

RABIES

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The Problem:

- Rabies free means no indigenously acquired human/ animal infection for 2 yrs.
- **World:** Australia, New Zealand, U.K., Ireland, Iceland, Taiwan, Cyprus, Japan, & Malta are "Rabies Free".
- Finland, Norway, Sweden also rabies free.
- Reliable data on **Rabies are not available** in many areas of the world, making it difficult to assess its full impact on human & animal health..

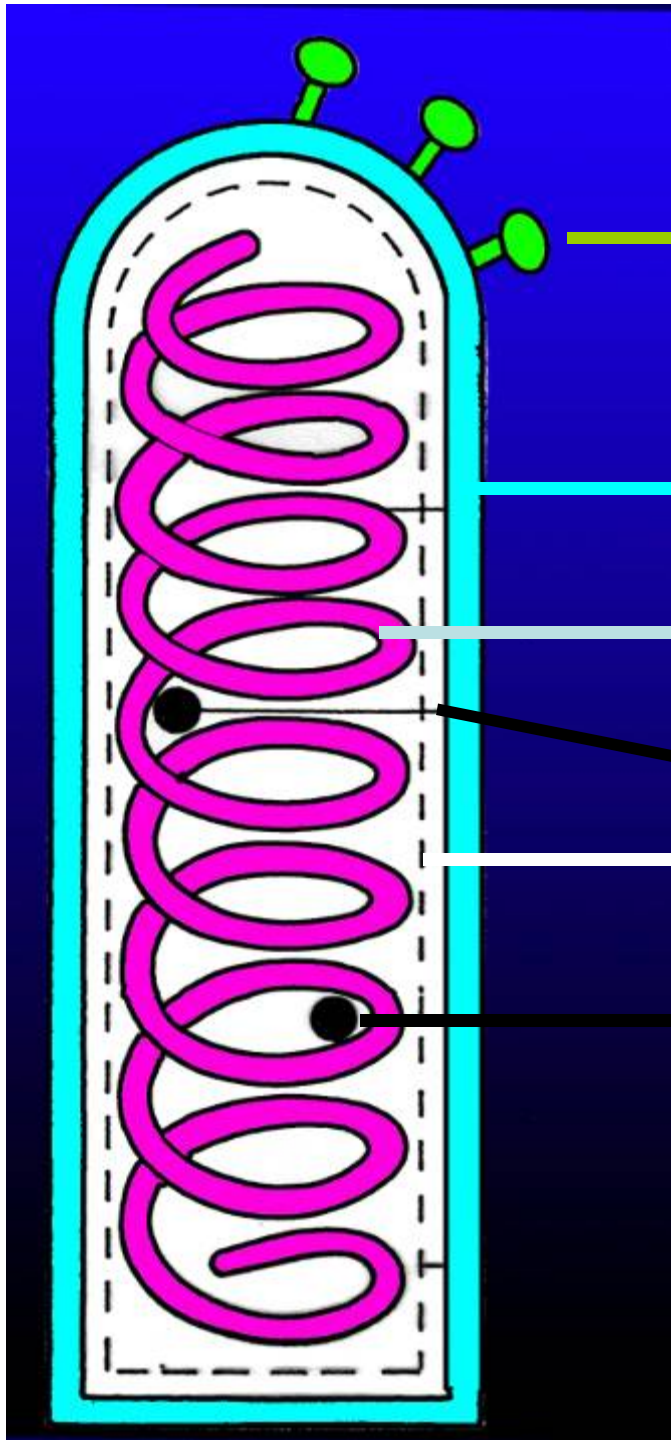
In India,

- Rabies occurs in **all the parts of the country with Exception of Lakshadweep, & Andman, Nicobar**
- **> 95 % cases are bitten by dogs.**
- The **dog population** in India - **25 million**, & most of them are not protected against rabies
- 96 % of human rabies cases are due to bites from Rabid dogs

Epidemiological determinants

Agent factors

- Causative agent (**Lyssavirus type 1**) a bullet shaped neurotropic enveloped, non-segmented RNA virus.
- It belongs to the family **Rhabdoviridae** — serotype 1 (Lyssavirus, type 1) & Serotype 2, 3 & 4 are *rabies related* but **antigenically distinct viruses**; they cause rabies like disease in man & animals .
- Rabies virus particles contain **2 distinct Antigen**, **major antigens a glycoprotein (G protein) antigen** from the virus membrane & **An internal (N) nucleoprotein antigen..**



Antigen from the virus membrane

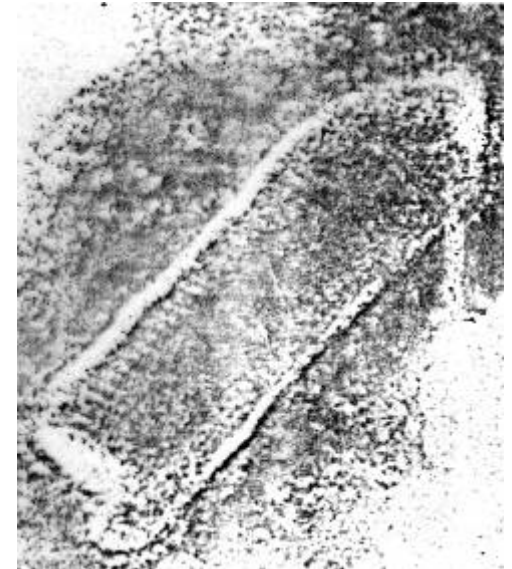
G: envelope glycoprotein
(spikes, trimmer, NT)

Lipid bilayer

N: nucleoprotein An internal
nucleo protein antigen
surrounding (-)ssRNA

M: matrix protein

Polymerase



130-240nm x 80nm

street virus & fixed virus.

- The virus recovered from naturally occurring cases of rabies is called **"street virus"**. It is pathogenic for all mammals & shows a long variable I.P. - **(20-60 days in dogs)..**

fixed virus

- Serial brain to brain passage of the street virus in **Rabbits modifies the virus** such that its **I.P. is reduced** until it becomes constant between **4-6 days**.
- Virus isolated at this stage is called a **fixed virus**.

- A "fixed" strain of virus defined as that has a **short, fixed & reproducible IP. (4-6 days)** when injected intracerebrally into suitable animals.
- It **does not form Negri bodies**. It no longer multiplies in extra-neural tissues..

RESERVOIRS OF INFECTION

- Rabies exists in 3 epidemiological forms :
 1. **urban rabies,**
 2. **Wild life (sylvatic) rabies &**
 3. **bat rabies.**

(1) *Urban rabies* : infection from wild life to domestic dogs results urban cycle which is maintained by the dog & is **responsible for 99% of human cases** in India.

A single rabid dog is capable of biting a large number of humans, animals ..

Wild - Fox



(b) Wild life rabies :

- Sylvatic form of rabies presents an intractable problem. It is an reservoir of infection. The wild life cycle is by the **jackal, fox, hyena & other wild life carriers which are the main reservoir & transmitters of rabies.**
- These animals maintain a **cycle amongst themselves** & transmit the infection to dogs & domestic animals. Man may contract rabies by wild life cycle of rabies..

South America



vampire bat

- **vampire bat**
- **Bovine losses from vampire transmitted rabies have been estimated at 5 Lacs to 1 million / year..**

(c) Bat rabies :

- In Brazil, Venezuela, Mexico, Trinidad, Tobago & parts of **U.S.A.** **vampire bat is an important host & vector of rabies.**
- These bats **feed on the blood** of animals & man. They can **transmit rabies to animals & humans.** **Rabies transmitted by the vampire bat it kill hundreds of thousands of cattle** annually.
- Humans are also affected especially when they sleep outdoors.
- **Rabid bats have been also found in Germany, Denmark and Holland ..**

Europe

bats

fox



Middle East

wolf



dog



North America



insectivorous bats



skunk

North America

fox



Raccoon



SOURCE OF INFECTION :

- The source of infection to man is the **saliva of rabid animals**. In dogs & cats, the virus may be present in the saliva for 3-4 days before the onset of C/F & during the course of illness till death .
- **The variability of the virus in saliva explains the fact why only about 50% of bites by proven rabid animals will result in rabies ..**

Mode of Transmission

- *Animal bites :*
- *Licks*
- *Aerosol*
- *Person —to —persons ..*

Transmission

- **Transmission** by bite of the infected animal. Even scratches by nails can transmit the infection as these are contaminated with saliva.
- Infection by aerosol in caves heavily contaminated with bat guano &
- In laboratory workers is reported.
- Corneal transplant from patients deceased from rabies is a rare but possible mode.
- Consumption of un-boiled milk of the rabid cattle is suspected to be a route of transmission.
Human to human transmission has also been reported..

Incubation Period

- In majority of cases **I.P.- 20-60 days.**
- However, it can be as **short as 5 days** & could be **several years.**
- **I.P.- is short if the bite is on head & face..**

Host Factors

- **Age and Sex:** All ages & both sexes are susceptible.
- **Occupation:**
 - **Veterinary staff,**
 - **Laboratory workers,**
 - **Dog-handlers, & hunters** are at a greater risk due to occupational exposure...

Pathogenesis

- At the site of introduction Rabies virus replicates in muscle or connective tissue cells
- It attaches to nerve endings & enters peripheral nerves. - *via* the **peripheral nerves towards the CNS**; most likely it "**ascends**" through the nerve .
- Following **infection of the CNS**, the **virus spreads centrifugally** in peripheral nerves to **many tissues**, including **skeletal & myocardial muscle**, **adrenal glands & skin**.
- The **salivary glands invasion** is crucial for the **transmission of the virus to another animal or human ..**

SIGNS & SYMPTOMS

- Itching, pain, or parasthesia at site of bite wound
- Fevers
- Myalgia
- Headache
- Irritability or depression
- Gastrointestinal upset
- Radiculopathy in bitten limb
- Proceeding to encephalopathy

C/F

- Rabies in man is called hydrophobia.
- The disease begins with **prodromal symptoms** such as headache, malaise, sore throat and slight fever lasting for 3-4 days.
- About 80% of patients complain of pain or tingling at the site of the bite. This is the only prodromal symptom which is specific ..

Aerophobia

- **Cold draught of air (sensory).**

Aerophobia (fear of air) may be present & is considered by some to be pathognomonic of rabies . It can be elicited by fanning a current of air across the face which causes **violent spasms of the pharyngeal & neck muscles**

...

C/F

- Examination may show **increased reflexes** and **muscle spasms** (motor) along with
- **Dilatation of the pupils &**
- **Increased perspiration,**
- **Salivation & Lachrimation** (sympathetic).
- **Mental changes** include fear of death, anger, irritability and depression..

hydrophobia

- The swallowing liquid become **unsuccessful**. At later stage the mere sight or sound of water may provoke spasm of the **muscles of deglutition**.
- This characteristic symptom of hydrophobia is **pathognomonic of rabies & is absent in animals...**

- The **duration of illness is 2 to 3 days**, but may be prolonged to **5-6 days** .
- The patient may **die abruptly** during one of the **convulsions** or may pass on to the **stage of paralysis & coma**.
- **Intensive care** may allow an occasional patient to survive. To date, **only 3 people** are on record who have been **survived** after rabies ..

Furious Rabies

Hydrophobia attack
(20 to 50% of patients)



Dump (paralytic) rabies (~20%)

Incubation Prodrome .1
 , Coma .2



- In paralytic form, the patient is conscious, & has Gullen-Barre like presentation.
- In addition, the patients have intact sensory function, fever, & urinary incontinence.
- Aerophobia & hydrophobia are seen in most of the cases.
- To date there are 7 cases reported to have survived the attack of the disease..

In Animals: (Dogs) :

- Two types of presentation have been described *Furious Rabies* & *Dumb Rabies*.
- In furious rabies, the animal exhibits **behavioural changes** (like irritability, aggressiveness, combat-iveness, biting without provocation, and biting anything), **Running amuck** (tendency to run away from home), **hoarseness** (change in voice) & **excessive salivation..**

In paralytic stage

- In paralytic stage, paralysis of limbs and jaws sets in. In dumb rabies the signs of excitation/ irritation are absent. Paralytic signs predominate. Animal rarely survives for more than a week after the onset of disease. .

Laboratory Diagnosis:

- **In Man:** Demonstration of antibodies in CSF is possible.
- Antigen detection at the site of the wound by immuno-florescence of skin biopsy,
- DOT BLOT hybridization, and RT-PCR are some other tests..

In Animals:

- The head of the animal is cut & sent to the laboratory in ice-packed and airtight container.
- Brain can be sent in 50% glycerol-saline. Fluores-cent antibody test can establish the diagnosis within few hours. Demonstration of Negri Bodies in brain is now considered to be of historic importance only.
- Other tests include Mouse inoculation test and detection of viral antigen in the corneal impressions..

MANAGEMENT OF ANIMAL BITES:

- **1. Local treatment,**
- **2. Anti-rabies vaccination,**
- **3. Passive immunization, and**
- **4. Advice to patient..**

Treatment - Isolation

- There is **no specific treatment for rabies.**
- Case management includes the following procedure :
- Patient should be **isolated in a quiet room**
- protected as far as possible from external stimuli such as
- bright light,
- noise or cold draughts which may precipitate spasms or convulsions..

LOCAL TREATMENT:

- The local treatment of bites & scratches consists of vigorous **washing with soap & water**. This is followed by **wash with 70% alcohol, & tincture, or 0.01% of iodine**.
- If possible, **suturing should be avoided** for 7 days. If it is absolutely necessary, it should be done with minimum sutures &
- wound must be infiltrated with anti-serum or HRIG.
- Antibiotic treatment can be given after the local treatment is completed..

Treatment

For preventing nerve invasion



- Wound treatment –
- Washing – soap & water
- wash with 70% alcohol & tincture, or 0.01% of iodine.
- suturing should be avoided
- Antibiotic treatment ..

Human Rabies Immunoglobulin



- **Human Rabies Immunoglobulin (HRIG)**
- **around the wound site and injected intramuscularly**
- **- Equine Rabies Immunoglobulin (ERIG) (anaphylaxis)..**

PASSIVE IMMUNIZATION

Human Rabies Immunoglobulin (HRIG) : 20 IU/kg body wt.
Maximum of 1500 IU

Equine Rabies Immunoglobulin (ERIG) : 40 IU/kg body wt.
Maximum of 3000 IU

ERIG must be administered only after the Test dose.

Test dose (ERIG)

Follow the Manufacturer Guidelines or Inject 0.1 ml of 1:10 dilution of the ERIG in normal saline, Intra Dermally over flexor aspect of forearm.

Observe for : Wheal, Erythema, Induration, Itching, Tachycardia,
Fall in Blood Pressure, Feeble Pulse.

Positive test reaction: Induration >10mm with or without constitutional symptoms.

Treatment

- **Relieve anxiety & pain by use of sedatives**
Morphin in doses of 30-45 mg may be given repeatedly.
- (c) If spastic muscular contractions are present use drugs with curare—like action.
- (d) Ensure hydration & diuresis.
- (e) Intensive therapy in the form of respiratory & cardiac support may be given.

ADVICE TO PATIENT:

- The patient should **avoid Strenuous work & Alcohol** till treatment is on.
- **Steroids** & other immuno-suppressants should be avoided.
- Patient should also be explained about the need for taking the **entire course** of vaccination..

EDUCATION OF PET OWNERS

- **Get your pet regularly and periodically examined by a qualified veterinarian.**
- **Get your pet vaccinated at 3 months of age & again 1 month later; B.D. must be given every yr.**
- **Obtain a Municipal License, put a collar and keep your pet under leash in public places.**
- **Do not allow your pet to come in contact with community / street dogs / cats or other animals. Inform the Municipal authorities about sick / mad dogs.**
- **Take t/t even after pet dog bite including pups.**

Reservoir Control

Domestic animals

- **Vaccination programs for all dogs and cats.**
- **Removal of strays & unwanted animals.**
- **Animal Birth Control (ABC) for stray dogs.**
- **Contraceptive vaccines for control of dog population ..**

- **Classification
of
Exposures**

- WHO has recommended following classification of wounds for PEP.
- **Category I:** No treatment in the absence of exposure, if history reliable:
 - touching or feeding of animals
 - licks on intact skin
- **Category II:** Vaccine and disinfection for minor exposure:
 - nibbling of uncovered skin
 - minor scratches or abrasions without bleeding
 - licks on broken skin
- **Category III:** Wound treatment plus rabies immunoglobulins plus vaccine for all severe exposures:
 - single or multiple Trans-dermal bites or scratches
 - contamination of mucous membrane with saliva (i.e. licks) ..

Classification of Exposures

Class I

(slight Risk)

licks on healthy unbroken skin

**consumption of unboiled milk of the
suspected animal**

scratches without oozing of blood

licks on fresh cuts

scratches with oozing of blood ..

Class II

(moderate risk)

- **Licks On Fresh Cuts**
 - **Scratch With Oozing Of Blood**
 - **All Bites Except Those On Head, Neck, Face ,Palms & Fingers**
 - **Minor Wounds Less Than 5 In Number**
- ..**

Class III (severe risk)

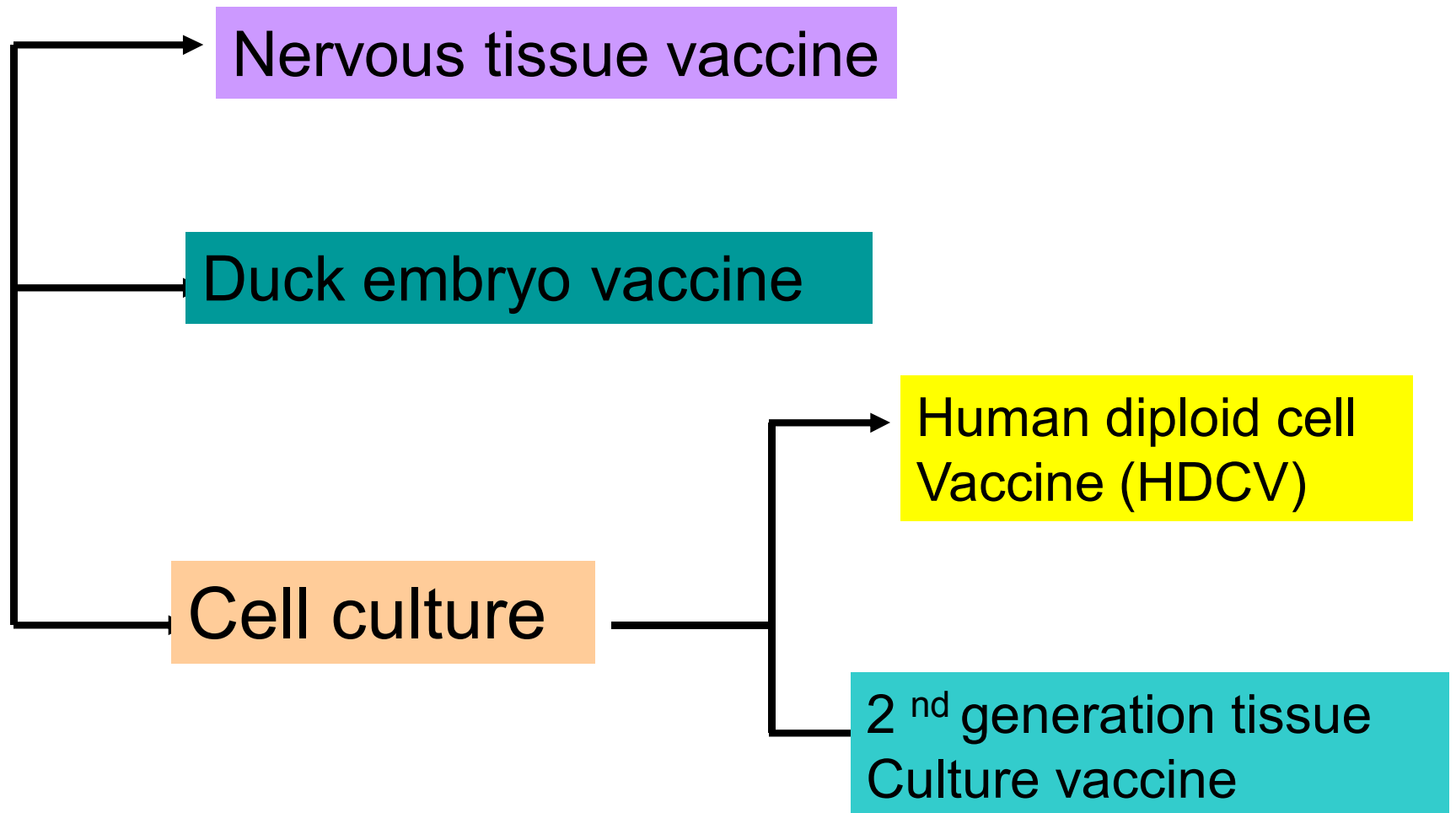
- **All Bites Or Scratches With Oozing Of Blood On Head, Neck,, Face , Palms & Fingers**
- **Lacerated Wounds On any Part the Body.**
- **Multiple Wounds 5 or More In Number**
- **Bites From wild Animals ..**

CATEGORY III EXPOSURES

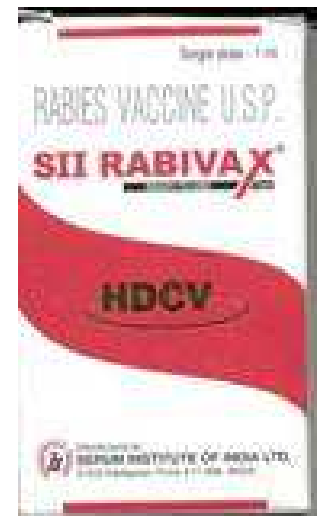
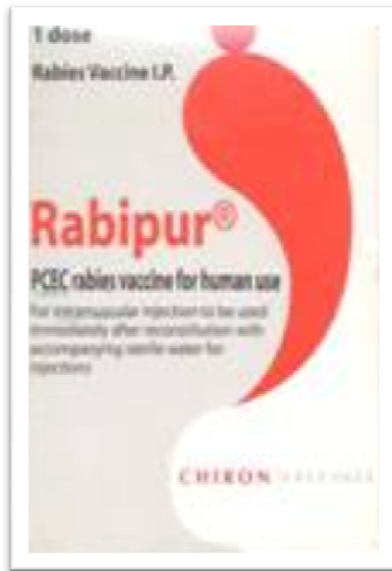


- **Anti-Rabies
Vaccine**

Anti-Rabies Vaccine



MODERN VACCINES AVAILABLE IN INDIA (March 2006)



Dosage schedule of BPL inactivated vaccine per day (Recommended by CRI, Kasauli)

Class of T / t	adults	Children (Wt $\leq$ 30 kg)	Duration of t/t	Booster
Class I	2 ml	2 ml	7 days	Nil
Class II	5 ml	2 ml	10 days	3 wks later 1 booster only
class III	5 ml	2 ml	10 days	-1 st on 7 th day - 2 nd on $\geq$ 2 wks of 10 th injection

3. Cell culture vaccine

A. Human Diploid Cell Vaccine (HDCV)

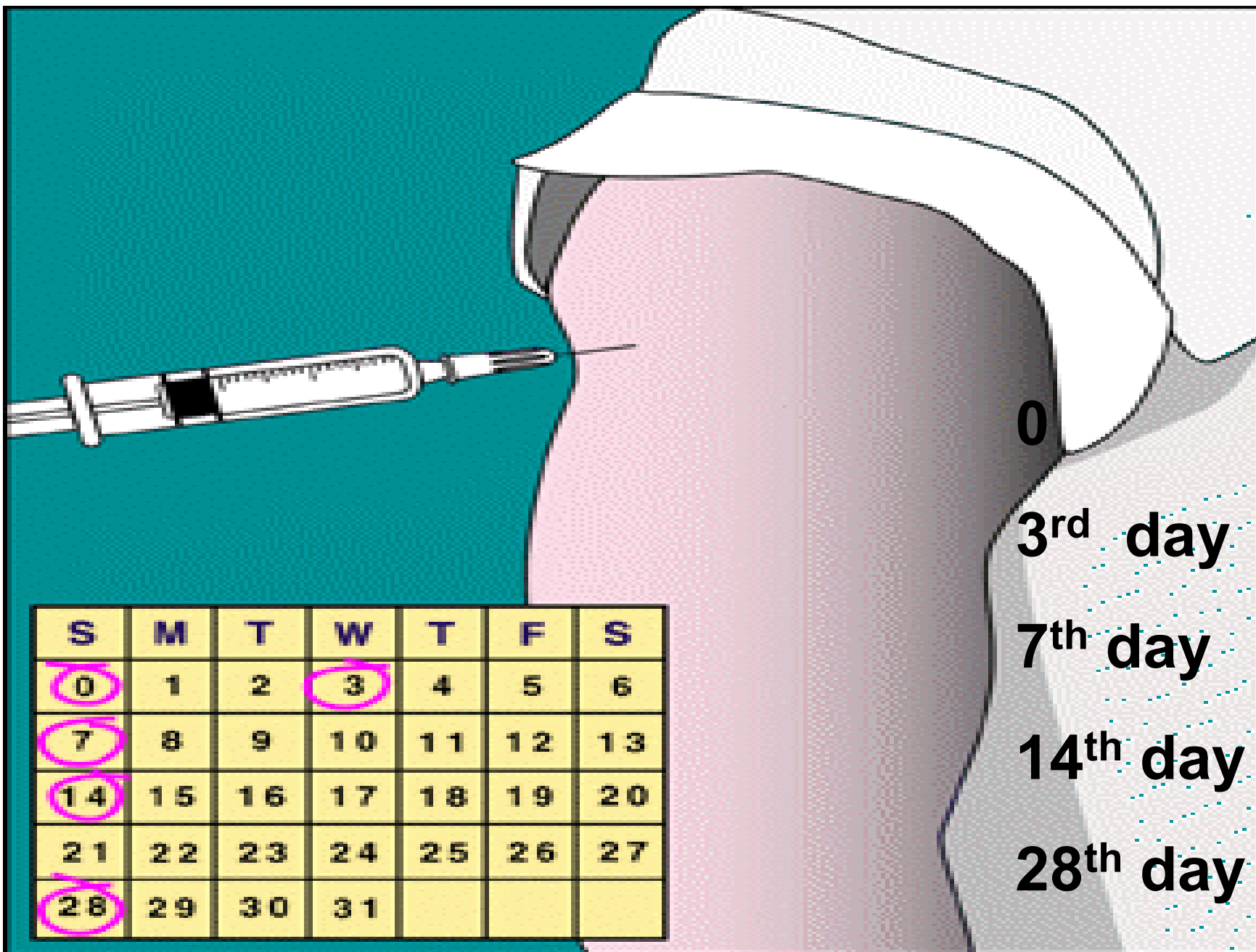
B. Second Generation Tissue Culture Vaccine (non—human origin)

A. Human Diploid Cell Vaccine (HDCV)

**Propagation Of 'Fixed Virus' On Human
`Diploid Fibroblast Cell**

Safe & Highly Potent

Use For Pre & Post Exposure.

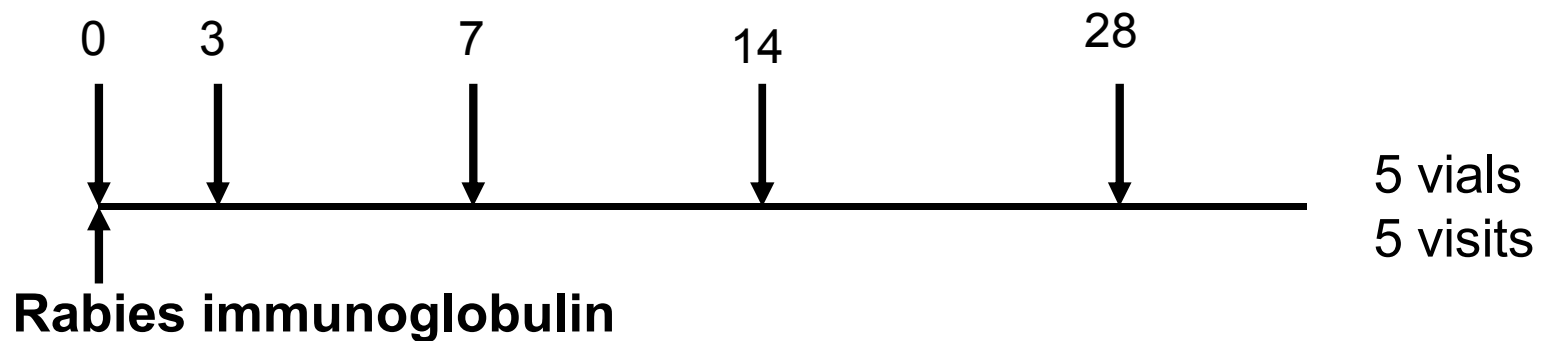


Intramuscular schedules

a. Intramuscular schedules

6 doses (1 ml each) on days 0, 3, 7, 14 & 28 & a booster on 90 days.

Intramuscular on deltoid



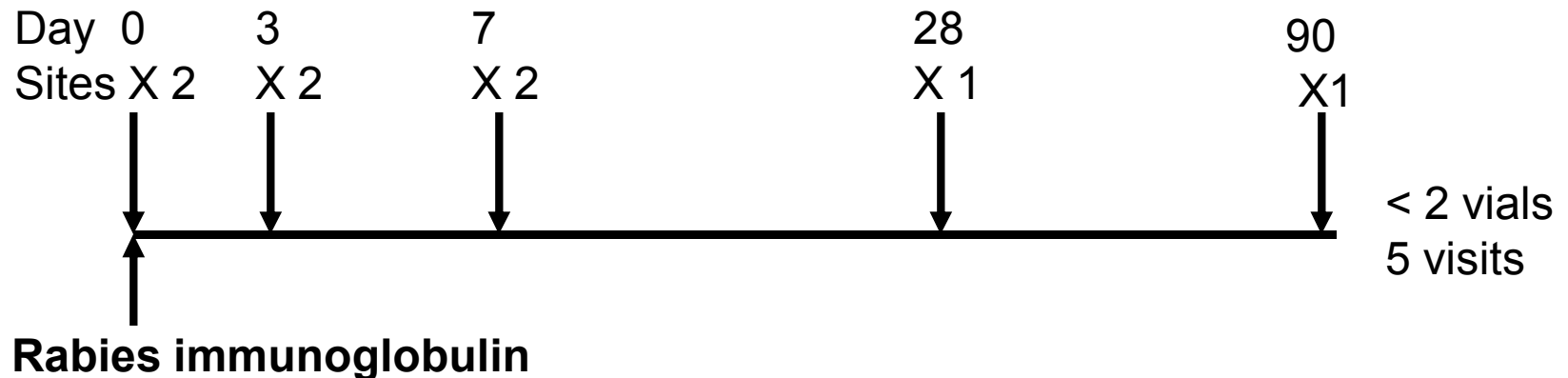
Intradermal Schedules

- **Intradermal Schedules**

- a. **2 –site intradermal schedules- (2-2-2-0-1-1)**

for use with purified vero cell vaccine (PVRV) , purified primary chick embryo cell vaccine (PCECV) and purified duck embryo vaccine (PDEV)

Dose – one id dose= one fifth of im dose (1.0 or 0.5 ml) id per site



Re-exposure:

- 3 IM injections of HDCV are indicated on days 0, 3, and 7, if the bite is severe.
- If bite is not severe, only two doses on days 0 and 3 are indicated.

Pre-exposure Prophylaxis:

- This is indicated
- Those who have a risk of exposure to rabies virus
- occupation. These include veterinarians,
- trappers, dogcatchers, & -oratory workers working with rabies virus.
- **cell culture vaccines.** These are given IM in 1-ml dose or intradermally 0,1ml dose, on the days 0, 7 and 28. Boosters are indicated every 2 years as long as risk of exposure exists.

PASSIVE IMMUNIZATION

WHO studies and some studies in Iran have showed efficacy of combined use of vaccine and anti-rabies serum (ARS).

Aim is to offer immediate protection that can protect till the immunity by active immunization reaches protective level.

Equine Anti-Rabies serum:

- **(EARS)** This is given
- in the dose of 40 IU / Kg body weight. (Maximum 3000 units).
- Half the serum is infiltrated locally. If the area of bite is large, the serum can be diluted with normal saline
- ARS requires prior sensitivity testing. Serum sickness & anaphylaxis are the major adverse reactions with ARS.

Human Rabies Immuno-Globulin

- **(HRIG):** This is administered in a single dose of 20 units / kg body weight.
- As much of HRIG as possible is injected around the wound & reminder if any, is injected IM.
- HRIG does not require prior sensitivity testing.

THANK YOU