एपिसोड 23

स्वास्थ्य विभाग की पहल

शुक्रवार की शाम, डाक्टर्स के नाम

प्रदेश के जाने-माने चिकित्सकों से सीधे जुड़ें और उनके अनुभवों का लाभ उठाएँ

दिनांक : 16 अगस्त, 2024 | समय : सांय 6:00 बजे से 7:30 बजे तक

— वेबकास्ट का विषय —

रैबीज़ प्रोफिलैक्सिस एंड एनिमल बाइट मैनेजमेंट

वक्ता

डॉ. मनीष कुमार सिंह

(MD (SPM-Gold Medalist KGMU), PGDHHM
FIAPSM, FIPHA, FIMSA, FIMAAMS, MAMS)

एसोशिएट प्रोफेसर, सामुदायिक चिकित्सा विभाग,
डॉ. राम मनोहर लोहिया आयुर्विज्ञान संस्थान, लखनऊ

आयोजक

राज्य स्वास्थ्य एवं परिवार कल्याण संस्थान (SIHFW)
इंदिरा नगर, लखनऊ, उत्तर प्रदेश

YouTube LIVE STREAMING

यह कार्यक्रम स्वास्थ्य विभाग और राज्य स्वास्थ्य एवं परिवार कल्याण संस्थान (SIHFW), उत्तर प्रदेश की पहल पर उत्तर प्रदेश टेक्निकल सपोर्ट यूनिट (UPTSU) के सहयोग से हो रहा है।

Principal Secretary, Medical Health & Family Welfare, U.P.
Shri Partha Sarthi Sen Sharma

Director Administration & Director, SIHFW
Shri Shiv Sahay Awasthi

Rabies Prophylaxis & Animal Bite Management

Dr. Manish Kumar Singh

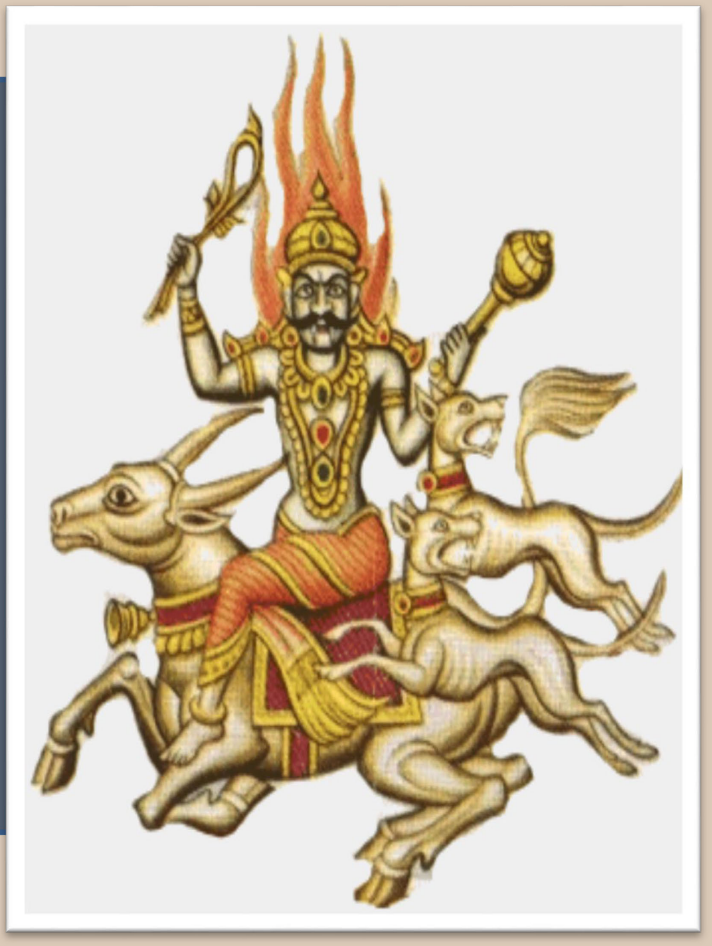
Associate Professor

Department of Community Medicine

Dr. RMLIMS, Lucknow, UP

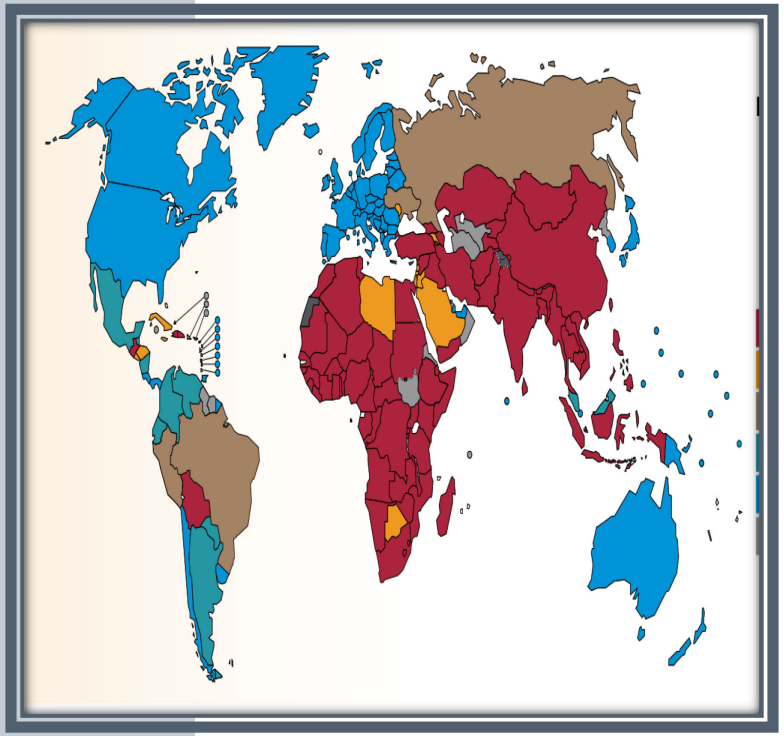
Historical Perspective

- Rabies is a 100% fatal viral zoonotic disease.
- The Word “Rabies” has its origin in Sanskrit, ‘Rabhas’ means **“to do violence”.**
- Causative agent is Lyssa Virus, of Rhabdo virus family [named after Lyssa, the Greek spirit of madness, frenzy and rage]

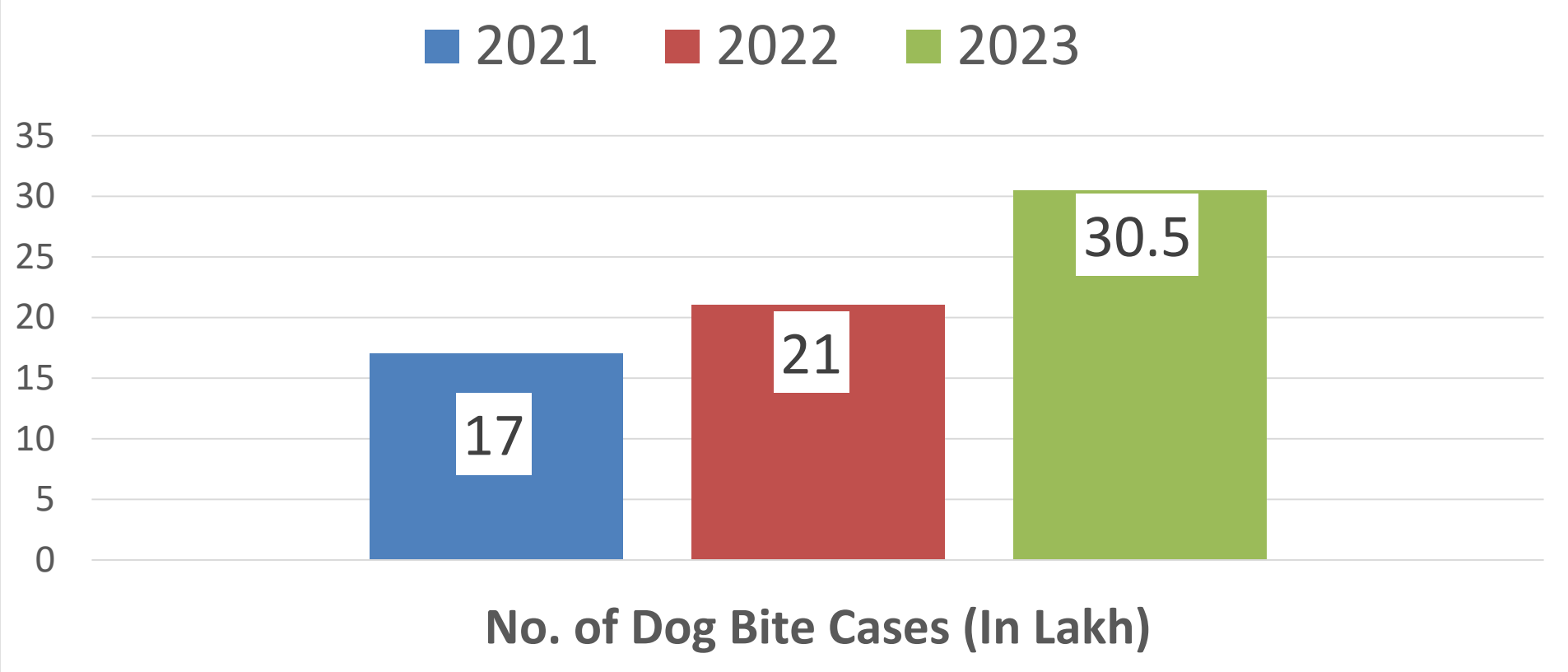


Burden of Rabies

- It is estimated to cause 59 000 human deaths annually. 1 person every 9 minutes of every day
- Asia (59.6%) and Africa(36.4%) togeather contribute about 95% of human deaths
- India accounts for 60% of rabies deaths in Asia and 35% of deaths globally (About 20,000)
- 40% of people who are bitten by suspect rabid animals are children under 15 years of age

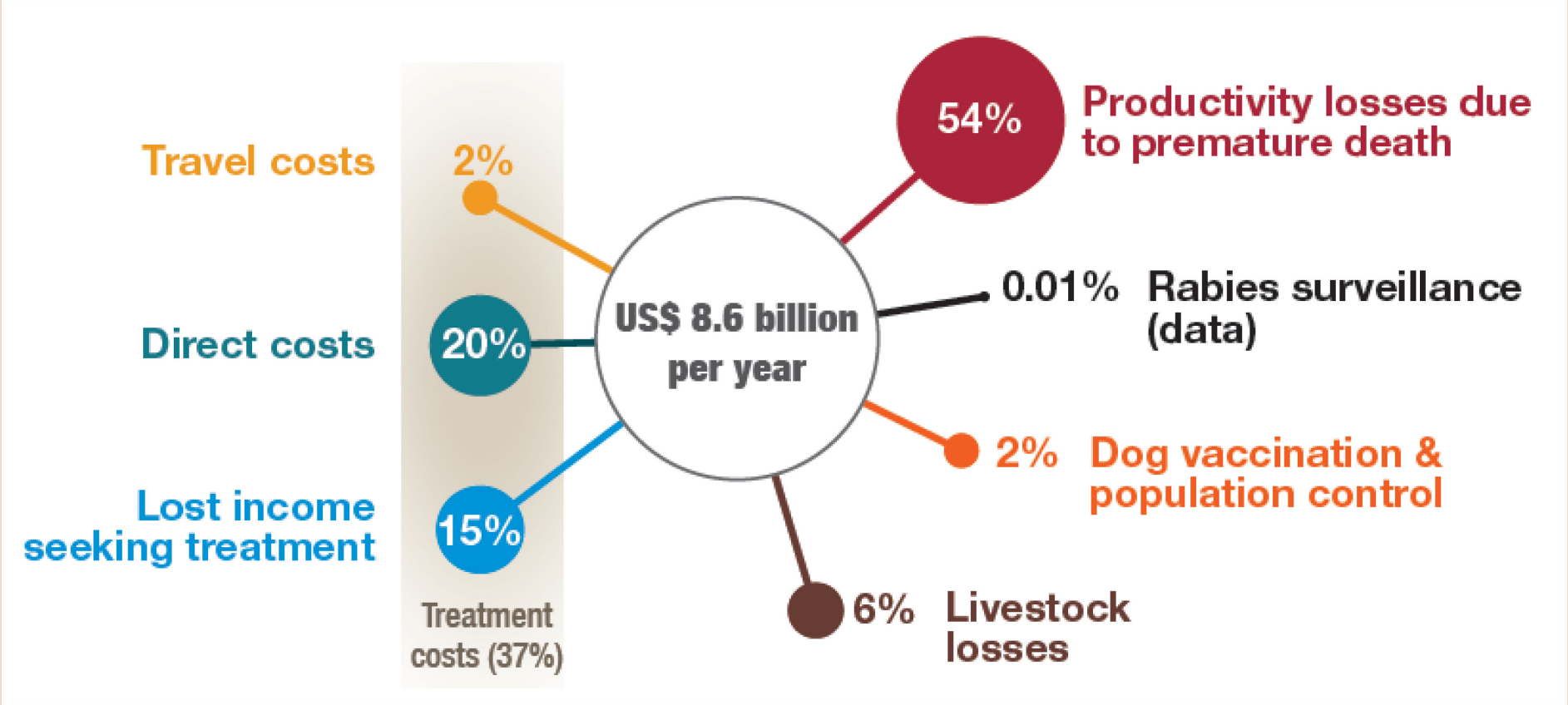


Trends in Dog Bite Cases -IDSP



2023 -Dog bite cases in India have seen a 45 % year-on-year increase. (i.e. 6 Dog bite cases every minute)

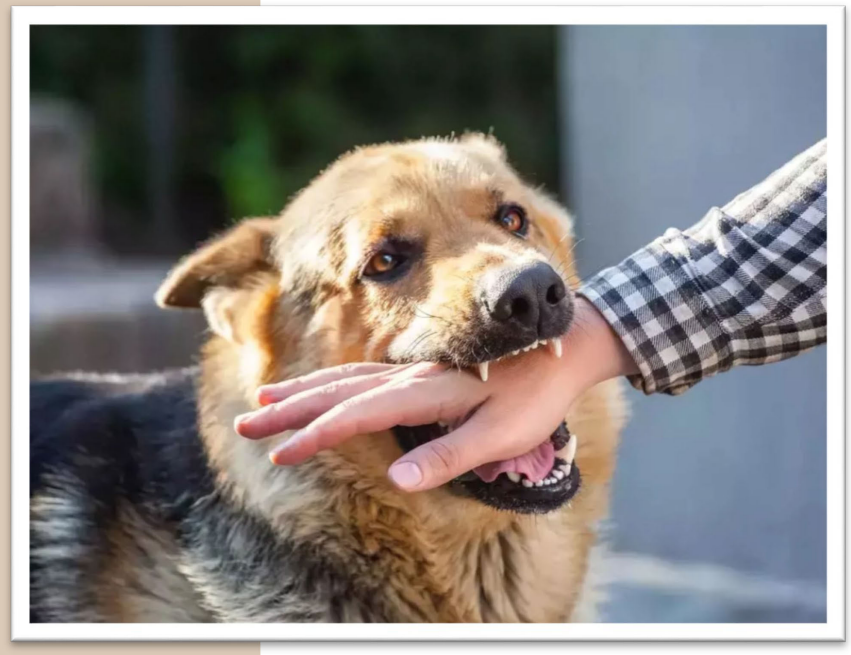
Global Economic Burden of Rabies



India –In 2023, About 46.5 Lakh shots of Anti Rabies Vaccine were administered & 286 deaths reported (IDSP Data)

Routes of Transmission

- Transdermal bite or scratch by infected animal
- Direct contact of infectious material, usually saliva with victim's mucosa or fresh skin lesions
- Rarely by inhalation of virus containing aerosol or via infected organ transplant
- Human-to-human transmission [Theoretically possible] but never been confirmed.



Which animals transmit rabies?

&

Which do not??

Animals Transmitting Rabies in India

Domestic :-

- Dogs & Cats

Wild :-

- Foxes & Jackals
- Monkeys
- Mongoose
- Bears

Peridomestic :-

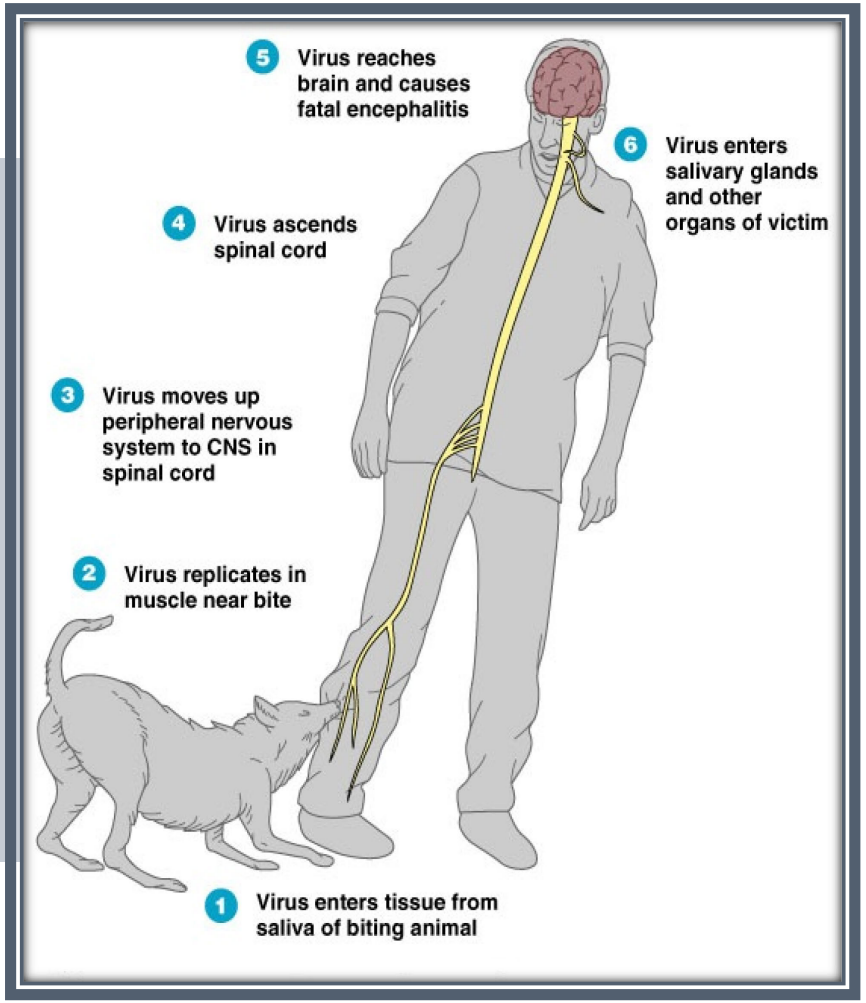
- Cows & Buffaloes
- Sheep & Goats
- Pigs
- Donkeys
- Horses
- Camels

Not reported :-

- Bats*
- Rodents*
- Birds
- Squirrel

Incubation Period of Rabies (in Human)

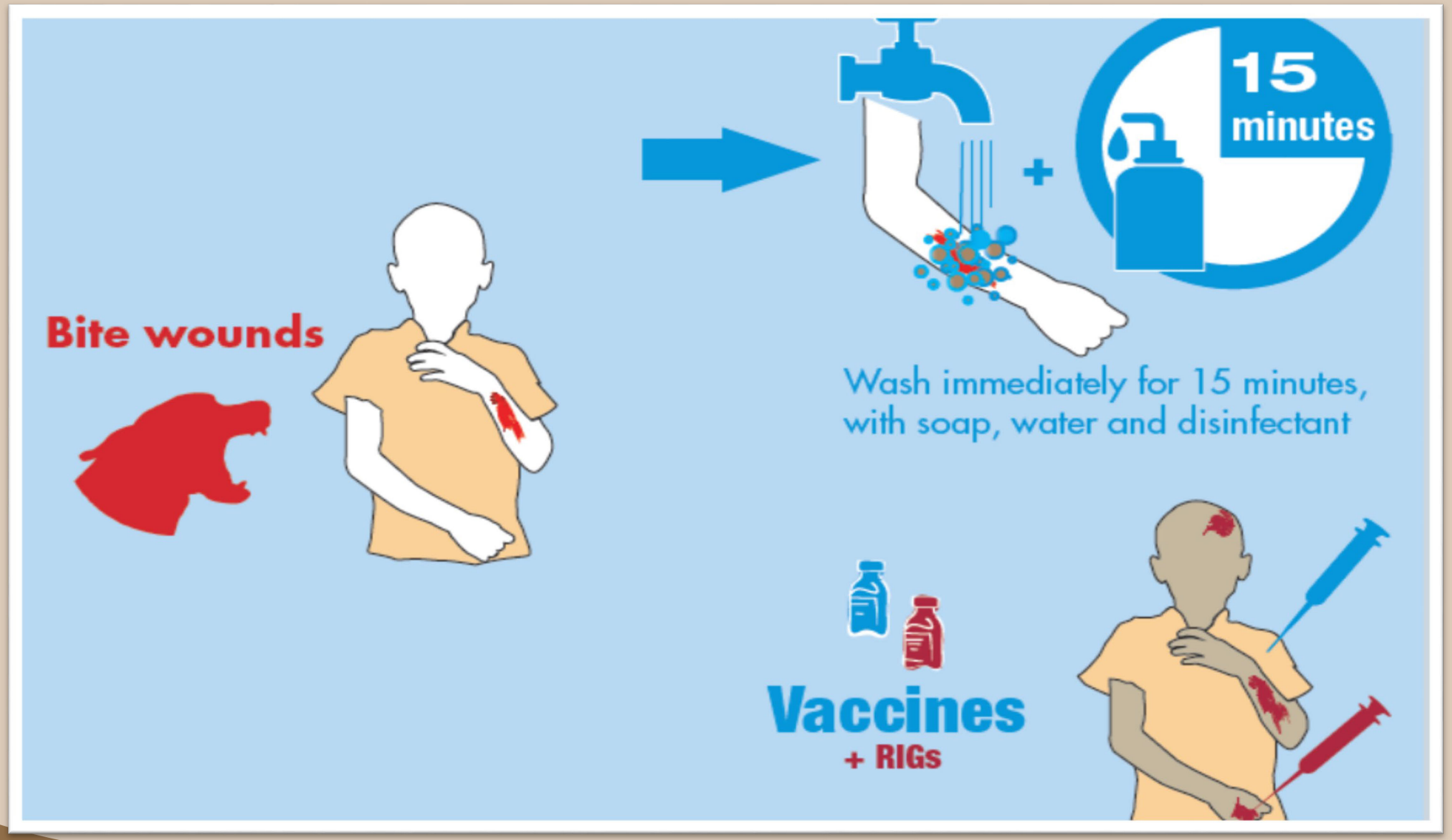
- Highly variable - Ranges between **6 days to 6 years**
- Average **: 30 – 90 days**
- Bites on head or face have shorter Incubation Period -upto 1 month
- Bites on extremities have longer Incubation Period - upto 3 months



Strategies for Prevention of Rabies

- Dog vaccination -To interrupt virus transmission to humans
- Human vaccination
  - Pre exposure
  - Post-exposure

Post Exposure Prophylaxis-PEP



PEP -STEP 1- Local Wound Treatment

DO'S

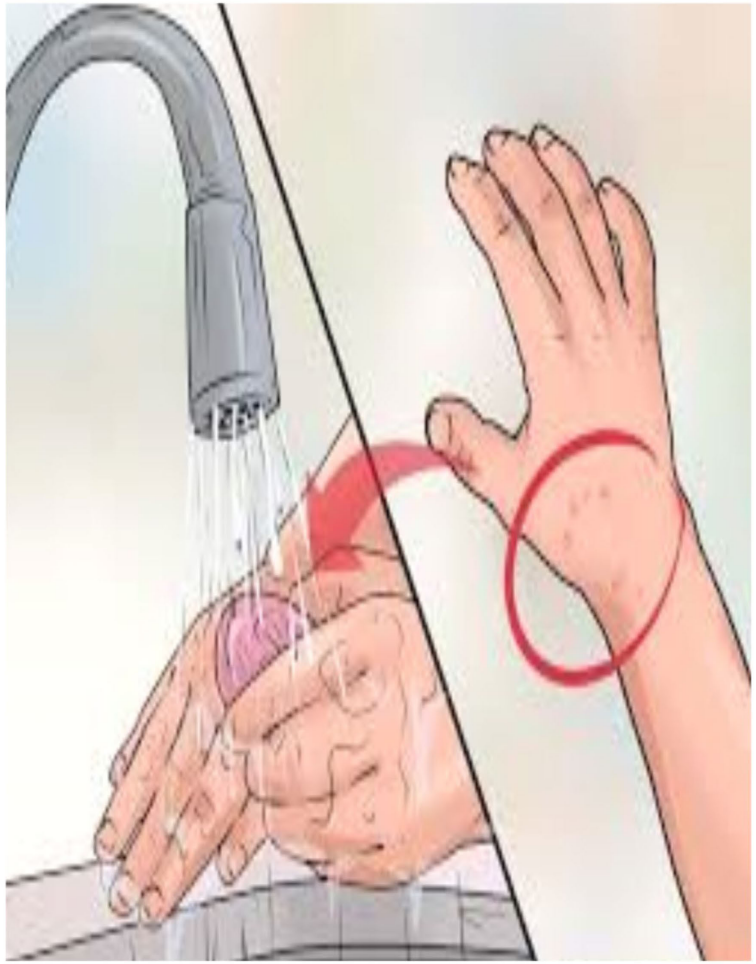
MECHANICAL: Wash under Running tap water

CHEMICAL: Soap (Preferably detergent)

Disinfectants - Povidone Iodine, Spirit, antiseptics

BIOLOGICAL: Infiltrate immunoglobulins/Monoclonal Antibodies

Avoid Suturing. Only if essential 1 - 2 loose sutures after administration of RIGs.



PEP -STEP 1- Local Wound Treatment

DON'TS

- **Don’t apply irritants viz. soil, chilies, oil etc.**
- **Don’t cauterize**
- **Don’t touch the wound with bare hands**

PEP-STEP 2: Categorisation of Exposure

Category I

- Licks on unbroken skin
- Touching/ feeding animals

Category II

- Nibble, cuts, scratches without oozing of blood

Category III

- Licks on mucous membrane or broken skin
- Single or Multiple bites with breach of skin and bleeding

CATEGORY 3 EXPOSURE

PEP-STEP 3 : Decision on Treatment

Category I	• Counsel & Wash the area
Category II	• Local Rx of wounds • Anti rabies vaccine
Category III	• Local Rx of wounds • Anti rabies vaccine • RIG or Monoclonal Antibody

PEP-STEP 4: **Administering ARV-** (Intradermal Regimen)

- Updated Thai regimen–2 site regimen **2- 2- 2- 0- 2** [Days 0, 3, 7, _ ,28]
- Day "0" is date of administration of 1st Dose of ARV
- Dose - 0.1ml at each site [Total of 0.2 ml administered on each day.]
- Site: **Upper arm over each Deltoid or Anterolateral aspect of thigh**

- ✓ **Only the ARV (lyophilized vaccine along with the diluent of specified volume) approved by DCGI for ID administration should be used for ID route**
- ✓ **Every batch of ARV must have minimum potency of 2.5IU per IM dose, irrespective of whether administered by IM or ID**

Intra Dermal Regimens for PEP- Advantage

- Cost effective.
- Less number of visit
- Studies in India confirm safety efficacy and feasibility.
- Notified by DCGI for use in India. (February 2006)

*Animal bite victims on Chloroquine therapy and immunosuppressed should be given ARV by intramuscular route.

PEP-STEP 4 : Administering ARV-Intramuscular Regimen

- Essen regimen – 5 doses on days 0, 3, 7, 14, 28 (also k/a – 1-1-1-1-1 regimen)
- Day 0 (zero) is the date of the administration of the first dose of vaccine
- Dose =1 ml
- Site: Deltoid / Anterolateral aspect of mid thigh (children).

Never administer ARV in Gluteal region

Important Precautions

- Use aseptic technique to withdraw the dose
- Store in a refrigerator at 2^0C to 8^0C
- Reconstituted vaccines -Use as soon as possible or within 6 to 8 hours, if kept at 2^0C to 8^0C.
- Vaccine dosage and number of injections is same for all ages
- Do not rub the injection site, Do not apply anything

Scenario For Discussion

SCENARIO -1

Sonu a 7 year old boy, son of Mr Arun was chased by a neighbour's dog while playing and had scratches on the fore hand. Mr Arun is very worried and talks to Mr Sumeet, his neighbour.

Mr Sumeet tells him that there is nothing to worry. He has his dog vaccinated fully. Even his daughter Rani had a similar scratch last month ?

Mr Arup seeks your opinion as a specialist ?

How should this case be managed ?

PEP-STEP 4B : **Administering Immunoglobulin**

- **Equine RIG (ERIG) dose** : 40 IU per kg body weight
  - ERIG produced in India contains 300 IU per ml
- **Human RIG (HRIG) dose** : 20 IU per kg body weight
  - HRIG is available in concentration of 150 IU per ml.

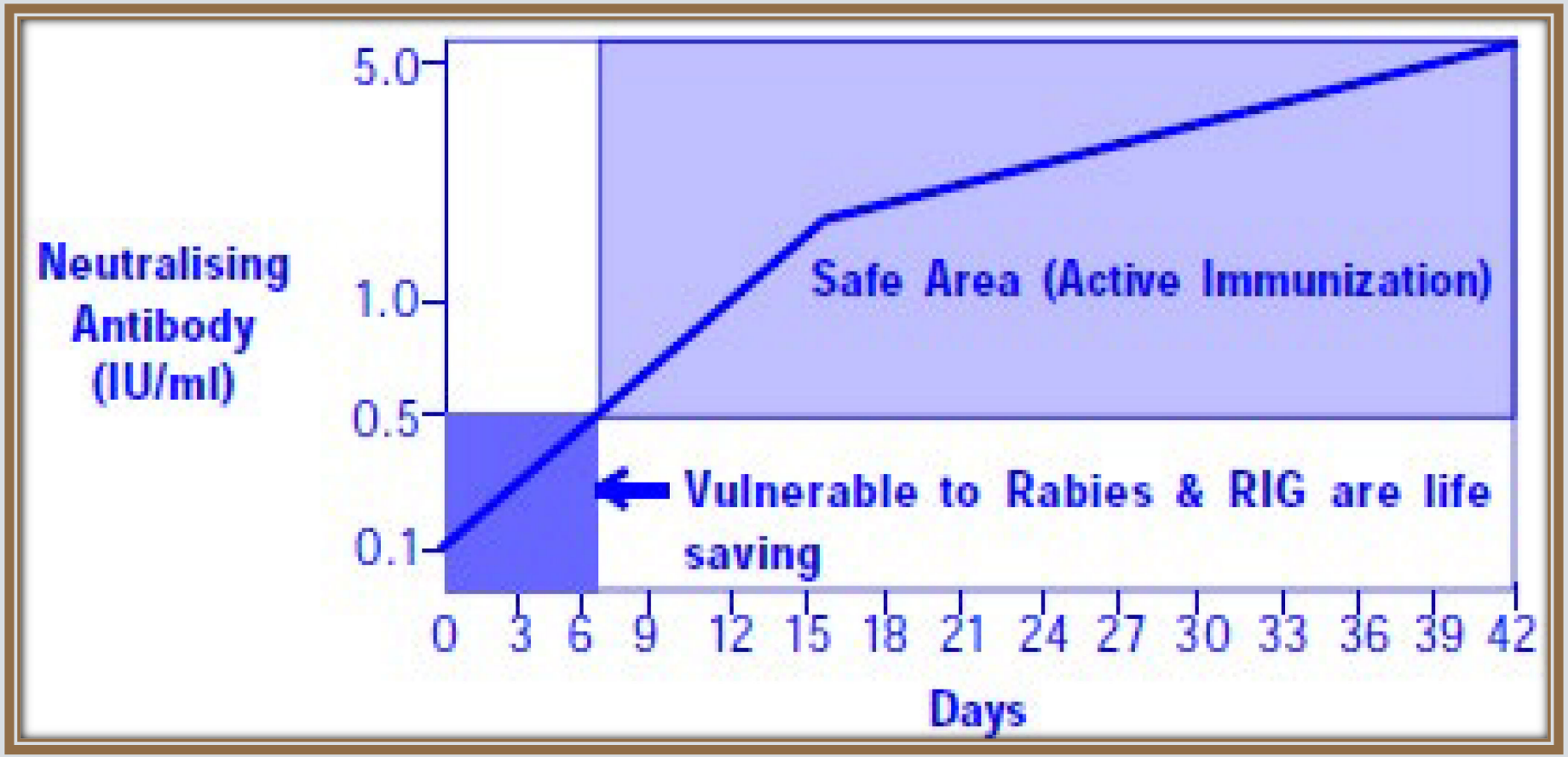
ERIG as per WHO does not require a sensitivity test before administration

Test dose (ERIG)- Recommended by some manufacturers

0.1 ml of 1:10 dilution of the serum in normal saline Intradermal over flexor aspect of forearm or as per Manufacturer guidelines.

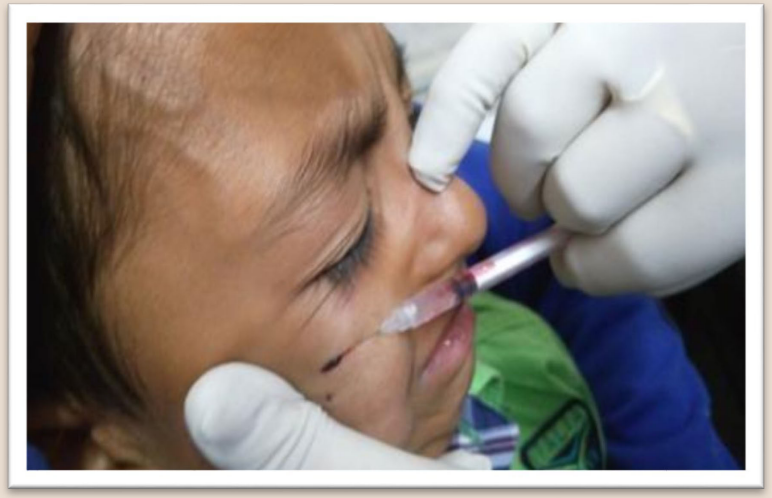
Observe for : Wheal, Erythema, Induration, Itching, Tachycardia, Fall in Blood Pressure, Feeble Pulse.

Why Rabies Immunoglobulin ?



RIG : Infiltration in wounds

- ✓ Bring RIG to room temperature (25ºC to 30ºC) before administration
- ✓ Infiltrate as much as anatomically feasible into all wounds and around the wounds; remaining if any SHOULD NOT be given Intra Muscularly. Never be given Intravenously
- ✓ If RIGs is insufficient (by volume) dilute it with sterile normal saline (upto equal volume).
- ✓ Not required in cases that have received complete PEP or PrEP
- ✓ Multiple needle injections into the wound(s) should be avoided
- ✓ ERIG are very safe [Rare occurrence of anaphylactic shock - 1/150,000]. If anaphylactic reactions occur- Give Adrenalin (subcutaneously or IM)
  - Adults -0.5 ml of 0.1 % solution (1 in 1000, 1mg/ml) & Children 0.01ml/kg body weight



Scenario For Discussion

SCENARIO 2

Mohan, 10 year old boy from Village **Rudauli** from Barabanki was bitten by a street dog in the village while returning from school. There was bleeding. His parents work as labourers. They went to a nearby physician who gave him 1 dose of Anti Rabies Vaccine in the left anterolateral part of midthigh and asked them to come back after 3 days for another dose. Mohan took 2 doses , but his parents being from a poor socioeconomic status, could not afford another dose and consulted the ANM. Who asked them to show at the CHC.

You being the CHC physician, How will you manage this case?

PEP-STEP 5 : **Medical advice to Vaccinee**

- Counseling to minimize emotional & physical stress
- Avoid immune suppressants (Steroids, anti- malarial) if possible.
- Avoid consumption of alcohol during course of treatment.
- Complete the course of vaccination

Should we observe the animal?

- Valid only for dogs and cats
- Start treatment and observe for 10 days
- Modify PEP in case of IM Regimen (ID Route complete the regimen irrespective of status of animal)

Scenario For Discussion

SCENARIO 3

Mr Ramesh and his family were going out for a vacation and asked their neighbours Mr Ghosh to feed their pet in their absence. They will be back in 15 days. Srishti, 19 year old girl of Mr Ramesh is very fond of the dog and agreed to feed him. One day while feeding the dog he scratched on her hand.

Mr Ramesh was worried and asked his neighbour regarding the vaccination status of the dog, who convinced him that the dog was perfectly vaccinated

Mr. Ramesh showed to a doctor at a government hospital, who advised intradermal schedule of vaccination. On her 3rd Visit, Srishti informs the doctor that the dog is perfectly fine and there is no change in behaviour

What would you advice on further course?

Management of Re-exposure

- Proper wound toilet
- No RIG recommended
- One site IM or ID - 2 boosters (Day 0 & Day 3)*
- All incomplete/partial vaccinations - Treat as fresh case
- Re-exposure following PEP with NTV, Vaccine of unproven potency, Incomplete course of PEP or PrEP – Treat as fresh case

Scenario For Discussion

Scenario 4

Rani a 32 year pregnant women in her 2nd Trimester is bitten by a street dog. She shows herself at the Infectious disease hospital. Rani was bitten in her childhood by a dog and she had received the complete course of vaccine then.

What advice you would give her ?

Scenario For Discussion

Scenario 5

Ravi and his friend's had gone for camping to Dhanaulti hills. Ravi had a rodent bite. He was very tense and consulted you for advice ?

What will you advise him ?

Rabies Monoclonal Antibody

- Monoclonal antibodies are immunoglobulins that have a high degree of specificity (mono-specificity) for an antigen or epitope.
- Monoclonal antibodies are typically derived from a clonal expansion of antibody producing human plasma cell
- To be used in combination with rabies vaccine and injected at sites separate from the rabies vaccine for PEP.

As per WHO position paper on Rabies 2018, if available use of monoclonal antibody instead of RIG is preferred.

Available online at www.sciencedirect.com
ScienceDirect
Vaccine 25 (2007) 2800–2810
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www.elsevier.com/locate/vaccine

Identification and characterization of a human monoclonal antibody that potently neutralizes a broad panel of rabies virus isolates☆

Susan E. Sloan[a], Cathleen Hanlon[b], William Weldon[b], Michael Niezgoda[b], Jesse Blanton[b], Josh Self[b], Kirk J. Rowley[a], Robert B. Mandell[a,1], Gregory J. Babcock[a], William D. Thomas Jr.[a], Charles E. Rupprecht[b], Donna M. Ambrosino[a,*]

[a] *Massachusetts Biologic Laboratories, University of Massachusetts Medical School, 305 South Street, Jamaica Plain, MA 02130, United States*
[b] *Division of Viral and Rickettsial Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road, NE, MS G33, Atlanta, GA 30333, United States*

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Abstract

Rabies is a zoonosis that results in millions of human exposures worldwide each year. Human monoclonal antibodies (HuMAbs) that neutralize rabies virus may represent one viable strategy for post-exposure prophylaxis in humans, and have many advantages over current human or equine rabies immune globulin. Transgenic mice carrying human immunoglobulin genes were used to isolate human monoclonal antibodies that neutralized rabies virus. Several HuMAbs were identified that neutralized rabies virus variants from a broad panel of isolates of public health significance. HuMAb 17C7 was the most promising antibody identified because it neutralized all rabies virus isolates tested. HuMAb 17C7 recognizes a conformational epitope on the rabies virus glycoprotein which includes antigenic site III. HuMAb 17C7 protected hamsters from a lethal dose of rabies virus in a well-established in vivo model of post-exposure prophylaxis.

Monoclonal antibody (mAb) have been demonstrated to be safe and effective in clinical trials and have been found to neutralize a broad panel of globally prevalent RABV isolate

Vaccine 30 (2012) 7315–7320

Contents lists available at SciVerse ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Safety and pharmacokinetics of a human monoclonal antibody to rabies virus: A randomized, dose-escalation phase 1 study in adults☆

Nithya Gogtay[a], Urmila Thatte[a], Nilima Kshirsagar[a], Brett Leav[b], Deborah Molrine[b], Peter Cheslock[b], Subhash V. Kapre[c], Prasad S. Kulkarni[c,*], SII RMab author group[1]

[a] KEM Hospital and Seth GS Medical College, Mumbai, India
[b] MassBiologics, University of Massachusetts Medical School, Boston, MA, USA
[c] Serum Institute of India Ltd, Pune, India

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ABSTRACT

Background: Rabies is an essentially fatal disease that is preventable with the timely administration of post-exposure prophylaxis (PEP). The high cost of PEP, which includes vaccine and hyperimmune globulin, is an impediment to the goal of preventing rabies in the developing world. Recently a recombinant human IgG_1 anti-rabies monoclonal antibody (SII RMab) has been developed in India to replace serum-derived rabies immunoglobulin. The present study was conducted to demonstrate the safety of SII RMab and to determine the dose resulting in neutralizing serum antibody titers comparable to human rabies immunoglobulin (HRIG) when administered in conjunction with rabies vaccine in a simulated PEP regimen.

Methods: This randomized, open label, dose-escalation phase 1 study was conducted in healthy adults at a large tertiary care, referral, public hospital in India. Safety was assessed by active surveillance for adverse events along with standard laboratory evaluations and measurement of anti-drug antibodies (ADA). Anti-rabies antibody levels were measured by rapid fluorescent focus inhibition test (RFFIT) and ELISA. The study duration was 365 days.

Findings: SII RMab was well tolerated with similar frequency of local injection site reactions to HRIG. The geometric mean concentrations of rabies neutralizing antibody in the vaccine plus SII RMab 10 IU/kg cohort were comparable to the vaccine plus HRIG 20 IU/kg cohort throughout the 365-day study period; day 14 geometric mean concentrations 23.4 IU/ml (95% CI 14.3, 38.2) vs. 15.3 IU/ml (95% CI 7.72, 30.3; p = NS), respectively. Future post-exposure prophylaxis studies of SII RMab at a dose of 10 IU/kg in conjunction with vaccine are planned.

Advantages of Rabies Monoclonal Antibody (RMAb)

Improved safety: No transmission of blood borne pathogens

Expanded availability: Unlimited production capacity.

Concentrated Product: lowers infiltration volume & easy to administer full dose in wounds.

Product	Recommended dose	Formulation concentration	Dose in IU for Avg 75 kg adult	Dose in mL for Avg 75 kg adult
ERIG	40 IU/kg	300 IU/mL	3000	10 mL
HRIG	20 IU/Kg	150 IU/mL	1500	10 mL
Rabishield	3.33 IU/Kg	40 IU/mL	250	6.25 mL
Twin Rab	40 IU/kg	600 IU/mL	3000	5 mL

Pre Exposure Prophylaxis

Regimen	Dose	Days
Intramuscular	1 full dose of vaccine (0.5ml/1 ml)	0,7 and booster dose either on day 21 or 28
Intradermal	0.1 ml at single site.	

Scenario For Discussion

Scenario 6

Harish reports to you that his kid was bitten by a street dog 5 days ago. They had shown to a local doctor who gave them 2 doses of ARV intramuscular in the Gluteal region. He could not afford the cost, so decided to visit a government facility

You being the doctor at the government facility, What would you advise him ?

Summary

- Take a proper history in all animal bite cases with regards to animal, previous history of vaccination, vaccine.
- Wash all wounds for 15 min under running tap water with soap
- Examine and Categorize the EXPOSURE & Decide on the vaccination /IRG administration
- Emphasize on complete course of Vaccination
- Counsel the animal bite victim.

References

1. National Guidelines for Rabies Prophylaxis, 2019. National Rabies Control Programme
2. World Health Organization -https://www.who.int/news-room/factsheets/detail/rabies
3. National Rabies Control Program, MOHFW https://rabiesfreeindia.mohfw.gov.in/

Thank You

END RABIES:
COLLABORATE, VACCINATE

WORLD RABIES DAY
SEPTEMBER 28