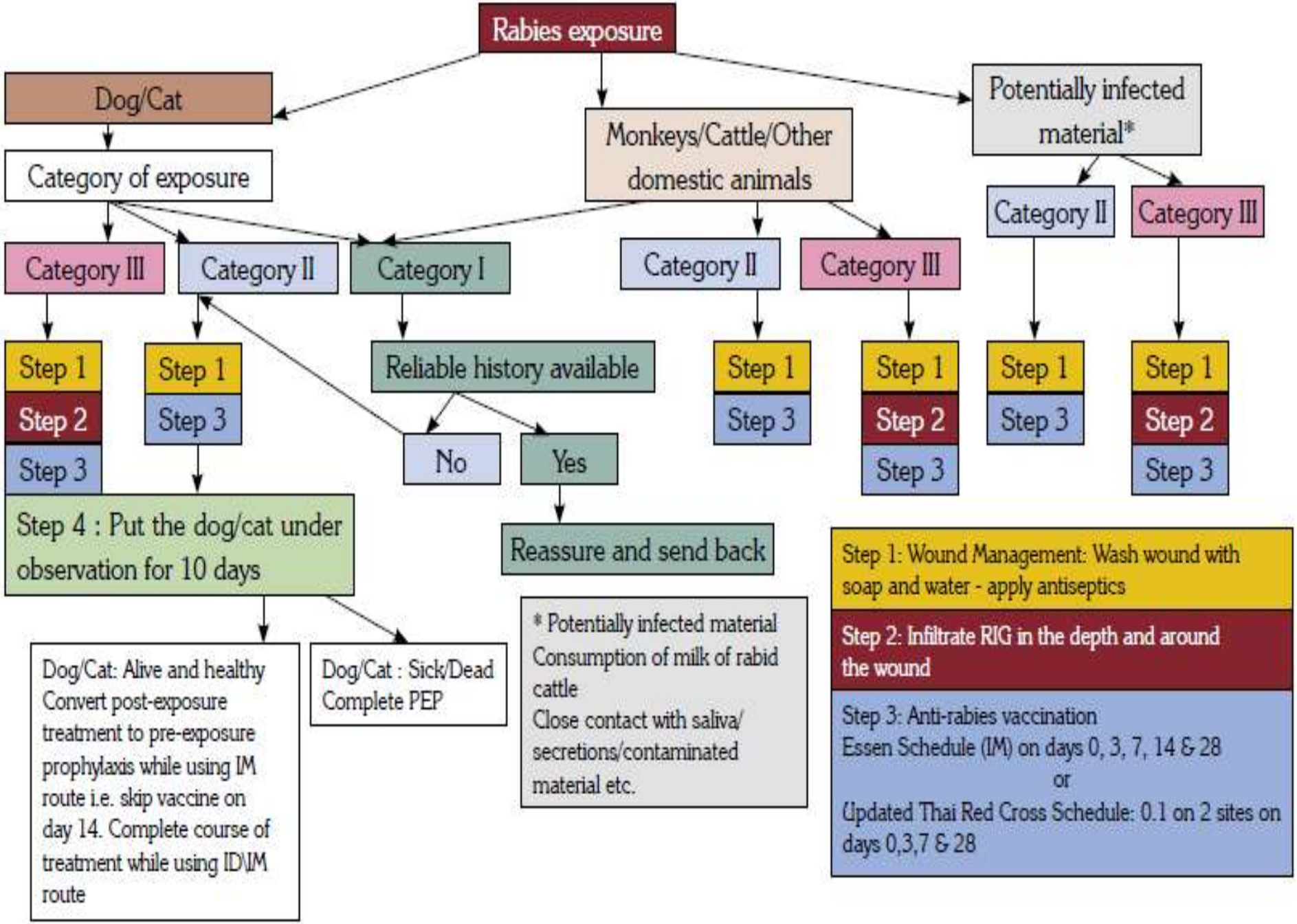
☑Most rabies deaths are caused by temporary brain dysfunction with little to no damage occurring to the brain itself

☑Willoughby et al at Children's Hospital of Wisconsin put Jeanna Giese into an induced coma with ketamine & midazolam ("Milwaukee protocol")

☑Amantadine & Ribavarin was given

First & only person to survive rabies without vaccine

☑Giese brought out of coma after 6 days once immunity regained


Rabies exposure
Dog/Cat
Monkeys/Cattle/Other domestic animals
Potentially infected material*
Category of exposure
Category III
Category II
Category I
Category II
Category III
Category II
Category III
Step 1
Step 2
Step 3
Step 1
Step 3
Reliable history available
Step 1
Step 3
Step 1
Step 2
Step 3
Step 1
Step 3
Step 1
Step 2
Step 3
No
Yes
Step 4 : Put the dog/cat under observation for 10 days
Reassure and send back
Dog/Cat: Alive and healthy
Convert post-exposure treatment to pre-exposure prophylaxis while using IM route i.e. skip vaccine on day 14. Complete course of treatment while using ID\IM route
Dog/Cat : Sick/Dead
Complete PEP
* Potentially infected material
Consumption of milk of rabid cattle
Close contact with saliva/ secretions/contaminated material etc.
Step 1: Wound Management: Wash wound with soap and water - apply antiseptics
Step 2: Infiltrate RIG in the depth and around the wound
Step 3: Anti-rabies vaccination
Essen Schedule (IM) on days 0, 3, 7, 14 & 28
or
Updated Thai Red Cross Schedule: 0.1 on 2 sites on days 0,3,7 & 28