





Biosafety and Biosecurity Measures in the Epidemiological Surveillance of Rabies Virus and Other Lyssaviruses in Mexico

November 19th, 2019

How big is the LATAM Region?

-21 "Spanish speaking" countries

- 7 in Central America
- 16 in the Caribbean
- 12 in South America

+ dependent territories.....



What do we know about Mexico?



However we also know that.....



How big is the challenge?



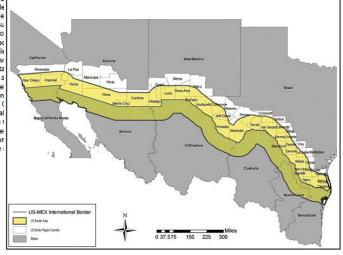
Aduanas interiores

RESEARCH

The U.S.-Mexico Border Infectious Disease Surveillance Project: Establishing Bi-national Border Surveillance

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and Martin Cetron* for the Border Infectious Disease Surveillance Project Working Group¹

In 1997, the Centers for D the Mexican Secretariat of He began the development of the veillance (BIDS) project, a su diseases along the U.S.-Mexic a binational team implemented system for hepatitis and febrile The network developed surv surveillance coordinators, esta Mexican border laboratories, a sharing and notification of se BIDS facilitated investigation Tamaulipas and measles in demonstrates that a binational eral participation can create a crosses an international borde structure, and political barrier collaboration will enhance the tion projects such as RIDS



Source: SHCP 2019

°276 puntos de revisión





What do we know about epidemiology efforts in the region?



Zika virus: Epidemiological surveillance of the Mexican Institute of Social Security

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surveillance of the Mexican Institute of Social

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Abstract

At the end of 2015, the first cases of Zika were identified in southern Mexico. During 2016. Zika spread as an outbreak to a large part of the country's coastal zones.

Methodology

The Zika epidemiological surveillance system records cases with clinical symptoms of Zika virus disease (ZVD) and those confirmed by means of a reverse polymerase chain reaction (RT-PCR) assay. This report includes the suspected and confirmed cases from 2016. Incidence rates were estimated by region and in pregnant women based on the proportion of

In total, 43,725 suspected cases of ZVD were reported. The overall incidence of suspected cases of ZVD was 82.0 per 100,000 individuals and 25.3 per 100,000 Zika cases. There were 4,168 pregnant women with suspected symptoms of ZVD, of which infection was confirmed in 1.082 (26%). The estimated incidence rate of ZVD for pregnant women nationwide Copyright: © 2019 Grajales-Mutiz et al. This is an was 186.1 positive Zika cases per 100,000 pregnant women. open access article distributed under the terms of

The incidence of Zika in Mexico is higher than that reported previously in the National System of Epidemiological Surveillance. Positive cases of Zika must be estimated and reported.

Introduction

Zika virus (ZIKV) was originally identified in a sentinel rhesus monkey in the Zika Forest of Uganda in 1947. The virus is a member of the family Flaviviridae, genus Flavivirus, and is mainly transmitted to humans by Aedes genus of mosquitoes [1]. The first recorded outbreak Epidemiology and Infection

cambridge.org/hyg

Analysis of influenza data generated by four epidemiological surveillance laboratories in Mexico, 2010-2016

Original Paper

Cite this article: Fernandes-Natano L et of (2019), Analysis of influenza data generated by four epidemiological surveillance laboratories in Mexico, 2010-2016. Epidemiology and Infection 147, e183, 1-10, https://doi.org/ 10.1017/\$0950268819000694

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Key words:

Infectious disease epidemiology; influenza; molecular biology

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Evaluation and Reform of Mexican National Epidemiological Surveillance System

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To generate timely and reliable information for decision making in local health centers, Mexico's National Epidemiological Surveillance System (SINAVE) was evaluated and reformed. The reform was achieved by consensing a conceptual model

data from 16 468 local ation from all health ind instruments were crethened epidemiologists' nd assessed control ac-

DOM RECAN WITH AN of SINAVE by means

tative interview, with a everal perceived probe first national meeting the cutoff. Participants also considered which diseases should be reported immediately or weekly and whether a case study should be conducted. Listings were subjected to a frequency analysis, and three standardized formats were defined: a Weekly Report of New Cases of Disease (EPI-1-95), a Case Study (EPI-2-95). and an Outbreak Study (EPI-3-95). A pilot test was conducted for a 2-month period. Problems were discussed, and errors were

detected and corrected. At a third national meeting. the simple conceptual model of SINAVE reform, formats, manuals, and training program was reconstant A Simple Information

an epidemiology bulletin, and a training plan.

A National Committee for Epidemiological Surveillance (CONAVE) was created through ministerial agreement to make surveillance statutory and compulsory in the National Health System.6 CONAVE was conceived and designed according to the model of academic committees. With Mexico's complex health system, CONAVE has a unique value, because, for the first time, all organizations had been actively involved at SINAVE, and the Official Mexican Norm for Epidemiology Surveillance mandates that inconformment /Discount 4 \ 7

Measles in Mexico, 1941–2001: Interruption of Endemic Transmission and Lessons Learned

José Ignacio Santos,12 Miguel Angel Nakamura,12 Miriam Veras Godoy,12 Pablo Kuri,3 Carlos Álvarez Lucas,3 and Roberto Tapia Conver

'National Center for Child and Adolescent Health, 'National Immunization Council, 'National Center for Epidemiological Surveillance, and "Under-Secretary for Disease Prevention and Protection, Ministry of Health, Mexico

In Mexico, measles occurred in a cyclical endemic-epidemic pattern until the early 1970s. Beginning in 1973, routine vaccination augmented by mass vaccination campaigns led to a decrease in the incidence of measles until the 1989-1990 regional pandemic, when the measles attack rate rose to 80 cases per 100,000, resulting in 5899 deaths. Since the pandemic, measles elimination efforts in Mexico have resulted in increasing coverage to >95% among children aged 1-6 years with 2 doses of either measles or measlesmumps-rubella vaccine since 1996 and in coverage of 97.6% among children aged 6-10 since 1999. Surveillance data suggest that the transmission of indigenous measles virus was interrupted in 1997. After almost 4 years without measles cases, in April 2000, measles virus was reintroduced into Mexico and 30 laboratory-confirmed cases were reported. Detection of relatively few cases in nonprogrammatic age groups affirms the high immunization coverage and the sensitivity of measles surveillance in Mexico. We conclude that the specific strategies adopted for measles elimination have enabled Mexico to eliminate the endemic transmission of measles.

Mexico, a country with many problems but without rage

Published: - Nov 18, 2019

Mexico is the first country in the world declared free of rabies in humans transmitted by dogs, according to the World Health Organization





Representative pathogens identified in last 40 years (and counting....)

1972 Norovirus from diarrhea outbreak Norwalk Ohio 4 yrs. earlier 1994: Human herpesvirus 8=Kaposi's sarcoma-associated herpesvirus 1973 Rotavirus Major cause of infantile diarrhea worldwide 1994 Sabia virus Brazilian hemorrhagic fever 1975 Parvovirus B19 Fifth disease; Aplastic 1997: First Human outbreak of H5N1 1976 Cryptosporidium parvum Acute enterocolitis 1998: TT virus: a Transfusion Transmitted Hepatitis 1977 Ebola virus Ebola hemorrhagic fever 1998: Nipah virus: Encephalitis 1977 Legionella pneumophila Legionnaires' disease 1999: Anaplasma phagocytophilum (Human Granulocytic Ehrlichiosis/Anaplasmosis) 1977 Hantaan virus Hemorrhagic fever with renal syndrome (HFRS) 2000: Helicobacter canadensis another cause of diarrhea 1977 Campylobacter sp. Enteric pathogens distributed globally 2001: Human metapneumovirus (hMPV): Resp infections 1980 Human T-cell lymphoma leukemia lymphotropic virus-I (HTLV I) 2002: Corynebacterium appendicis: appendicitis 1981 Staphylococcus Toxic shock syndrome with toxin tampon use 2002: Dysgonomonas mossii :sepsis 1982 Escherichia coli; O157:H7 hemolytic uremic syndrome 2002: Kytococcus schroeteri: sepsis 2003: SARS - CoV 1982 HTLV II Hairy cell leukemia 1982 Borrelia burgdorferi Lyme disease 2003: "Bird flu" H5N1 new clad of birds & humans 1983 Human immunodeficiency Syndrome-AIDS virus (HIV) 2004: Human cornoavirus NL63 (HCoV-NL63) 1983 Helicobacter pylori Gastric ulcer 2005: Porocephalus taiwana: a new pathogenic pentastomid 1988 Human herpesvirus-6 (HHV-6) Roseola subitum 2006: Prevotella baroniae septicemia and wound infection 1989 Ehrlichia chaffeensis Human ehrlichiosis 2007: New Orya-Fever Tike agent: Bartonella rochalimae sp. Nov 1989 Hepatitis C Parentally transmitted non-A, non-B hepatitis 2008 Lujo virus (Novel Arena virus of Africa) 1990 Recognition that Pneumocystis jiroveci was unique from P. carinii 2008 Mycobacterium chimaera (subtype of MAC) 1991 Guanarito virus Venezuelan hemorrhagic fever 2009 H1N1-2009 Pandemic 1991 Mycoplasma penetrans urogenital infection 2009 Wohlfahrtiimonas chitiniclastica sepsis 1992 Vibrio cholerae New strain associated with O139 epidemic cholera 2010 Negativicoccus succinicivorans 1992 Bartonella henselae Cat-scratch disease; bacillary angiomatosis 2011 Influenza A(H3N2)v virus 1992 Tropheryma whippelii Whipples Disease 2012 Middle East Respiratory Syndrome (MERS- CoV) 1992 Barmah Forest (BF) virus - Arbovirus Australia 2013 influenza A(H7N9) 1993 Hantavirus Hantavirus pulmonary syndrome isolates 2013 Severe fever with thrombocytopenia syndrome Virus (new bunyavirus)

2014 Avian influenza A H10N8

1994: Asian Taeniasis: Human Tapeworm infection

How epidemiological surveillance works in Mexico

 System for Epidemiological Surveillance (SUIVE) created in 1981.

 SUIVE publishes weekly bulletins detailing potential "emerging and re-emerging" diseases.



Talking about epidemiological surveillance.....

PRO/AH/EDR> Rabies - Americas (44): USA, dog, skunk, raccoon, fox, human exp

RABIES - AMERICAS (44): USA, DOG, SKUNK, RACCOON, FOX, HUMAN EXPOSURE

A ProMED-mail post

http://www.promedmail.org

ProMED-mail is a program of the

International Society for Infectious Diseases

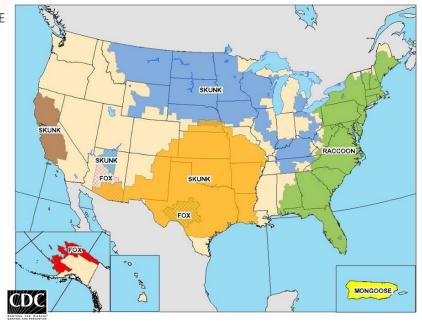
<http://www.isid.org>

In this post:

- [1] South Dakota/North Dakota: puppy, possible human exposure
- [2] North Carolina: fox, human exposure
- [3] New York: raccoon, human exposure
- [4] Massachusetts: skunk, human exposure
- [5] South Carolina: puppy, human exposure

[1] South Dakota/North Dakota: puppy, possible human exposure

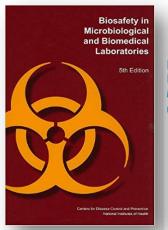
Date: Fri 30 Aug 2019 Source: Jamestown Sun [edited]



< https://www.jamestownsun.com/lifestyle/pets/4639568-After-puppy-tests-positive-for-rabies-health-departments-in-the-Dakotas-seek-owners-of-littermates>

Infectious diseases and the challenges that we face

- Epidemiological context
- Limited support/risk assessment
- "New Regulations"
- Language, cultural barriers, professional background ... ICS > 03 > 03.100 > 03.100.70



LABORATORY **BIOSAFETY** MANUAL

FOURTH EDITION



ISO 35001:2019

Biorisk management for laboratories and other related organisations



But... how could we monitor something that it is difficult to detect?





Rabies



In North America, rabies still persists in terrestrial meso-carnivore species and bats.

- Specific variants of the rabies virus are adapted to species.
- Wildlife species include: skunks, foxes, coyotes, and bats.



Rabies: Status in Mexico

- No human cases transmitted by dogs since 2006...
- Last canine case in 2017...

In 2017:

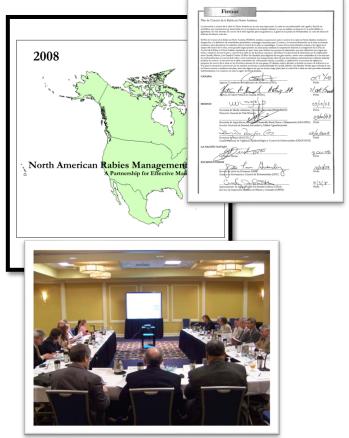
- 75% of positive cases diagnosed were puppies...
- Confirmed cases were non-vaccinated animals...



The North American Rabies Management Plan (NARMP)

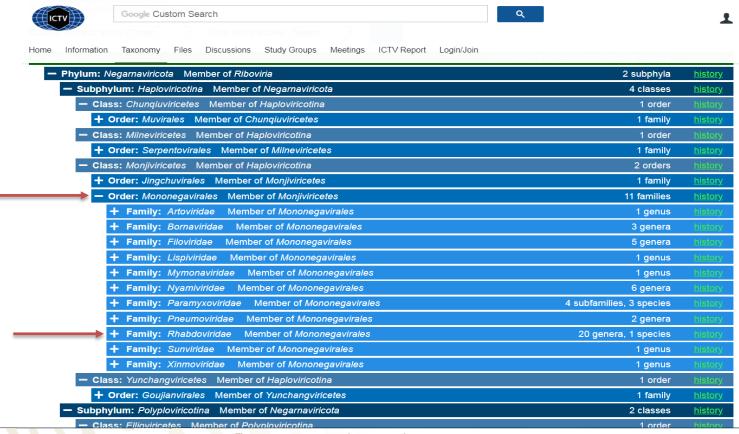
 NARMP establishes a protocol for rabies management in North America.

 "Key strategy" in facilitating the planning processes.





Taxonomy of Lyssaviruses





Taxonomy of Lyssaviruses (cont.)

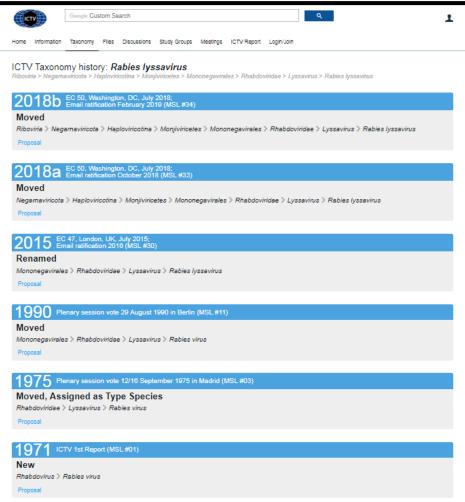
Google Custom Search	Q	
	I genus	
ne Information Taxonomy Files Discussions Study Groups Meetings ICTV Report Login/Join		
+ Family: Paramyxoviridae Member of Mononegavirales	4 subfamilies, 3 species	history
+ Family: Pneumoviridae Member of Mononegavirales	2 genera	history
- Family: Rhabdoviridae Member of Mononegavirales	20 genera, 1 species	history
+ Genus: Almendravirus Member of Rhabdoviridae	5 species	<u>history</u>
+ Genus: Alphanemrhavirus Member of Rhabdoviridae	2 species	
+ Genus: Caligrhavirus Member of Rhabdoviridae	3 species	
+ Genus: Curiovirus Member of Rhabdoviridae	4 species	
+ Genus: Cytorhabdovirus Member of Rhabdoviridae	11 species	history
+ Genus: Dichorhavirus Member of Rhabdoviridae	5 species	history
+ Genus: Ephemerovirus Member of Rhabdoviridae	8 species	histor
+ Genus: Hapavirus Member of Rhabdoviridae	15 species	history
+ Genus: Ledantevirus Member of Rhabdoviridae	16 species	history
+ Genus: Lyssavirus Member of Rhabdoviridae	16 species	histor
+ Genus: Novirhabdovirus Member of Rhabdoviridae	4 species	histor
+ Genus: Nucleorhabdovirus Member of Rhabdoviridae	10 species	histor
+ Genus: Perhabdovirus Member of Rhabdoviridae	3 species	histor
+ Genus: Sigmavirus Member of Rhabdoviridae	7 species	histor
+ Genus: Sprivivirus Member of Rhabdoviridae	2 species	histor
+ Genus: Sripuvirus Member of Rhabdoviridae	5 species	histor
+ Genus: Tibrovirus Member of Rhabdoviridae	7 species	histor
+ Genus: Tupavirus Member of Rhabdoviridae	3 species	history
+ Genus: Varicosavirus Member of Rhabdoviridae	1 species	history
+ Genus: Vesiculovirus Member of Rhabdoviridae	16 species	histor
Species: Moussa virus Member of Rhabdoviridae		history

Source: ICTV Mayo 2019 https://talk.ictvonline.org/taxonomy/

New species submitted

Source: ICTV Mayo 2019 https://talk.ictvonline.org/taxonomy/



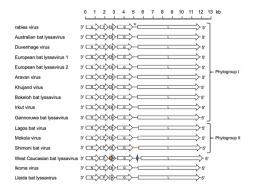


Genus Lyssavirus

Virus Taxonomy: 2018b Release

EC 50, Washington, DC, July 2018 Email ratification February 2019 (MSL #34)

- Genu	s: Lyssavirus
Species:	Aravan lyssavirus
Species:	Australian bat lyssavirus
Species:	Bokeloh bat lyssavirus
Species:	Duvenhage lyssavirus
Species:	European bat 1 lyssavirus
Species:	European bat 2 lyssavirus
Species:	Gannoruwa bat lyssavirus
Species:	Ikoma lyssavirus
Species:	Irkut lyssavirus
Species:	Khujand lyssavirus
Species:	Lagos bat lyssavirus
Species:	Lleida bat lyssavirus
Species:	Mokola lyssavirus
Species:	Rabies lyssavirus
Species:	Shimoni bat lyssavirus
Species:	West Caucasian bat lyssavirus



Derivation of names

Lyssavirus: from Lyssa, the Greek goddess of madness, rage, and frenzy.

Related, unclassified viruses

Virus name	Accession number	Virus abbreviation
Taiwan bat lyssavirus	MF472710	TBLV
Kotalahti bat lyssavirus	MF960865	KBLV

Virus names and virus abbreviations are not official ICTV designations.



Source: ICTV Mayo 2019 https://talk.ictvonline.org/taxonomy/

New species

Source: Lyssaviruses and Bats: Emergence and Zoonotic Threat. Viruses 2014, 6, 2974-2990; doi:10.3390/v6082974

Rabies virus (RABV) (1865) Lagos bat lyssavirus (LBV) (1956) Mokola virus(MOKV) (1974) Duvenhage virus (DUVV) (1971) European bat lyssavirus 1 [EBLV-1] (1968) European bat lyssavirus 2 [EBLV-2] (1986) Australian bat lyssavirus (ABLV) (1996) Aravan virus (ARAV) (2003) Irkut virus (IRKV) (2003) Khujand virus (KHUV) (2003) West Caucasian Bat Virus (WCBV) (2005) Shimoni virus (SHIBV (2009) Bokeloh bat lyssavirus (BBLV) (2010) Ikoma lyssavirus (IKOV) (2012) Lleida bat lyssavirus (LLEBV) (2012) Gannoruwa bat lyssavirus (GBLV) (2016) Taiwan bat lyssavirus (TWBLV) (2016/2017) Kotalahti bat lyssavirus (KBLV) (2017)

No.	Virus	Distribution	
1	RABV 🖠	Global 🕶	
2	ARAV	Eurasian 🛶	6982
3	KHUV	Eurasian 🛶	
4	BBLV	European 🕶	100
5	EBLV-2	Europe 🕶	
6	ABLV 🛊	Australia 🛶	
7	IRKV 🖠	Eurasian 🛶	
8	EBLV-1 ₩	European 🛶	
9	DUVV 🛊	African 🕶	9 100 79 86 81
10	MOKV 🛊	African	100
11	SHIBV	African *	- // 100
12	LBV	African 🕶	0
			11 /// 100
			$ \begin{array}{c c} A & B & D & 12 & C \end{array} $
13	WCBV	Eurasian 🕶	Phylogroup III/IV?
13 14	WCBV IKOV	Eurasian 🕶	



Relationship between Lyssaviruses and bats

species

Geographical distribution	Lyssavirus species	Bat species most commonly associated with lyssavirus infection	Common name	Transmission from bats implicated in human fatalities
The Americas	Rabies virus (RABV)	Eptesicus fuscus	Big brown bat	Yes
		Tadarida brasiliensis	Mexican/Brazilian free-tail bat	Yes
		Lasionycteris noctivagens	Silver-haired bat	Yes
		Perimyotis subflavus	Tri-coloured bat	Yes
	Ī	Desmodus rotundus	Vampire bat	Yes
		Eidolon helvum	Straw coluored fruit bat	No
Africa	Lagos Bat Virus (LBV)	Rousettus aegyptiacus	Egyptian fruit bat	No
		Epomorphorus wahlbergi	Wahlberg's epauletted fruit bat	No
	Shimoni Bat Virus (SHIBV)	Hipposideros commersoni	Commerson's leaf-nosed bat	No
	Duvenhage virus (DUVV)	Miniopterus sp?	Undefined	Yes
		Nycteris thebaica	Egyptian slit-faced bat	Yes
Eurasia	European Bat Lyssavirus type 1 (EBLV-1)	Eptesicus serotinus	Serotine bat	Yes
	European Bat Lyssavirus type 2 (EBLV-2)	Myotis daubentonii	Daubenton's bat	Yes
	Bokeloh Bat Lyssavirus (BBLV)	Myotis nattereri	Natterer's bat	No
	Aravan virus (ARAV)	Myotis blythi	Lesser mouse-eared bat	No
	Irkut Virus (IRKV)	Murina leucogaster	Greater tube-nosed bat	Yes
	Khujand Virus (KHUV)	Myotis mystacinus	Whiskered bat	No
	West Caucasian Bat Virus (WCBV)	Miniopterus schreibersii	Common bent-winged bat	No
	Lleida Bat Lyssavirus (LLEBV) *	Miniopterus schreibersii	Common bent-winged bat	No
Australosis	Australian Bat Lyapavinus (ADLV)	Pteropus alecto	Black flying fox and related sp.	Yes
Australasia	Australian Bat Lyssavirus (ABLV)	Saccolaimus flaviventris	Yellow-bellied sheath-tailed bat	Yes





Article types Clinical Trial Review Customize ...

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Publication dates

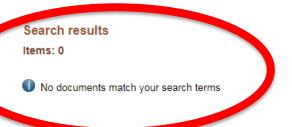
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Species Humans

Other Animals

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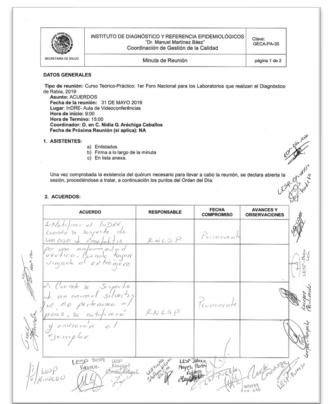
The solution...

A strategic measure for increasing Rabies and other Lyssaviruses surveillance in the country and one action plan for the containment of these pathogens for an eventual introduction in NA.



Step 1: training (ISST), sign agreement and evaluation of lab capabilities



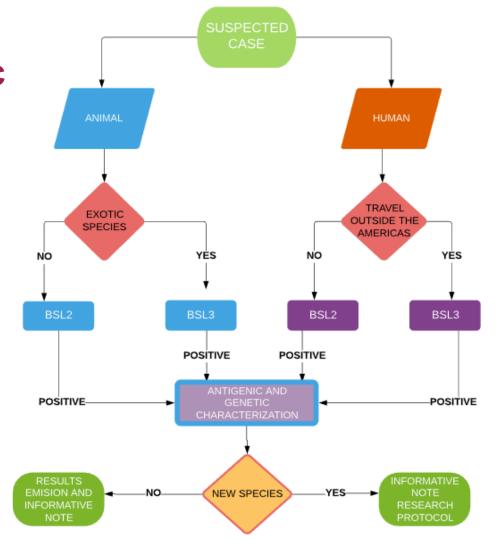






Step 2: Diagnostic and containment algorithm





Working on a National Level

















Biosafety and Biosecurity measures for PH labs

- Annual training from 2008 up to date....
- Specific emergency response drills (lab diagnosis and contaiment).
- More than 120 staff trained...
- Strengthening of the inspection and surveillance program.









Additional measures

- National cooperation with other agencies...
- Strategic communication national and international...
- Trained and certified shippers for the transport of Infectious Substances...





Concluding remarks (International Level)

What we need to keep doing:

Improve the exchange of information on epidemiologic events...

Facilitate the international cooperation



Concluding remarks (National Level)

- Existing guidelines for epidemiological surveillance
- Emergency preparedness and response protocols.
- Experience and training (basic and specific).



General Direction of Epidemiology

Direction of Diagnosis and Reference Direction of Services and Technical Support

Department of Virology (Rabies Lab Staff)

Department of Bacteriology

Department of Parasitology

Department of Molecular Biology

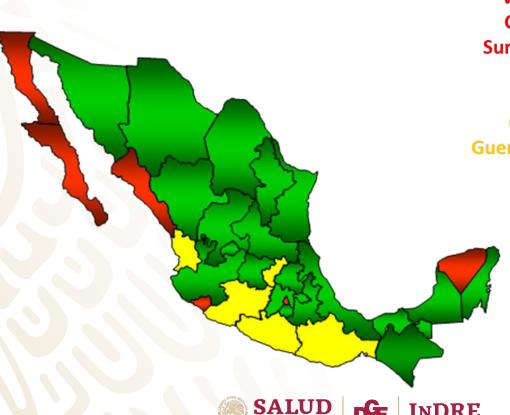
Department of Emerging Diseases

Department of Sample Control and Services

RNLSP



Rabies Laboratories Network



Without laboratory: Baja California, Baja California Sur, Sinaloa, Colima, Ciudad de Mexico and Yucatan.

Quality control: Nayarit, Guerrero, Oaxaca, Queretaro y Michoacan

Diagnosis by FAT

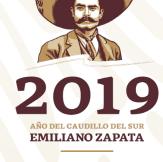
All is about emerging and re-emerging infectious diseases/pathogens.....

"Sooner or later everything old is new again".....



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Thank you for your attention

