

# RABIES: A NEGLECTED, RE-EMERGING ZOOONOSIS



**Charles E. Rupprecht, VMD, MS, PhD**

*Chief, Rabies Program*

Division of High Consequence Pathogens and Pathology  
National Center for Emerging and Zoonotic Infectious Diseases  
Centers for Disease Control and Prevention



# Myths about Rabies



**Rabies is rare**

**Rabies is not widespread**

**Nothing can be done to make an impact towards  
rabies elimination**

# Rabies 101

- ❑ **An acute, progressive viral encephalomyelitis**
- ❑ **The highest case fatality rate of any conventional etiological agent**
- ❑ **Leading viral zoonosis**
  - International burden
  - Veterinary and public health significance
- ❑ **Distributed on all continents but Antarctica**
- ❑ **One of the oldest described infectious diseases, known for more than 4 thousand years**

# Rabies: An Ancient Disease

## □ 2300 BC

- Dog owners in Babylon fined heavily for deaths caused by their dogs biting people

## □ 800–700 BC

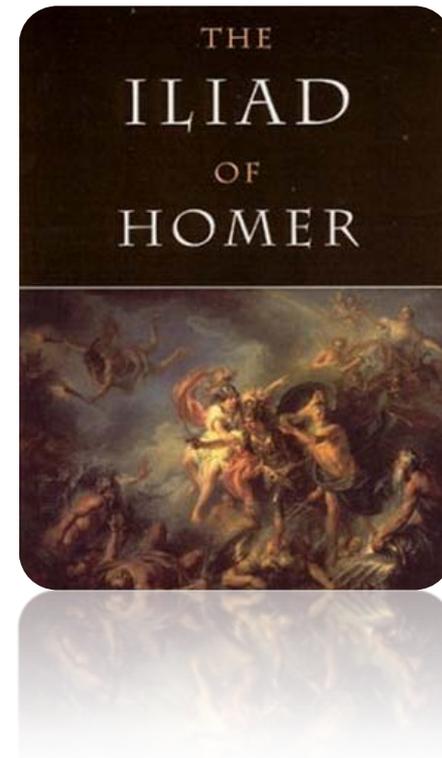
- Homer likens Hector to a “raging dog” in *The Iliad*

## □ 1271

- 1<sup>st</sup> large rabies outbreak reported (Germany)

## □ 1703

- 1<sup>st</sup> case of rabies reported in the Americas by a priest in Mexico



# Rabies: Etiology



## □ RNA viruses in the family *Rhabdoviridae*, genus *Lyssavirus*

- The type species of the genus is Rabies Virus
- Historically, at least 6 other lyssavirus species cause rabies, some lacking cross reactivity to commercial biologics
- Recently, the International Committee on Virus Taxonomy ratified 4 new lyssavirus species from Eurasian bats
- Additional pathogen discovery is expected

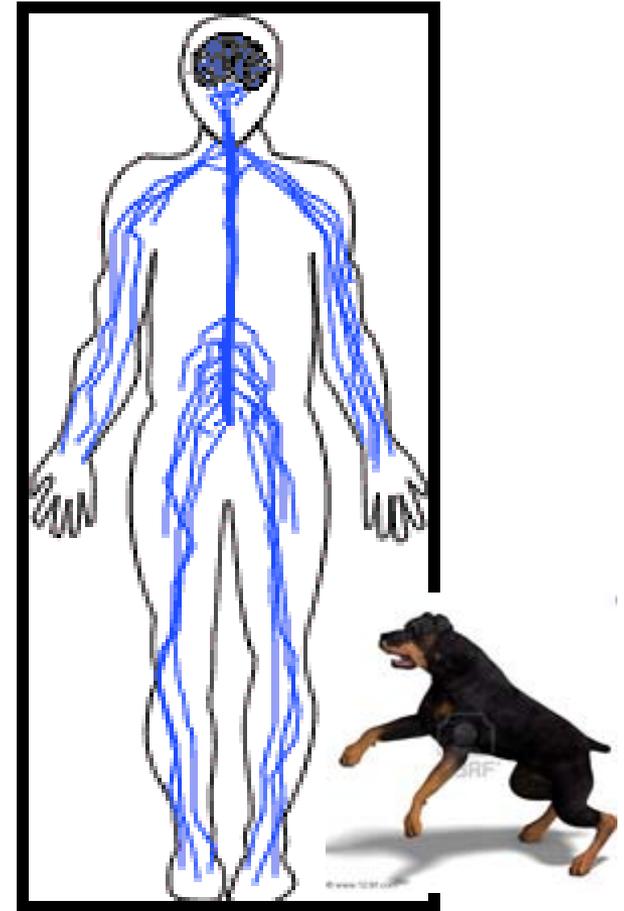
## □ All mammals appear susceptible; major reservoirs

- Carnivora: Dogs, foxes, raccoons, skunks, etc.
- Chiroptera: Insectivorous, hematophagous, and frugivorous bats



# Rabies: Pathogenesis

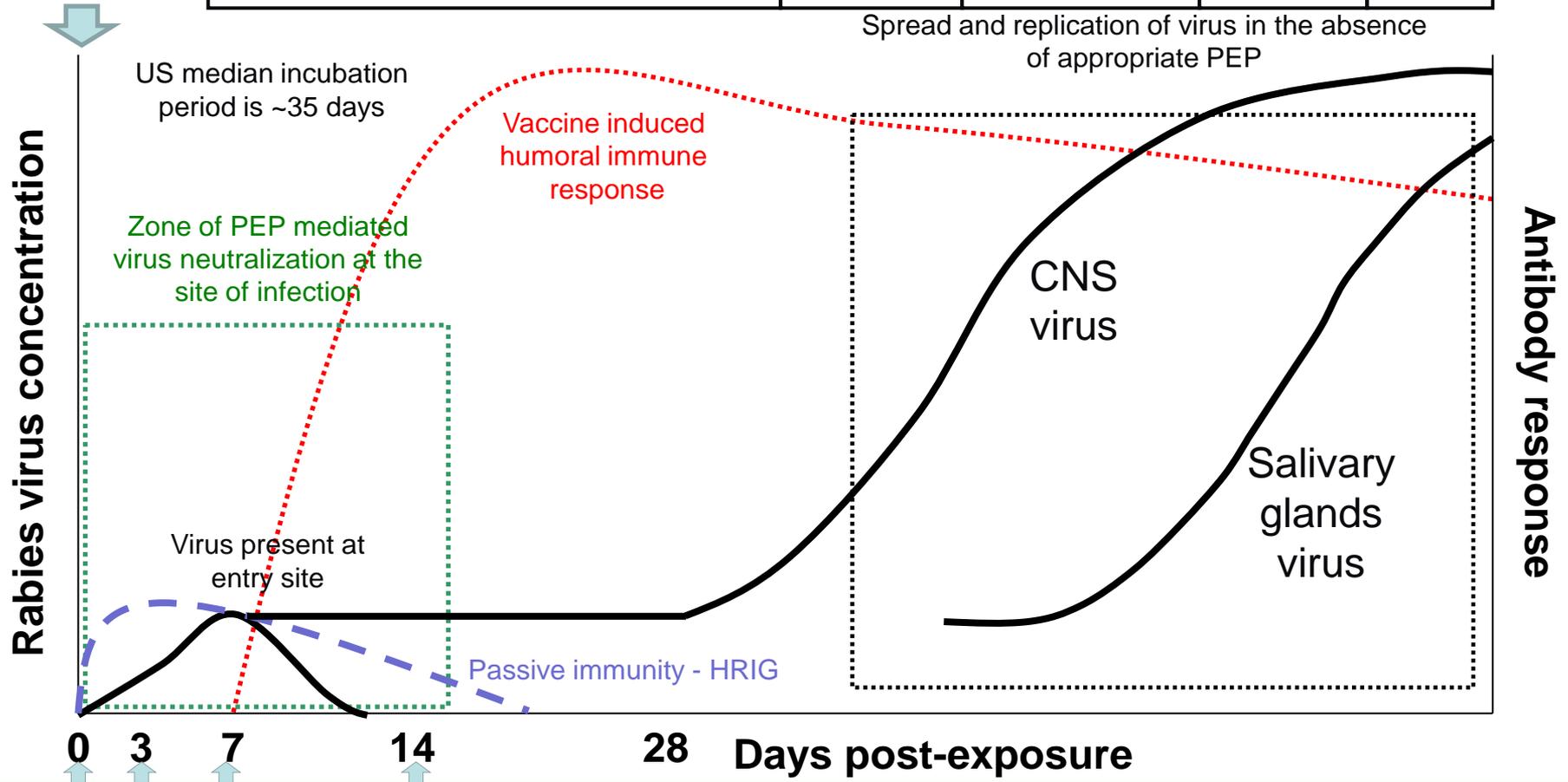
- ❑ **Transmission primarily via bite**
- ❑ **Viruses are highly neurotropic**
  - Enter peripheral nerves
  - Centripetal travel by retrograde flow in axoplasm of nerves
  - Replicate in CNS
  - Centrifugal flow to innervated organs, including the primary portal of exit, the salivary glands
- ❑ **Viral excretion in saliva**





# Infection

Incubation period (5 days to > 2 years)	Prodrome (0-10 days)	Acute neurologic period (2-7 days)	Coma (5-14 days)	Death
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# Rabies: Clinical Stages

## ❑ Incubation period

- Range: 6 days to >2 years
- Average: 4–6 weeks

## ❑ Prodromal stage

- Nonspecific signs

## ❑ Acute neurologic phase

## ❑ Coma

## ❑ Death

- Vs. extremely rare reports of experimental treatment and recovery from rabies after the onset of clinical signs



# Rabies: Diagnosis

- ❑ **History of animal exposure and typical neurologic clinical signs**
- ❑ **Laboratory diagnosis**
  - Gold standard: Postmortem demonstration of viral antigens in CNS by DFA
  - National laboratory protocol in 2000
  - In humans, antemortem detection of virus or viral amplicons, antibodies, or antigens (sera, CSF, saliva, nuchal biopsy)



# Rabies: Global Burden

- ❑ **Human rabies exposures/year: Tens of millions**
- ❑ **Estimated human rabies deaths/year: >55,000**
  - Africa (rural): 3.6/100,000
  - India (rural): 2.5/100,000
  - Pakistan: 1.2/100,000
  - China: 0.2/100,000
- ❑ **Most cases occur in Africa and Asia, and in children**
- ❑ **Reservoirs**
  - **Domestic dog: Single most important animal reservoir**
  - **Wildlife important, especially in developed countries of Europe and North America**

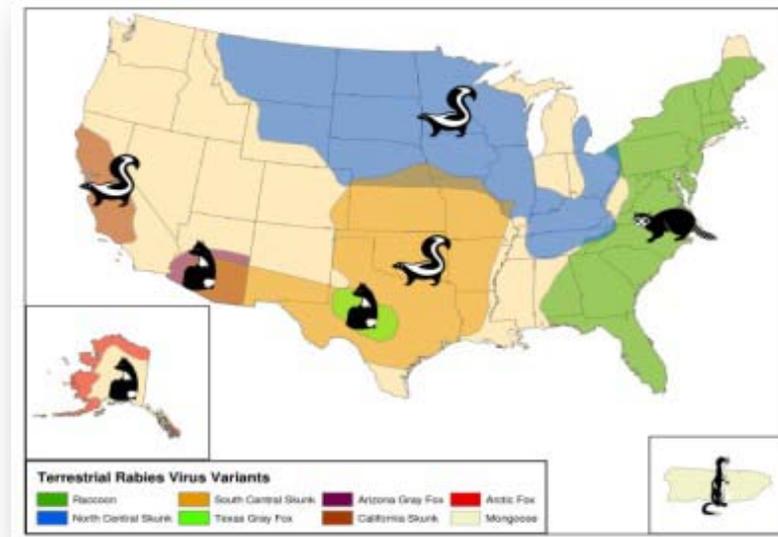
# Rabies in the United States

## ❑ Human rabies: Uncommon

- 20,000–40,000 exposures/year
- 1–8 cases/year

## ❑ Animal rabies

- 7,000 –10,000 cases/year
- Dog rabies transmission eliminated
- Wildlife hosts include raccoons, skunks, foxes, mongooses (Puerto Rico), and bats
- Distributed in every state but Hawaii

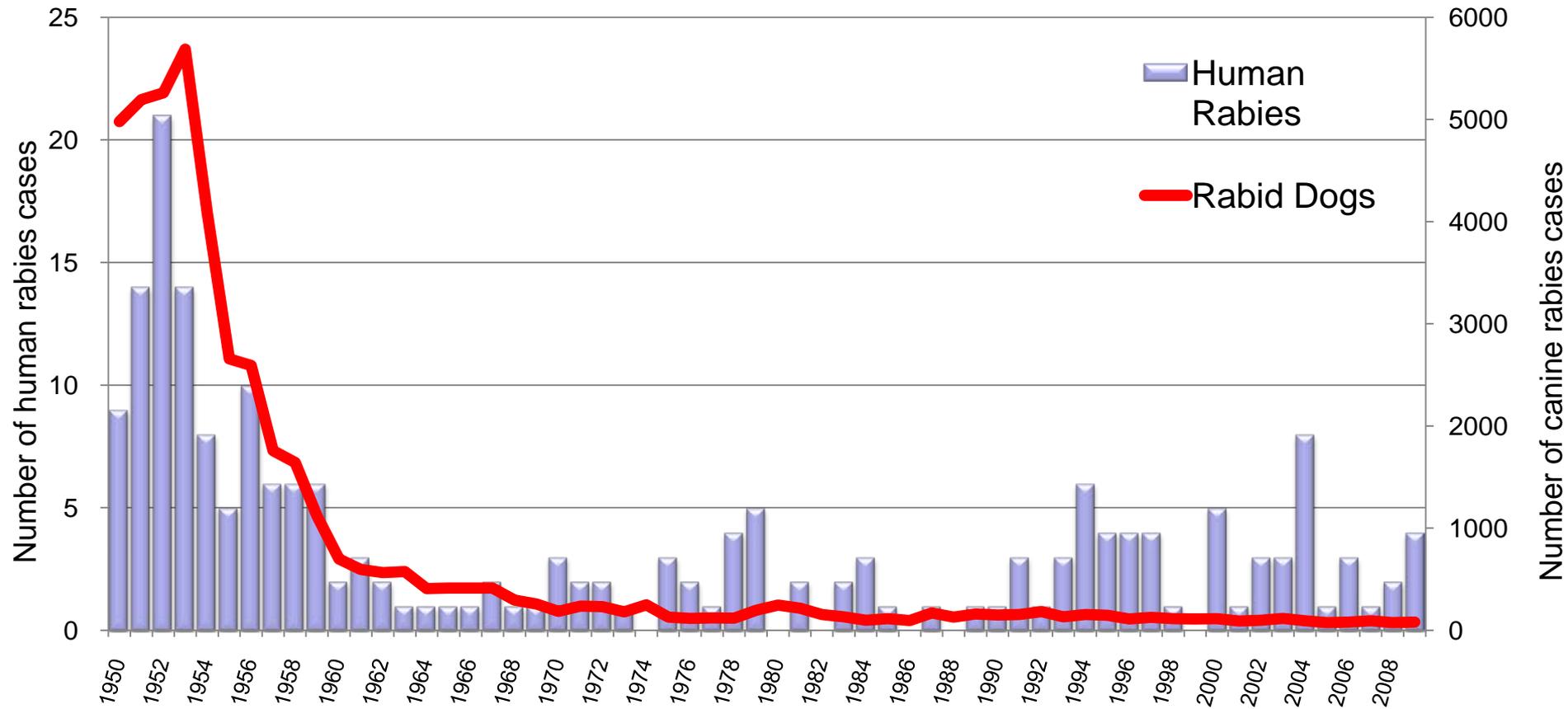


# Why Focus on Dogs?

- ❑ Worldwide >90% of rabies exposures are from dogs
- ❑ Worldwide >99% of human rabies deaths are via dogs
- ❑ Bite wounds, stress, and trauma from dogs rabies
- ❑ Rabies control and elimination is possible in dogs
- ❑ Roaming infected dogs are obstacles to success
- ❑ Oral Rabies Vaccination (ORV) and contraception hold promise to enhance rabies control



# Rabies in the United States: Effect of Animal Control on Human Fatalities



# Rabies: Foundations of Prevention and Control

- ❑ Dog rabies vaccination, *en masse*
- ❑ Minimization of human exposures to infected animals
- ❑ Prompt wound care and prophylaxis with vaccine and rabies immune globulin after exposure
- ❑ Regulations to support the disease-free status of many localities, due to the introduction of rabid animals (e.g., Bali)



# Goals Towards Global Rabies Prevention and Control in the 21<sup>st</sup> Century

- ❑ **Counter viral emergence from wildlife reservoirs**
- ❑ **Develop humane methods for population management of free-ranging animals**
- ❑ **Translate progress in canine rabies elimination**
  - From developed to developing countries
  - On a realistic, sustainable, regional basis
  - Based upon ideal models
- ❑ **Create of new international advocacy and effective blueprints for rabies prevention and control**
- ❑ **Establish dynamic, multidisciplinary partnerships via renewed intersectoral cooperation**

# RABIES MANAGEMENT AT THE HUMAN-ANIMAL INTERFACE



**Dennis Slate, MS, PhD**  
*National Rabies Management Coordinator*  
US Department of Agriculture  
Animal and Planet Health Inspection Service  
Wildlife Services



# Impact of Dog Rabies on Humans

- ❑ Worldwide, 90% of rabies exposures are from dogs
- ❑ Worldwide, 99% of human rabies deaths are from dogs
- ❑ Bite wounds, stress, and trauma from dogs rabies



- ❑ Burden of coexistence with dog rabies
- ❑ Rabies transmission at the dog–wildlife interface

# Dog Subpopulations: A Challenge to Achieving Control of Dog Rabies



## Home- Owned Pet

Specific owner: 72 million dogs in the US (2007)  
Generally accessible for vaccination by injection

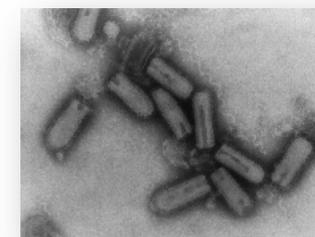
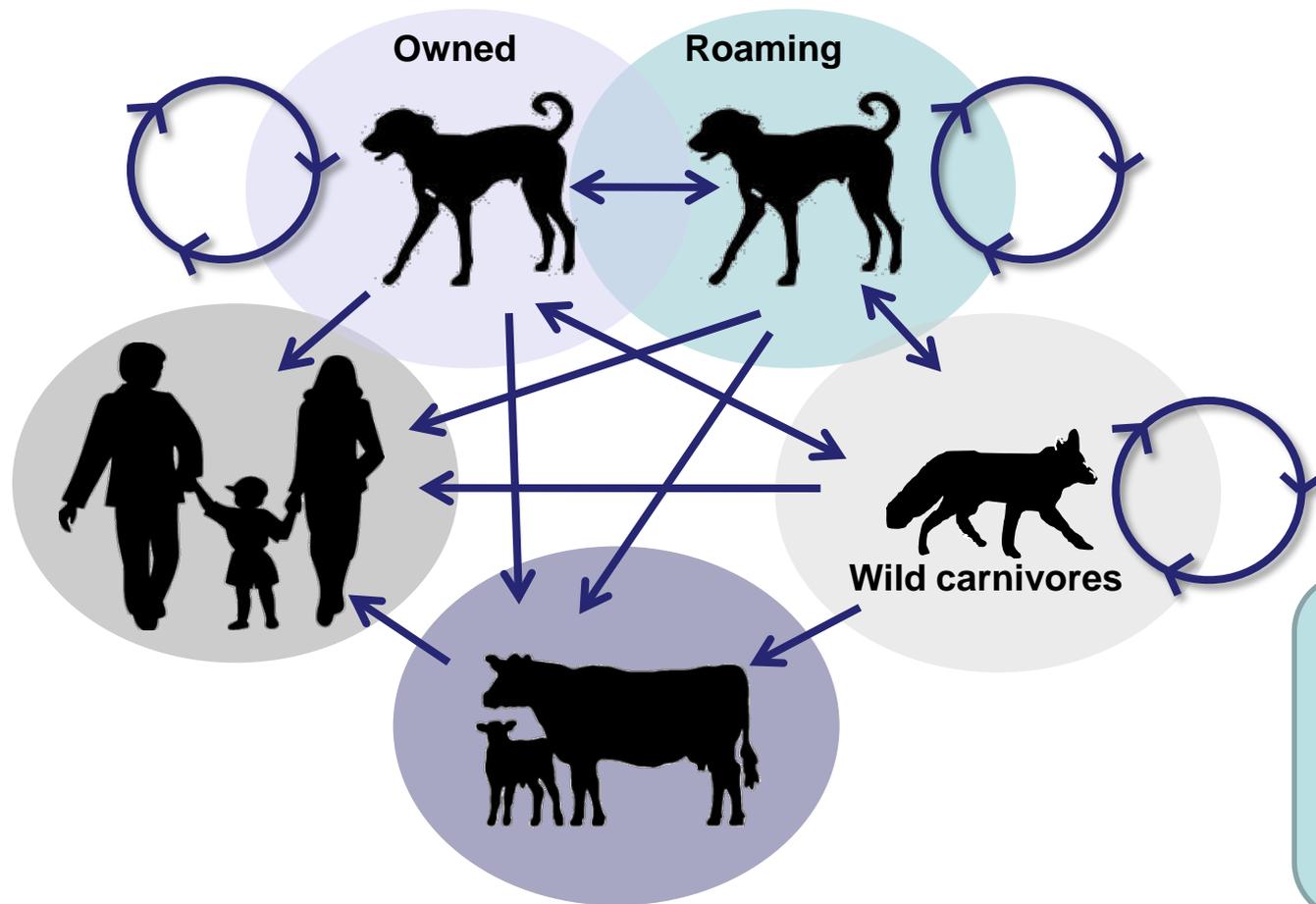


## Feral Roaming Street Community

No specific owner  
Not easily accessible for vaccination by injection



# Dog Rabies: Dynamics of Virus Transmission and Exposure



Transmission pathways

1-way →

2-way ↔

Circulating ↻

# Challenges for Control of Dog Rabies

- ❑ **Achieving adequate immunity in owned-dog population (50-70% level)**
- ❑ **Vaccination of free-roaming dogs**
- ❑ **Dog overpopulation may impede or prevent rabies control success**
- ❑ **Virus spillover at the dog-wildlife interface may confound success of dog and wildlife rabies control**

# Dog-Wildlife Interface

## Achieving objectives of dog and wild carnivore rabies control Profound conservation impacts

Species	Interface Event	Consequence
*African wild dog 	Spillover of canine variant into African wild dog	Threatens local extirpation
*Ethiopian wolf 	Spillover of canine variant into Ethiopian wolf	Threatens species extinction
Coyote 	Spillover of canine variant from Mexico into coyote	Creates a public health emergency in south Texas
Gray fox 	Spillover of gray fox variant into dog	Confounds success of ORV in gray foxes

\* Endangered species



# Effective Control of Dog Rabies May Require Integration of Additional Tools

- ❑ Education
- ❑ Quarantine
- ❑ Injectable vaccination campaigns
- ❑ Oral Rabies Vaccination (ORV)
- ❑ Contraception

**MMWR™**

*Recommendations and Reports*

April 18, 2008 / 57(RR02);1-9

**Compendium of Animal Rabies Prevention and Control, 2008\***  
**National Association of State Public Health Veterinarians, Inc. (NASPHV)**

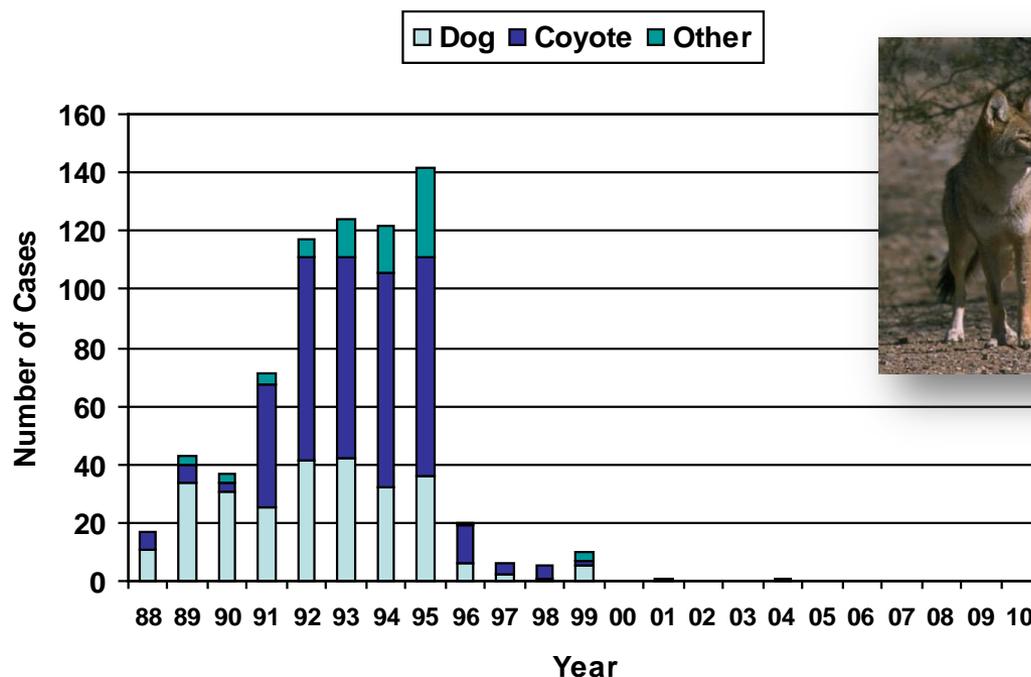
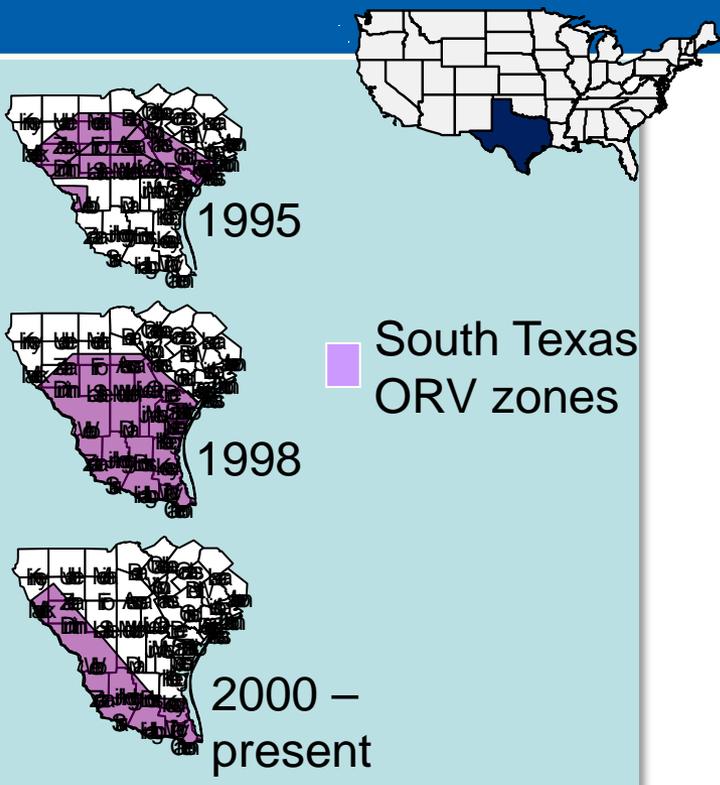


# Oral Rabies Vaccination Basics

- ❑ Delivering a vaccine-bait to a target species for consumption to create herd immunity
- ❑ Canada, Europe, and the United States are primary users
  - 42,166,134 ORV doses in 2009
- ❑ Cost is a potential limiting factor (\$1.23/dose)
- ❑ Led to elimination of specific rabies variants at the landscape scale



# Strategic Application of ORV in Texas



Canine variant rabies cases in south Texas: 1988-2010.

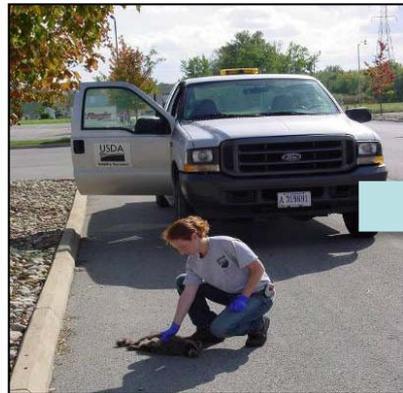
**Canine rabies spillover into coyotes**  
**Integration of ORV contributed to canine rabies elimination**  
**US declared free of canine rabies in 2007**

ORV, Oral rabies vaccination



# Enhanced Rabies Surveillance

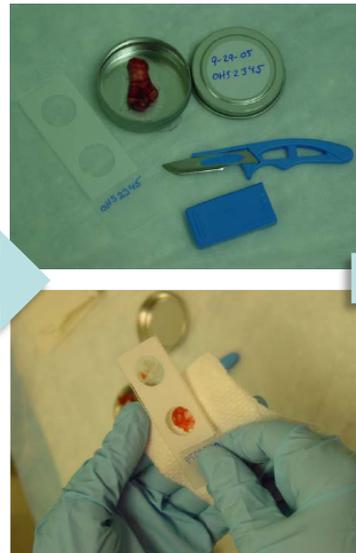
## dRIT- direct Rapid Immunohistochemistry Test



Road kill sample



Collecting brainstem sample



Slide preparation

Test determination via light microscope



negative

positive

**Inexpensive, quick and accurate test for detecting rabies**  
**Used in the US to enhance rabies surveillance to support ORV**

ORV, Oral rabies vaccination



# ORV Handout Trails to Vaccinate Free-ranging Dogs on Navajo Lands, Arizona 2006

- ❑ 373 dogs hand baited with Raboral V-RG
- ❑ 33/104 dogs tested had rabies virus neutralizing antibodies



ORV, Oral rabies vaccination



# Current and Future Contraceptive Approaches

## ❑ Surgery

- Intrusive, expensive, time-consuming, postoperative infections
- High efficacy

## ❑ Injectable EsterilSol™ (zinc gluconate)

- Males only, anesthetic to inject testicles, permanent contraceptive
- Currently not licensed in the United States

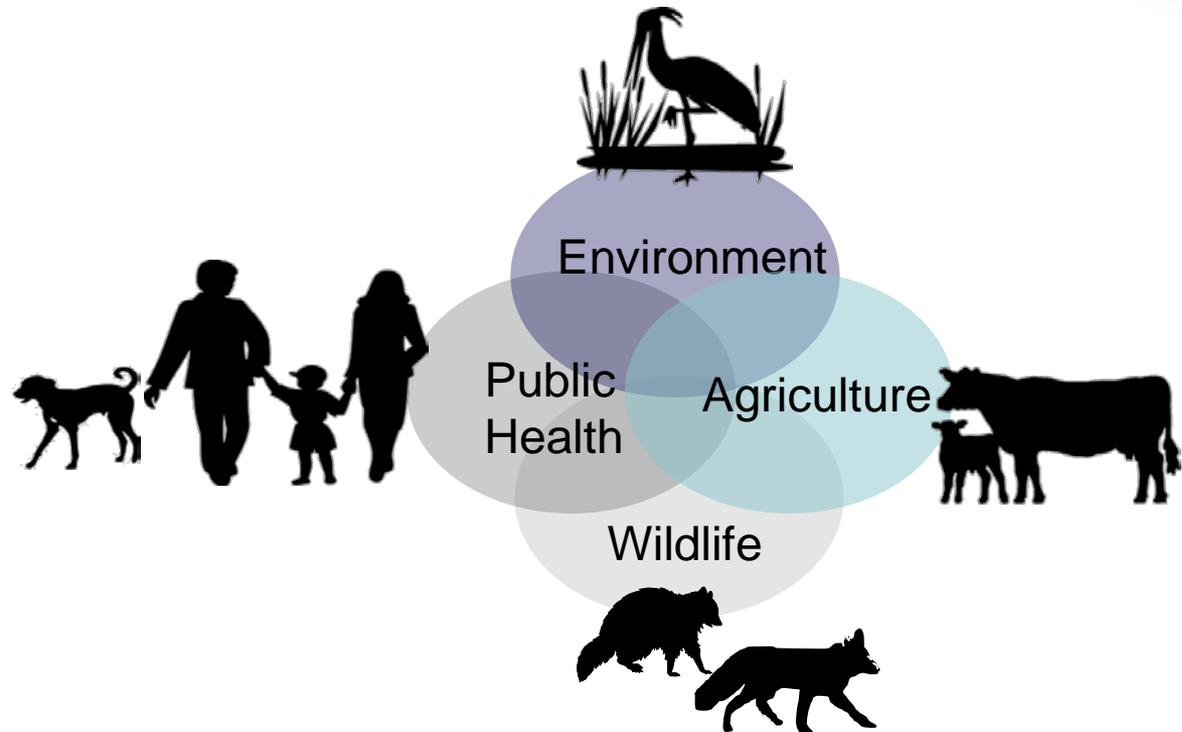
## ❑ Injectable GonaCon™ (GnRH vaccine)

- Immunocontraceptive effect persists 3–4 years in some species
- Effective in males and females for population control effects
- Captive dog trials underway with new formulation to evaluate adverse local immune reactions (e.g., granulomas)

# North American Rabies Management Plan

## International Collaboration and Coordination

- Information transfer
- Surveillance and monitoring
- Rabies control
- Research



# Successful Dog Rabies Control

- ❑ **Injectable vaccination campaigns for companion dogs**
  - **Integrates:**
    - **Contraception to reduce dog fecundity**
    - **ORV targeting free roaming dogs and wildlife**



# NEW APPROACHES TO RABIES ELIMINATION IN LATIN AMERICA



**Luis Fernando Leanes, MVD, MSc**

*Regional Advisor*

Zoonosis Diseases – Veterinary Public Health

Pan American Health Organization (PAHO)

World Health Organization





**Pan American  
Health  
Organization**



Regional Office of the  
World Health Organization



**World Health  
Organization**

- |  |  |
|--|--|
|  Anguilla               |  Cayman Islands                     |
|  Antigua and Barbuda    |  Chile                              |
|  Argentina              |  Colombia                           |
|  Aruba                  |  Costa Rica                         |
|  Bahamas                |  Cuba                               |
|  Barbados               |  Dominica                           |
|  Belize                 |  Dominican Republic                 |
|  Bermuda                |  El Salvador                        |
|  Bolivia                |  Ecuador                            |
|  Brazil                 |  US/MEX Border                      |
|  British Virgin Islands |  French Guiana                      |
|  Canada                 |  Grenada                            |
|  Guadalupe              |  Paraguay                           |
|  Guatemala              |  Peru                               |
|  Guyana                |  Puerto Rico                       |
|  Haiti                |  Saint Kitts and Nevis            |
|  Honduras             |  Saint Lucia                      |
|  Jamaica              |  Saint Vincent and the Grenadines |
|  Martinique           |  Suriname                         |
|  Mexico               |  Trinidad and Tobago              |
|  Montserrat           |  Turks and Caicos Islands         |
|  Netherlands Antilles |  Uruguay                          |
|  Nicaragua            |  US                               |
|  Panama               |  Venezuela                        |



# Overview

- ❑ Political decisions and mandates
- ❑ Epidemiological trends and progress made
- ❑ Remaining challenges
- ❑ Strategy for elimination and prevention of human rabies

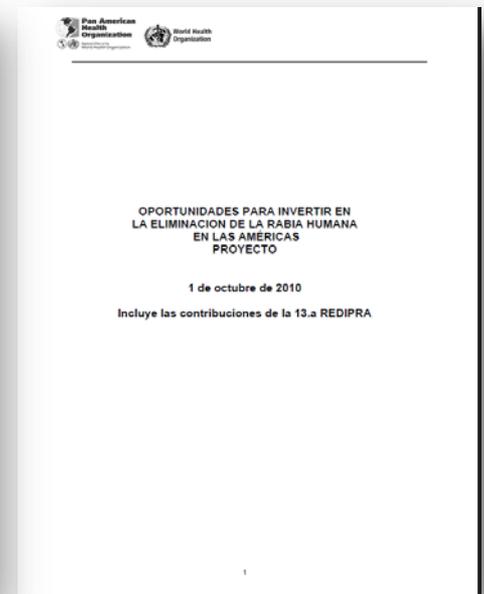
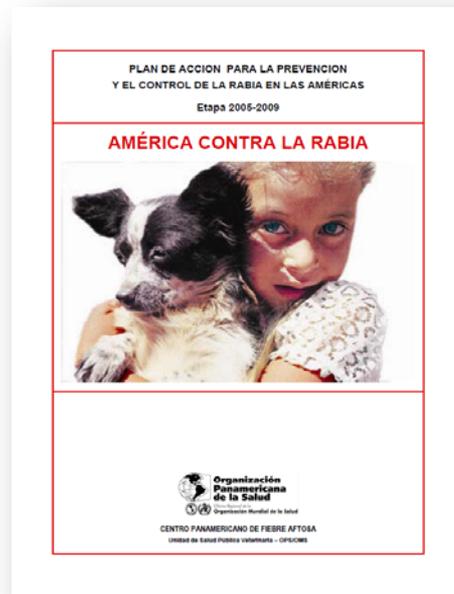


# Political Decision and Mandates

- ❑ **1983: 3<sup>rd</sup> Ministries of Health and Agriculture and PAHO Directive Council**
  - Launched rabies elimination initiative fostering National Plans
- ❑ **2008: PAHO Directing Council**
  - Elimination of human rabies transmitted by dogs by 2012
- ❑ **2010: Regional Meeting of the National Directors of Rabies Control Programs in Latin America (REDIPRA)**
  - Follow up of National Plans through 13 PAHO-sponsored meetings of National Rabies Directors with OIE, WSPA, GARC, and CDC

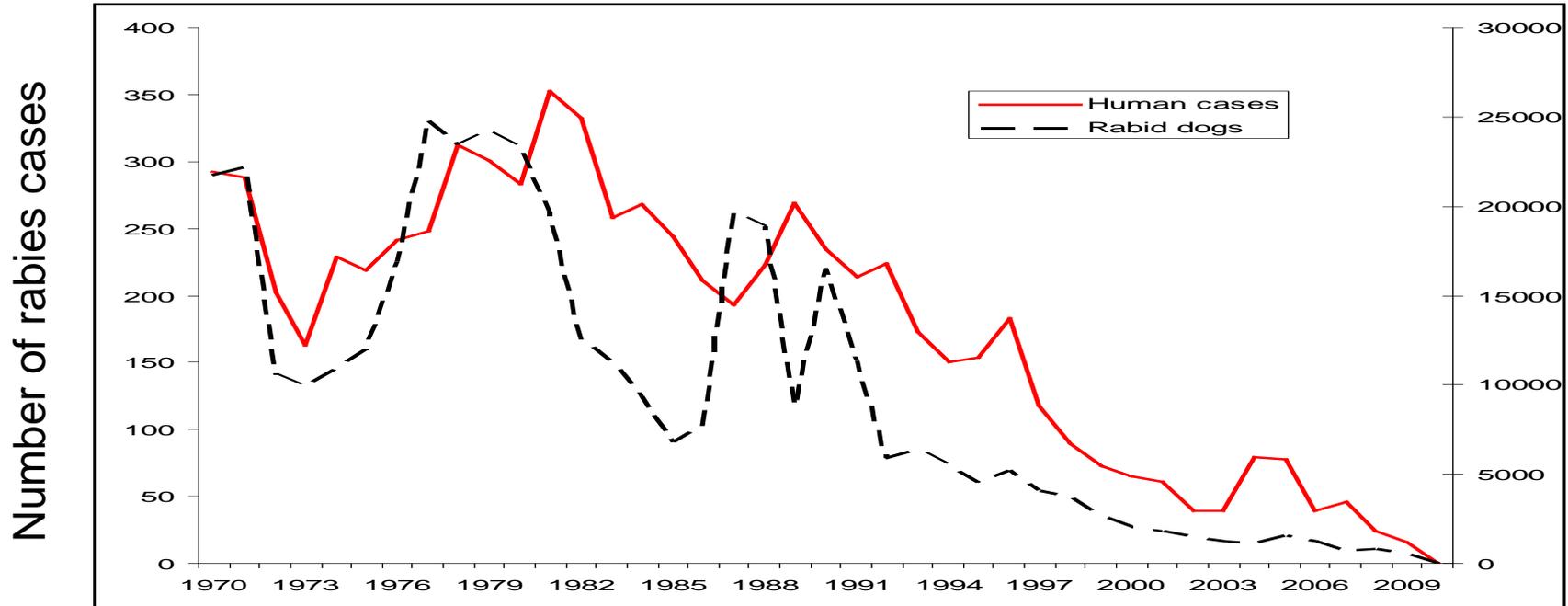
# National Plans

- ❑ Surveillance
- ❑ Pre- and post-exposure prophylaxis
- ❑ Veterinary vaccination schemes and dog population control



# Epidemiological Trends of Human and Canine Rabies Cases (N=7,228)

## Latin America, 1970–2009



1984: >300 human cases

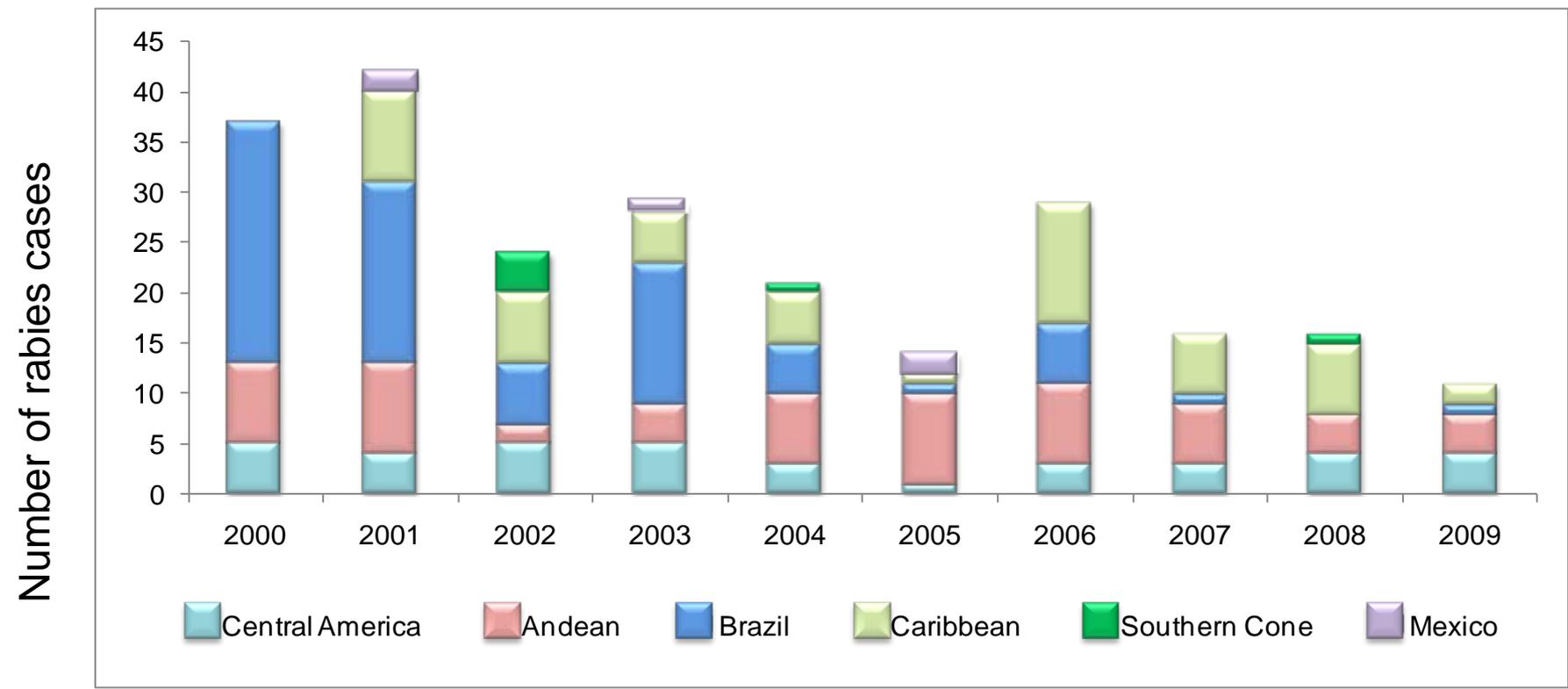
2009: 19 human cases; 95% reduction of human and dog cases



# Epidemiological Trends:

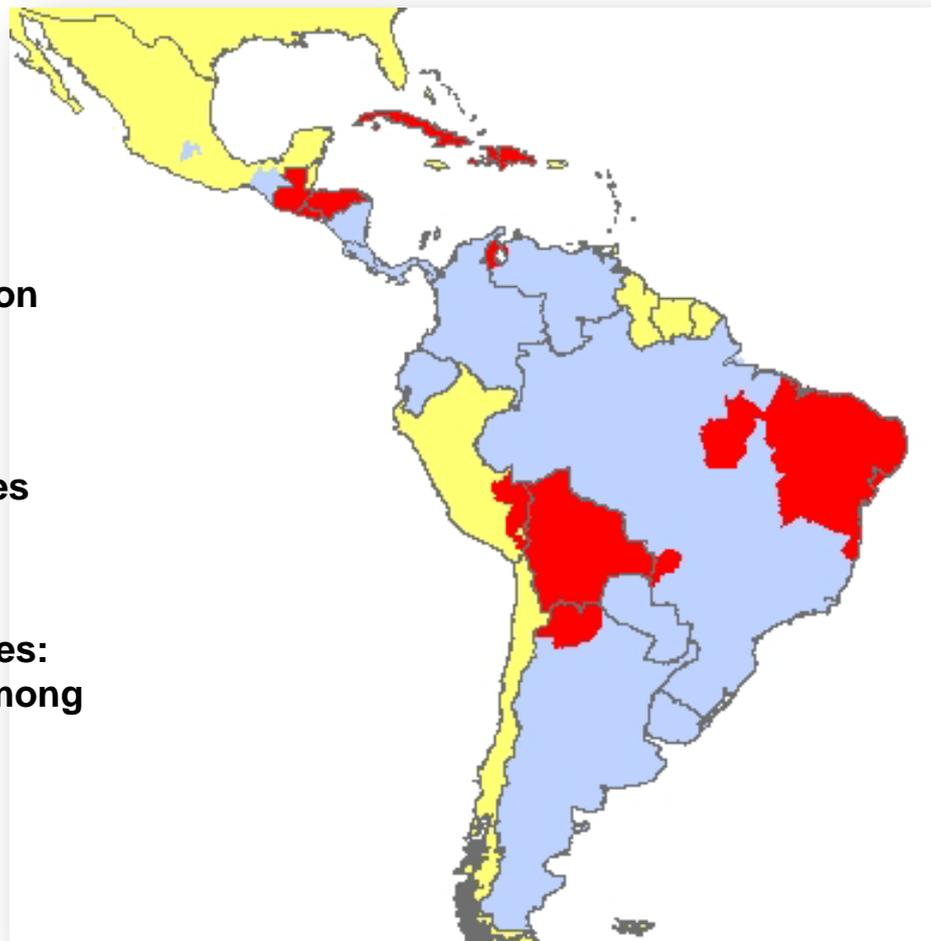
## Human Rabies Cases Transmitted by Dogs (N=239)

Latin America, 2000–2009



# Circulation of Rabies among Dogs Latin America, 2010

-  **Areas of low risk:**  
Achieved interruption of circulation  
of rabies among dogs
-  **Areas of moderate risk:**  
Non sustained circulation of rabies  
among dogs
-  **Areas of high risk for human rabies:**  
Sustained circulation of rabies among  
dogs



# Remaining Challenges: Human Rabies Transmitted by Dogs

- ❑ **Inadequate supply for canine vaccination**  
ELS, HON, DOR, HAI, CUB, BOL
- ❑ **Limited capacities for PEP**  
GUT, ARG, DOR
- ❑ **Coordination at local level**  
GUT, MEX, VEN, BRA
- ❑ **Coordination at borders**  
ELS-HON, HAI-DOR, ARG-BOL, PER-BRA



# Remaining Challenges: Wild Reservoirs – Human Cases

## Latin America, 2000–2009

Transmission by	Mexico	Cent- Am	Andean	Caribbean	Brasil	South- Cone	Total
Dogs	5	37	61	<b>54</b>	76	6	<b>239</b>
Vampire bats	4	3	69	<b>0</b>	73	0	<b>149</b>
Non-haematophagous bats	7	0	0	3	0	1	<b>11</b>
Non-specified bats	10	0	3	0	1	1	<b>15</b>
Cats	0	2	3	1	3	0	<b>9</b>
Cattle and horses	1	0	1	0	2	0	<b>4</b>
Wild carnivora	8	1	0	1	0	0	<b>10</b>
Not specified	0	4	10	2	8	1	<b>25</b>
<b>Grand Total</b>	<b>35</b>	<b>47</b>	<b>147</b>	<b>61</b>	<b>163</b>	<b>9</b>	<b>462</b>

# REDIPRA Strategies to Prevent Human Rabies

## Strengthen National Programs

- ❑ **Avoid relaxation when there are no human cases**
- ❑ **Manage urban transformations**
  - Stray dogs and migration
- ❑ **Prevent circulation of rabies among dogs and wild *Carnivora***
- ❑ **Ensure access to health care and human pos- and pre-exposure prophylaxis**

# One Health Approach

- ❑ **Veterinary vaccination schemes**
- ❑ **Diagnostic surveillance based on CDC monoclonal antibodies and molecular typing**
- ❑ **Animal control and welfare**
- ❑ **Post-exposure and pre-exposure prophylaxis**



**Interdisciplinary collaborations in all aspects of health care  
for humans, animals and the environment**

<http://onehealthinitiative.com>



# RENEWED ADVOCACY AND EFFECTIVE PARTNERSHIPS FOR RABIES PREVENTION AT THE COMMUNITY LEVEL



**Deborah J. Briggs, PhD**

*Director*

Global Alliance for Rabies Control



# Why Do People Still Die of Rabies?

- ❑ **Lack of awareness on all levels about**
  - Responsible pet ownership – vaccinating pets
  - Need for post-exposure prophylaxis (PEP)
  - Primary wound care
- ❑ **Rabies immunoglobulin (RIG) not available**
- ❑ **Rabies vaccines not available**
  - Greater cost of travel
  - Increased risk of rabies onset
- ❑ **Rabies vaccines are too expensive**
  - Likelihood of giving up
  - Delays because of need to raise money



# Overview

- ❑ **Global partnerships and efforts for rabies prevention**
- ❑ **From blueprint to local implementation**



# Recent Examples of Innovative Programs for Global Rabies Prevention and Control

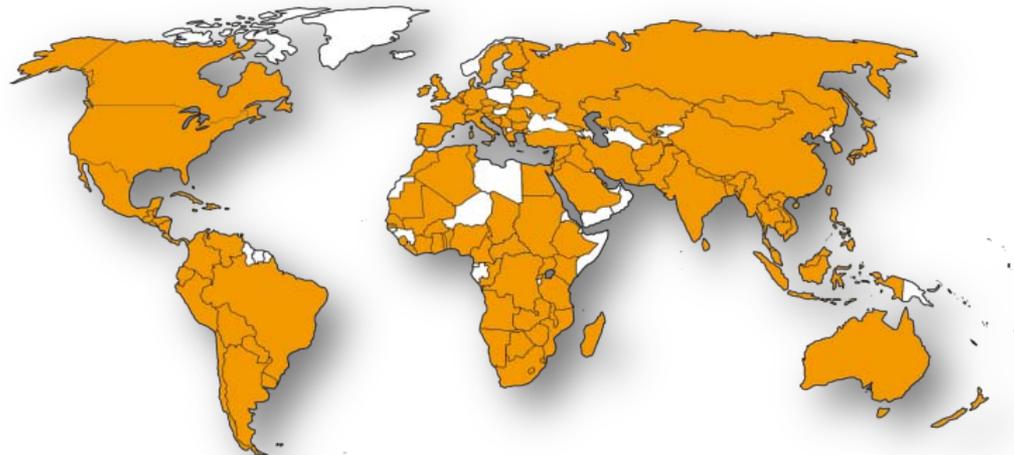
- ❑ **World Rabies Day, launched 2007**
  - Focal point for increasing global awareness
- ❑ **Global Alliance for Rabies Control, established 2007**
  - Registered 501 c3 in US; registered charity in Scotland
- ❑ **Partners for Rabies Prevention, established 2008**
  - Informal group of global stakeholders
  - Public, private, NGOs, funding organizations
- ❑ **E-global communications**
  - Bank of free educational materials
- ❑ **Pilot projects for One Health rabies control**
  - Example: Bohol Philippines, 2007–2011

# World Rabies Day September 28



## □ Since September 2007...

- 135 participating countries
- 150+ participating schools of public health, veterinary and medical colleges have hosted one or more 'rabies-awareness' events
- ~300K Web visitors, 214 countries/territories



GLOBAL ALLIANCE  
FOR  
RABIES CONTROL

World Rabies Day is an  
initiative of the Global Alliance  
for Rabies Control

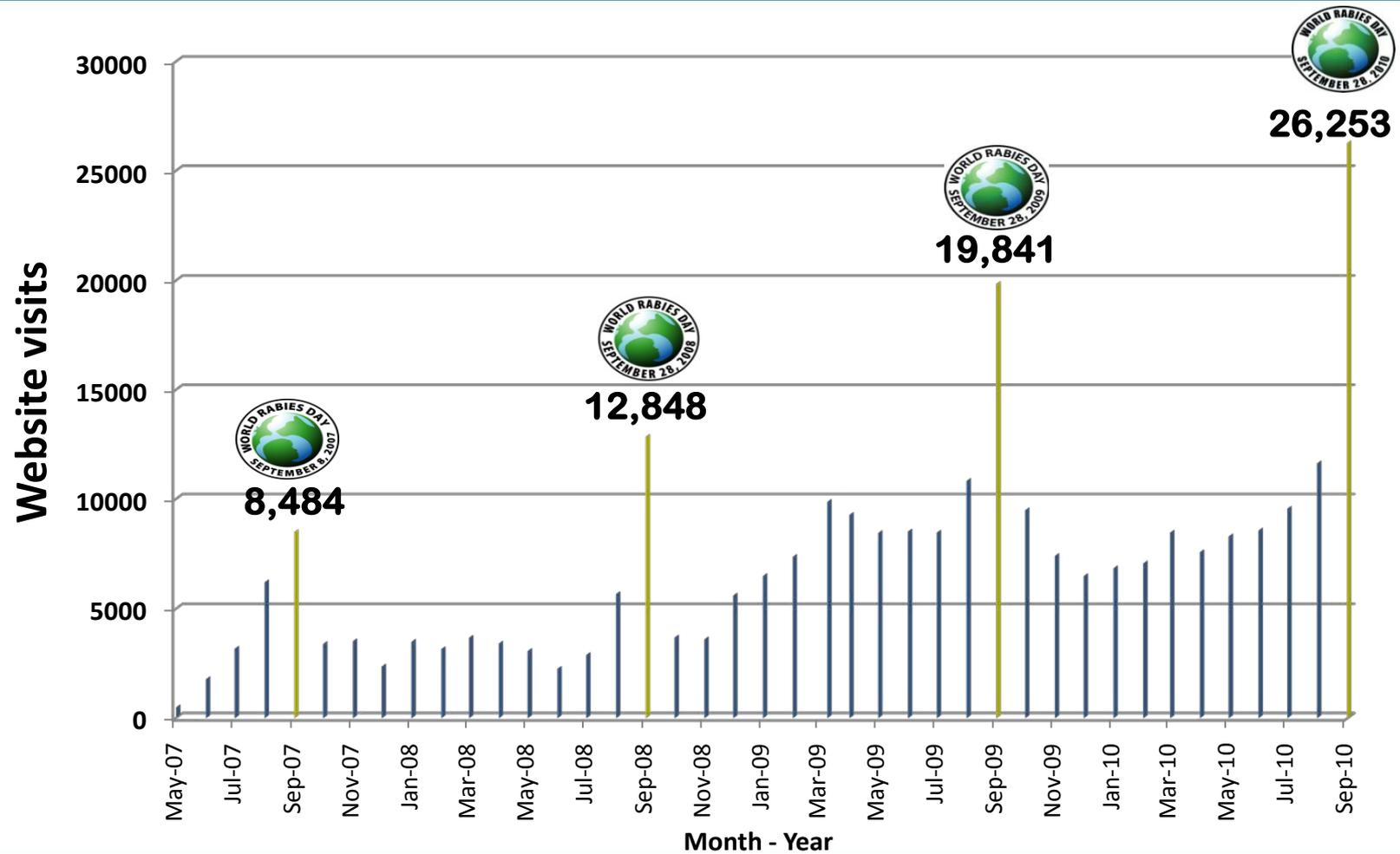
**Find out more:**

- > Our Mission
- > Plan an Event
- > Perspectives
- > Veterinary Resources
- > Latin America Best Event
- > Rabies Vacc. Guide

**New Video!**  
"Understanding Rabies"

[www.worldrabiesday.org](http://www.worldrabiesday.org)





# Impact of World Rabies Days

- **Since September 2007...**
  - >1,200 reported events
  - 4.6 million animals vaccinated
  - 150 million people educated

Children bringing pets to be vaccinated  
in Napak, Uganda during WRD 2010  
Photo: Dr Inangolet Francis Olaki



# Impact of World Rabies Days

- ❑ New animal vaccination programs in endemic countries
- ❑ New and invigorated educational programs
- ❑ Global community networks
- ❑ Listed on UN website of globally observed health days



Classroom education in Iraq



Vaccination clinic in Mozambique

# Impact of World Rabies Day: Mozambique

## □ Prior to World Rabies Day 2007

- Dogs unvaccinated due to local superstition
- Lack of support from government
- Basic educational materials not available

## □ As of World Rabies Day 2010

- Partnership between veterinary clinics and Maputo Veterinary University
- Multiple vaccination clinics held throughout Mozambique
- National government funding rabies vaccinations on WRD
- Education of locals; construction of animal record database





# The World Rabies Days: Evaluation of the Impact

- ❑ **Continuous evaluation of global programs**
- ❑ **Annual evaluation of World Rabies Day campaign**
- ❑ **In 2010, questions about the effort as a whole were included**
  - 213 surveys returned: English, French, Portuguese, and Spanish
  - 96.3%: “Rabies Education Programs Are Saving Lives”
  - 89.6%: “World Rabies Day Is Making a Difference”
  - 95.0%: “Will Host a World Rabies Day Event in 2011”

# Partners for Rabies Prevention (PRP)



## □ Informal group of stakeholders

- Public and private: Bring time, talent, treasure to table
- GARC, CDC, FAO, OIE, PAHO/WHO, WSPA, etc.
- Discuss common strategies
- Evaluate needs, timelines, deliverables

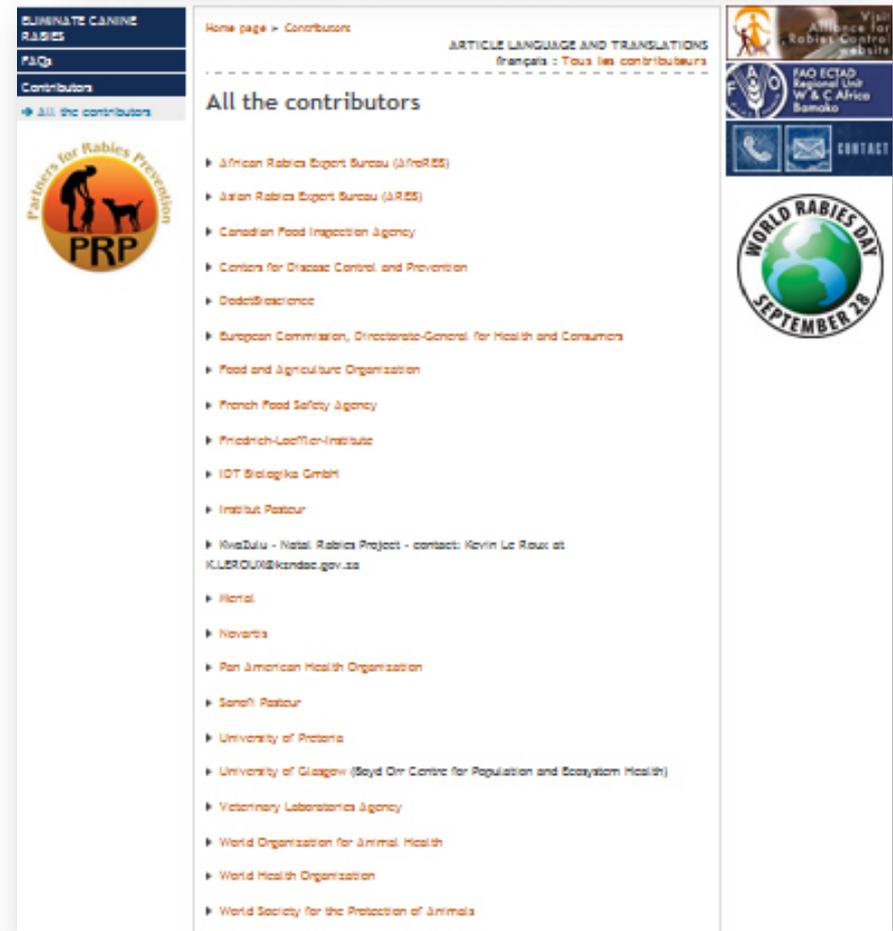
## □ Secretariat: Global Alliance for Rabies Control (GARC)

## □ Activities

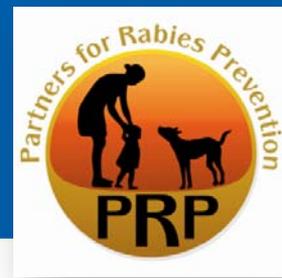
- Road map: 2008
- Blueprint for Canine Rabies Control: 2009–2010
- Next step: Evaluate the global burden of rabies



- ❑ Free access on line
- ❑ Examples of ongoing programs
- ❑ Links to documents
- ❑ Information on
  - Cost
  - Planning
  - Funding



# Blueprint: The Concept



- ❑ **Aimed at assisting and guiding individual countries on implementation of canine rabies control programs**
  - If rabies is present
  - If rabies is reintroduced after a period of absence
- ❑ **New concept – not meant to replace existing documents**



# Overview

## □ Global partnerships and efforts for rabies prevention

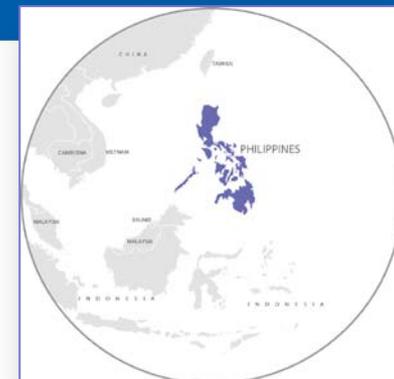
### □ From blueprint to local implementation

- Istanbul and India: International workshops on development and implementation of the communications plan delineated in the Blueprint
- India: The Blueprint is a source of reference for human rabies prevention
- West Africa: The Blueprint used to improve communications networking and to set up dog vaccination programs
- Requests for translation into several different languages



# Bohol, Philippines: Controlling Canine Rabies and Preventing Human Deaths

- ❑ Partnership with government and the Global Alliance for Rabies Control
- ❑ Additional funds from WHO and other NGOs
- ❑ Initiated in 2007
- ❑ Cost
  - Estimated \$2.5 million/year in cost-savings by eliminating dog rabies in Philippines
  - Costs would be repaid in 4–11 years



# Bohol Philippines: Controlling Canine Rabies and Preventing Human Deaths

- ❑ **Community mobilization**
  - 140 to >15,000 persons involved in program
- ❑ **Vaccination**
  - 70% of dog population
- ❑ **Increased access to postexposure prophylaxis (PEP)**
  - New clinics
  - Expanded training
- ❑ **Integration of rabies education into school curriculum**
  - 182,000 children educated
- ❑ **CDC training of direct Rapid Immunohistochemical Test (dRIT) and evaluation of diagnostics**

# Bohol Philippines: Controlling Canine Rabies and Preventing Human Deaths

## HEALTH IMPACT

- ❑ **No human or dog rabies deaths reported since Oct 2008**
  - In 2 prior years 10 cases/year reported
- ❑ **Currently undergoing evaluation by the Philippine Ministry of Health for rabies-free status**

# Lessons Learned

## ❑ Rabies prevention is possible

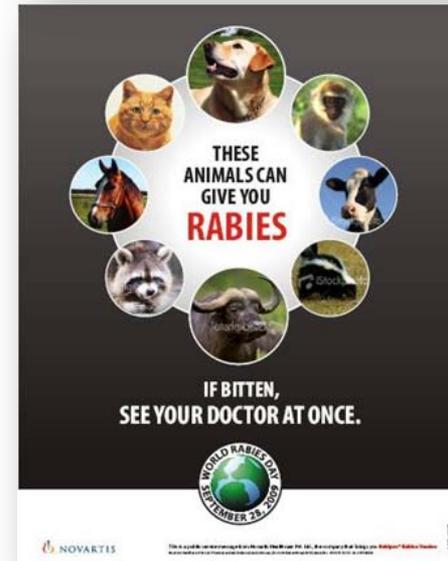
- Need support from multiple sectors
- Public/private partnerships are critical – pooling of resources

## ❑ Communication networks are powerful

- World Rabies Day
- First global webinar included >2,000 participants from 34 countries

## ❑ Many tools are already in place

- Vaccines, reduced regimens, dRIT, websites, etc.



# Needs, Challenges, and Way Forward

- ❑ **Investment in new tools (dog population control)**
- ❑ **Shorter pre-exposure vaccination regimens**
  - Especially important to vulnerable or isolated populations  
e.g., Amazonia
- ❑ **Improved global and national surveillance**
- ❑ **Reassessment of global burden to fully understand burden of rabies and to develop impact models that assess strategic interventions**
- ❑ **Novel strategies and methods to ensure sustainability to prevent reintroduction**



# PUBLIC HEALTH GRAND ROUNDS

Office of the Director

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