

# **Rabies**

**What you  
should know**



**CMC VELLORE , MPH STUDENTS**

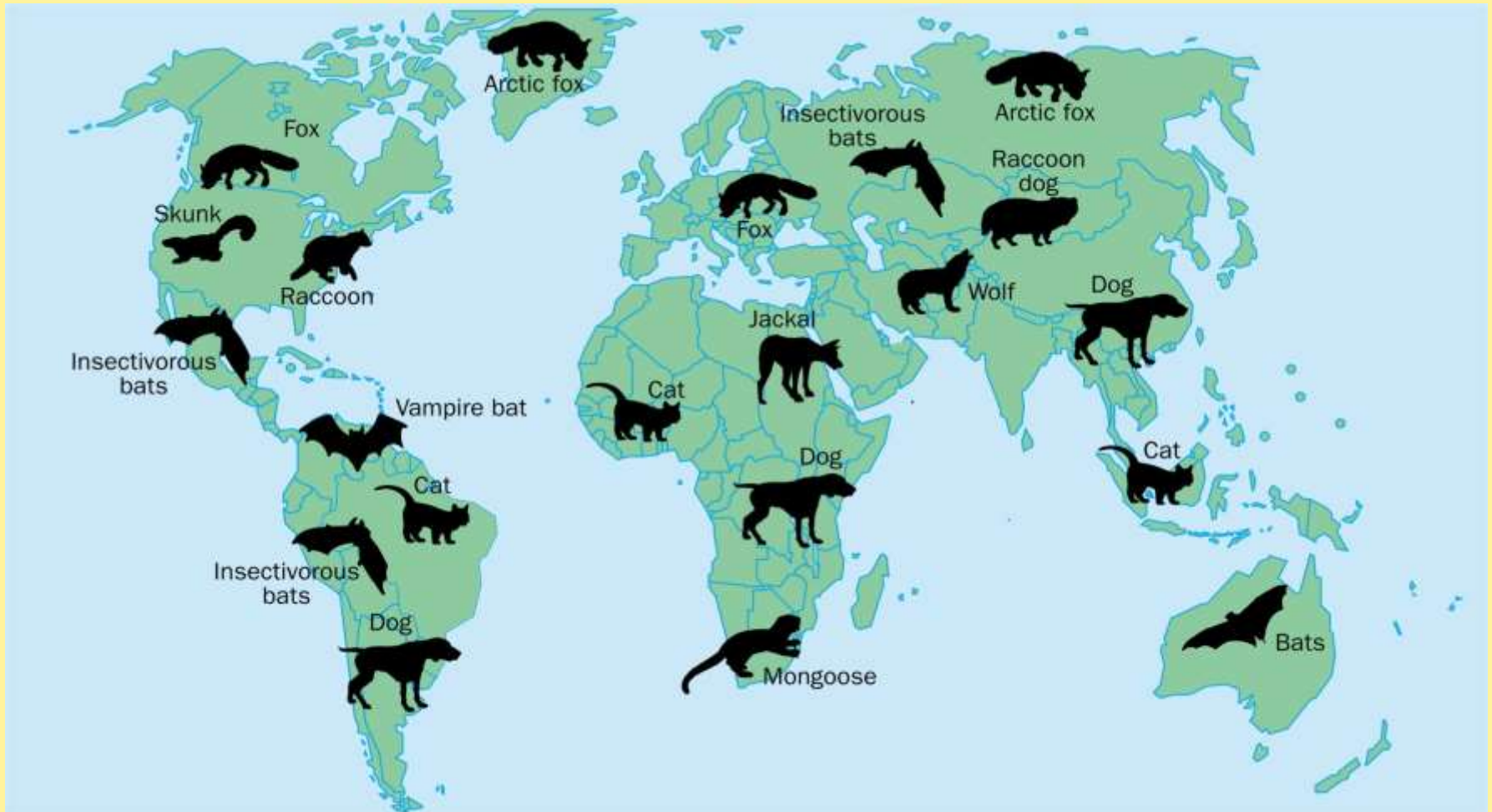
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- Rabies, also known as hydrophobia, is a highly fatal viral disease that causes inflammation of the brain in humans and other mammals.
- It is caused by **Lyssavirus type 1**.
- Transmission of Rabies to human-
  - Bites (95%),
  - Scratches &
  - Licks from infected animals.



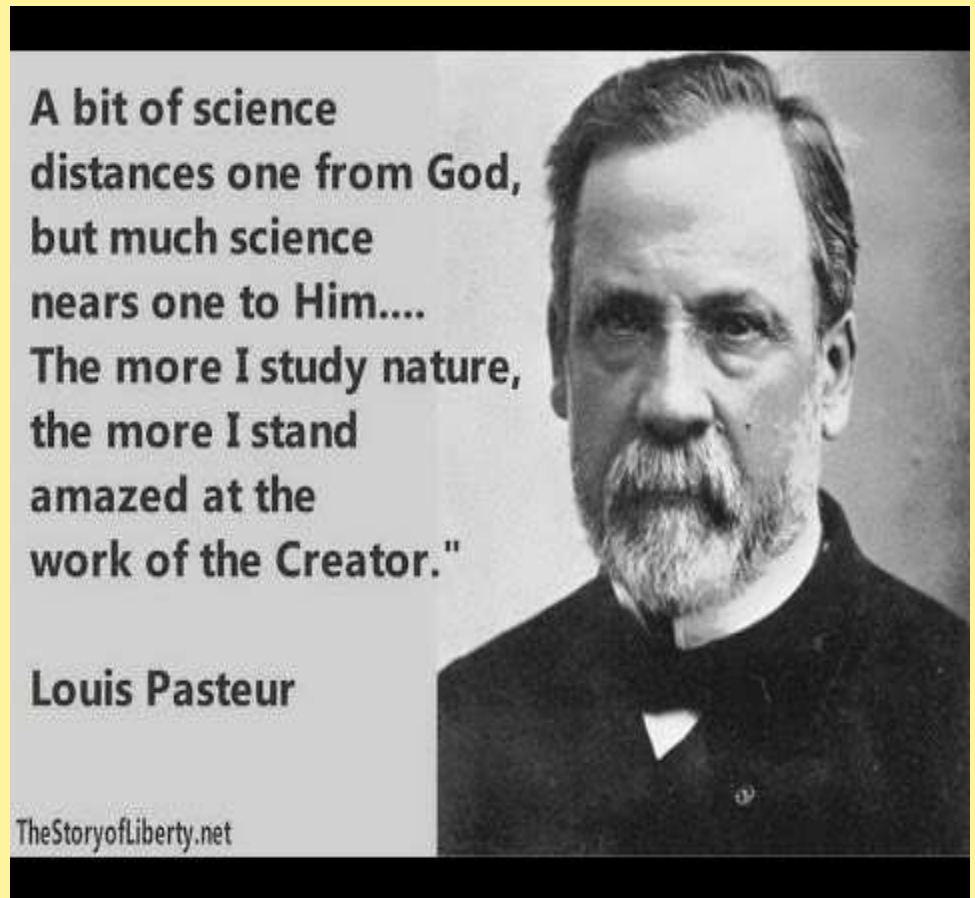
- It is a zoonotic disease of warm blooded animals such as – Dogs, Skunk, Cats, Jackals, bats and wolves.



# History of Rabies

- Man described the disease in 2300 B.C.
- The word 'Rabies' originated from "*rabhas*", meaning "*to do violence*". It comes from ancient Indian Sanskrit dating 3000 B.C.
- Since Roman times, man established the link between the infectivity of a rabid dogs saliva and the spread of the disease.
- Because there is no cure, those that had been bitten by a rabid dog would commonly commit suicide to avoid the painful death that would inevitably follow.

- Louis Pasteur (a French biologist, microbiologist and chemist) was the first person to diagnose that rabies targets the Central Nervous System (CNS)



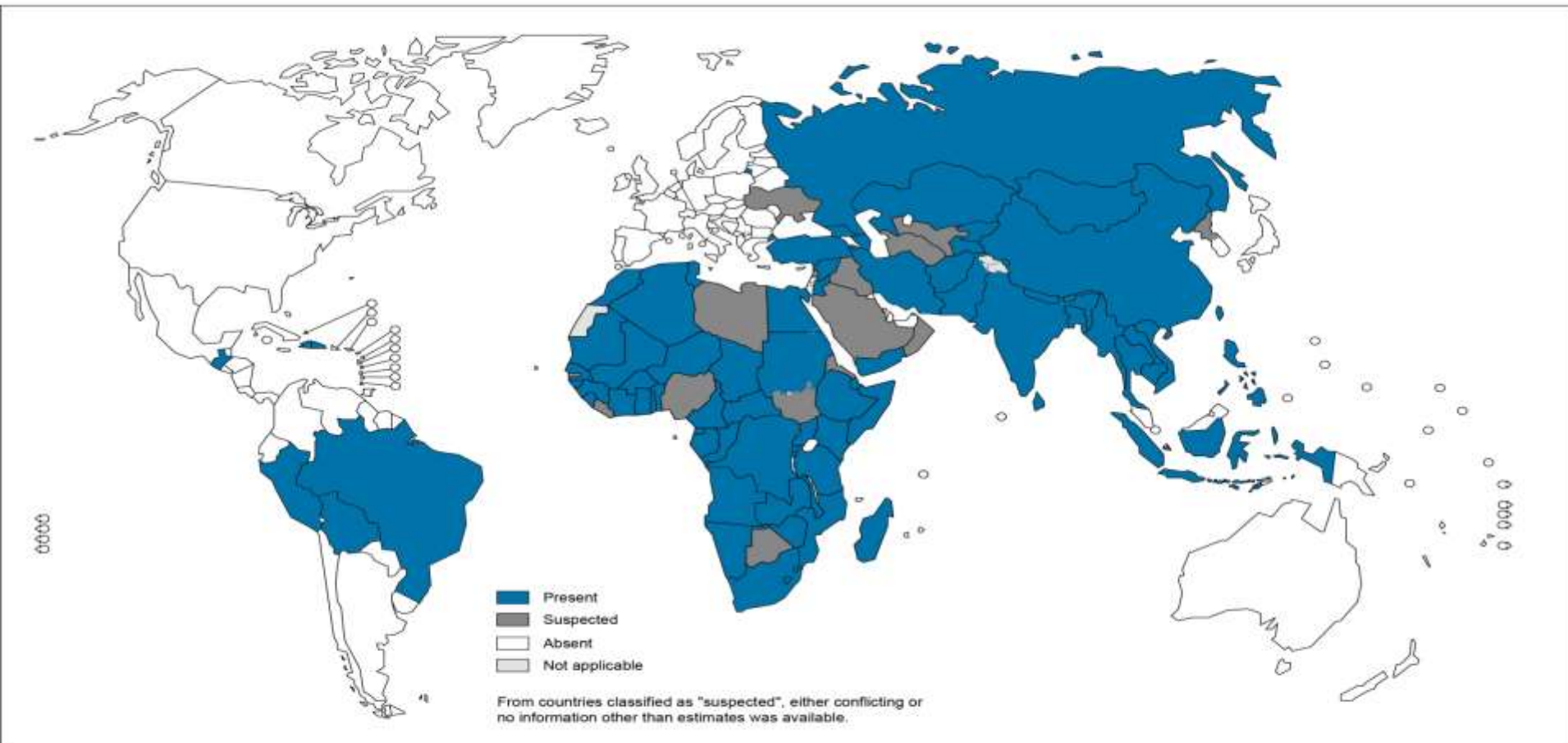
- In **1890** created the rabies vaccine and saved 9 year old Joseph Meister after he had been bit by a rabid dog



# Global Burden

- **A very wide distribution-** Human rabies is present in 150 countries and territories and on all continents, except for Antarctica.

Presence of dog-transmitted human rabies based on most recent data points from different sources, 2010-2014



- **Globally**: estimates indicate that human mortality is highest in Asia, with the highest incidence and deaths reported in India, followed by Africa.
- The virus claims an estimated of 59,000 (95% confidence intervals (CI):25–1,59,000) human lives annually, mostly in Africa and Asia.
- Over 95% of rabies deaths in humans result from virus transmission through the bites of infected dogs

Source: **Human rabies: 2016 updates and call for data**, *Weekly epidemiological record*  
Authors: WHO/ Department of Control of Neglected Tropical Diseases

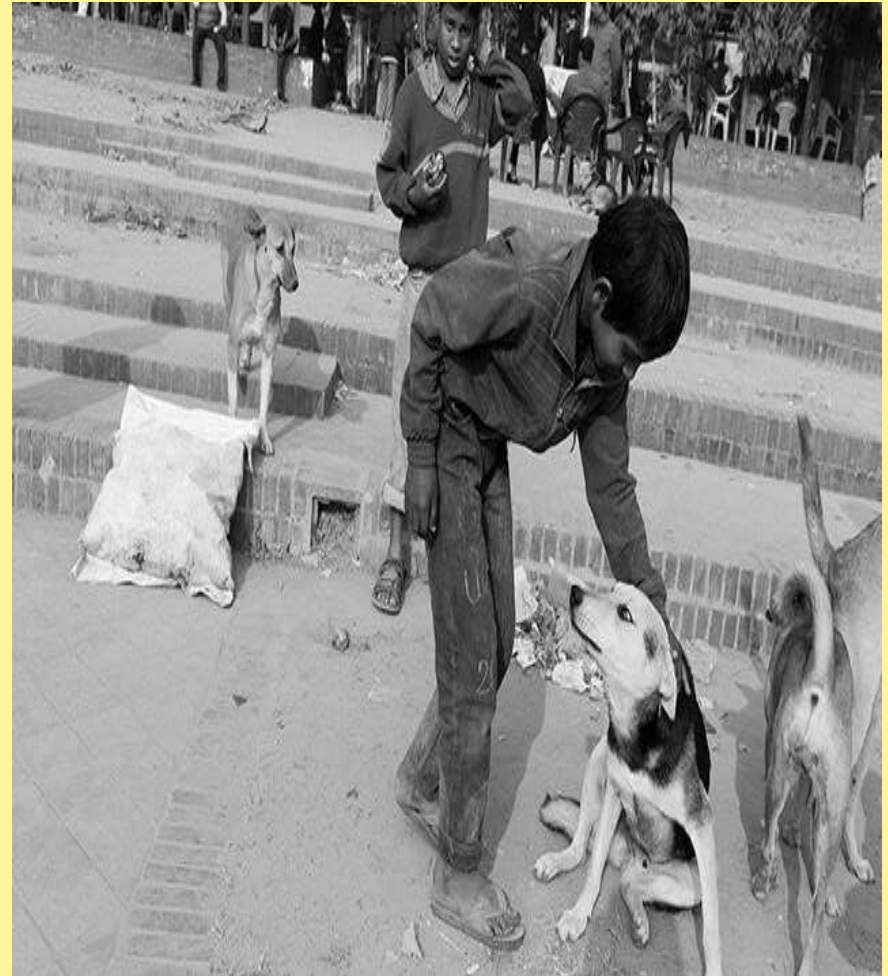
# Burden in India

- India is endemic for rabies accounting for 36% of the world's deaths.
- True burden of rabies in India is not fully known; although as per available information, it causes 18,000 - 20,000 deaths every year.
- 30%-60% (approx) of reported rabies cases and deaths in India occur in children under the age of 15 years

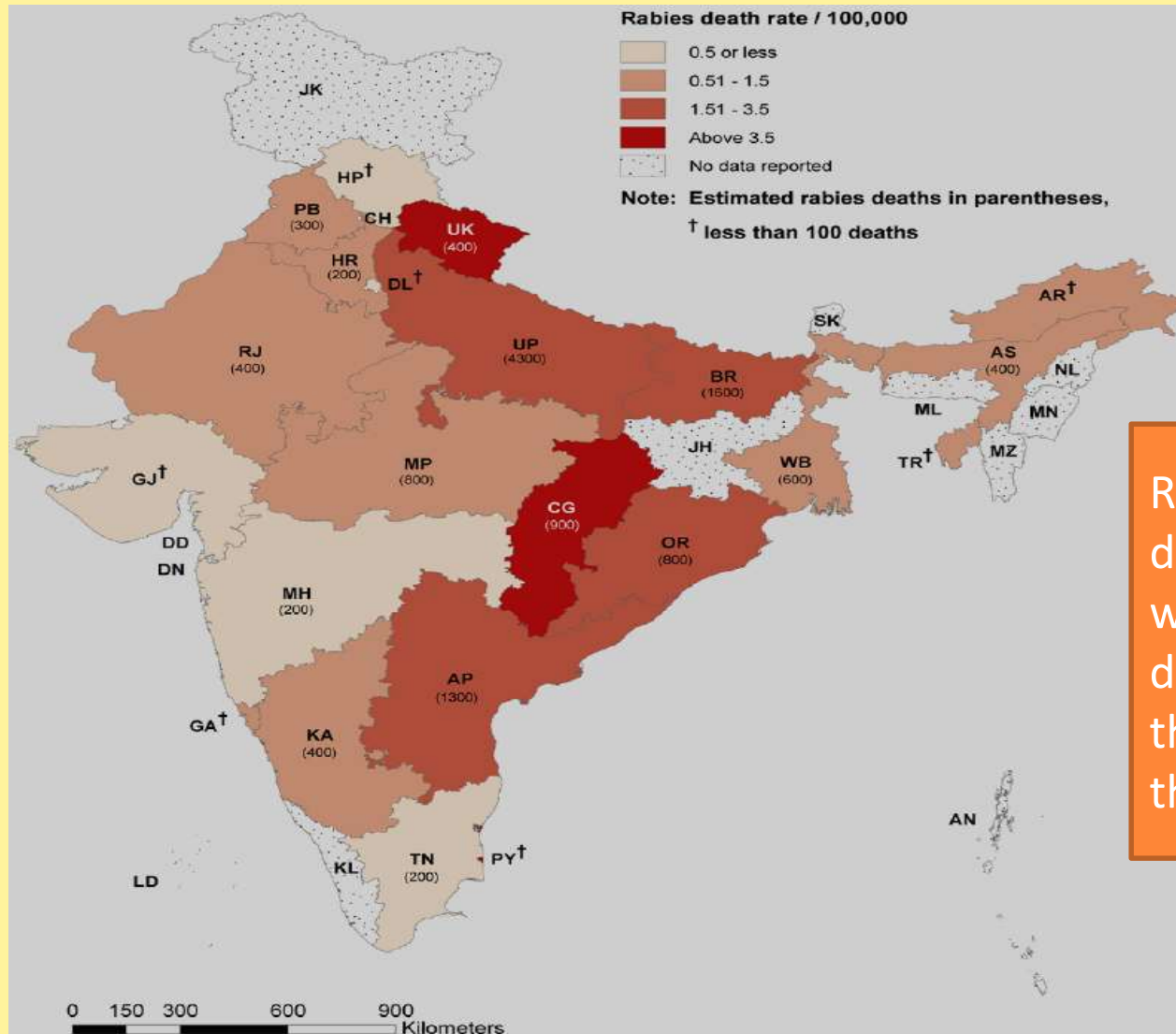


# Why Children are at more risk in India?

- Children are more likely to pat and play with animals.
- Less likely to let an adult know if an animal has bitten them
- More likely to get severe bites to their heads, face and hands.



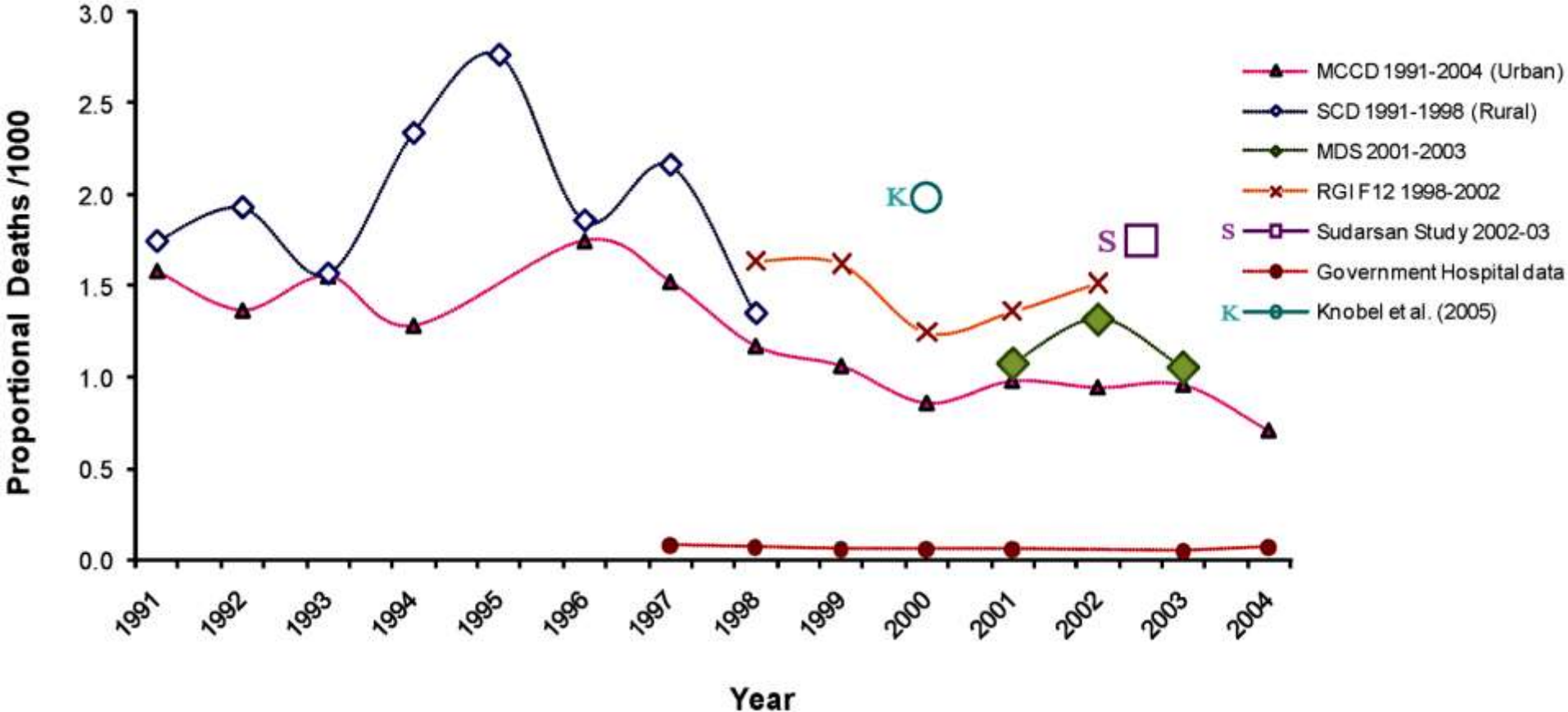
# Burden of Rabies- State wise



Rabies deaths are widely distributed throughout the country

**Source:** Suraweera, Wilson & Morris, Shaun & Kumar, Raj & A Warrell, David & Warrell, Mary & Jha, Prabhat. (2012). Deaths from Symptomatically Identifiable Furious Rabies in India: A Nationally Representative Mortality Survey. PLoS neglected tropical diseases. 6. e1847. 10.1371/journal.pntd.0001847.

# Reports & Study findings on Rabies in India

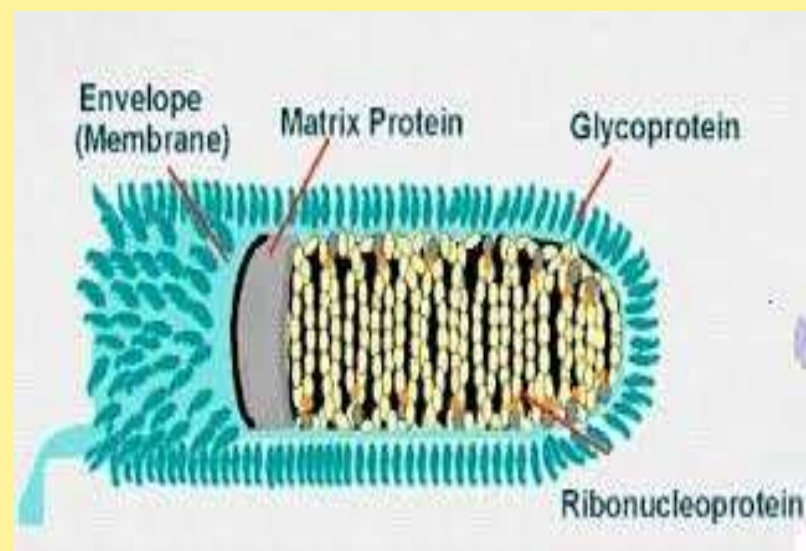
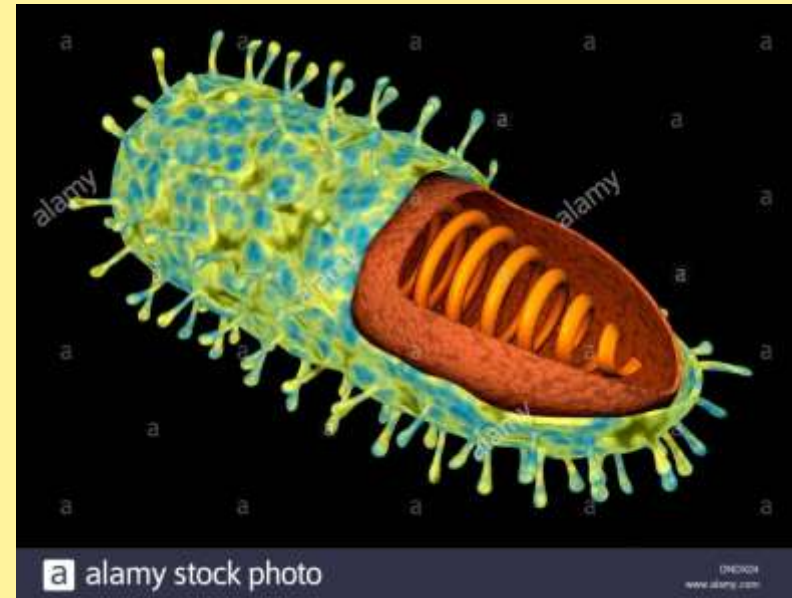


1. MCCD - Medically Certified Causes of Death, Annual Report
2. SCS - Survey of Cause of Death
3. MDS - Million Death Study
4. RGI - Registrar General of India
5. Re-evaluating the burden of rabies in Africa and Asia. *Knobel DL, Cleaveland S, Coleman PG, Fèvre EM, Meltzer MI, Miranda ME, Shaw A, Zinsstag J, Meslin FX Bull World Health Organ. 2005 May; 83(5):360-8.*
6. Government hospital data from the routine data collection of the Union Ministry of Health and Family Welfare

# EPIDEMIOLOGY

# AGENT

- Rhabdovirus
- Lyssavirus type 1
- Bullet shaped virus
- Size is 180 \*75nm
- Has a lipoprotein envelope
- Knob like spikes or glycoprotein G.
- Matrix protein layer
- Genome –unsegmented ,linear, negative sense RNA.





# TYPES OF RABIES VIRUS

|          | <u>STREET VIRUS</u>  | <u>FIXED VIRUS</u>   |
|----------|--|--|
|          | The virus recovered from naturally occurring cases of rabies is called street virus.   | The virus which has a short , fixed and reproducible incubation period is called fixed virus.  |
| SOURCES  | It is naturally occurring virus . It is found in saliva of infected animal   | It is prepared by repeated culture in brain of rabbit such that its IP is reduced and fixed.   |
| FEATURES | <ol style="list-style-type: none"><li>1. It produce negri bodies</li><li>2. Incubation period is 20 to 60 days.</li><li>3. It is pathogenic for all mammals</li><li>4. Cannot be used for preparation of vaccine</li></ol> | <ol style="list-style-type: none"><li>1. It does not form negri bodies</li><li>2. Incubation period is constant between 4-6 days.</li><li>3. It can be pathogenic for humans under certain conditions.</li><li>4. It is used to prepare anti-rabies vaccine.</li></ol> |

# RESERVIOUR OF INFECTION

- **URBAN RABIES:**

1. 99% cases in India is from dogs and cats.
2. A single infected dog capable of transmitting over an area of 40 km.

- **WILD LIFE RABIES :**

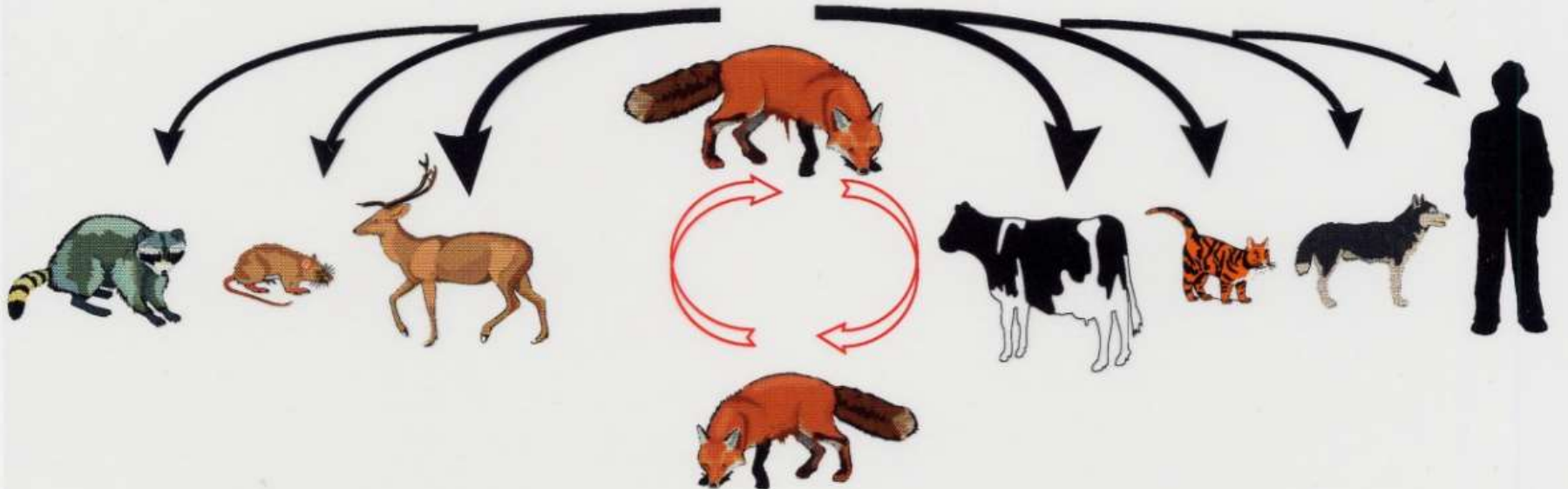
1. sylvatic rabies
2. Unidentified reservoir of infection
3. Foxes, jackals, hyenas , skunks etc.
4. Transmit infection among themselves and to dogs and man.

- **BAT RABIES:**

1. Latin American countries ,USA
2. Vampire bats feed on blood of humans and animals.
3. Cause havoc to cattle population
4. Not reported in India
5. Constant sources of infection to man and animals
6. Transmission by bite and aerosols.

# 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 3-8 weeks
- Maybe short that is 4 days or maybe prolonged for years.
- Depends on site of bite

Severity of bite

Number of wounds

Amount of virus injected

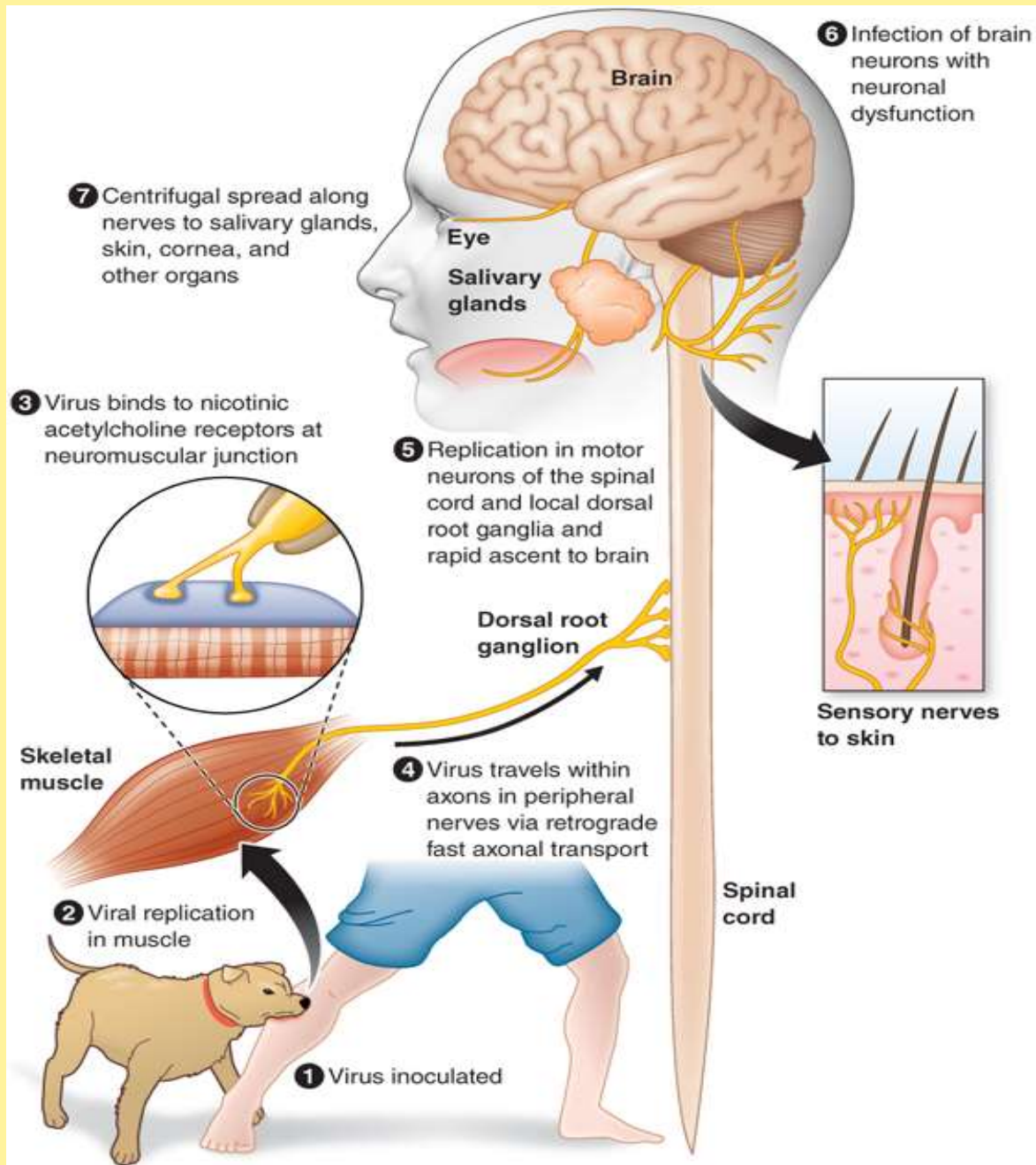
Species of biting animal

Protection provided by clothing

Treatment taken or not.



# **PATHOGENESIS**



# **RABIES IN MAN**

- Know as **hydrophobia** (fear of water)
- **Duration of disease:** 2-3 days prolonged to 5-6 days (exceptional cases)
- Prodromal symptoms (3-4 days)
  - Headache
  - Malaise
  - Sore throat
  - slight fever
- Followed by excitation and stimulation off all parts of nervous system
  - Sensory system
  - Nervous system
  - Motor system
  - Sympathetic system
  - Mental system

- Patient becomes intolerant to noise, bright light, cold draught of air (sensory).
- Aerophobia (fear of air ) may be present.
- Increased reflexes and muscle spasms(motor).
- Dilatation of pupil and increased perspiration , salivation , lacrimation.(sympathetic).
- Fear of death , irritability , anger and depression (mental changes).
- Patient dies abruptly due to convulsions or pass to coma and paralysis.



# DIAGNOSIS

- On basis of clinical history of bite by rabid animal
- Characteristic signs and symptoms
- Confirmatory tests
  - Antigen detection by immunofluorescence (skin biopsy).
  - Virus isolation (saliva and other secretions)
- Immunofluorescence of corneal impression smears proven unreliable.

# TREATMENT

- No specific treatment
- Case management
  - Isolation in a quiet room protected as far as possible from external stimuli to prevent spasms and convulsions
  - Relieve anxiety and pain by use of sedatives
    - Morphine 30-54 mg
  - If spastic muscle contractions present use drugs with curare like action
  - Ensure hydration and diuresis
  - Intensive therapy in the form of respiratory and cardiac support

- Patients with rabies are highly infectious virus is present in all secretions like saliva , tears, vomits, urine, and other body fluids.
- Nursing personnel should be warned of risks and protect themselves with PPE
- Persons with open wounds and cut should not attend the patients
- In places where rabies cases are encountered frequently pre exposure prophylaxis (2-3 doses HDC vaccine ) recommended.

# PREVENTION OF HUMAN RABIES

**This may be considered under 3 heads**

- Post-exposure prophylaxis.
- Pre-exposure prophylaxis.
- Post-exposure treatment of persons who have been vaccinated previously

# POST-EXPOSURE PROPHYLAXI

1. General consideration
2. Local treatment of wound
  - (a) Cleansing
  - (b) Chemical treatment
  - (c) Suturing
  - (d) Antibiotics and anti-tetanus measure
3. Immunization



# Immunization

- Rabies vaccines prequalified by WHO do not contain preservatives such as thimerosal.
- The shelf-life 3 years
- Stored at +2°C to +8°C and protected from sunlight.
- Following reconstitution with the accompanying sterile diluents, the vaccines should be used immediately, or within 6-8 hours if kept at the correct temperature.
- All CCEEVs should comply  $\geq 2.5$  IU per single intramuscular dose .

# Categories of contact and recommended post-exposure prophylaxis (PEP)

| Categories of contact with suspect rabid animal   | Post-exposure prophylaxis measures  |
|---|---|
| <b>Category I</b> - Touching or feeding animals, licks on intact skin   | None  |
| <b>Category II</b> - Nibbling of uncovered skin, minor scratches or abrasions without bleeding  | Immediate vaccination and local treatment of the wound  |
| <b>Category III</b> - Single or multiple transdermal bites or scratches, licks on broken skin; contamination of mucous membrane with saliva from licks, contacts with bats. | Immediate vaccination and administration of rabies immunoglobulin; local treatment of the wound |

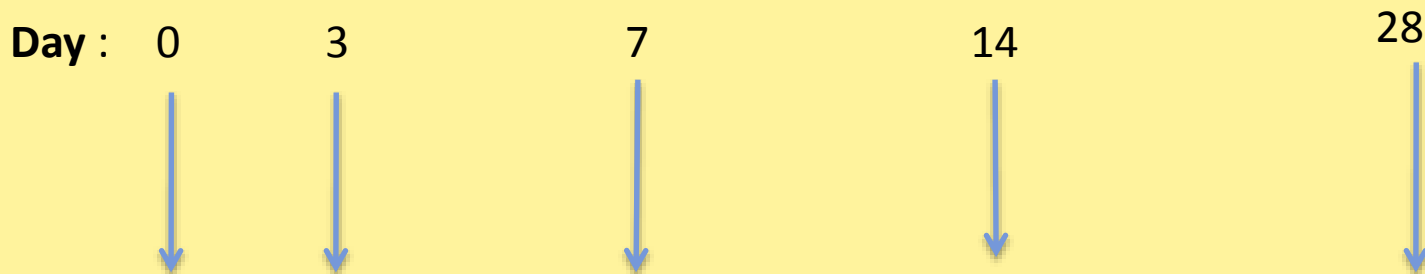
**All category II and III exposures assessed as carrying a risk of developing rabies require PEP This risk is increased if :**

- The biting mammal is a known rabies reservoir or vector species
- The animal looks sick or has an abnormal behaviour
- A wound or mucous membrane was contaminated by the animal's saliva
- The bite was unprovoked
- The animal has not been vaccinated
- And if biting animal cannot be traced or identified.

# Intramuscular administration of vaccine for post-exposure prophylaxis

- Essen regimen : The 5-dose regimen prescribes 1 dose on each of days 0, 3, 7, 14, and 28

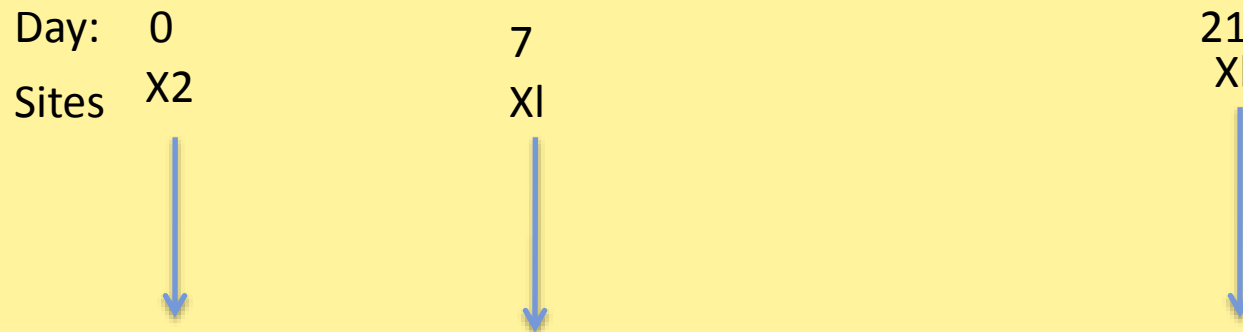
**Dose:** one IM dose (1.0 or 0.5 ml) into deltoid (or thigh)



Rabies immunoglobulin

- Zareb regimen: The 4-dose abbreviated multisite regimen prescribes 2 doses on day 0 (1 in each of the 2 deltoid or thigh sites) followed by 1 dose on each of days 7 and 21, as shown below.

**Dose : one IM dose (LO or 0.5 ml) into deltoid (or thigh)**

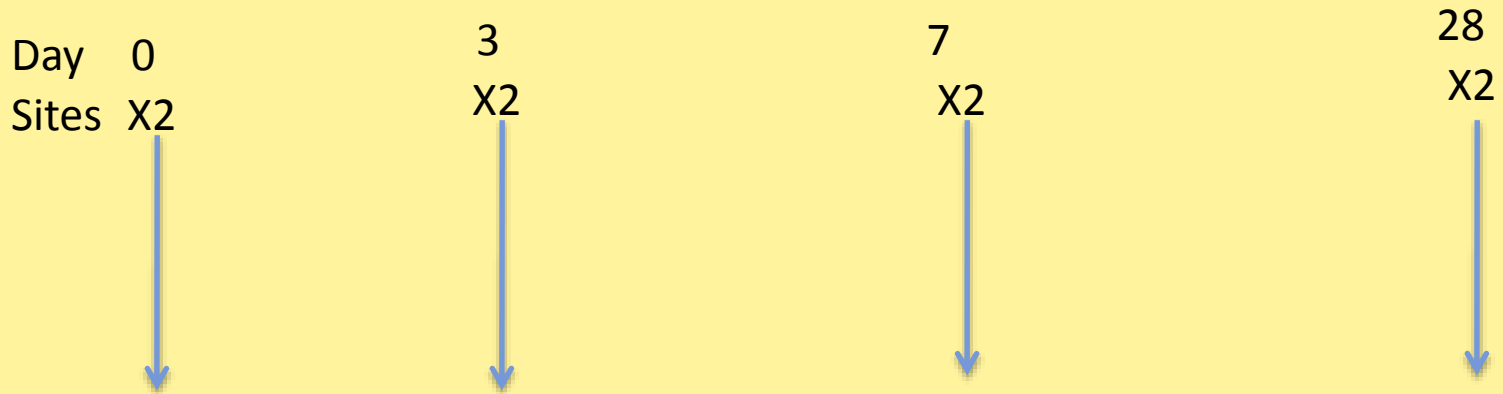


# Intradermal administration for post-exposure prophylaxis

- The 2-site regimen prescribes injection of 0.1 ml at 2 sites (deltoid or thigh) on days 0, 3, 7 and 28. The day 14 dose is missed

## 2-site intradermal regimen (2+2+2+0+2)

Dose : one JD dose one fifth of IM dose (0.1 ml) ID per site



# **Post-exposure prophylaxis for previously vaccinated individuals**

- For rabies-exposed patients who can document previous complete pre-exposure vaccination or complete post exposure prophylaxis with a CCEEV, 1 dose delivered intramuscularly or a CVV delivered intradermally on days 0 and 3 is sufficient

# Immunization of immunocompromised individuals

- In immunocompromised individuals including patients with HIV/AIDS, a complete series of 5 doses of intramuscular CCEEV in combination with comprehensive wound management and local infiltration with human rabies immunoglobulin is required for patients with category II and III exposures.



# Pre-exposure prophylaxis

- IM or 0.1 ml ID on days 0, 7 and either day 21 or 28.  
For clinicians and persons attending to human rabies cases, veterinarians, animal handlers

# Adverse events following immunization

- In general, CCEEVs have been shown to be safe and well tolerated. However, in 35-45% of vaccines, minor and transient erythematic, pain and/or swelling may occur at the site of injection, particularly following intradermal administration of a booster.
- Mild systemic adverse events following immunization (AEFI), such as transient fever, headache, dizziness and gastrointestinal symptoms, have been observed in 5-15 % of vaccines

# **RABIES IN DOGS**

# RABIES IN DOGS

- **INCUBATION PERIOD** : Ranges from 3-8 weeks but it may be as short as 10 days or as long as 1 year.
- **CLINICAL PICTURE:**  
It manifest in 2 forms : Furious rabies and dumb rabies.
- **FURIOUS RABIES** : Typical mad- dog syndrome.

- **CHANGE IN BEHAVIOUR**- Loses its fear of people , aggressive, bites unusual objects- stick , straw and mud.
- **RUNNING AMUCK**: Tendency to run away from home and wander.
- **CHANGE IN VOICE**: Barks and growls in a hoarse voice or unable to bark
- **EXCESSIVE SALIVATION**: Foaming at the angle of mouth
- **PARALYTIC STAGE**: Later stage paralysis of the whole body leading to coma and death.



- **DUMB RABIES:** Exciting and irritating stage is lacking .
- Its predominantly paralytic.
- Dog withdraws from being seen and disturbed.
- Dies in about 3 days.



## LAB DIAGNOSIS :

- **FLUORESCENT ANTIBODY TEST:** Highly reliable and best single test for rabies antigen detection.
- If brain is negative by FRA test , person need not be treated.
- **MICROSCOPIC EXAMINATION:** Negri bodies identifies 75-90% of cases.

- **MOUSE INOCULATION TEST** : Intracerebral mouse inoculation of the infected brain tissue show signs of rabies between 6-8 days if infected.
- **CORNEAL TEST**: Antigen detection in corneal impressions or in frozen skin biopsies by FRA.
- **CONTROL MEASURES**
- **IMMUNIZATION OF DOGS**: Mass vaccination of dog. All dog must receive Primary immunization – 3,4 months and booster dose at regular interval.
- **BPL inactivated nervous tissue vaccine**: Revaccination done after 6 month and every year subsequently
- **Modified live virus vaccine**: Booster every 3 years.

# CONTROL OF URBAN RABIES

- Cost effective approach is the elimination of stray dogs and ownerless dogs combined with mass immunization at least 80% of the area.
- Registration and licensing of all domestic dogs
- Restrain in public places.
- Immediate destructions of dogs and cats bitten by rabid animals.
- Quarantine for 6 month of imported dogs.
- Health education
- ORAL VACCINE: For the immunization of foxes.





# CONCLUSION

- It's a fatal disease, and dangerous public health problem.
- Mostly European countries are totally saved from this disease by practicing prevention measures.
- Public health education workshops should be organized to educate people about responsible pet ownership and routine veterinary care.
- Prevention can be by either by eliminating exposures to rabid animals Or by providing exposed persons with prompt local treatment of wounds combined with the administration of human rabies immune globulin and vaccine.
- Local governments should initiate and maintain effective programs to ensure vaccination of all dogs, cats, and ferrets and to remove strays.