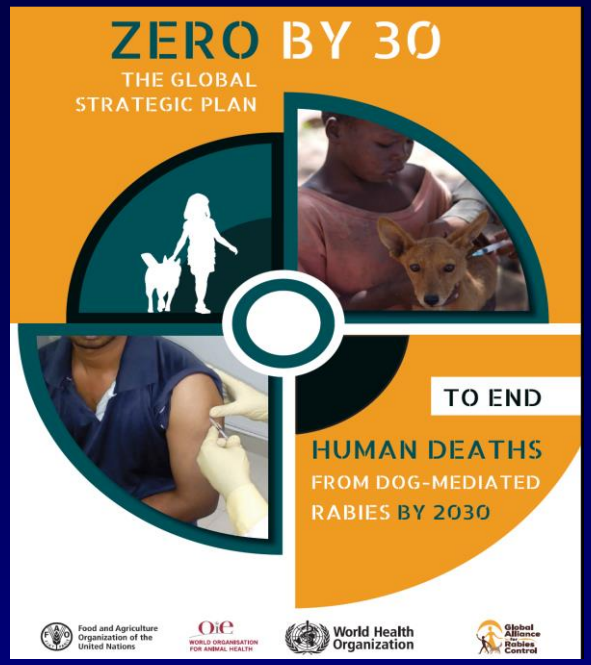

Prevention and Management of Rabies

Queen Saovabha Memorial Institute (QSMI),
WHO Collaborating Centre for
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Thai Red Cross Society, Thailand

Disclosure (2020 – 2025)

Prof. Terapong Tantawichien: has received support for

- Travel for International Conference (Bionet, Siam Pharm)
- Lectureships (GlaxoSmithKline, Pfizer, MSD, Roche, Thai Meiji, Siam Pharm, Sanofi , Biovalys, Biogenetec……).
- Advisory board for zoster vaccine/pneumococcal vaccine (MSD),rabies vaccine (GSK), dengue vaccines (Sanofi, MSD, Takeda), influenza vaccine(Sanofi)

Prof. Terapong Tantawichien: has received research funds from

- MPH, Thailand (shorten rabies PET) 2019-2020
- NSTDA/Bionet (Asia)-Spearhead project (Tdap: recombinant pertussis toxin)-2019-2024)
- Sanofi (Rabies vaccine:VRV-12) 2020-2021
- Sanofi (Rabies vaccine: VRV-14) 2020-2021
- Baiya (Covid-19 vaccine phase I) 2021-2023
- Sanofi (Yellow fever vaccine) 2021-2025
- Jansen (RSV vaccine) 2021-2023
- Baiya (Covid-19 vaccine phase IIa) 2023-2024
- Chula (Covid-19 mRNA vaccine phase II) 2023-2024
- Jansen (*E.coli* vaccine phase III) 2023-2025
- Bionet (Asia) (Recombinant pertussis vaccine phase IV) 2025

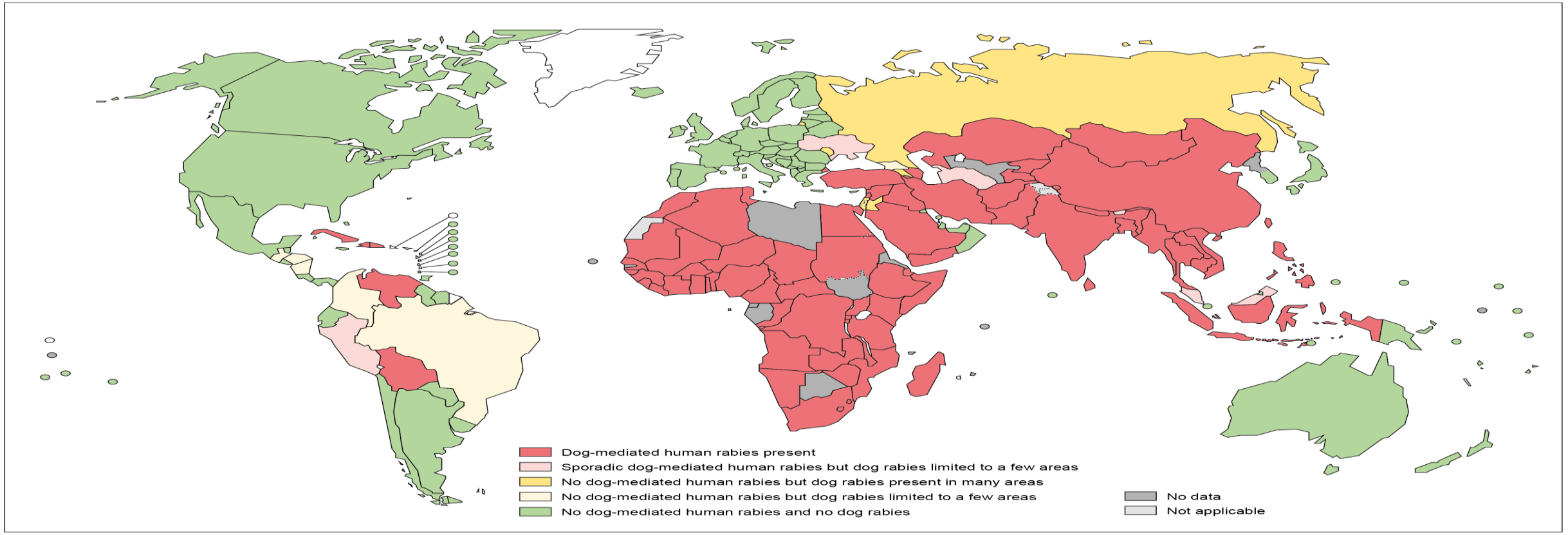
Prevention and Management of Rabies Overview:

- Epidemiology and Human Rabies in Asia
- Management of Human Rabies
- Post-Exposure Rabies Prophylaxis
- Pre-Exposure Rabies Prophylaxis

Rabies :Zoonotic disease: RNA virus: Family *Rhabdoviridae*,

- **Acute, progressive encephalomyelitis and clinical disease almost always fatal**
- Human rabies is most common in people aged under 15,however, all aged groups are susceptible.
- Reported incidence of human rabies cases is often incomplete and the estimated of 50,000 deaths per year may be an underestimated.

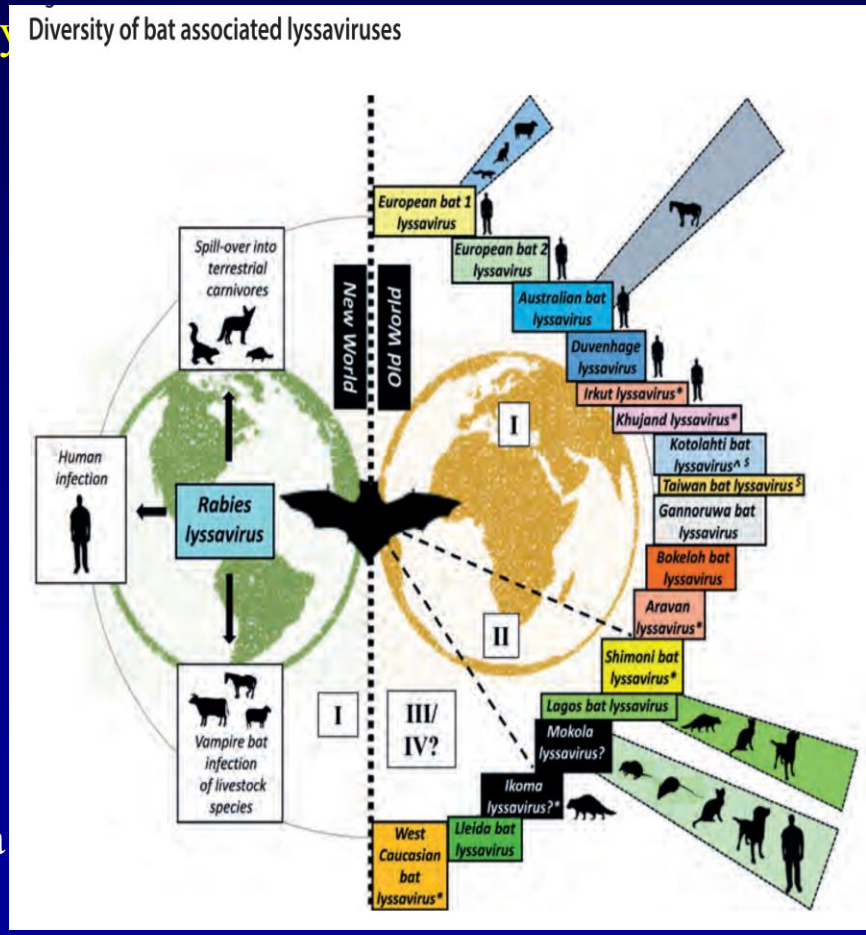
Presence of dog-mediated human rabies, by country, 2022



Data Source: World Health Organization
Map Production: Control of Neglected Tropical Diseases (NTD)
World Health Organization

World Health Organization

Recognized (WHO2013)	Primary host	Geographical range and species
Rabies virus (RABV)	*Carnivora* and bats (*Chiroptera*)	Terrestrial mammals worldwide except in Australia, Antarctica ; bats New World only
Australian bat lyssavirus (ABLV)	Pteropodid bats (at least 4 species of *Pteropus* genus) and insectivorous bats (*Saccolaimus albiventris*)	Australia
European bat lyssavirus 1 (EBLV1)	Insectivorous bats (predominantly *Eptesicus serotinus*)	Most of Europe
European bat lyssavirus 2 (EBLV2)	Insectivorous bats (predominantly *Myotis daubentonii* and *M. dasycneme*)	NW Europe
Khujand virus (KHUV)	Insectivorous bat *Myotis mystacinus*	Central Asia
Aravan virus (ARAV)	Insectivorous bat *Myotis blythi*	Central Asia
Bokeloh bat lyssavirus(BBLV)	Insectivorous bat *Myotis nattereri*	France, Germany
Irkut virus (IRKV)	Insectivorous bat *Murina leucogaster*	Eastern Asia
Duvenhage virus (DUVV)	Insectivorous bats	Sub-Saharan Africa
Lagos bat virus (LBV)	Pteropodid bats of several genera	Sub-Saharan Africa
Mokola virus (MOKV)	Unknown	Sub-Saharan Africa
Shimoni bat virus (SHIBV)	Insectivorous bat *Hipposideros commersoni*	Kenya
West Caucasian bat virus (WCBV)	Insectivorous bats from genus *Miniopterus*	South-east Europe
Ikoma lyssavirus (IKOV)	Not known	United Republic of Tanzania



WHO Techncal Series 2018

Table 1. Current situation and management experience of rabies around the globe.

Region	Situation	Iconic events	Limiting/promoting factors
Europe	Low incidence; Risk of travelers importing cases	Oral rabies vaccination programs have been adopted by all European countries since the late 1980s and are still ongoing.	Frequent tourism and communication bring input pressure; Regional conflicts may pose a risk of outbreak; The strong economic foundation of developed countries supports animal immunity.
Asia	Severe mortality and economic burden; Positive measures and actions are being implemented	A few developed countries (Japan, Singapore, South Korea) have adopted large-scale dog vaccination and stray dog population control plans; In 2004, the Asian Rabies Expert Bureau (AREB) was established.	Limited resource investment, including vaccine accessibility and improved monitoring systems; Lack of political commitment and departmental coordination; The public has a low level of education and weak awareness of prevention and control.
Africa	A large number of rabies deaths; Lack of accurate data	Tunisia has begun mass vaccination campaigns for dogs in the 1980s; In 2008, the Africa Rabies Expert Bureau (AfroREB) was established;	Insufficient understanding of rabies monitoring and burden; Lower national priority levels; Lack of sustainable plans for canine rabies control.
North America	A significant reduction in rabies cases in the United States and Mexico while Haiti still faces challenges	"Plan of Action for the Elimination of Urban Rabies from the Principal Cities of Latin America" (OPS, 1983)	The Pan American Health Organization (PAHO) coordinates canine vaccination, contact person treatment, and epidemiological monitoring.
South America	Most cases of rabies occur in countries such as Bolivia and Brazil		
Oceania	Free of dog-mediated rabies but high risk of traveler's cases	Australian Veterinary Emergency Plan (AUSVETPLAN) (Animal Health Australia, 2011)	Strict dog management and legal governance tools
Antarctica	Free of all lyssaviruses but with no laboratory-based surveillance	–	Uninhabited

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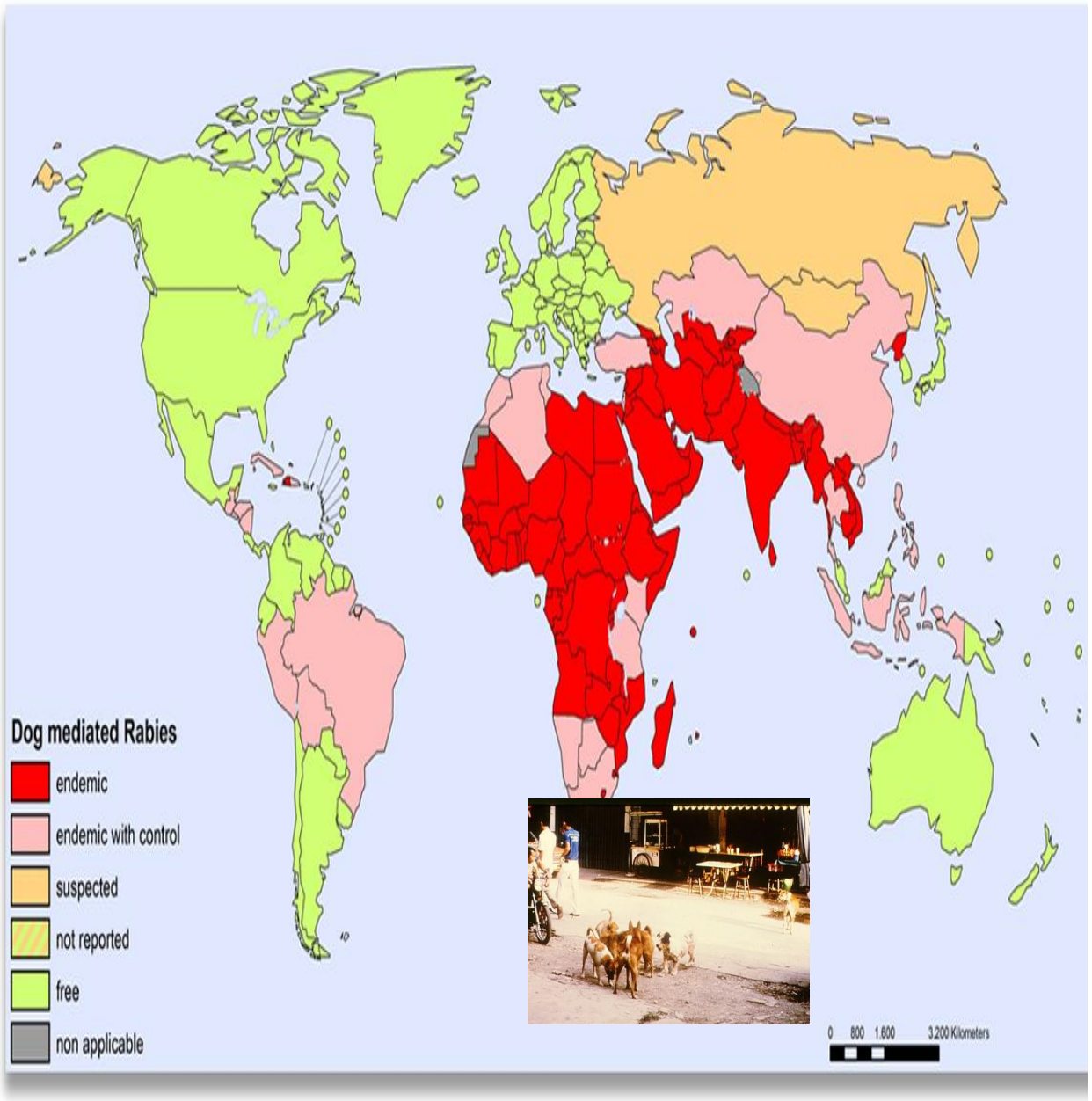
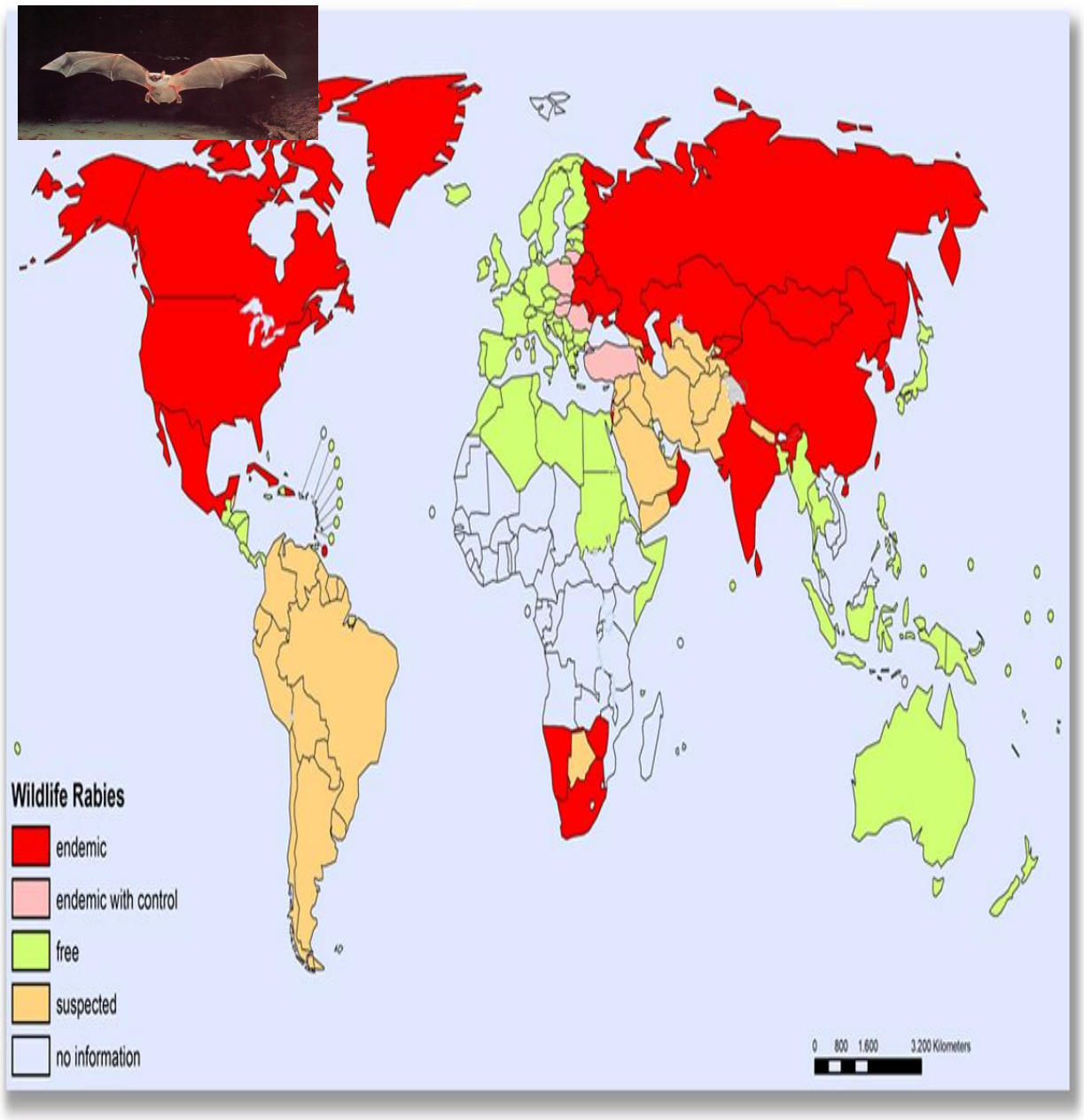
Occurrence of canine rabies



Occurrence of wildlife mediated rabies



https://www.who-rabies-bulletin.org/site-page/occurrence-rabies

Table 1: Distribution per year of human rabies and dog bite cases in countries of the southeast Asia region.

Country	Estimated no. of dog bites	Estimated no. of human rabies cases	Estimated no. of human cases per million population	Source of information
Bangladesh	300,000	2,000–2,500	13	Ministry of Health and Family Welfare, Bangladesh
Bhutan	5000	<10	3	Ministry of Health, Bhutan
DPR Korea	Not available	Not available	Not available	N/A
India	17,400,000	18,000-20,000	18	Assoc. for Prevention and Control of Rabies in India (APCRI)
Indonesia	100,000	150–300	1.3	Ministry of Health, Indonesia
Maldives	0	0	0	N/A
Myanmar	600,000	1000	22	Ministry of Health, Myanmar
Nepal	100,000	<100	4	Ministry of Health and Population, Nepal
Sri Lanka	250,000	<60	3	Public Veterinary Services, Sri Lanka
Thailand	400,000	<25	0	Ministry of Public Health, Thailand
Timor Leste	1,000	0	0	Ministry of Health, Timor-Leste
SE ASIA TOTAL	19,156,000	21,345–23,995		

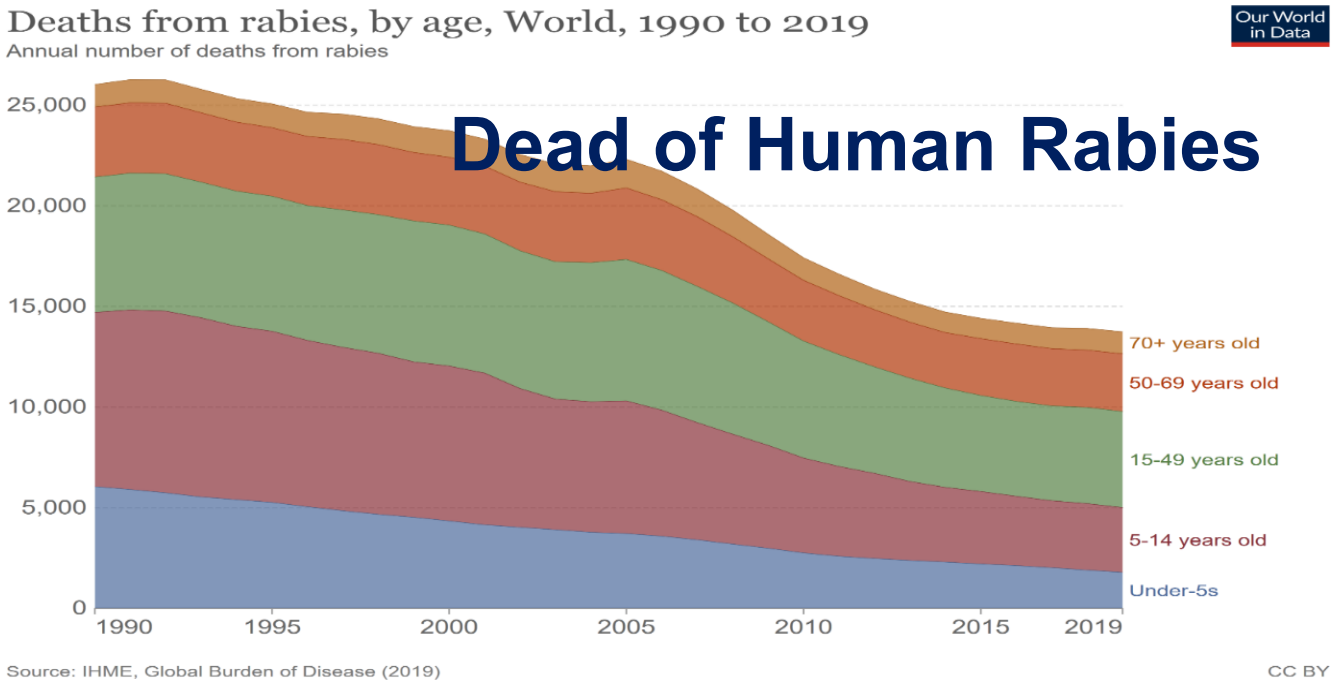
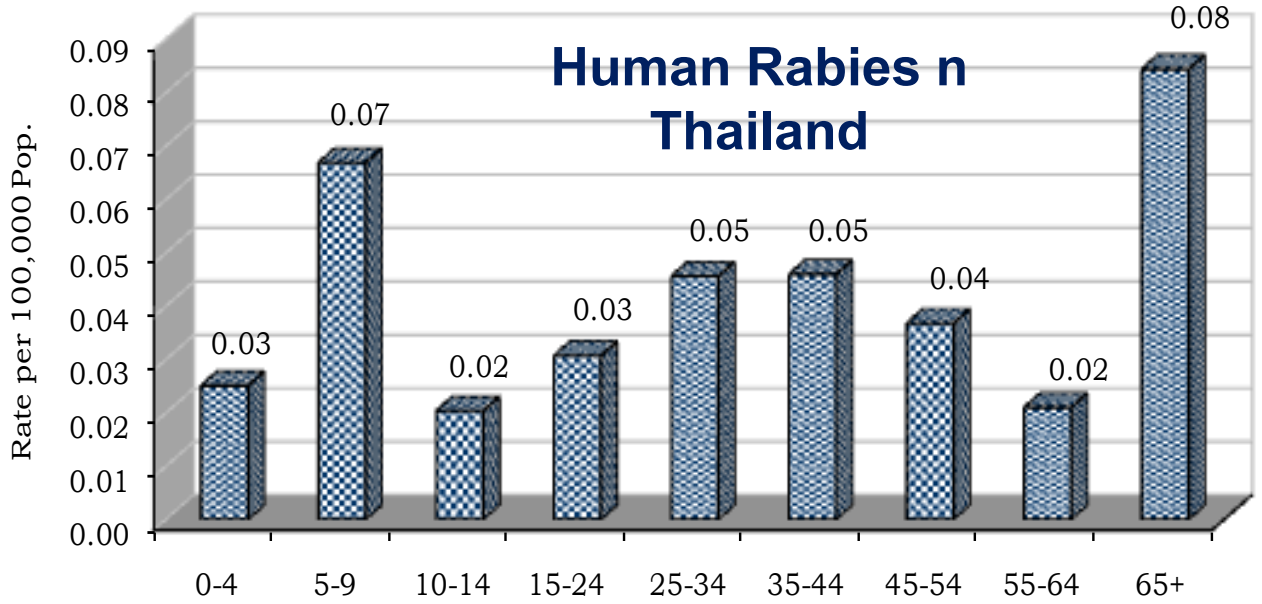


Fig. 4 Reported Cases of Rabies per 100,000 Population by Age-Group, Thailand, 2006.



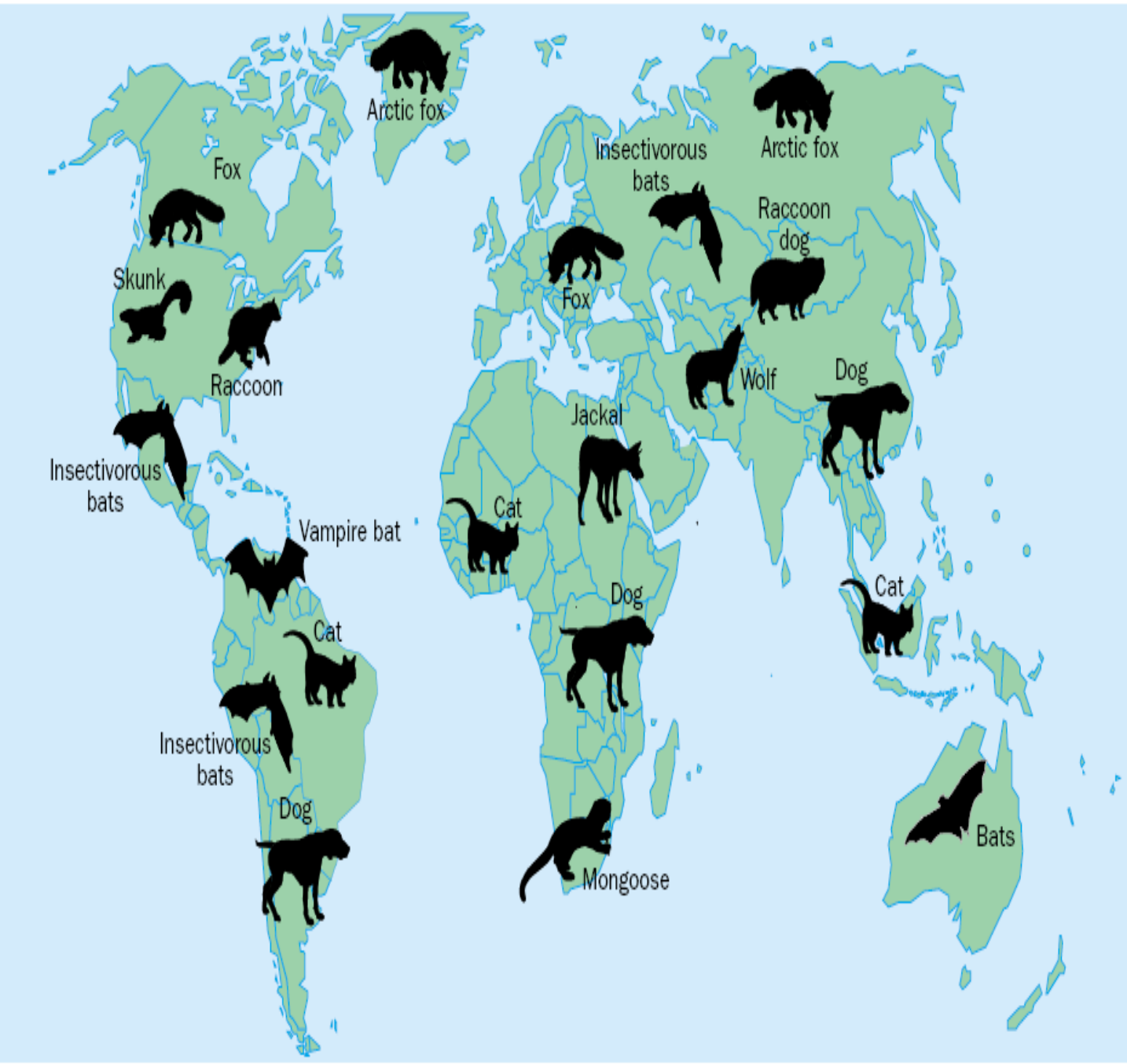


Figure 5. Global distribution of mammalian rabies reservoirs and vectors.

Charles E Rupprecht,Lancet 2004

Table 2. Cases of Animal Rabies in the United States. Rupprecht, CE NEJM 2004

Animal*	Average No. of Cases, 1998–2002	Geographic Focus†
Raccoon	2962	Eastern United States
Skunk	2257	California, upper and lower Midwest, eastern United States
Bat	1175	Entire United States, except Hawaii
Fox	443	Alaska, Texas, southwestern United States
Cat	276	Entire United States, except Hawaii
Cattle	106	Entire United States, except Hawaii
Dog	105	Entire United States, except Hawaii
Horse or mule	62	Entire United States, except Hawaii
Mongoose	58	Puerto Rico
Woodchuck	50	Eastern United States
Bobcat	30	Entire United States, except Hawaii
Sheep or goat	9	Entire United States, except Hawaii
Other wild animal	24	Entire United States, except Hawaii
Other domestic animal	3	Entire United States, except Hawaii

* All mammals are considered to be susceptible to rabies, and incidental (or spillover) infection from wild-animal reservoirs may occur in any species.
† Rabies may occur in an exposed animal in any location; the geographic foci listed here are based on current epidemiologic trends. No cases of rabies have been reported in Hawaii or in American Samoa, the Commonwealth of the Northern Mariana Islands, Guam, or the U.S. Virgin Islands.

Bat Rabies in the US and Canada Serres GD;CID 2008:46

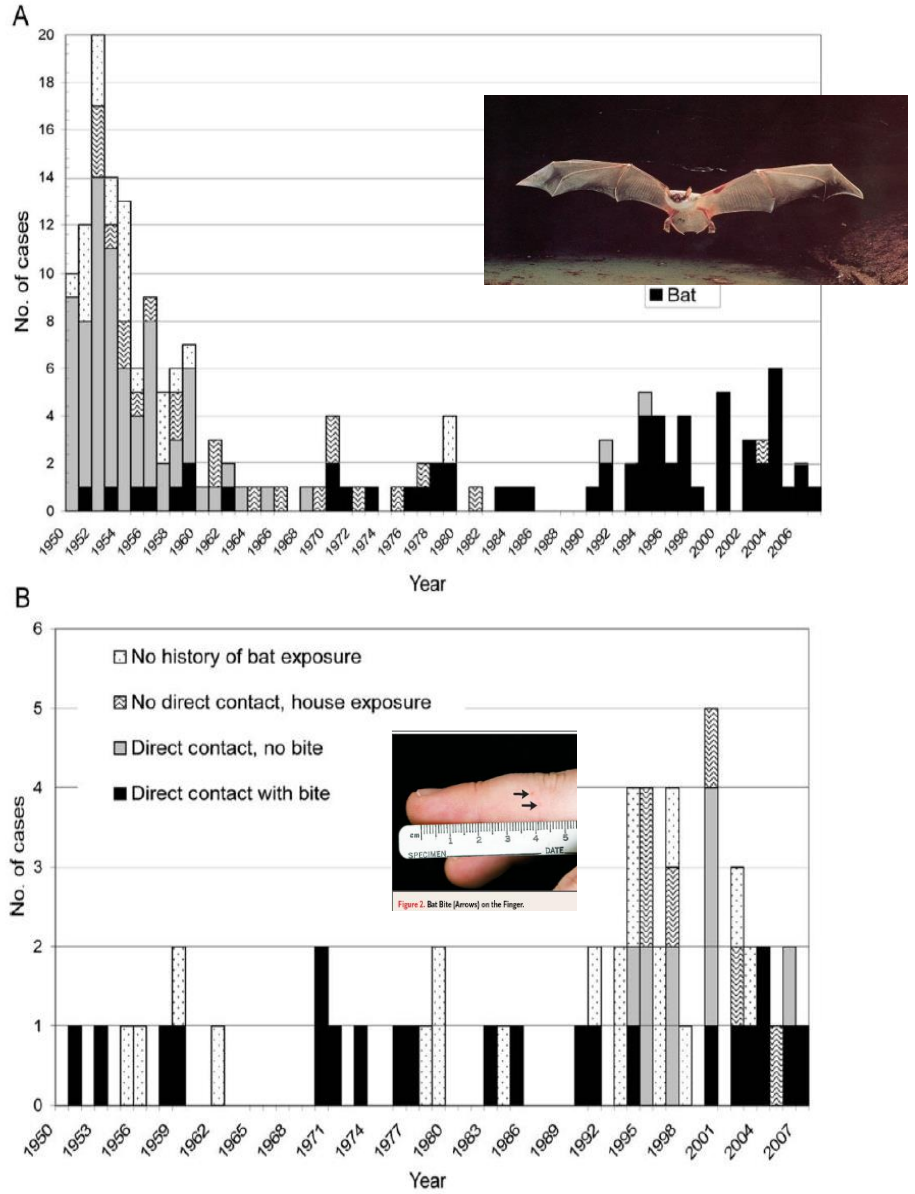


Figure 1. *A,* Number of human cases of indigenously acquired rabies in Canada and the United States since 1950, including cases involving organ transplantation, by type of source animal. N/A, not available. *B,* Number of human cases of indigenously acquired bat rabies in Canada and the United States from 1950 through 2007, excluding organ transplant cases.

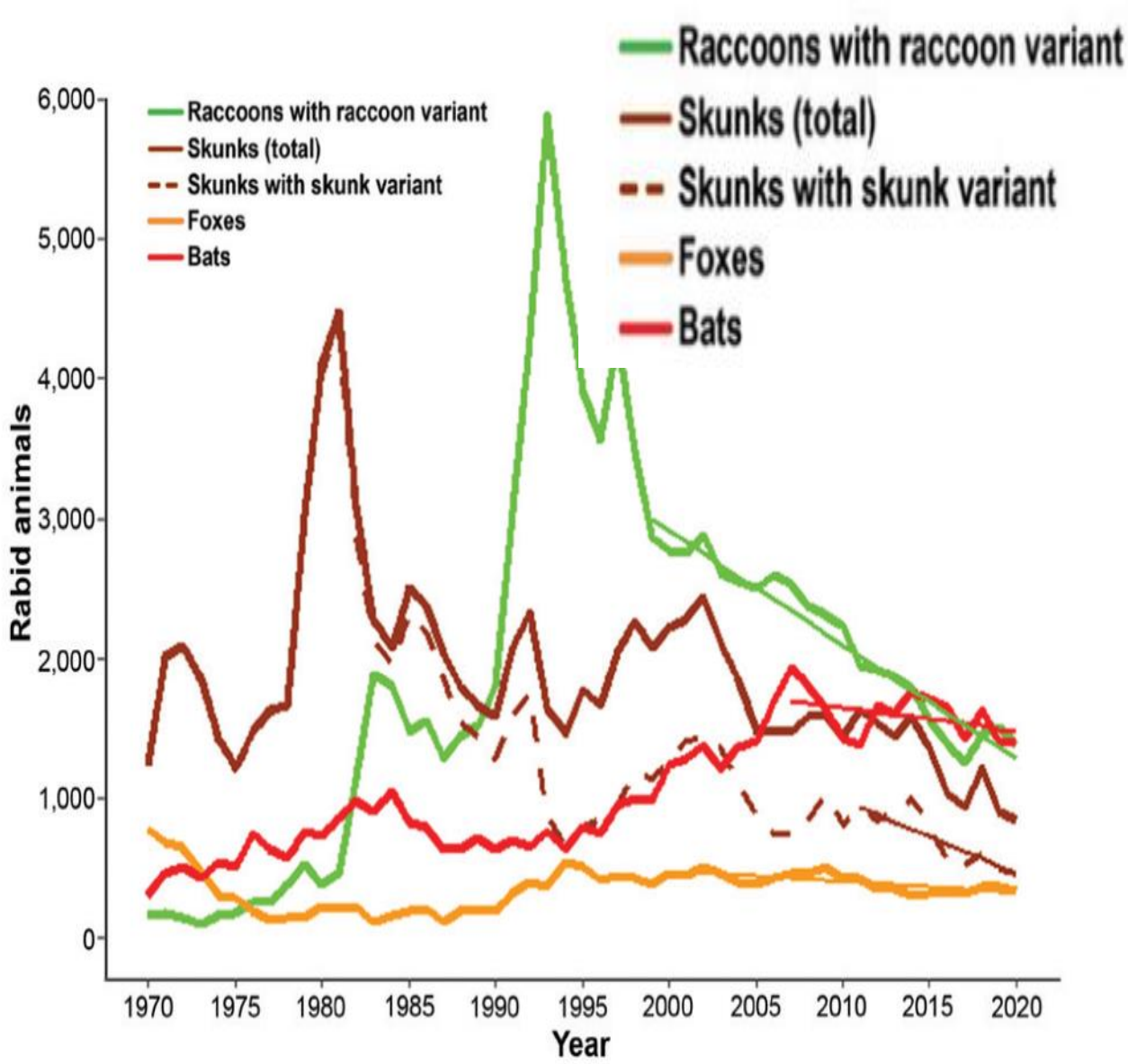
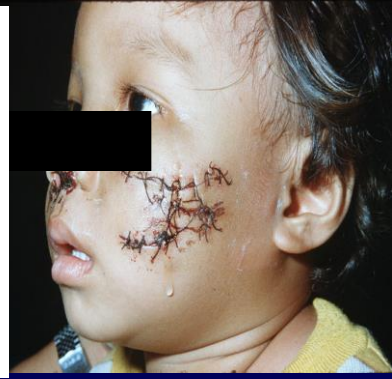


Figure 2—Cases of rabies among wildlife in the US, by year and species, 1970 through 2020.

Ma X; JAVMA | JULY 2022 | VOL 260 | NO. 10



Mass vaccination of dogs is not effective in most of Asia and Africa.

Street dogs represent the most frequent risk for bite exposure, followed by monkeys, cat, especially those that live near temples in parts of Asia. In some countries, control of the dog population is almost impossible to implement because of cultural and religious beliefs and because some animal welfare organizations have hindered human efforts to control the canine population.

A prospective study on the incidence of dog bites and management in a rural Cambodian, rabies-endemic setting

Aurelia Ponsich [a,b], Flavie Goutard [a,c], San Sorn [d], Arnaud Tarantola [a,*]

Acta Tropica 2016(160)

Table 1
Attacks and severe attacks incidence per age categories.

	Number of attacks	Number of severe attacks	Number of pers.year	Attacks incidence 95% CI		Severe attacks incidence 95% CI	
<1 year old	0	0	15.5	0.0	[0–24.8]	0.0	[0–24.8]
1–5 years old	9	9	76.0	11.8	[5.4–22.5]	11.8	[5.4–22.5]
6–12 years old	10	8	126.2	7.9	[3.8–14.6]	6.3	[2.7–12.5]
13–17 years old	3	2	88.3	3.4	[0.7–9.9]	2.3	[0.3–8.2]
≥18 years old	18	14	496.3	3.7	[2.2–5.8]	2.9	[1.6–4.8]
Global	40	33	802.3	5	[3.5–6.6]	4.1	[2.8–5.8]

Animal-Associated Exposure to Rabies Virus among Travelers, 1997–2012

Philippe Gautret, Kira Harvey, Prativa Pandey, Poh Lian Lim, Karin Leder, Watcharapong Piyaphanee, Marc Shaw, Susan C. McDonald, Eli Schwartz, Douglas H. Esposito, Philippe Parola, for the GeoSentinel Surveillance Network[1]

Region of exposure, no. (%)¶						
Southeast Asia	570 (36)	414 (66)	99 (37)	10 (22)	37 (30)	1,129 (43)
South-Central Asia	406 (26)	146 (23)	21 (8)	3 (7)	22 (18)	598 (23)
Northeastern Asia	217 (14)	13 (2)	25 (9)	0	6 (5)	261 (10)
North Africa	76 (5)	6 (1)	45 (17)	1 (2)	9 (7)	137 (5)
Latin America	121 (8)	15 (2)	7 (3)	21 (46)	10 (8)	174 (7)

Table 2. Countries with 5 highest levels of exposure among 2,697 patients who sought care for animal exposure and received rabies postexposure prophylaxis at GeoSentinel Surveillance Network sites, January 1997–December 2012, by animal species

	Animal, country of exposure, no. (%) exposures					
No.	Dog, n = 1,618	NHP, n = 638	Cat, n = 271	Bat, n = 46	Other, n = 126	Total, n = 2,697
1	Thailand, 294 (18)	Indonesia, 200 (31)	Thailand, 59 (22)	Indonesia, 7 (15)	Thailand, 16 (13)	Thailand, 534 (20)
2	Nepal, 198 (12)	Thailand, 166 (26)	Turkey, 31 (11)	French Guyana, 5 (11)	India,10 (8)	Indonesia, 314 (12)
3	China, 197 (12)	Nepal, 82 (13)	China, 25 (9)	Peru, 4 (9)	Indonesia, 10 (8)	Nepal, 295 (10)
4	India, 124 (8)	India, 43 (7)	Indonesia, 17 (6)	Mexico, 3 (7)	China, 6 (5)	China, 241 (9)
5	Indonesia, 80 (5)	Vietnam, 21 (3)	Algeria, 15 (6)	Surinam, 3 (7)	Nepal, 6 (5)	India, 185 (7)

ZERO HUMAN DEATHS FROM DOG-MEDIATED RABIES BY 2030

less expenditure on rabies

fewer rabies exposures

validated rabies elimination in individual countries/regions

Reduce human rabies risk
- improved awareness and education
- increased access to healthcare, medicines and vaccines
- dog vaccinations

Provide guidance and data
- effective policies, guidance and governance
- ensuring reliable data to enable effective decision-making

Harness multi-stakeholder engagement
- demonstrate the impact of activities completed under the **United Against Rabies** collaboration

OBJECTIVE 1
to effectively use vaccines, medicines, tools and technologies

OBJECTIVE 2
to generate, innovate and measure impact

OBJECTIVE 3
to sustain commitment and resources

OBJECTIVES

operational capacity-building preparedness

educational & advocacy programmes awareness & commitment

monitoring & evaluation effectiveness & sustainability

The **UNITED AGAINST RABIES** collaboration was formed by four partners: WHO, FAO, OIE, GARC*

PROBLEM STATEMENT

Although 100% preventable, rabies kills more than 59,000 people in over 150 countries every year. The disease is nearly always fatal once symptoms appear.

* World Health Organization (WHO), Food and Agriculture Organization of the United Nations (FAO), World Organisation for Animal Health (OIE), and Global Alliance for Rabies Control (GARC)

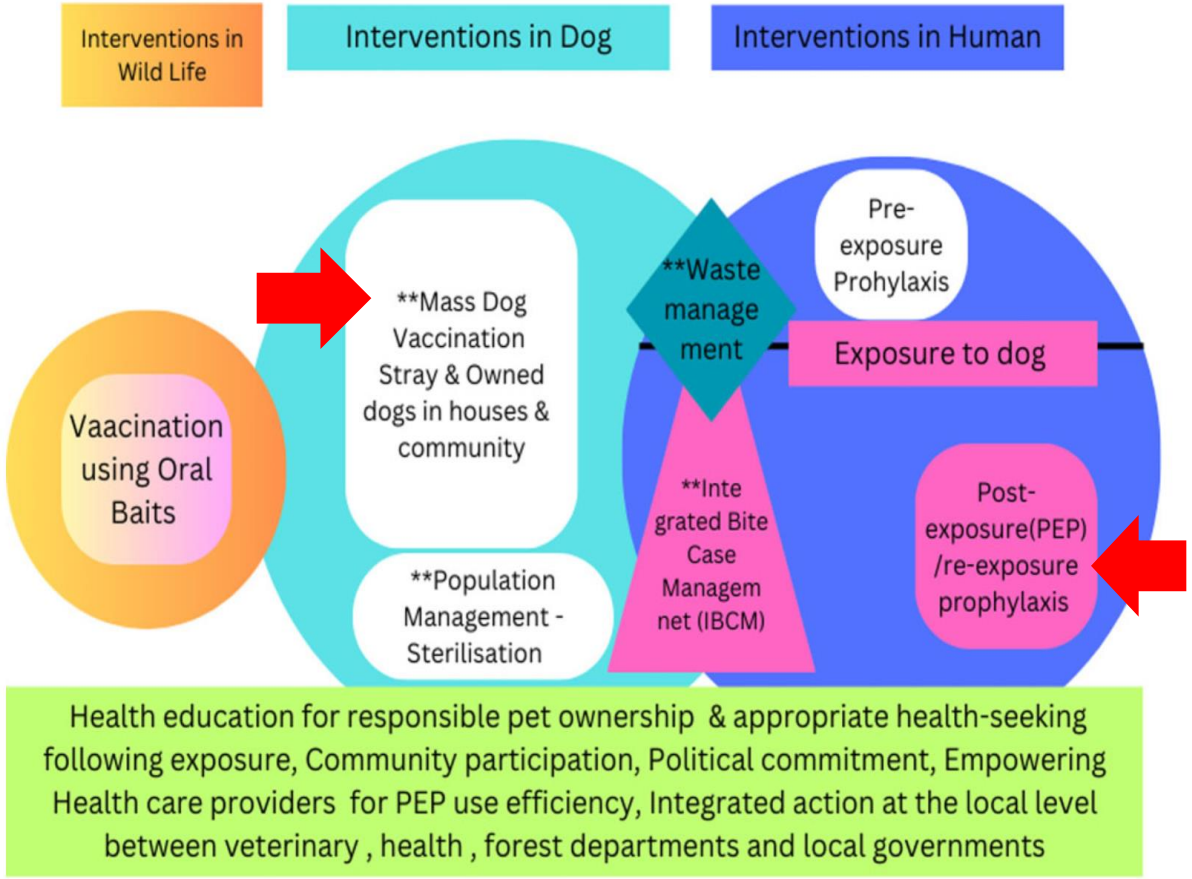
One Health approach to cost-effective rabies control in India

R.P. Lavan et al. / Vaccine 35 (2017) 1668–1674

Optimal One Health program to tackle rabies should incorporate mass dog vaccination and integrated bite case management in combination with efficient use of post-exposure prophylaxis along with a shift to a 1-week abbreviated ID rabies vaccine regimen in humans.

Collaborative **One Health Approach** involving human public health and veterinary agencies, with **Mass canine vaccination programs in endemic areas being the mainstay of strategies to eliminate dog-mediated human rabies. Post-exposure prophylaxis (PEP) is effective in preventing deaths.**

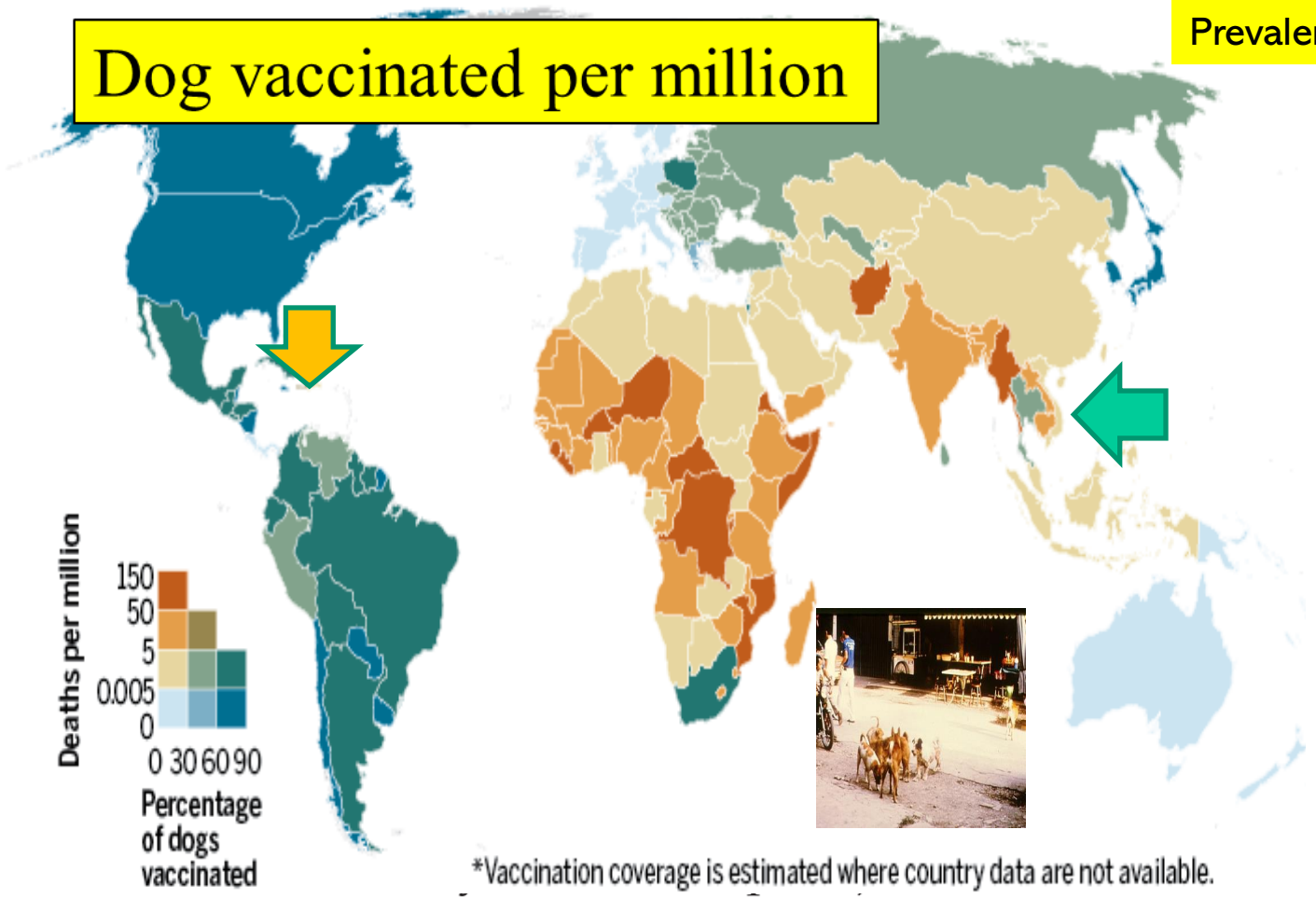
Indiscriminate culling of the dog population is expensive and there is little evidence that it is effective in controlling rabies in non-island locations.
Mass canine vaccination programs achieves a minimum 70% vaccination coverage have proven to be cost-effective in controlling zoonotic rabies in endemic, resource-poor regions.



Trans R Soc Trop Med Hyg 2024; **118**: 223–233

Framework of interventions for canine-mediated rabies elimination in humans.

Dog vaccinated per million



J. You/Science; (Data) K. Hampson et al., PLOS Neglected Tropical Diseases 9 (16 APRIL 2015) ©PLOS One

Prevalence of rabies in tested animals in Asian countries (2010–24)

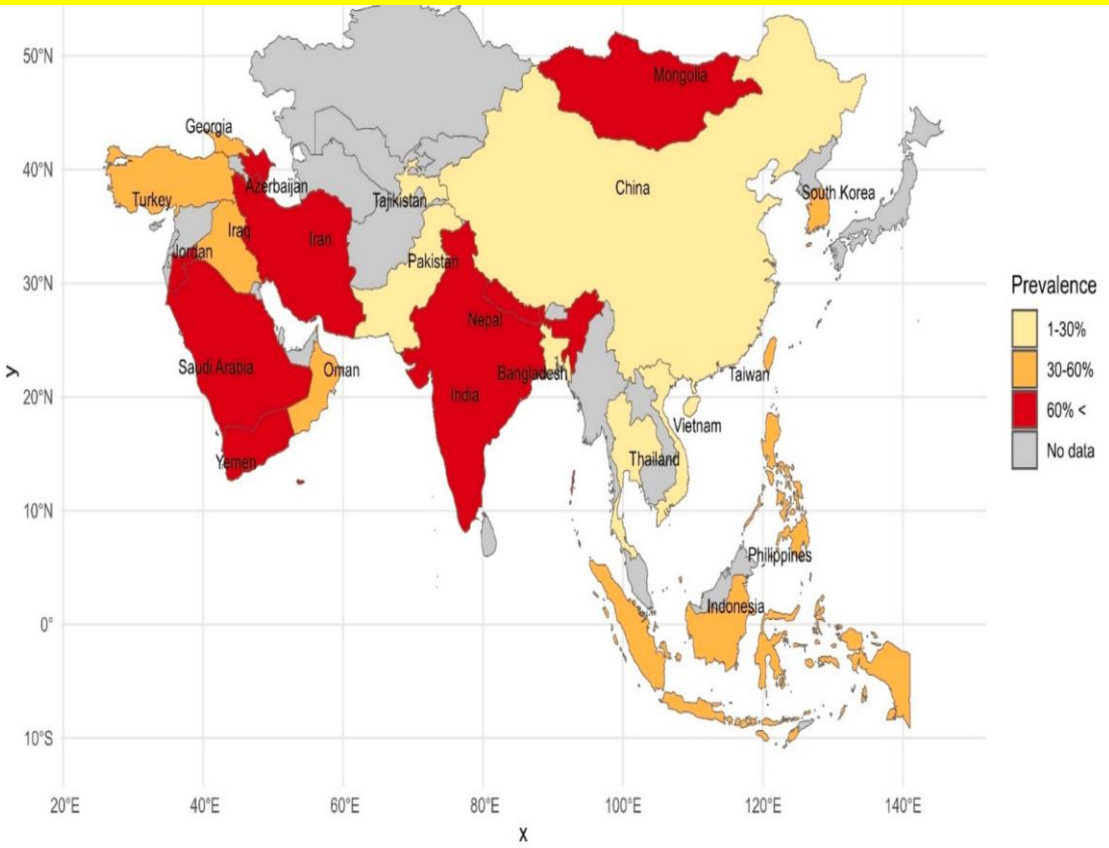


Fig. 1. Prevalence of rabies in tested animals in Asian countries (2010–2024).

F. Shams et al. One Health 20 (2025) 101102

Table 1. Examples from the published literature of vaccination campaigns that have met or failed to meet vaccination targets

Successful vaccination programs			Unsuccessful vaccination programs		
Country	Vaccination coverage, %	Reference	Country	Vaccination coverage, %	Reference
Zambia	80	(*29*)	Chad	19	(*30*)
Mexico	>90	(*31*)	Chad	24	(*32*)
Chad	74	(*30*)	Kenya	29	(*33*)
Thailand	70	(*34*)	Nigeria	17	(*35*)
Bolivia	85	(*36*)	South Africa	56	(*37*)
Tanzania	68	(*38*)	Tanzania	9	(*38*)

Oral rabies vaccine: a new strategy in the fight against rabies de

3 May 2021

https://www.who.int/news/item/03-05-2021-oral-rabies-vaccine-a-new-strategy-in-the-fight-against-rabies-deaths

ORV in Thailand

"Thailand applies an oral vaccine in its free-roaming dog population. Working with partners, we identified the most appropriate bait for Thai free-roaming dogs. We worked with five cities/towns to roll out oral rabies vaccination in their areas in 2020, vaccinating almost 2,000 free-roaming dogs. We achieved 65% of vaccination coverage in the free-roaming dog population in these areas. All parties agreed that this tool is feasible and practical to increase vaccination coverage in inaccessible dog populations. More importantly, there have been no rabies outbreaks reported in free-roaming dogs in any of these five municipalities since oral vaccination was conducted. We will be scaling up oral rabies vaccination in free-roaming dogs in 2021 to complement rabies vaccine shots." Karoon Chanachai, regional animal health advisor for the U.S. Agency for International Development's Regional Development Mission for Asia

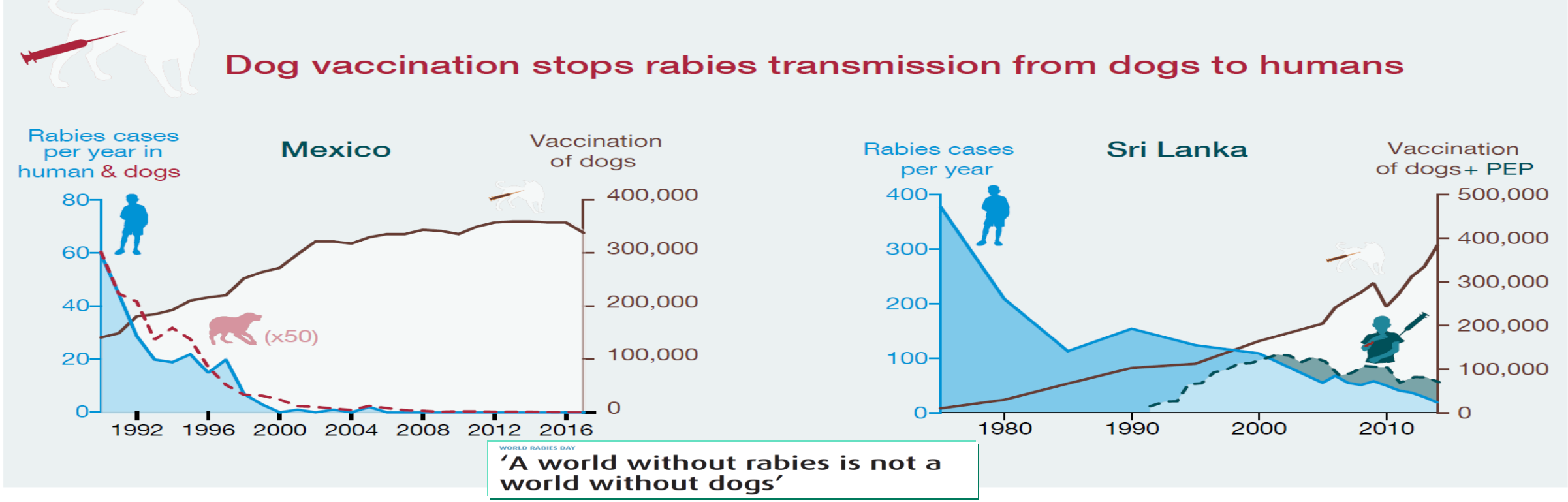


Figure 4. The knowledge, tools and technology to eliminate human rabies deaths are available and proven to work

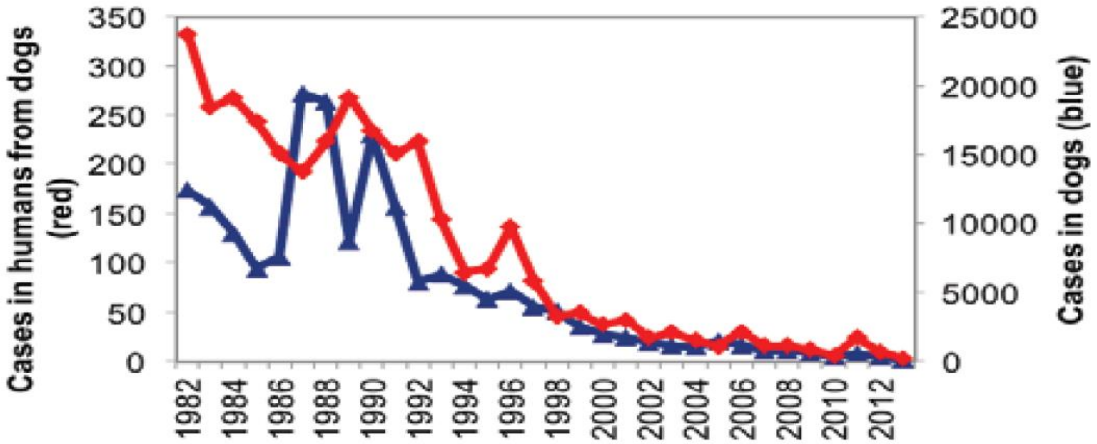
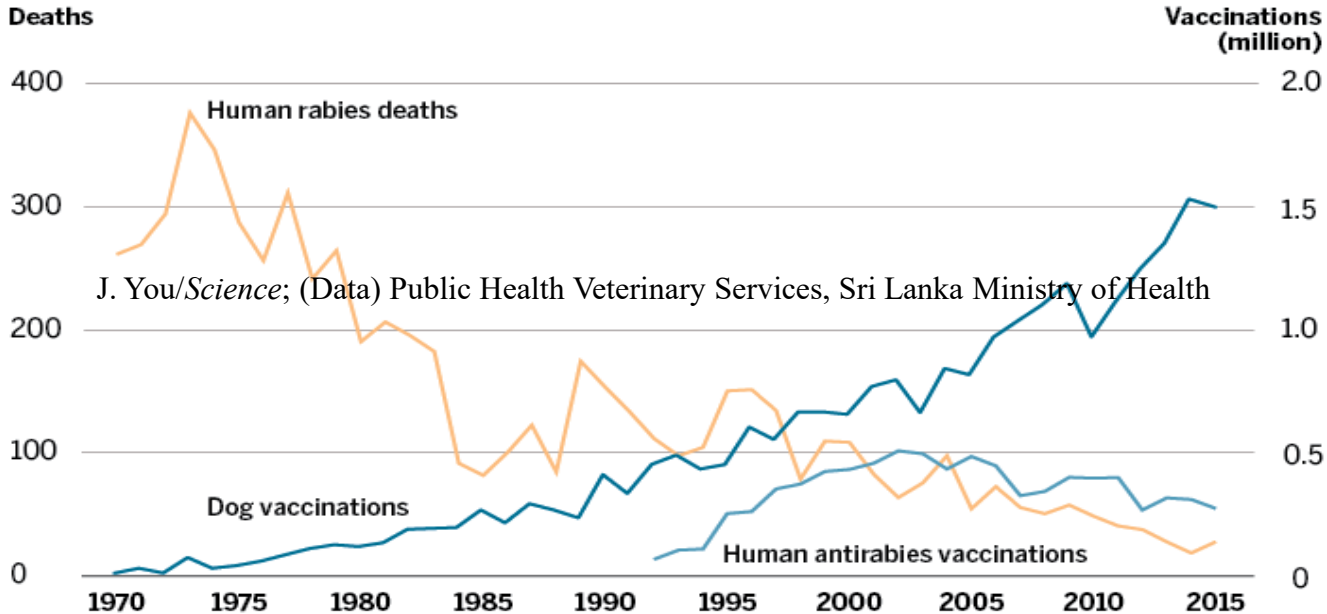


Figure A2.1. Numbers of human and dog rabies cases reported in Latin America and the Caribbean (1982–2012) Data courtesy of PANAFTOSA, Veterinary Public Health – PAHO/WHO



J. You/*Science*; (Data) Public Health Veterinary Services, Sri Lanka Ministry of Health

ปี (พ.ศ.)	Post-exposure prophylaxis	Animal rabies +
2009	196,698	28.43
2010	224,709	17.45
2011	164,827	12.93
2012	160,293	9.79
2013	157,022	2.49
2014	166,662	5.70
2015	167,192	3.78
2016	197,348	6.93
2017	295,592	9.86
2018	564,241	15.31
2019	431,107	5.15
2020	355,387	3.39
2021	235,179	3.09
2022	120,163	4.44

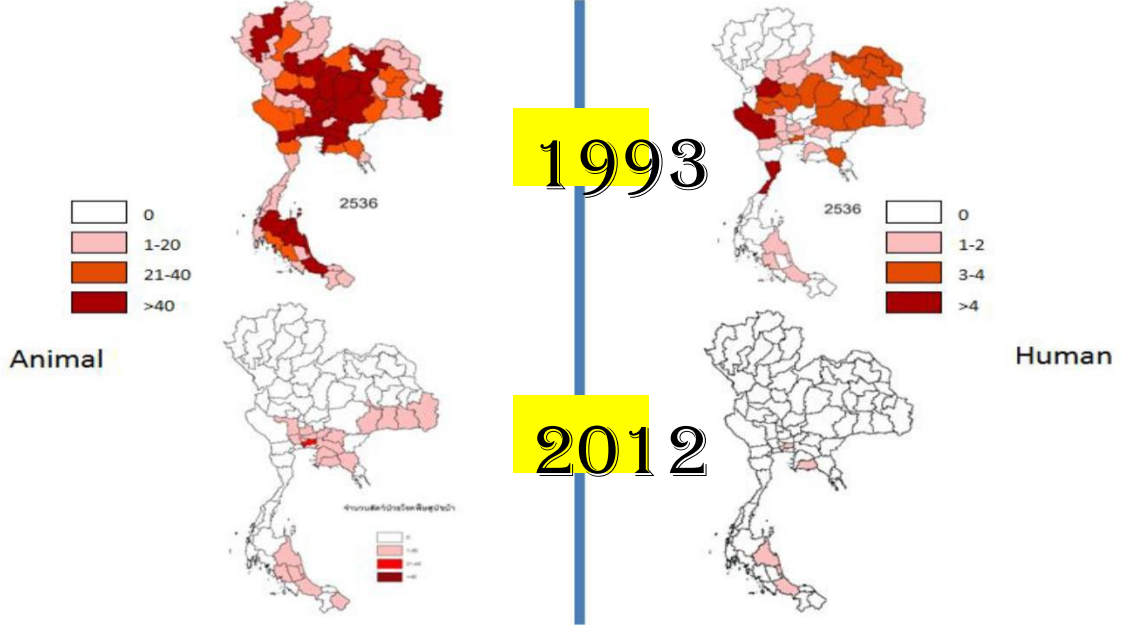
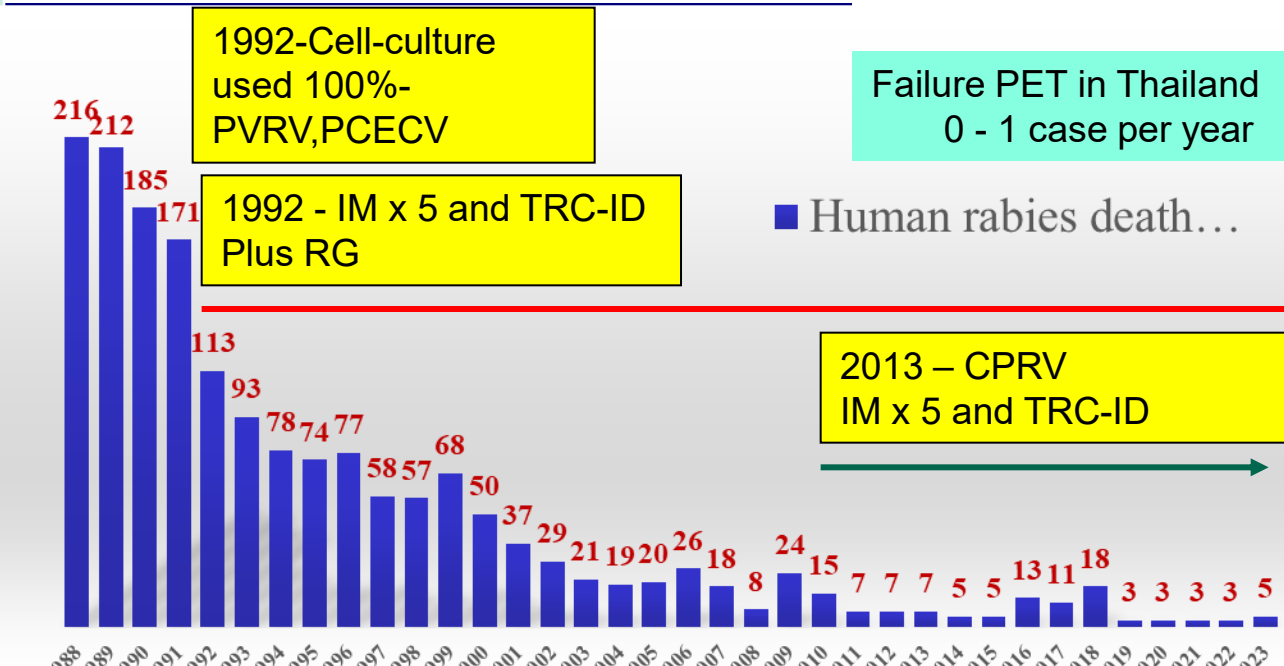
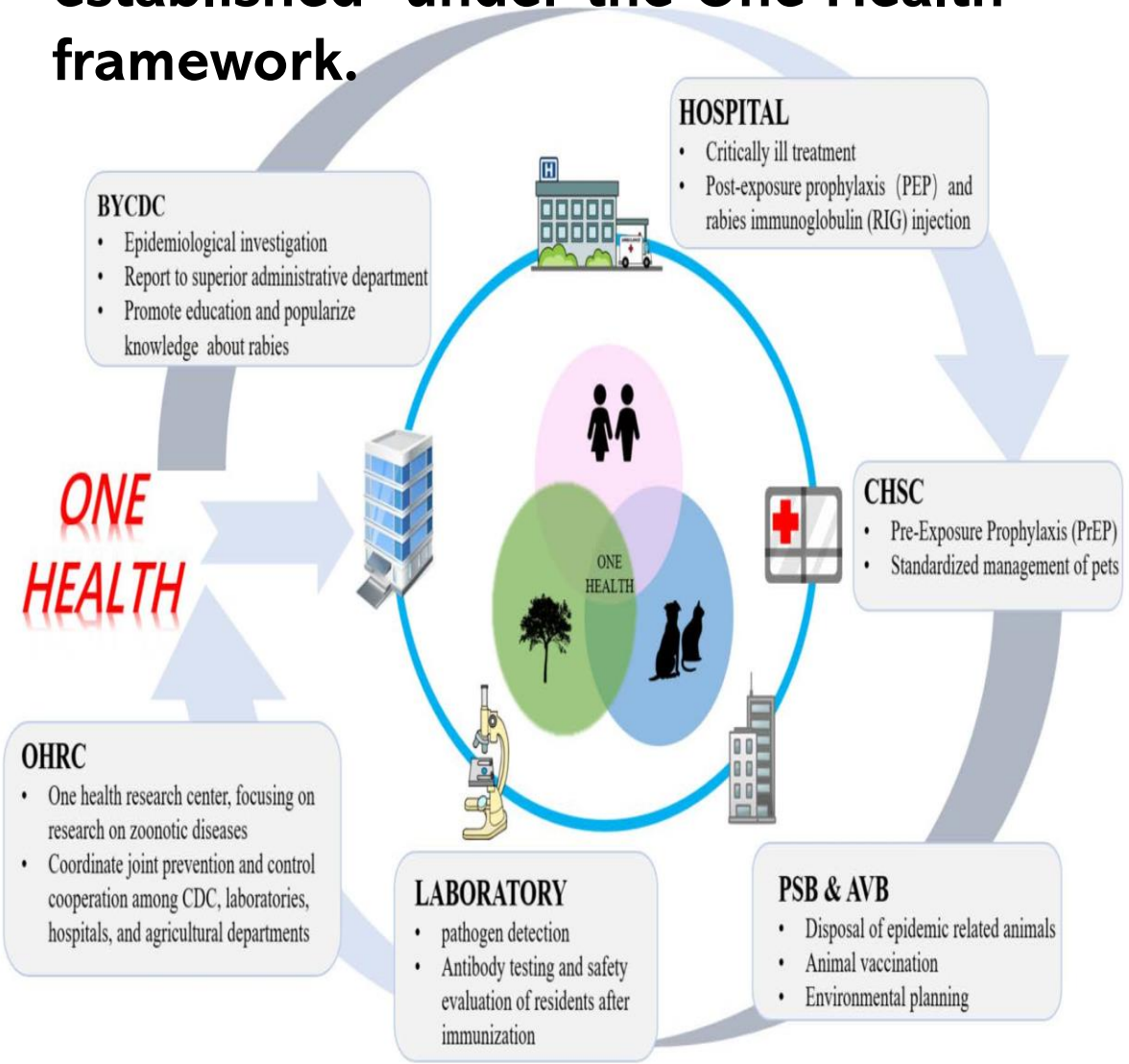


Figure 1 : Animal -Human Rabies Distribution (1993 – 2012)

Figure extracted from Warrell et al 2008



A multi-sectoral coordination mechanism for rabies prevention and control, established under the One Health framework.



Programs for rabies prevention, control, and elimination (Asia)

- Lack of motivation by government,
- Cultural issues
- Inadequate funding
- Lack of co-operation between national sectors
- Insufficient enforcement of animal rabies control
- Lack of high quality biological vaccination
- Lack of rabies awareness in our population

Zha RPLoS Negl Trop Dis 19(6): e0013159.

Prevention and Management of Rabies Overview:

- Epidemiology and Human Rabies in Asia
- **Management of Human Rabies**
- Post-Exposure Rabies Prophylaxis
- Pre-Exposure Rabies Prophylaxis

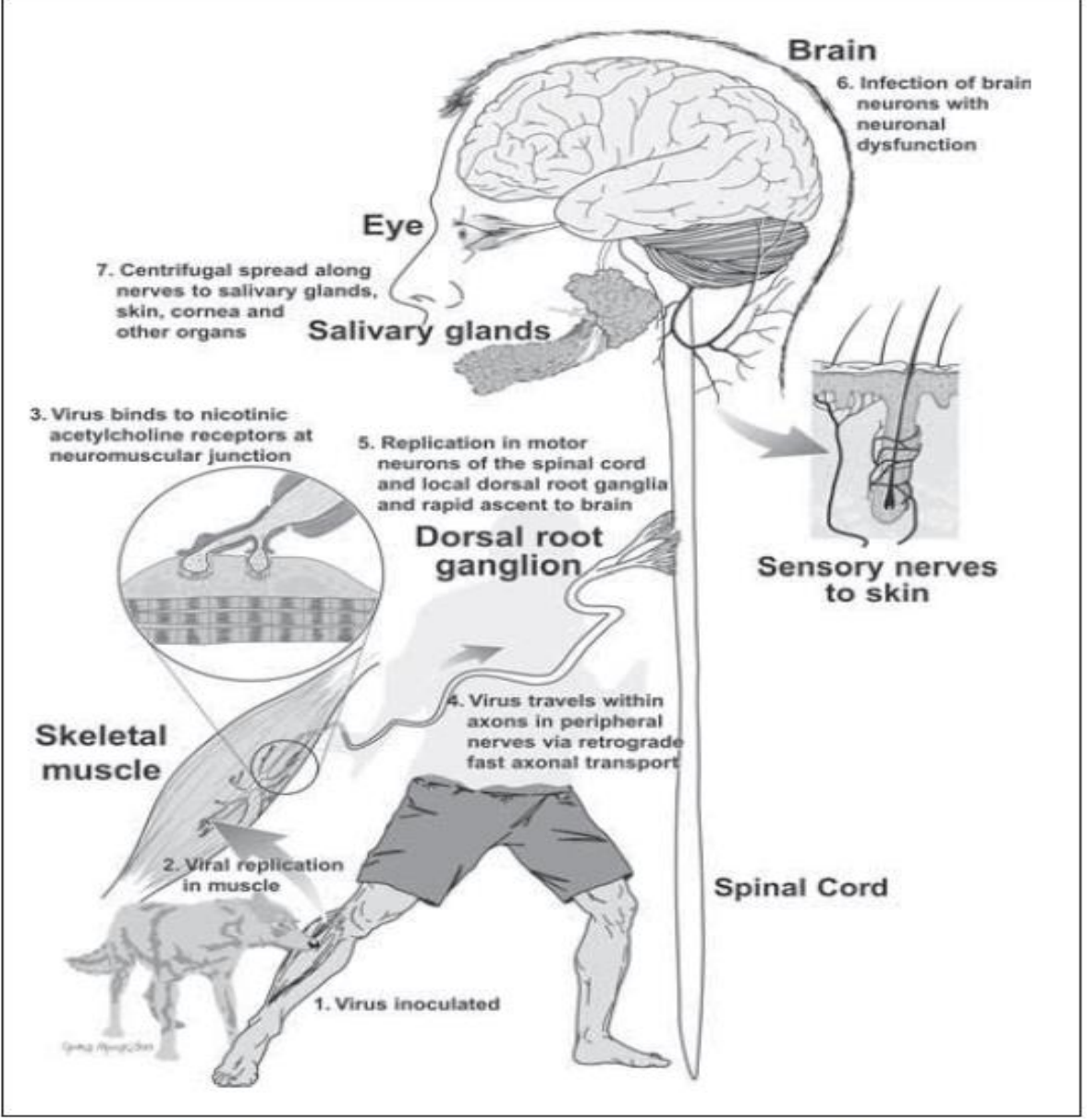


Figure 1: Schematic diagram showing the sequential steps in the pathogenesis of rabies after an animal bite/peripheral inoculation of rabies virus. (Reproduced from Jackson AC: Pathogenesis, in Rabies, edited by AC Jackson and WH Wunner, 2002, Academic Press, San Diego, pp 345-82;[10] Copyright Elsevier).

Rabies Virus Transmission

Rabies is spread between mammals by bites, by contamination of intact and abraded mucosal membranes with virus-laden saliva, by inhalation of aerosal, by ingestion of infected prey and transplacentally.

In man, rabies is nearly always secondary to bites, however, human infections caused by non-bite exposures including scratch, lick, and inhalation of aerosols and transplantation of infected cornea and organs also occur.

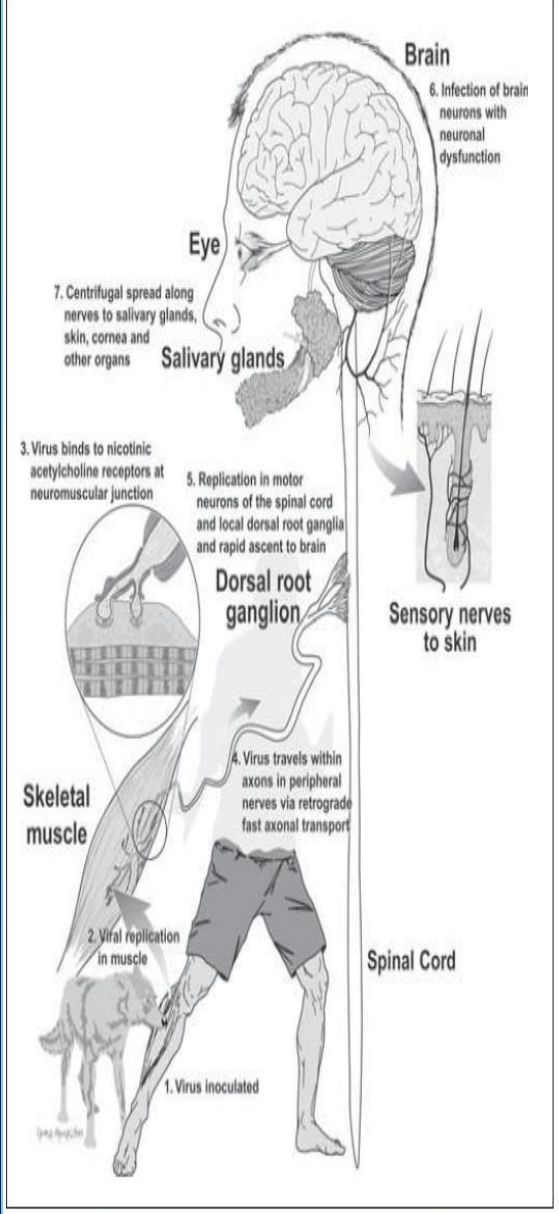
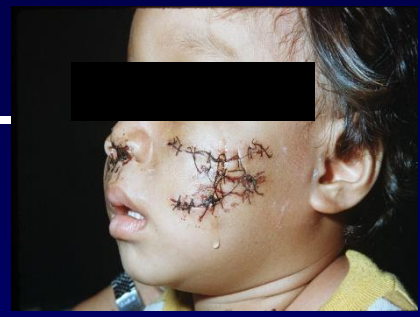


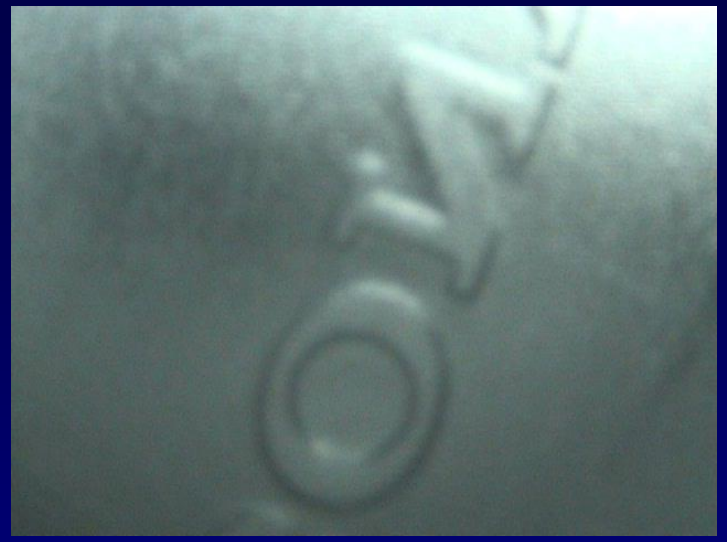
Figure 1: Schematic diagram showing the sequential steps in the pathogenesis of rabies after an animal bite/peripheral inoculation of rabies virus. (Reproduced from Jackson AC: Pathogenesis, in Rabies, edited by AC Jackson and WH Wunner, 2002, Academic Press, San Diego, pp 345-82,[10] Copyright Elsevier).

Duration of Different Stages Rabies

Stage	Type (% of cases)	Durations (% of cases)	Associated Findings
Incubation period		Under 30 day:25% 30-90 days: 50% 90 days to yr : 20% More than 1 yr: 5%	None
Prodrome and early symptoms		2-10 days	Paresthesiae ,itching or pain at the wound fever; malaise; anorexia; nauses; and vomiting.
Acute neurologic disease	Furious rabies (80%)	2-7 days	Hallucination; bizarre behavior, anxiety; agitation; hydrophobia; autonomic dysfunction
	Paralytic rabies (20%) Atypical rabies	2-7 days	Ascending flaccid paralysis
Coma			
Death*		0-14 days	

*Rare recoveries have been reported. (Data from Fishbein.)





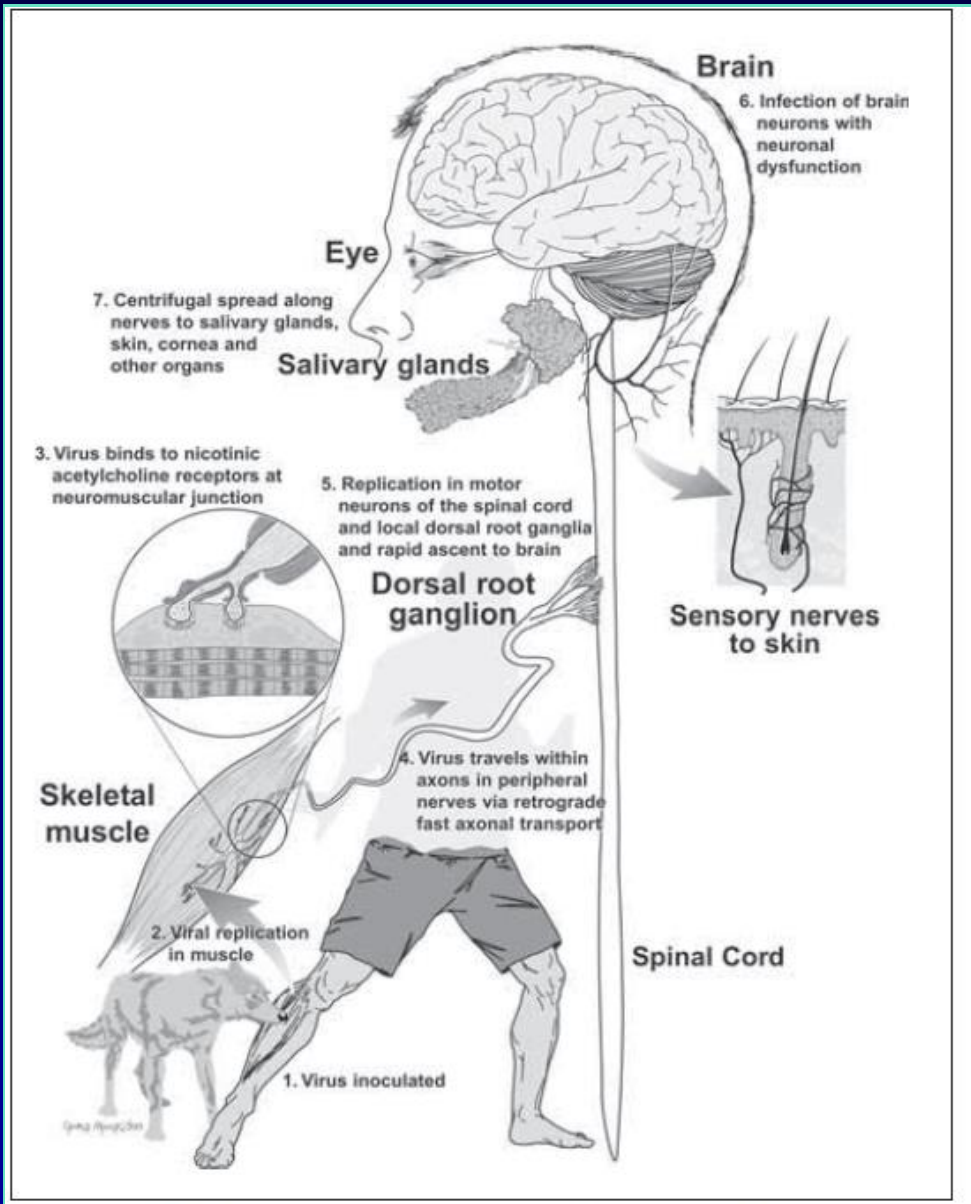


Figure 1: Schematic diagram showing the sequential steps in the pathogenesis of rabies after an animal bite/peripheral inoculation of rabies virus. (Reproduced from Jackson AC: Pathogenesis, in Rabies, edited by AC Jackson and WH Wunner, 2002, Academic Press, San Diego, pp 345-82;[10] Copyright Elsevier).

Diagnosis of human rabies

Definite : Presence of definite bite exposure plus 3 major cardinal manifestations
- Aerophobia/hydrophobia
- Fluctuating consciousness
- Autonomic stimulation signs

And/or one or more of the followings

1. Presence of Nab to rabies virus in serum/CSF in non-vaccinated patient
2. Virus isolation from suspensions of biopsy (brain or saliva)
3. Antigen detection by direct IF method (skin biopsy/brain)
4. Detection of rabies virus RNA in saliva by RT-PCR,NASBA
5. Local prodrome at the site of bite (and progress to involve the entire bitten region) plus above criteria

Probable

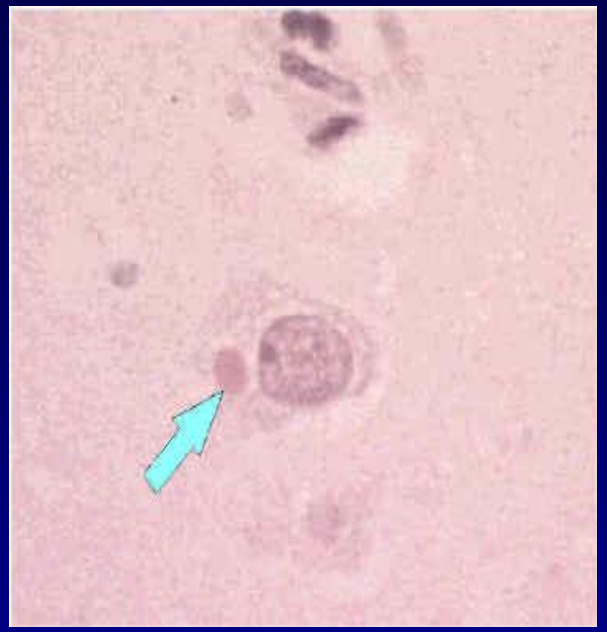
- Viral encephalitis (±bite exposure) plus clinical features (except phobic spasm)
- Atypical GBS (±bite exposure): Fever, percussion edema, SIADH, bladder incontinence

To date, there is no effective and validated etiological treatment for rabies once the symptoms have set.

Ribavirin
Interferon alfa
favipiravir (T-705)
Rabies vaccine
Rabies immunoglobulin
Monoclonal antibody
Ketamine
Corticosteroids

Anti-mortem diagnosis:

PCR- Saliva, urine, CSF,
extracted hair follicles, skin from the nape of neck containing hair follicles
Antibody-Blood, CSF



Human rabies in India: an audit from a rabies diagnostic laboratory

Reeta Subramaniam Mani, Ashwini Manoor Anand and Shampur Narayan Madhusudana

Caring for patients with rabies in developing countries – the neglected importance of palliative care

Arnaud Tarantola[1,2], Yoann Crabol[1], Bangalore Jayakrishnappa Mahendra[3], Sotheary In[1,2], Hubert Barennes[1], Hervé Bourhy[4], Yiksing Peng[1,2], Sowath Ly[1] and Philippe Buchy[5,6] Tropical Med Inter Health 2016

Prevention and Management of Rabies Overview:

- Epidemiology and Human Rabies in Asia
- Management of Human Rabies
- **Post-Exposure Rabies Prophylaxis**
- Pre-Exposure Rabies Prophylaxis

HUMAN RABIES PREVENTION

Prioritisation by authorities (One Health concept.)

National Policy - Co-ordination - Resource(funding..) - High biological products

Multicultural and religious influences

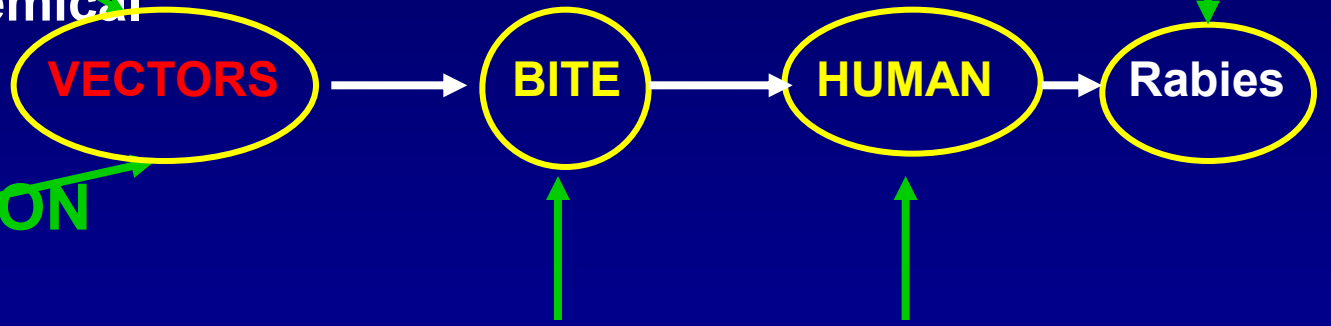
Pre-exposure prophylaxis.

CONTROL Vectors (dog..)

Elimination, culling
Sterilization- surgery, chemical

vaccinating the dog population ,achieving 'herd immunity'

ANIMAL IMMUNIZATION



Diagnosis/treatment

Few rabies cases receive laboratory Confirmation and report

Animal vaccine

Mass dog vaccination campaigns
Awareness about responsible pet ownership

Community education

PREVENT BITE

Education
Law of regulation
Bite report

IMMUNIZATION

Post-exposure prophylaxis

Seek alternative, non-medical treatments, Culture belief

Rabies Immunization

- **Post-Exposure Prophylaxis**

  Guideline and Regimens:

  IM and Important Issues of ID regimens in limited-resource countries

  Rabies Immunoglobulin:

  Inappropriate RIG Treatment

  Booster Vaccination:

  How and What's benefit ?

Guideline for Rabies post-exposure prophylaxis

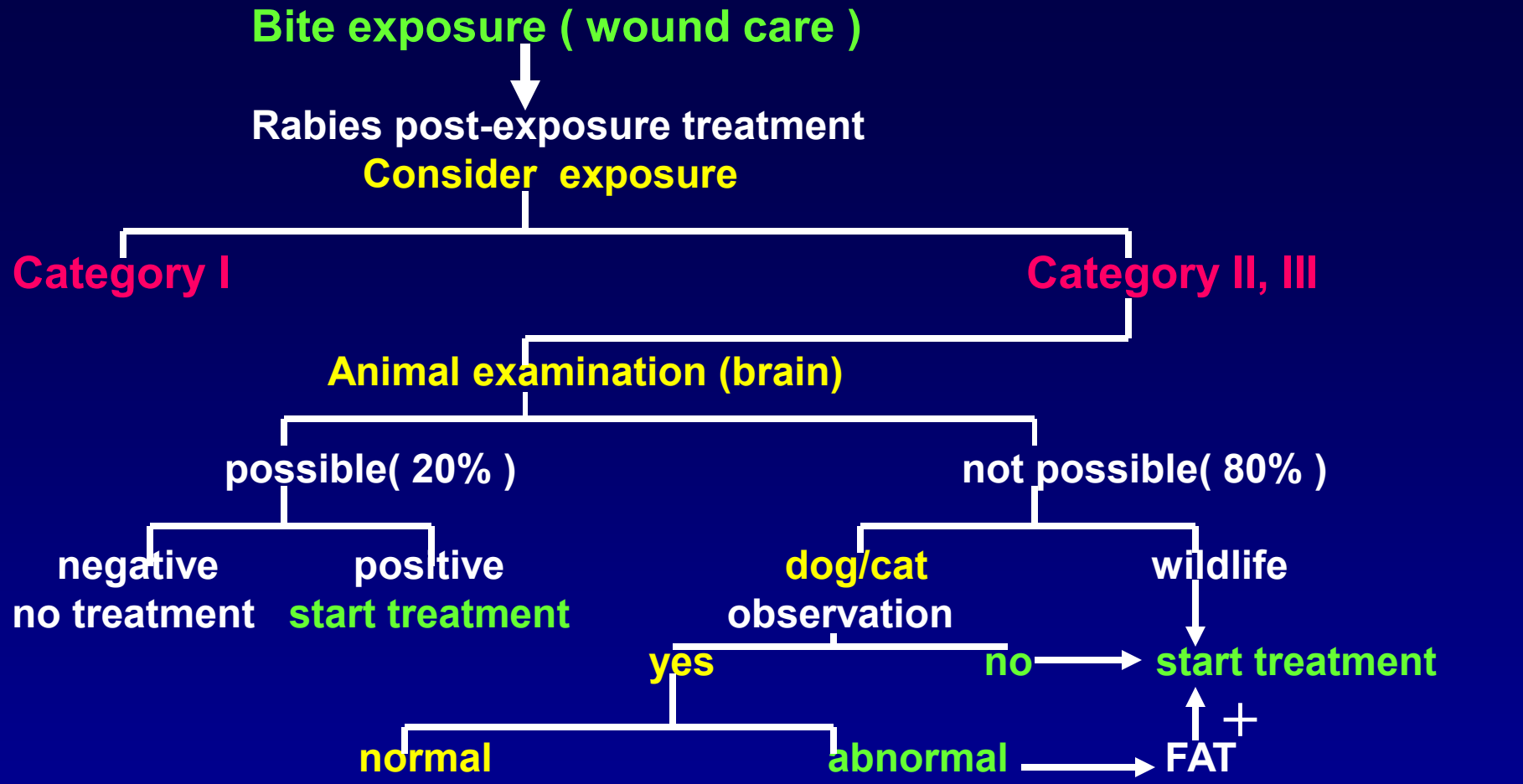
Factors that should be considered:

- Epidemiology of rabies in country
- Severity of rabies exposure (nature of injury)
- Species of the animal and clinical features of the animal responsible
- Vaccination history of the animal, and type and timing of vaccine used ((dog and cat)
- Availability of the animal (dog and cat) for observation
- Result of laboratory testing

The decision to administer post-exposure prophylaxis after an exposure to an apparently healthy animal should be based on a careful risk assessment by a qualified medical professional.

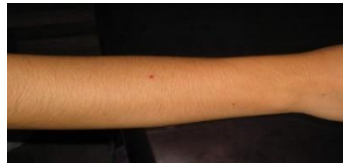
WHO 2018

Diagram for Post-Exposure Rabies Treatment in Thailand



Recommended post-exposure prophylaxis according to type of exposure (WHO 2018)

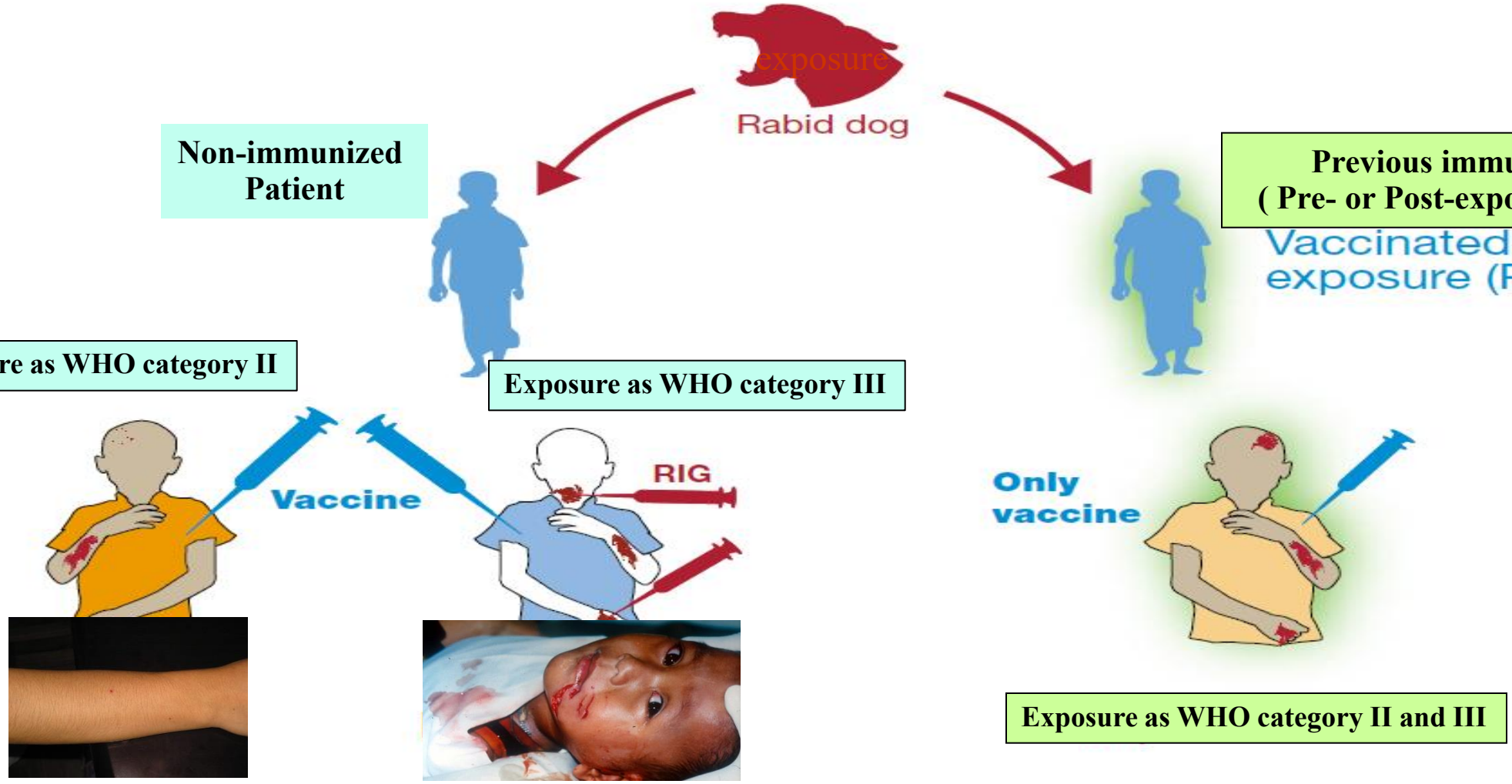
Category of exposure	Type of exposure to a domestic or wild animal suspected or confirmed to be rabid or animal unavailable for testing	Recommended post-exposure prophylaxis
I	Touching or feeding animals, licks on intact skin (no exposure)	None, if reliable case history is available[a]
I I	Nibbling of uncovered skin Minor scratches or abrasions without bleeding (exposure)	Administer vaccine immediately Stop treatment if animal remains healthy throughout an observation period of 10 days[b] or is proven to be negative for rabies by a reliable laboratory using appropriate diagnostic techniques. Treat as category III if bat exposure involved.
I I I	Single or multiple transdermal[c] bites or scratches, contamination of mucous membrane or broken skin with saliva from animal licks, exposures due to direct contact with bats (severe exposure).	Administer rabies vaccine immediately, and rabies immunoglobulin, preferably as soon as possible after initiation of post-exposure prophylaxis. Rabies immunoglobulin can be injected up to 7 days after administration of first vaccine dose. Stop treatment if animal remains healthy throughout an observation period of 10 days or is proven to be negative for rabies by a reliable laboratory using appropriate diagnostic techniques.



The incubation period of the majority of cases is 2–3 months, while 2–3% of cases have had an incubation period > 1 year, with an exceptional case of 8 years

If an apparently healthy dog or cat in or from a low-risk area is placed under observation, treatment may be delayed

Rabie Post-Exposure Prophylaxis



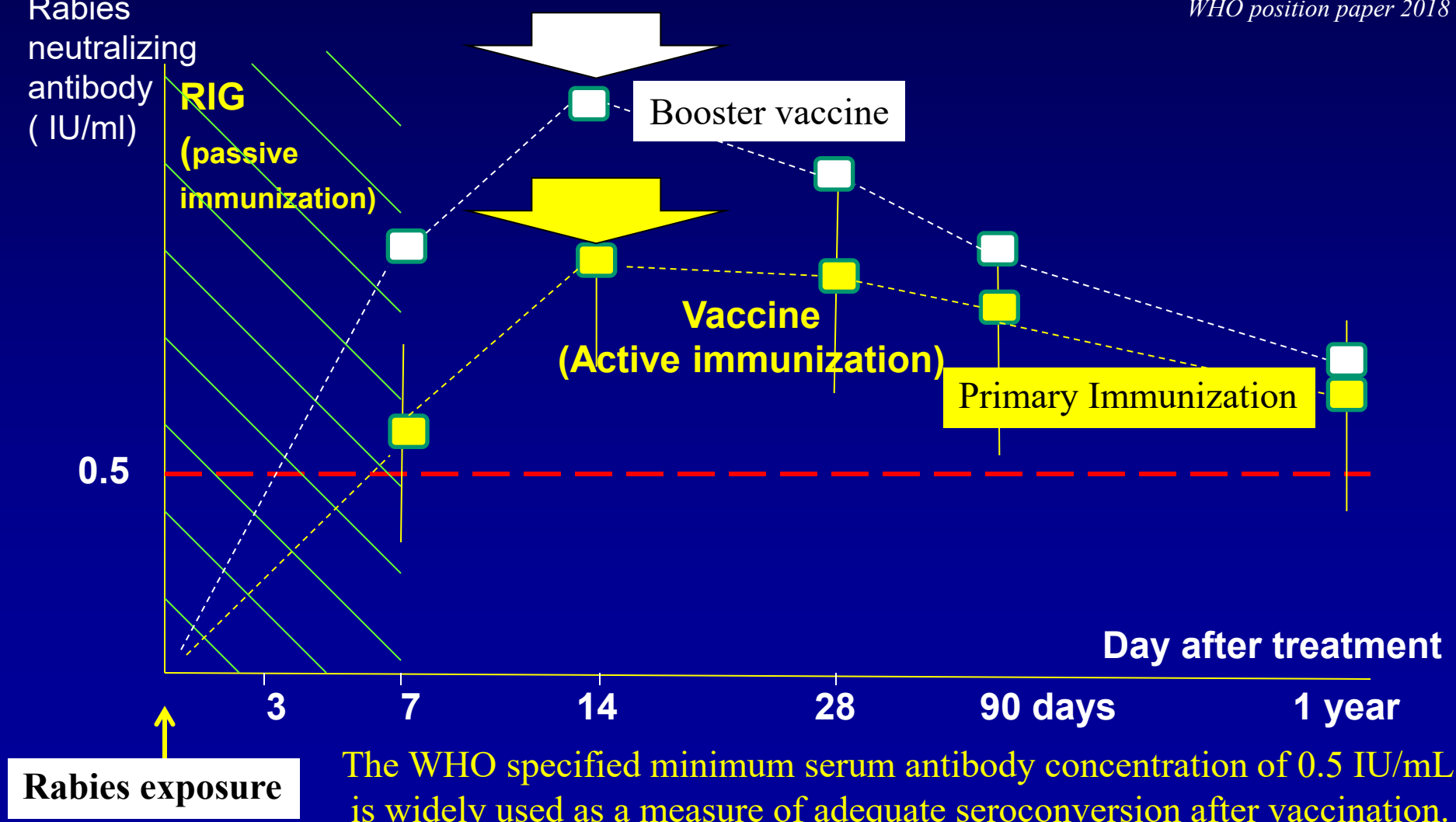
Post-Exposure Prophylaxis after Rabies Exposure

WHO/CDS/NTD/NZD/2018.04

Post-exposure rabies prophylaxis

The incubation period of the majority of cases is 1–3 months.4 An incubation period longer than 1 year has also been documented

WHO position paper 2018



The WHO specified minimum serum antibody concentration of 0.5 IU/mL is widely used as a measure of adequate seroconversion after vaccination.

Post-Exposure Prophylaxis (PEP) for Possible Rabies Exposure

Any animal bite/scratch should receive cleansing of wound with soap povidone iodine.

Non-immunized patient *will need to obtain full PEP* in the event of a possible exposure to a proven or suspected rabid animal.

Exposure WHO category II: rabies vaccine as regimen:

IMx5 (1-1-1-1-1-0- ESSEN) or IMx4 or **Zagrab (2-0-1-0-1)**
TRC-ID(2-2-2-0-2), IPC-ID (2-2-2-0-0),4-site ID(4-4-4-0-0)

Exposure WHO category III: rabies vaccine as regimen:

IMx5 (1-1-1-1-1-0- ESSEN) or IMx4 or Zagrab (2-0-1-0-1)
TRC-ID(2-2-2-0-2), IPC-ID (2-2-2-0-0),4-site ID(4-4-4-0-0)
plus rabies immune globulin (ERIG or HRIG)

Immunized patient (who have completed a pre-exposure (2 or 3 doses) or post-exposure rabies immunization (at least 0,3,7) received the only booster vaccination and do not require RIG (IM or ID)

- Booster regimen: 1 dose of IM or ID on days 0 and 3 OR 4 doses ID on day 0

(WHO Recommendation 2018)

Appropriateness of Intramuscular and Intradermal Regimen for Post-Exposure Prophylaxis (WHO Recommendation 2018)

Shorten regimens (ID and IM) for post-exposure prophylaxis

One or two weeks for post-exposure prophylaxis (comfortable)

- Less vaccine cost (reduced vaccine doses/volume)
- Prevent short supply of cell-culture rabies vaccine
- Reduction of indirect costs (loss of wage, transportation cost,….)
- Reduced adverse reactions
- Safe and efficacy

Recommended ID regimen of PEP

IPC-ID (2-2-2-0-0)

4-site ID 1 week (4-4-4-0-0)

TRC-ID (2-2-2-0-2)

Warrel-ID (4-0-2-0-1)

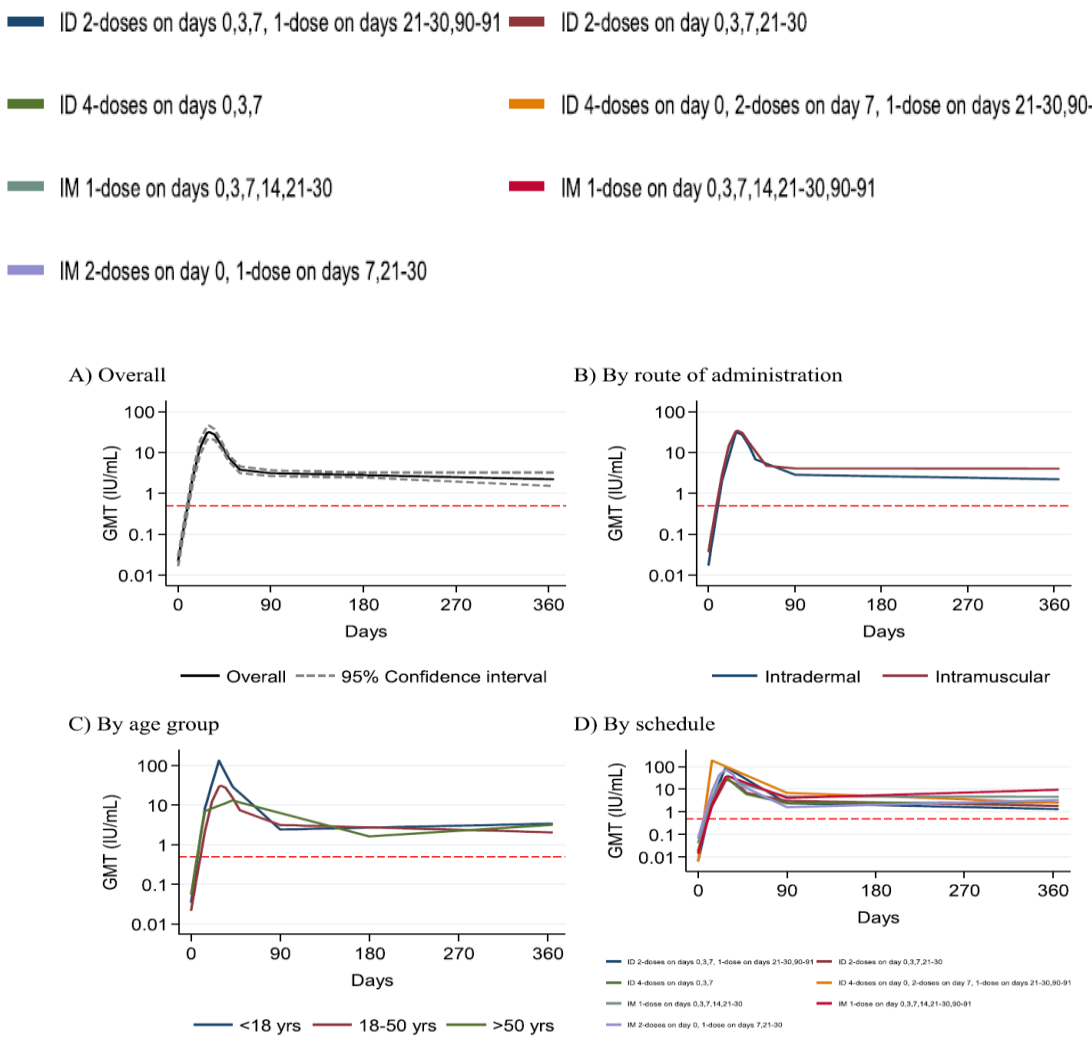
Recommended IM regimen of PEP

Zagrab- IM (2-0-1-0-1)

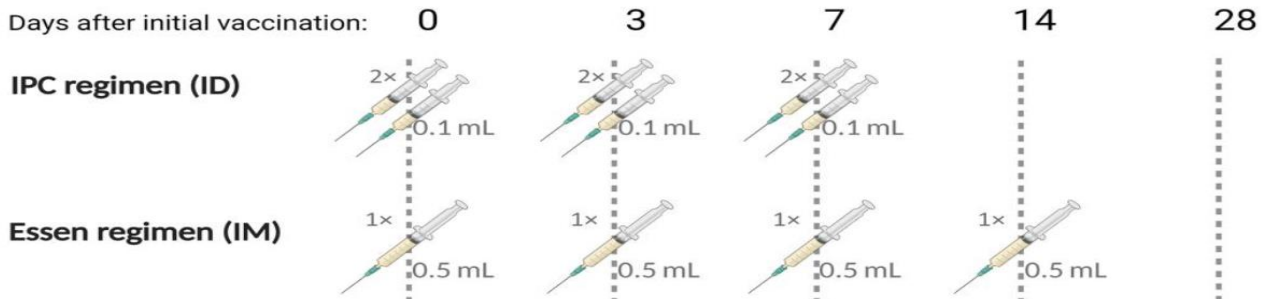
ESSEN- IM 5 doses /4 doses (*1-1-1-1-1* or 1-1-1-1)

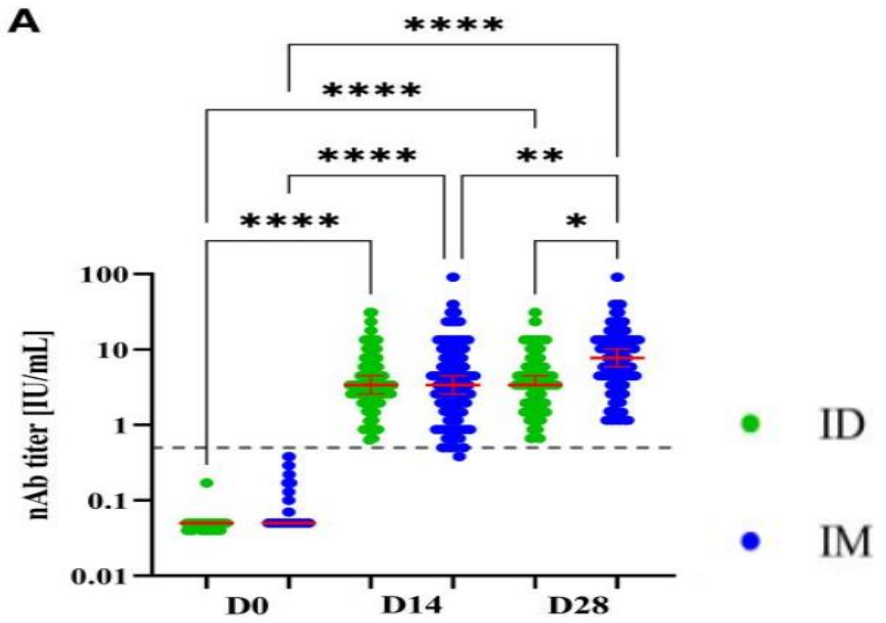
Immunogenicity after pre- and post-exposure rabies vaccination: A systematic review and dose-response meta-analysis

Chang Xu; Vaccine 2021; 39 (2021) 1044–1050

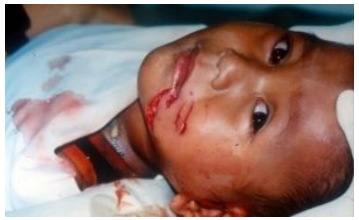


Side-by-side Comparative Study of the Immunogenicity of the Intramuscular and Intradermal Rabies Post-exposure Prophylaxis Regimens in a Cohort of Suspected Rabies Virus Exposed Individuals





WHO recommends PEP for category II and III exposures (see Table 1).



The WHO rabies exposure categories are:

Category I touching or feeding animals, animal licks on intact skin (no exposure);

Category II nibbling of uncovered skin, minor scratches or abrasions without bleeding (exposure);

Category III single or multiple transdermal bites or scratches, contamination of mucous membrane or broken skin with saliva from animal licks, exposures due to direct contact with bats (severe exposure).

Table 1: PEP recommendations by category of exposure

	Category I exposure	Category II exposure	Category III exposure
Immunologically naive individuals of all age groups	Wash exposed skin surfaces. No PEP required.	Wound washing and immediate vaccination: - 2-sites ID on days 0, 3 and 7[6] OR - 1-site IM on days 0, 3, 7 and between day 14-28[7] OR - 2-sites IM on days 0 and 1-site IM on days 7, 21[8] RIG is not indicated.	Wound washing and immediate vaccination - 2-sites ID on days 0, 3 and 7[6] OR - 1-site IM on days 0, 3, 7 and between day 14-28[7] OR - 2-sites IM on days 0 and 1-site IM on days 7, 21[8] RIG administration is recommended.
Previously immunized individuals of all age groups	Wash exposed skin surfaces No PEP required.	Wound washing and immediate vaccination*: - 1-site ID on days 0 and 3; OR - at 4-sites ID on day 0; OR - at 1-site IM on days 0 and 3); RIG is not indicated.	Wound washing and immediate vaccination*: - 1-site ID on days 0 and 3; OR - at 4-sites ID on day 0; OR - at 1-site IM on days 0 and 3; RIG is not indicated.

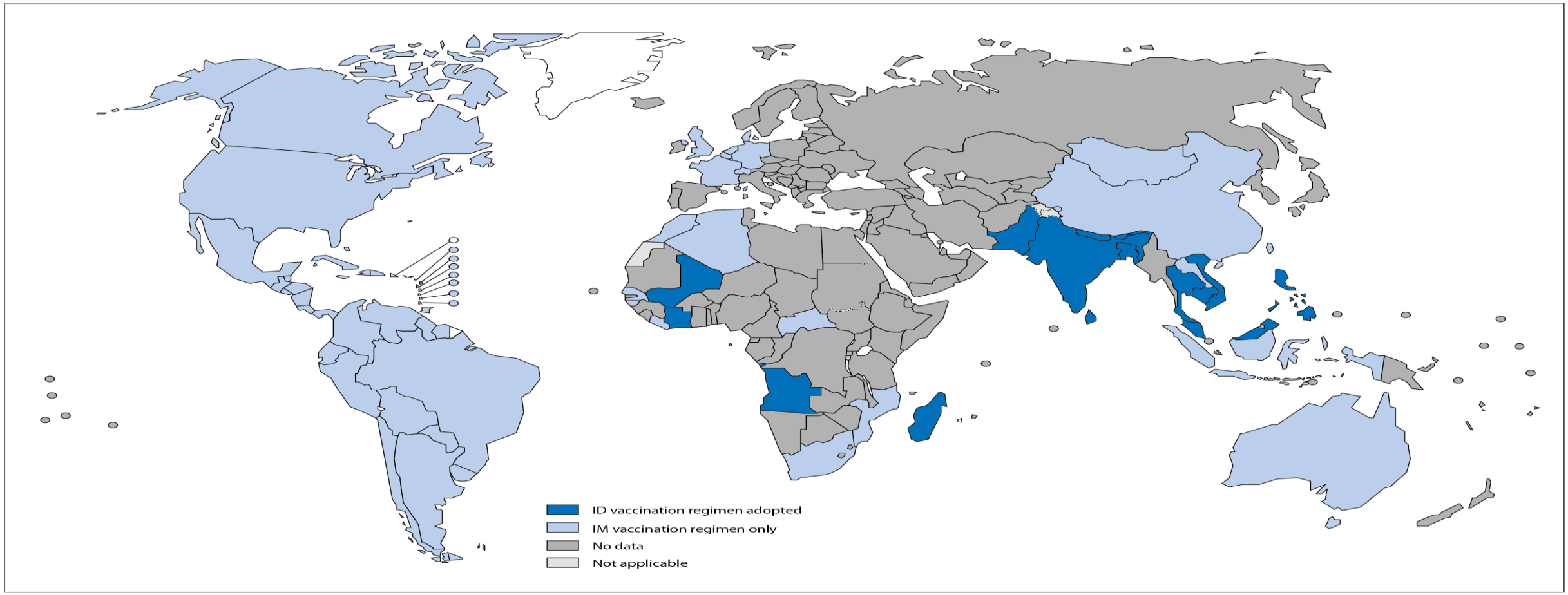
* *except if complete PEP already received within <3 months previously*

WHO Recommendation 2018

Evaluation of Cost-Effective Strategies for Rabies Post-Exposure Vaccination in Low-Income Countries

PLOS Negleted Trop Dis 2011

Use of intramuscular (IM) or intradermal (ID) rabies vaccination regimens, by country, 2022



Data Source: World Health Organization
Map Production: Control of Neglected Tropical Diseases (NTD)
World Health Organization

World Health Organization

Overview of rabies post-exposure prophylaxis access, procurement and distribution in selected countries in Asia and Africa, 2017–2018

Vaccine 37 (2019) A6–A13

Table 1

Overview of administration route, dosage schedule, cost, and accessibility of rabies vaccine and rabies immunoglobulin (RIG) in the public and non-private sectors by country, in selected countries in Asia and Africa (N = 23), January 2017–May 2018.

Country	Route of administration[a]	Dosage schedule[b]	Vaccine accessibility[c]	Vaccine cost to patient	RIG accessibility[c]	RIG cost
Bangladesh[*] [†]	ID	Updated Thai Red Cross	Widely accessible	Free	Accessible	Free-US $ 15/vial
Bhutan[†]	ID	Updated Thai Red Cross	Widely accessible	Free	Accessible	Free
India[*] [†]	ID IM	Updated Thai Red Cross Essen 5-dose	Accessible	Free	Limited	Free
Nepal[*]	ID IM	Updated Thai Red Cross Essen 5-dose	Accessible	Free	Limited	–
Sri Lanka[†]	ID	Updated Thai Red Cross	Widely accessible	Free	Accessible	Free
Pakistan[*]	ID IM	Updated Thai Red Cross Essen 5-dose	Limited	Free	Limited	Free
Cambodia[*]	ID IM	Updated Thai Red Cross Essen 5-dose	Limited	Free – US$ 15/dose	Limited	US$ 37/patient
China[†]	IM	Zagreb Essen 5-dose	Widely accessible	US$ 50/course[d]	Widely accessible	US$ 25–50/vial
Mongolia	IM	Essen 5-dose	Widely accessible	Free	Limited	Free
Philippines[†]	ID	Updated Thai Red Cross	Widely accessible	Free	Accessible	US$ 28–32/vial
Vietnam[†]	ID IM	Updated Thai Red Cross Essen 5-dose	Accessible	US$ 7–13/dose	Accessible	US$ 15–27/vial

[*] Gavi-eligible countries; countries with a Gross National Income per capita below or equal to US$ 1580 on average over the past three years (2015–2017).

Post-Exposure Prophylaxis (PEP) for Possible Rabies Exposure

Any animal bite or scratch should receive prompt local first aid by thorough cleansing of wound with soap and povidone iodine.

Non-immunized patient *will need to obtain full PEP* in the event of a possible exposure to a proven or suspected rabid animal.
RIG and a series of vaccination for severe exposure.

Concern: - Different rabies post-exposure guideline in each country
- Different rabies post-exposure vaccine regimens, alternative routes of administration.
- Available of cell-culture vaccine (generic vaccines)
- Rabies immunoglobulin (equine or human) may not be available

Immunized patient (who have completed a pre-exposure or post-exposure rabies immunization) received the only booster vaccination and do not require RIG (IM or ID)

Imovax® / Merieux Inactivated Rabies Vaccine (MIRV)	Rabipur®/ RabAvert®	Chirorab®	Cocav (Кокав)	Indirab®	Abhayrab ®	Speeda™ / Rabies Vaccine (Vero cell) for Human Use, Freeze-dried	Bioshoot / Rabies Vaccine (Vero cell) for Human Use, Freeze-dried
Sanofi Pasteur SA, ฝรั่งเศส	Bavarian Nordic A/S, เดนมาร์ก	Chiron Behring Vaccine*, อินเดีย	NPO Microgen, รัสเซีย	Bharat Biotech, อินเดีย	Human Biologicals Institute, อินเดีย	Liaoning Cheng Da Biotechnology, จีน	Changchun Zuoyi Biological, จีน
Human diploid cell, MRC-5 strain (HDCV)	Primary cultures of Chicken fibroblast (PCECV)	Purified Chick Embryo Cell Vaccine (PCECV)	Primary Syrian Hamster Kidney Cell Culture (PHKCV)	Chromatographically Purified Vero Cell (PVRV)	Purified Vero Rabies Vaccine (PVRV)	Chromatographically Purifier Vero Cell Rabies Vaccine (PVRV)	Vero Cell (PVRV)
Wistar rabies PM/WI 38–1503–3M strain	Flury Low Egg Passage (LEP)	Flury LEP strain	Rabies virus Vnukovo-32 strain	Pitman Moore Strain	L. Pasteur 2061/ Vero Rabies strain	L.Pasteur PV-2061	CTN-1V strain (fixed strain)

HDCV® / Rabies Vaccine (Human Diploid Cell) for Human Use, Freeze-dried	Rabies Vaccine (Human Diploid Cell) for Human Use, Freeze-dried	Rabies Vaccine (Hamster Kidney Cell) for Human Use	Rabies Vaccine (Hamster Kidney Cell) for Human Use	Rabies Vaccine (Hamster Kidney Cell) for Human Use	Rabies Vaccine (Hamster Kidney Cell) for Human Use*	TRCS Speeda	Abhayrab-PF®	Sure Rab™
Chengdu Kanghua Biological Products, จีน	Beijing Minhai Biotechnology, จีน	Henan Grand Biopharmaceutical, จีน	Bohui Biopharmaceutical, จีน	Jilin Yatai Bio-Pharmaceuticals, จีน	Lanzhou Institute of Biological Products**, จีน	สถานเสาวภา สภากาชาดไทย, ไทย	Human Biologicals Institute, อินเดีย	Bio-Med, อินเดีย
Human Diploid Cell (HDCV)	Human Diploid Cell (HDCV)	Hamster Kidney Cell (HKCV)	Hamster Kidney Cell (HKCV)	Hamster Kidney Cell (HKCV)	Hamster Kidney Cell (HKCV)	Chromatographically Purifier Vero Cell Rabies Vaccine (PVRV)	Purified Vero Rabies Vaccine (PVRV)	Vero cell culture (PVRV)
Pitman-Moore strain, MRC-5 cells	PM strain	NA	NA	NA	NA	L.PASTEUR PV-2061 strain	L. Pasteur 2061/ Vero Rabies strain	Pitman Moore Strain

Rabies Vaccine (Vero cell) for Human Use, Freeze-dried	Rabies Vaccine (Vero cell) for Human Use*	Yisheng Junan® / Rabies Vaccine (Vero cell) for Human Use, Freeze-dried	Rabies Vaccine (Vero cell) for Human Use*	Rabies Vaccine (Vero cell) for Human Use, Freeze-dried	Rabies Vaccine (Vero cell) for Human Use, Freeze-dried	Rabies Vaccine (Vero cell) for Human Use, Freeze-dried	Rabies Vaccine (Vero Cell) for Human Use
Changchun Institute of Biological Products**, จีน	Wuhan Institute of Biological Products**, จีน	Liaoning Yisheng Biopharma***, จีน	Fosun Apexvax (Dalian) Biopharmaceutical, จีน	Jiangsu CuroVax, จีน	Hualan Biological Vaccine, จีน	Shandong Yidu Biotechnology, จีน	Liaoning Chengda Biotechnology, จีน
Vero cell (PVRV)	Vero cell (PVRV)	Vero cell (PVRV)	Vero cell (PVRV)	Vero cell (PVRV)	Vero cell (PVRV)	Vero cell (PVRV)	Vero cell (PVRV)
aGV strain	L. Pasteur PV2061 strain (fixed strain)	NA	CTN-1V strain	NA	CTN-1V strain	PV strain	L. Pasteur 2061 strain

- If any doses are delayed, vaccination should be resumed, not restarted.

- A change in the route of administration or in vaccine product during a PEP or PrEP course is acceptable if such a change is unavoidable. Restarting the series of injections is not necessary; vaccination should continue according to the schedule for the new route of administration.

WHO Position paper ; Weekly Epidemiol Rec 2018; 93:201-20 (April)

Switching in Post Exposure Prophylaxis

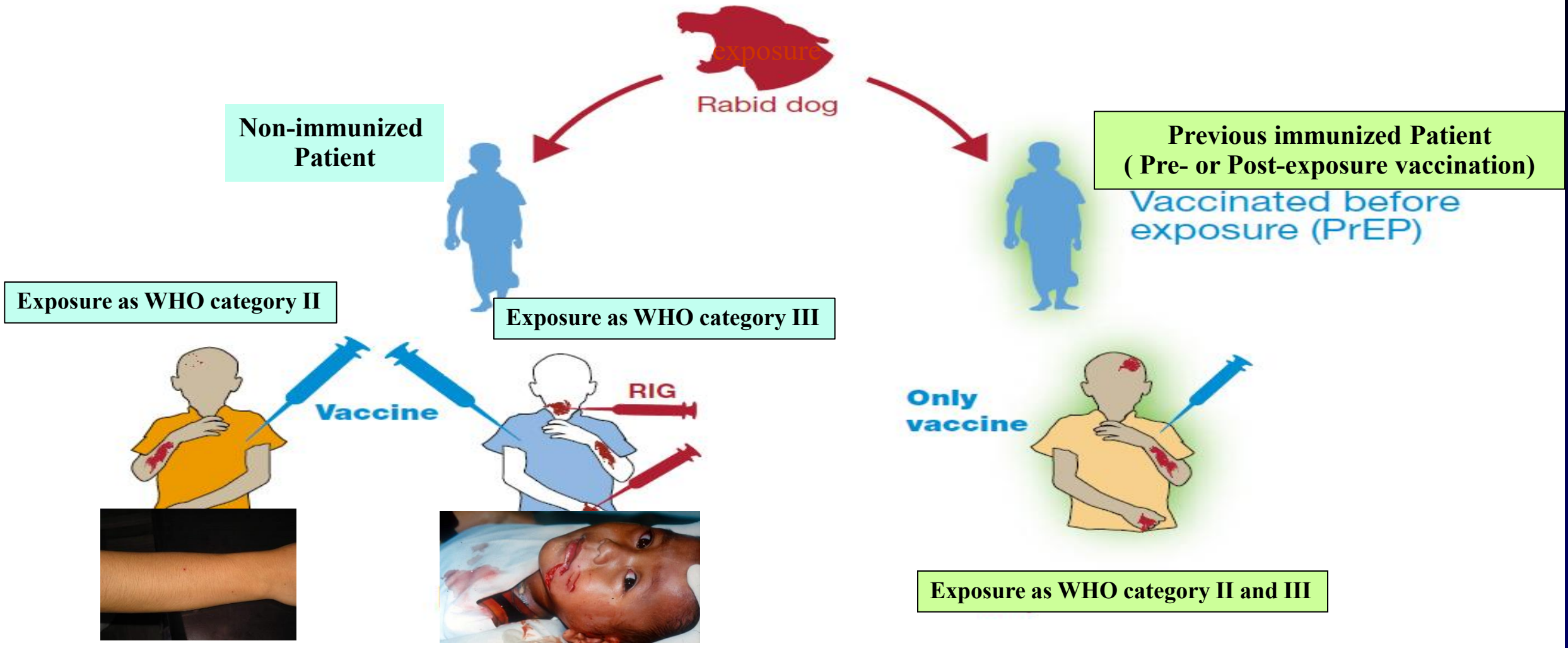
Brand switching:

Type of vaccine- 1) Chick embryo vaccine (PCECV), 2) Vero cell vaccine (PVRV,CPRV), 3) Human derived vaccine (HDCV), 4) Duck embryo vaccine (PDEV)

Regimen (Route of injection) switching

IM and ID (IM change to ID OR ID change to IM

Rabies Immunoglobulin for Post-Exposure Prophylaxis



Post-Exposure Prophylaxis after Rabies Exposure

Prioritization of RIG allocation *WHO Position paper April 2018*

However, data from rabies-endemic settings have shown that even in the absence of RIG, with thorough wound washing plus immediate vaccination and completion of the PEP course, >99% of patients survive.

If a limited amount of RIG is available, RIG allocation should be prioritized for exposed patients based on the following criteria:

- Multiple bites; Deep wounds;
- Bites to highly innervated parts of the body, such as head, neck,hands
- Patients with severe immunodeficiency;
- History of biting animal indicative of confirmed or probable rabies;
- Bite/ scratch / exposure of mucous membrane by bat can be ascertained.

Table 5: Estimated probability of rabies transmission following the bite of a rabid dog, by anatomical site (Cleaveland et al. 2002)

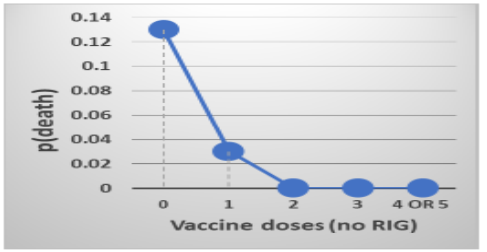
Area of bite	Transmission risk
Head/Neck	30-60%
Arm	15-40%
Hand	15-40%
Finger	15-40%
Genitalia	15-40%
Trunk	0-10%
Leg	0-10%
Foot	0-10%

Question 14: Details new evidence

Transmission risk
(Cleaveland et al. 2002)

Probability of death in rabies exposed & number of vaccine doses (no RIG)

Tanzanian data n= 2,196



Cambodian data n= 265

Preliminary data (2003-2014) ***0 deaths:***
- Among 62 persons exposed to rabid dogs
- Among 203 persons exposed to untested, but sick dogs
- Even though **NO RIG**

Interventions improving chance of survival after a rabies exposure:
- Thorough wound washing + same day vaccine administration
  → **99% patients survived even without RIG**
- Use of quality vaccine
- Completion of full course of PEP regimen

Use of rabies immune globulin (RIG)

Group 1) Non-immunized patients : WHO category III

- **Equine rabies immune globulin(ERIG) = 40 IU/kg**
- **Human rabies immune globulin (HRIG) = 20 IU/kg**
- **Monoclonal antibody (cocktail)**

Inadequate RIG supply in rabies endemic countries

: single dose at the same time as the first dose of vaccine (site of RIG injection distant from site of vaccine injection)

: It is not indicated beyond the seventh day after the first dose of rabies vaccine, regardless of whether the day 3 and day 7 doses were received, because an active antibody response to the CCV has already started, and there may be interference between active and passive immunization.

: It should be infiltrated around and into all wounds

- After calculating the RIG dose, only the amount of RIG necessary for infiltrating into and around the wound is administered, as much as anatomically possible.

Post-exposure prophylaxis, including rabies immunoglobulin, should always be administered when category III exposure is recognized, even months or years after contact. *WHO 2018*

Prioritization of RIG allocation

However, data from rabies-endemic settings have shown that even in the absence of RIG, with thorough wound washing plus immediate vaccination and completion of the PEP course, >99% of patients survive.

Rabies mAbs licensed or in clinical development

Name	Developer	Stage	Clinical trials registry number
Licensed			
Rabishield (SII RMab)	Serum Institute of India PVT. LTD. (SIIPL)	Phase 1, 2/3 clinical trials completed and licensed in December 2016	CTRI/2009/091/000465[17] CTRI/2012/05/002709[18]
Twinrab™ (RabiMabs)	Zydus Cadila in India	Phase 1/2, 3 clinical trials completed and licensed in September 2019	CTRI/2015/06/005838[19] CTRI/2017/07/009038[20]
Applying for licensure			
rhRIG	NCPC (China) in collaboration with MITT (USA)	Phase 1, 2 and 3 clinical trials completed	NCT02559921[21] ChiCTR1900023809[22] ChiCTR1900023785[23] ChiCTR1900023236[24] ChiCTR1900021478[25]
In active clinical development			
SYN023 (CTB011/CTB012)	Synermore Biologics in China	Phase 1 and 2 clinical trials completed and phase 3 clinical trials are planning	CTR20190281[26] NCT02956746[27] NCT04644484[28]
Withdrawn from development			
CL184 (CR57/CR4098)	Crucell in Netherlands	Phase 1 and 2 clinical trials completed	ISRCTN18660493[29] ISRCTN12693237[29] NCT00708084[30] NCT01228383[31]

Human rabies despite post-exposure prophylaxis: a systematic review of fatal breakthrough infections after zoonotic exposures

Erin R Whitehouse; Lancet Infect Dis 2022: Online Dec 2022

	All cases (n=122)	Breakthrough infections with reported or possible deviations from core practices (n=68)*	Breakthrough infections without deviations from core practices (n=54)*
WHO classification of human rabies case[4]			
Confirmed	56/122 (46%)	24/68 (35%)	32/54 (59%)
Probable	66/122 (54%)	44/68 (65%)	22/54 (41%)
Age, years			
0–9	42/122 (34%)	17/68 (25%)	25/54 (46%)
10–19	27/122 (22%)	20/68 (29%)	7/54 (13%)
20–29	9/122 (7%)	7/68 (10%)	2/54 (4%)
30–39	8/122 (7%)	5/68 (7%)	3/54 (6%)
40–49	5/122 (4%)	2/68 (3%)	3/54 (6%)
50–59	17/122 (14%)	8/68 (12%)	9/54 (17%)
60–69	8/122 (7%)	5/68 (7%)	3/54 (6%)
70–79	4/122 (3%)	3/68 (4%)	1/54 (2%)
≥80	2/122 (2%)	1/68 (1%)	1/54 (2%)

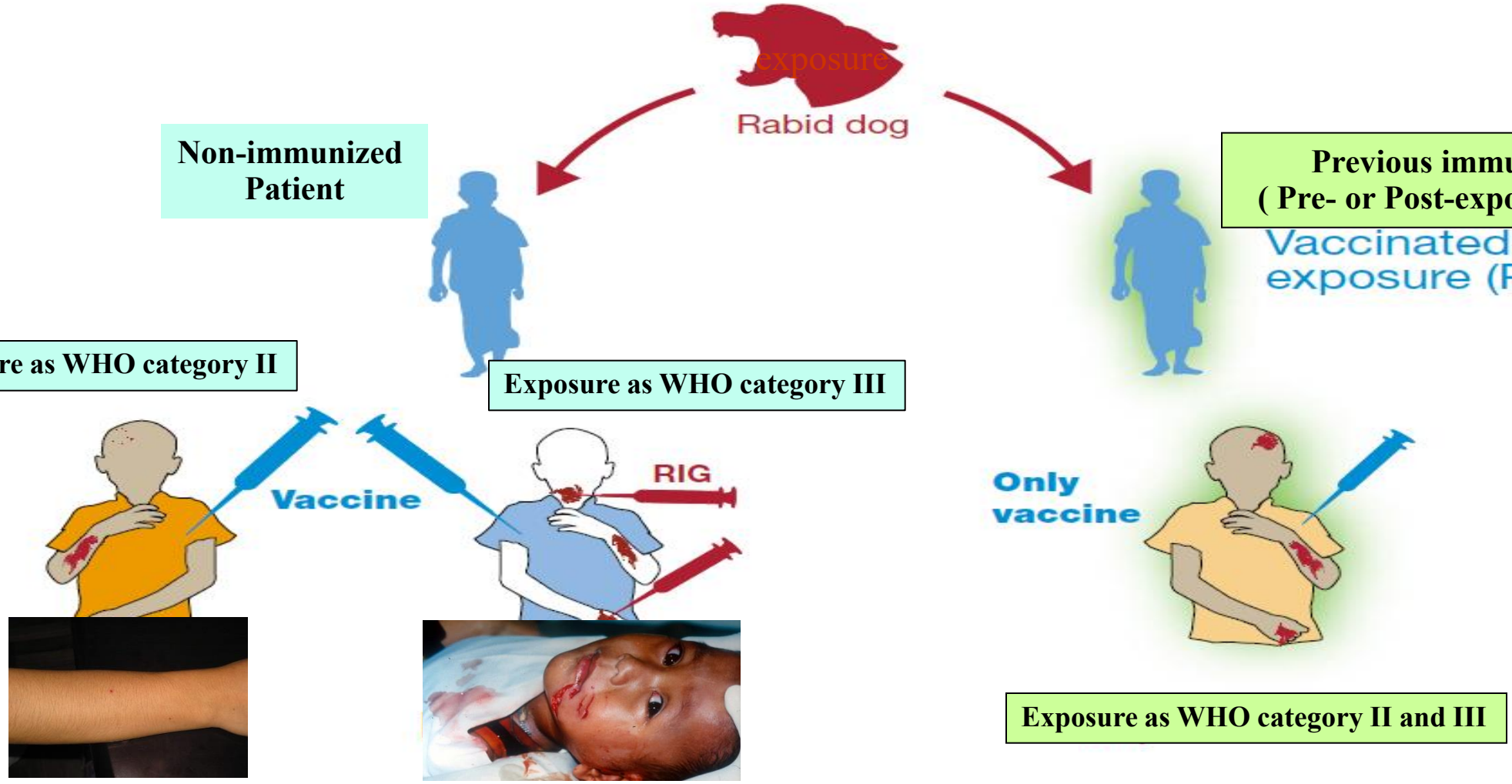
86 breakthrough infections(cleaning wound with vaccine administration):

- median time from exposure to symptom onset was 20 days (IQR 16–24).
- 77% participants received PEP within 2 days of an exposure.
- **Severe wounds** (multiple wound sites or bites to the head, face, or neck) **(69%).**
- **Deviations from core practices (56%):**

Possible causes-

Errors administration of RIG,
Delays in seeking health care,
Comorbidities or immunosuppression.

Rabie Post-Exposure Prophylaxis



Post-Exposure Prophylaxis after Rabies Exposure

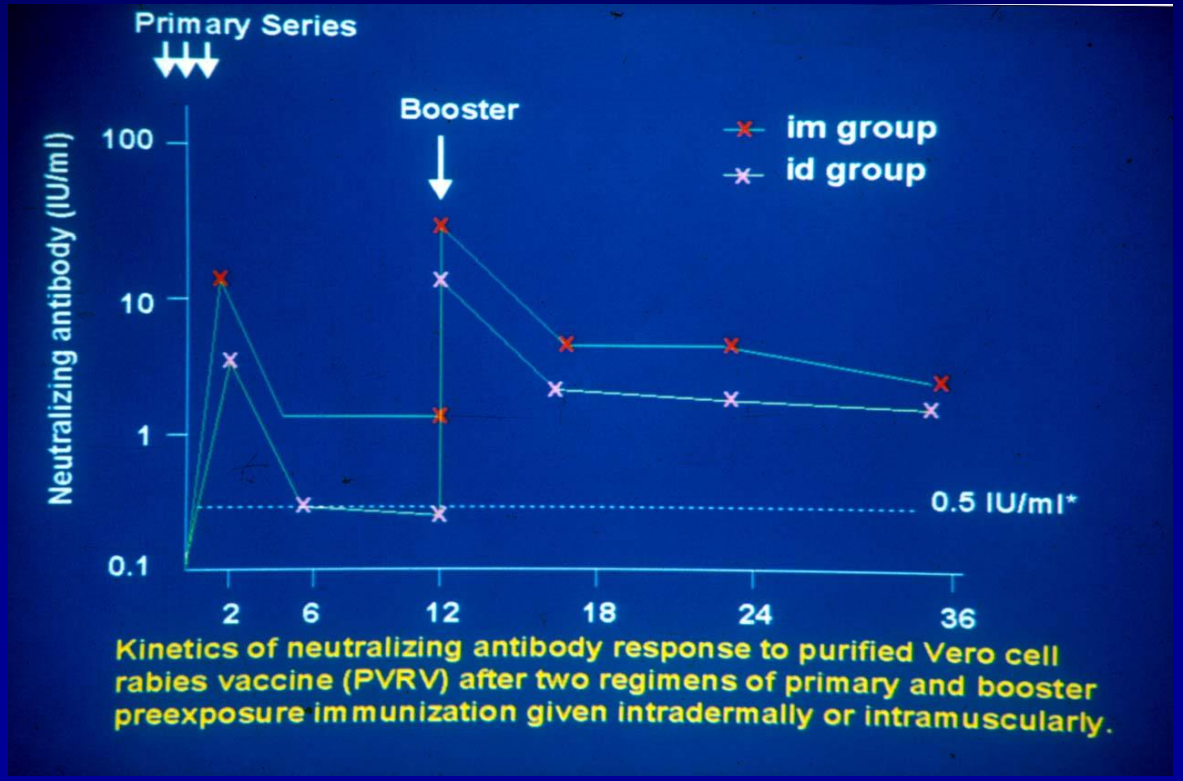
WHO/CDS/NTD/NZD/2018.04

PET for previously vaccinated individuals

• Patients who can document previous complete pre-exposure vaccination or complete post-exposure prophylaxis with a CCV.
•
• People vaccinated against rabies who have demonstrated rabies-virus neutralizing antibody titres of ≥0.5 IU/ml.

Vaccination cards recording previous immunizations are invaluable.

The WHO recommends booster vaccination if there is an additional occurrence of potential exposure.
RIG is not indicated in such cases.



Kinetics of neutralizing antibody response to purified Vero cell rabies vaccine (PVRV) after two regimens of primary and booster preexposure immunization given intradermally or intramuscularly.

WHO Position Paper : Wkly Epidemiol Rec 2010(August 6)

Rabies Antibody Response After Booster Immunization: A Systematic Review and Meta-analysis

Annefleur C. Langedijk,[1,a] Cornelis A. De Pijper,[1,a] Rene Spijker,[2,3] Rebecca Holman,[4] Martin P. Grobusch,[1] and Cornelis Stijnis[1]

[1]Center for Tropical Medicine and Travel Medicine, Department of Infectious Diseases, Division of Internal Medicine and [2]Medical Library, Academic Medical Center, University of Amsterdam, [3]Cochrane Netherlands, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, and [4]Clinical Research Unit, Academic Medical Center, University of Amsterdam, The Netherlands

Clinical Infectious Diseases® 2018;XX(XX):1–16

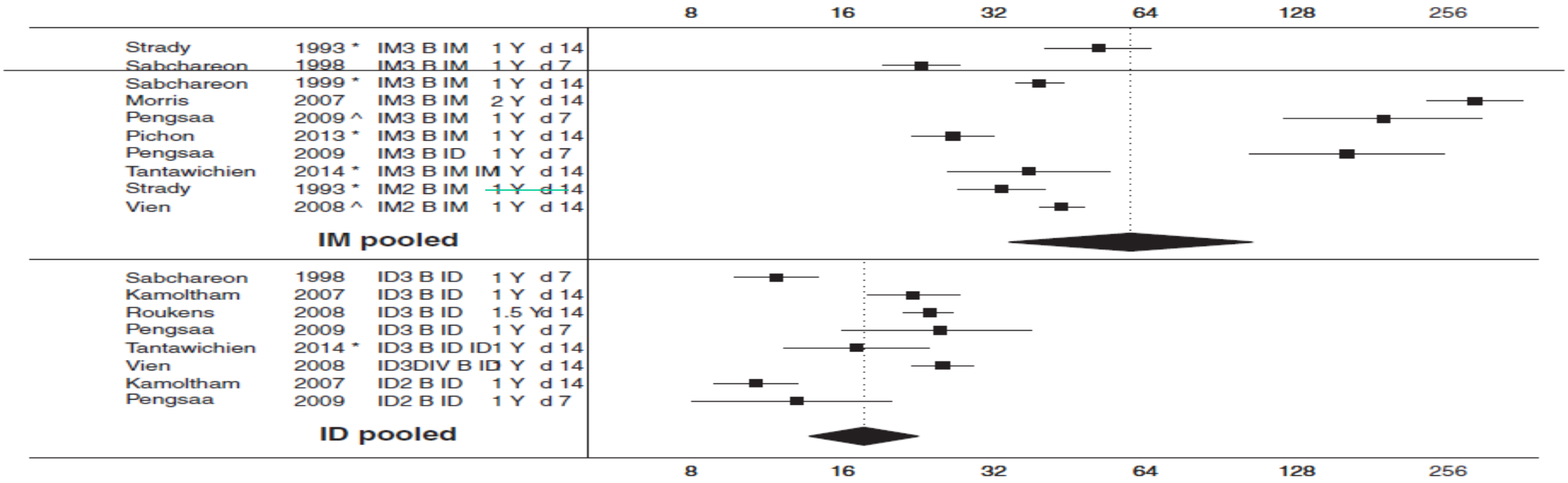
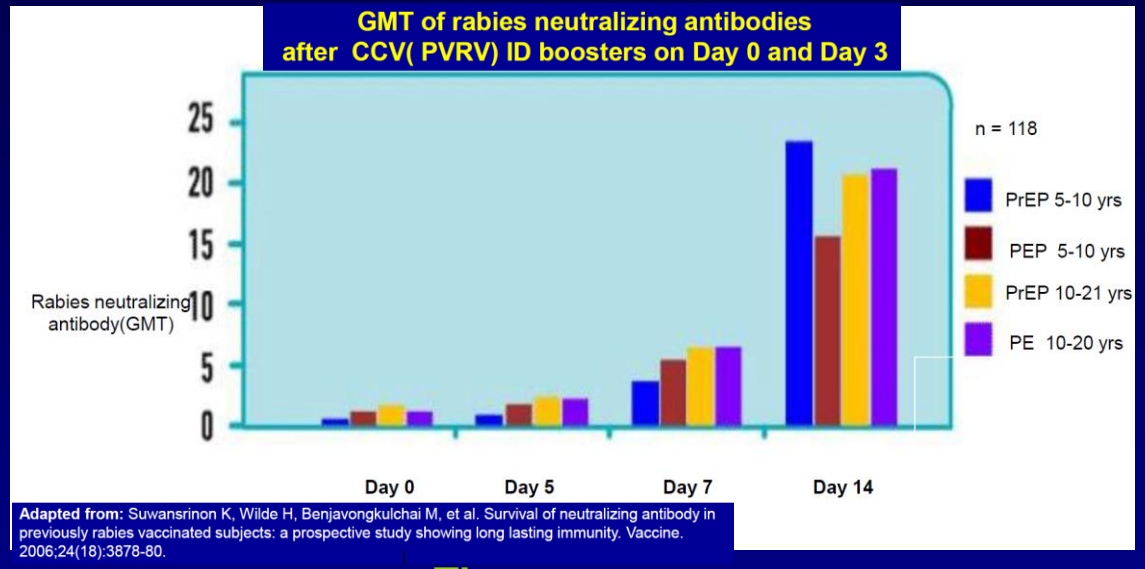
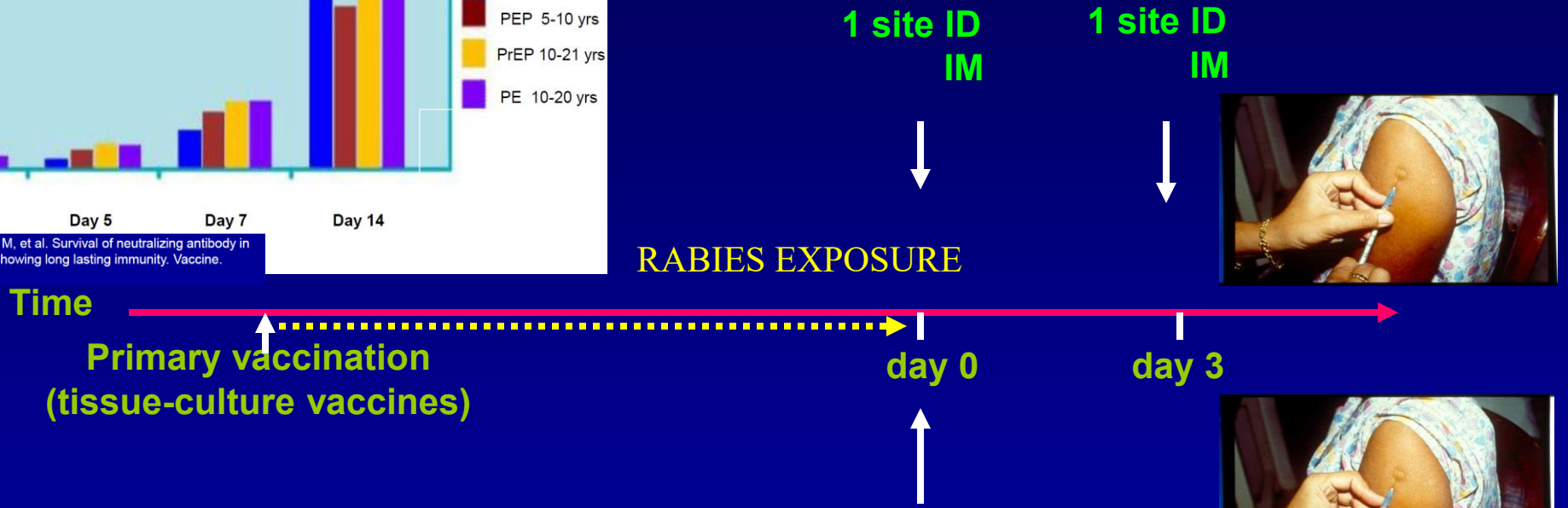


Figure 6. Geometric mean titers after boostering for intramuscular and intradermal schedules as reported in studies included in the meta-analysis of this review. Cumulative means and 95% confidence intervals are depicted as diamonds. Studies in this meta-analysis were limited to short-term boostability. The interval between primary and booster immunization is given in years; days are defined as the interval between booster immunization and antibody measurement. *Combined research arms. ^1/2 dose. Abbreviations: B, booster; d, day; ID, intradermal; ID2, 2-dose intradermal pre-exposure schedule; ID3, 3-dose intradermal pre-exposure schedule on days 0, 7, and 21–28; ID3DIV, 3-dose intradermal pre-exposure divergent schedule; IM, intramuscular; IM2, 2-dose intramuscular pre-exposure schedule; IM3, 3-dose intramuscular pre-exposure schedule on days 0, 7, and 21–28; Y, year.

WHO recommendation: Booster doses

- One doses of intramuscular (IM) or intradermal (ID) vaccination on days 0 and 3.
- a single-visit 4-site ID regimen consisting of 4 injections of 0.1 mL of CCV equally distributed over deltoids or anterior thighs or supra-scrapular areas.





WHO Position Paper : Wkly Epidemiol Rec 2010(August 6)
WHO 2013,WHO2018

Rabies Immunization in Special Hosts

Pregnant woman

Co-morbid illness- CKD with dialysis,
Chronic liver disease, DM (unpublished)

Severe Immunosuppressive conditions

- Lymphoma, autoimmune diseases
- Steroid user (> 20mg/day)
- HIV/AIDS

Our studies of patients with HIV/AIDS have shown that some with CD4 counts < 100-200 mount a significantly lower or no detectable neutralizing antibody response to rabies virus.

Proper, thorough wound treatment accompanied by local infiltration of RIG and a complete series of **five intramuscular** doses of rabies CCEEV is required for category II and III exposures.
When feasible, the rabies virus neutralizing antibody response should be determined 2–4 weeks after vaccination. WHO 2013

Prevention and Management of Rabies Overview:

- Epidemiology and Human Rabies in Asia
- Management of Human Rabies
- Post-Exposure Rabies Prophylaxis
- **Pre-Exposure Rabies Prophylaxis**

Pre-exposure immunization is recommended for anyone at increased risk of exposure to rabies virus.

Individuals at high risk of rabies exposure include:

- Persons at occupational risk
  (Laboratory personnel, animal handlers, veterinarians, and others at *risk for contracting rabies*)

- Travelers to remote rabies endemic areas
  (Travelers who are likely to have exposures to dogs or cats in canine rabies – *endemic countries* are being advised)

- Sub-populations in endemic settings with limited access to timely and adequate post-exposure prophylaxis
  (particularly in areas with *extremely high bite rates*)

What and Why Pre-exposure Prophylaxis

- Post-exposure booster vaccination after pre-exposure prophylaxis
- Periodic booster doses of vaccine are not required after primary rabies vaccination, except as an additional precaution for people whose occupation puts them at continual or frequent risk of exposure
- More economical compared with post- exposure prophylaxis of selected population.(booster dose after exposure)
- Avoid risk and adverse effect of rabies immunoglobulin in post-exposure treatment
- No failures reported in patients who received Prevent infection in uncertain exposure.

(The only way to prevent PEP failure in the areas where rabies is endemic and where RIG is not widely available would be to pre-immunize the entire potentially exposed population.)

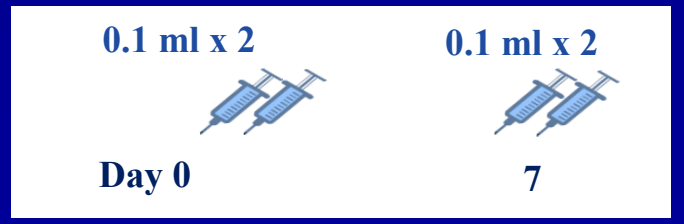
Regimens for Rabies Pre-exposure Prophylaxis

➢ IM regimen (1-1):

1 dose of vaccine to be given on days 0 and 7 **(7 - 28)**

➢ ID regimen (2-2):

0.1 ml volume of vaccine to be given 2 sites on days and 7 **(7 - 28)**



Advise to Travelers Who Visiting a Rabies Endemic Area

Avoid contact with wild animals and unknown domestic animals

Pre-exposure rabies vaccination is not a general requirement for travel to any country.

The decision must be based on

- The probability of rabies exposure:
  - The incidence of rabies in the area,
  - The probability of contact with an rabies susceptible animal, either wild or domestic, dogs and cats;Travelers with extensive unprotected outdoor exposure in rural areas,(younger age, duration of stay ?)
- The probability of being provided with the best possible treatment,
  - The availability of efficacious CCVs and RIG
  - If bitten by an animal that is potentially infected with rabies, immediately wash and flush the wound and visit specialized centers, as they are likely to be more aware of the rabies situation and the best current PET modalities.

Am. J. Trop. Med. Hyg., 82(6), 2010, pp. 1168–1171
doi:10.4269/ajtmh.2010.09-0699

Rabies Exposure Risk among Foreign Backpackers in Southeast Asia

Watcharapong Piyaphanee,* Prapimporn Shantavasinkul, Weerapong Phumratanaprapin, Piyada Udomchaisakul, Pongdej Wichianprasat, Maneerat Benjavongkulchai, Thitiya Ponam, and Terapong Tantawichian

TABLE 5
Risk of rabies exposure

	n	%
Total number of backpackers	870	100
During this trip in Southeast Asia*		
Number of backpackers bitten	6	0.69
Number of backpackers licked	31	3.6
Among the exposure group ($N = 37$)		
Exposure within the first 10 days	20	54
Exposure on days 11–30 of the trip	9	24
Exposure > 30 days after arrival	8	22

*Average stay = 30.06 days.

Have Traveled to		
Thailand	870	100.0
Lao PDR	132	15.2
Cambodia	124	14.3
Vietnam	111	12.8
Malaysia	49	5.6

Rabies Postexposure Prophylaxis in Returned Injured Travelers From France, Australia, and New Zealand: *Philippe Gautret ; J Travel Med 2008*

261 returning travelers seeking care following an animal-related injury acquired abroad from 1997 to 2005.

Only 6.8% of injured patients were previously vaccinated against rabies, while 75.4% of the cohort experienced a severe injurious contact with animals (WHO category III).

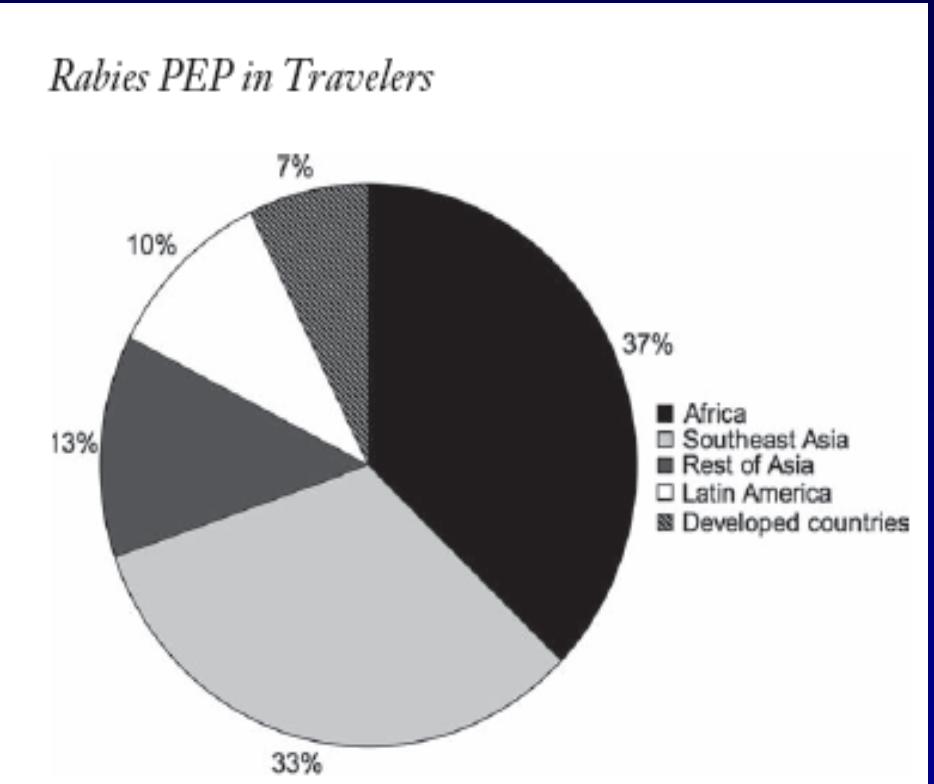


Figure 1 Region of exposure in 261 injured travelers.

Of travelers who sustained a high-risk injury, only 24% received both vaccination and rabies RIG. Of the travelers who did not receive RIG, 43% had received a first dose of vaccine more than 7 days after return and before presenting to a clinic in their home country.

Pre-exposure immunization is recommended for anyone at increased risk of exposure to rabies virus.

Individuals at high risk of rabies exposure include:

- Persons at occupational risk
  (Laboratory personnel, animal handlers, veterinarians, and others at *risk for contracting rabies*)

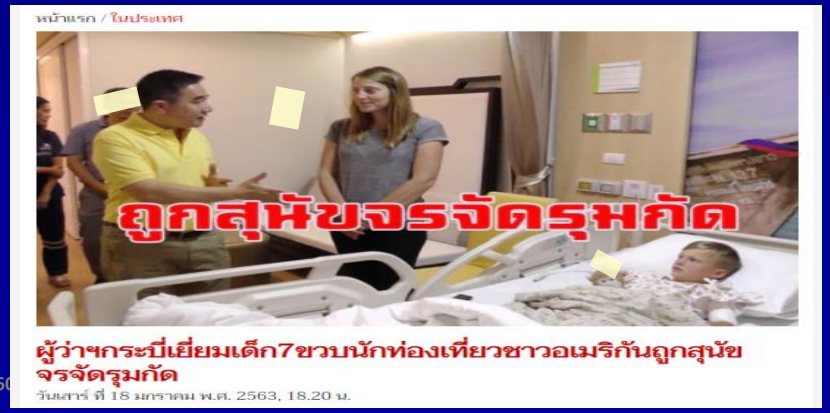
- Travelers to remote rabies endemic areas
  (Travelers who are likely to have exposures to dogs or cats in canine rabies – *endemic countries* are being advised)

- Sub-populations in endemic settings with limited access to timely and adequate post-exposure prophylaxis
  (particularly in areas with *extremely high bite rates*)

Why do we focus on children in rabies endemic countries ?

- Play and feed known and unknown animals
  (dogs and cats - unvaccinated animals)
- Play outside their home and unable to protect themselves
  (stray dogs, cats)
- Risks of bites at face , head and neck
  (increased risk of infection and shorten incubation period)
- Undetected or hide exposure

Children are at high risk of rabies through animal bites



Reference: https://www.khaosod.co.th/around-thailand/news_5075186, 2. https://www.naewna.com/local/467145

Health Economic Assessment of a Rabies Pre-Exposure Prophylaxis Program Compared With Post-Exposure Prophylaxis Alone in High-Risk Age Groups in the Philippines

Beatriz Quiambao, Inter J Infect Dis 2020:97;38-46

PrEP+PEP program (PrEP + booster PEP) vs PEP alone.

Results: Over a 20-year period, in a cohort: 1 million 5-year-old children

PrEP+PEP was expected to prevent 297 deaths compared with PEP alone.

From both payer and societal perspectives,
the resulting incremental cost-effectiveness ratios were 36 035 (US$759; 2016 US$ conversion) and 18 663 (US$393) Philippine Pesos (PHP) - quality-adjusted life-years gained - respectively, which are both below the willingness-to-pay threshold of PHP140 255 (US$2 953).

A Cost-Effectiveness Analysis of Pre-Exposure Prophylaxis to Avert Rabies Deaths in School-Aged Children in India

Abhishek Royal; Vaccines 2023, 11, 88.

Cost-utility analysis of pre-exposure prophylaxis rabies vaccine in 5-year-old children in Thailand

Sutinee Soopairin (submitted)

Results: The base-case analysis showed that the PrEP rabies vaccine had an incremental cost-effectiveness ratio (ICER) of THB 312.87 per quality-adjusted life year (QALY) saved, which is cost-effective under the willingness-to-pay threshold of THB 160,000 per QALY saved in Thailand. Additionally, the scenario analysis showed that intradermal vaccine administration costs less due to lowered use of vaccine volume.

ZERO HUMAN DEATHS FROM DOG-MEDIATED RABIES BY 2030

less expenditure on rabies

fewer rabies exposures

validated rabies elimination in individual countries/regions

Reduce human rabies risk
- improved awareness and education
- increased access to healthcare, medicines and vaccines
- dog vaccinations

Provide guidance and data
- effective policies, guidance and governance
- ensuring reliable data to enable effective decision-making

Harness multi-stakeholder engagement
- demonstrate the impact of activities completed under the **United Against Rabies** collaboration

OBJECTIVE 1
to effectively use vaccines, medicines, tools and technologies

OBJECTIVE 2
to generate, innovate and measure impact

OBJECTIVE 3
to sustain commitment and resources

OBJECTIVES

operational capacity-building preparedness

educational & advocacy programmes awareness & commitment

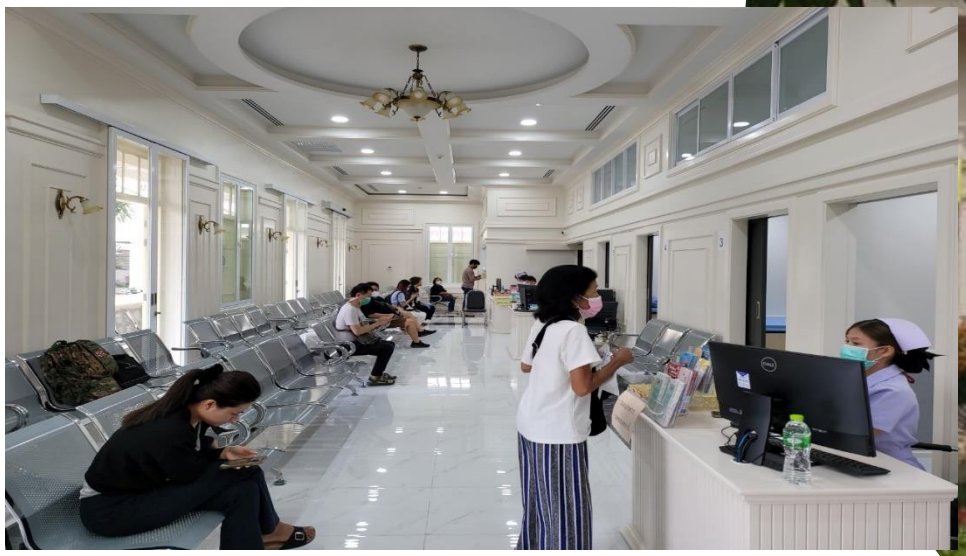
monitoring & evaluation effectiveness & sustainability

The **UNITED AGAINST RABIES** collaboration was formed by four partners: WHO, FAO, OIE, GARC*

PROBLEM STATEMENT

Although 100% preventable, rabies kills more than 59,000 people in over 150 countries every year. The disease is nearly always fatal once symptoms appear.

* World Health Organization (WHO), Food and Agriculture Organization of the United Nations (FAO), World Organisation for Animal Health (OIE), and Global Alliance for Rabies Control (GARC)



Thank you