Center for Infectious Disease Research and Policy
University of Minnesota

CIDRAP Leadership Forum
September Intelligence Briefing

February 24, 2016

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1. **Mosquito-borne diseases**
   - Dengue, Chikungunya
   - Zika: travel, blood safety, vector control, sexual transmission, microcephaly, vaccines
2. **MERS-CoV**
   - Latest cases
   - Camels
   - Vaccines
3. **Influenza**
   - H1N1 surge
   - Vaccine
   - Avian
4. **Ebola**
5. **Vaccines**
   - Pertussis
   - HPV

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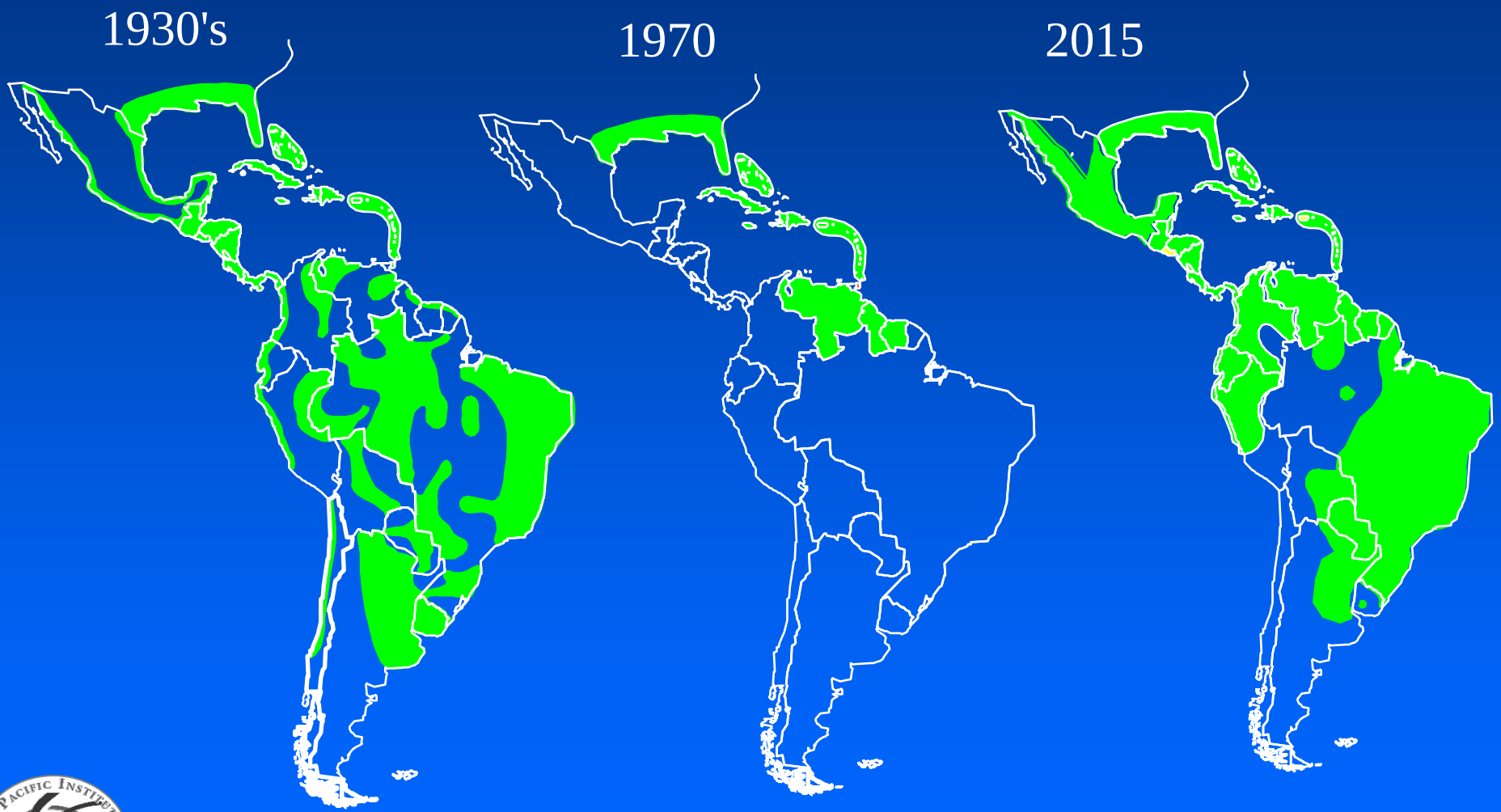
Aedes aegypti

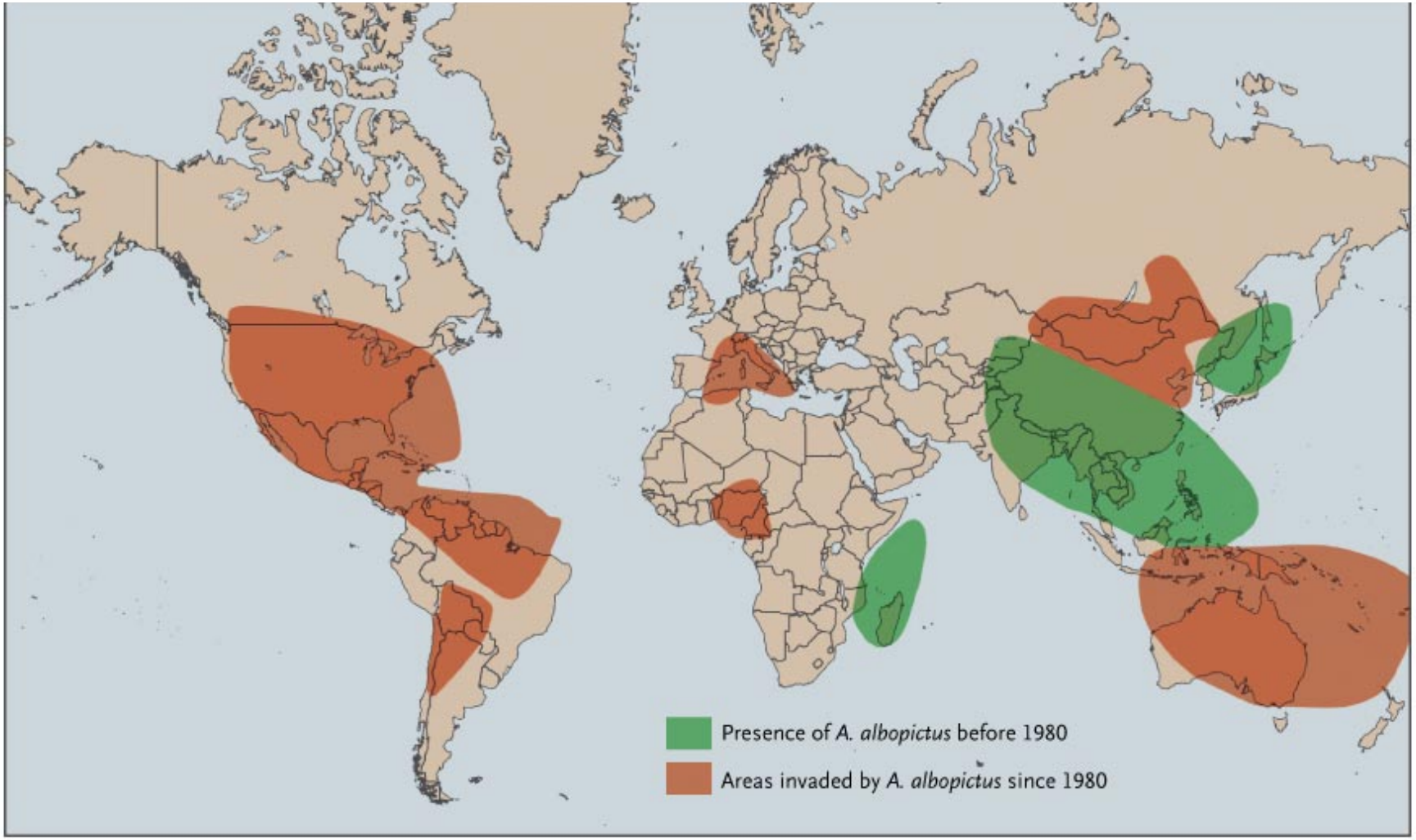
Aedes aegypti Distribution in the Americas



Adapted from Gubler, 1998

Aedes albopictus Female

World Distribution of the *Aedes albopictus* Mosquito



Charrel R et al. N Engl J Med 2007;356:769-771

The NEW ENGLAND JOURNAL of MEDICINE

Approximate distribution of *Aedes aegypti* in the United States*

Approximate distribution of *Aedes albopictus* in the United States*

REUTERS

Hawaii's Big Island declares emergency over dengue fever infections

The mayor of Hawaii's Big Island declared a state of emergency on Monday to deal with a growing outbreak of dengue fever, spread by infected mosquitoes, with 250 cases confirmed over the past four months.

As a result of Hawaii County Mayor Billy Kenoi's order people on the Big Island will be allowed to resume disposing of old tires in landfills, since tires which are left lying around are a known breeding spot for mosquitoes.

There have been 250 confirmed cases of dengue fever on the island since Oct. 29, making it the largest outbreak in the state since the 1940s, according to the mayor's declaration and Hawaii health officials.

Dengue fever causes flu-like symptoms and can develop into the deadly dengue hemorrhagic fever.

Hawaii Governor David Ige said in a statement he supported the efforts on the Big Island but would not issue a statewide emergency declaration unless the outbreak spread to other islands or expanded to include other diseases, such as the Zika virus.

Zika is spreading rapidly in South and Central America and the Caribbean and has been linked to severe birth defects in Brazil.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AQUI


BARRACA DA VÂNIA E JUNIOR

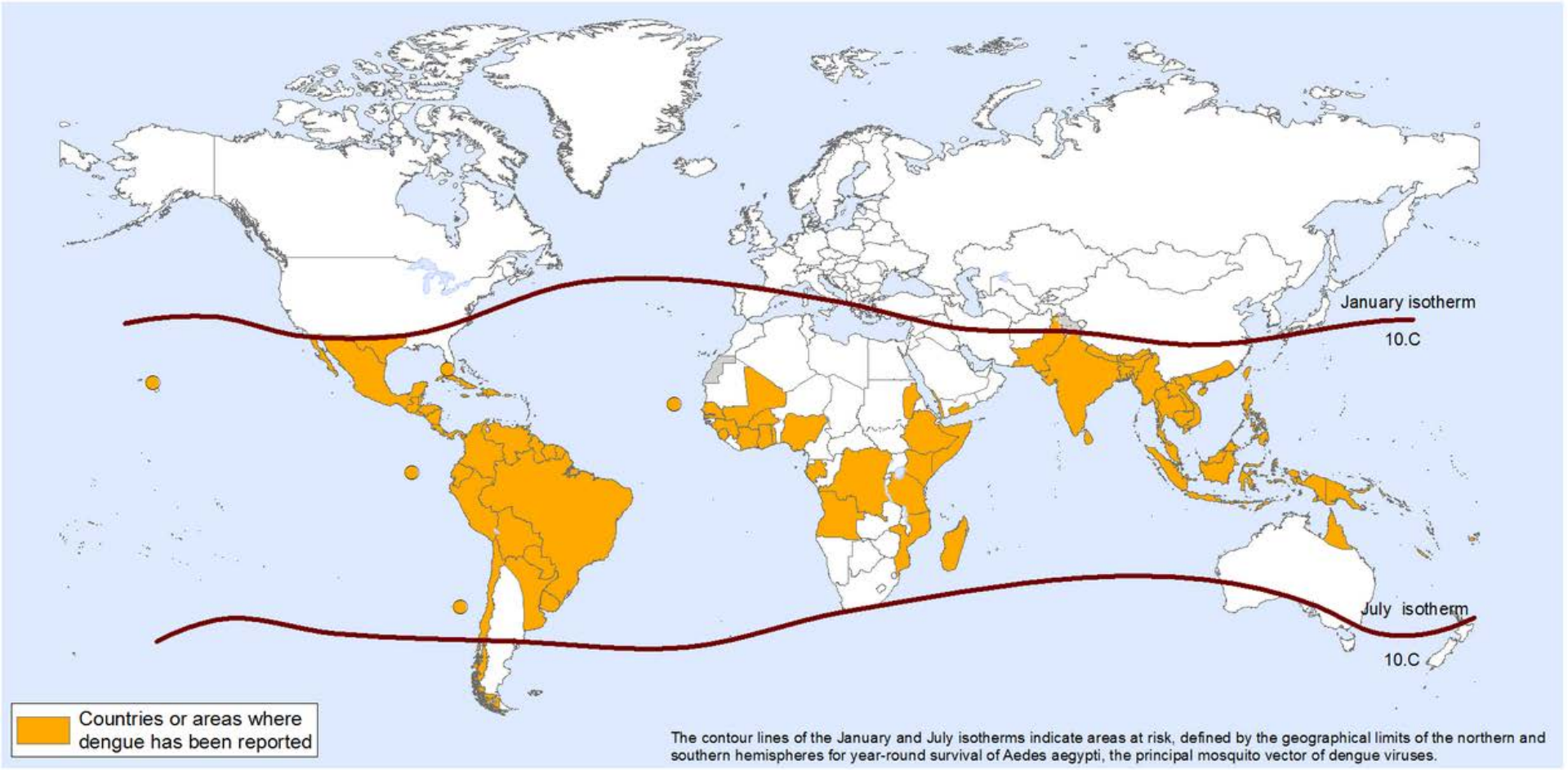
Global Burden of Dengue

- Some 2.5 billion people – two fifths of the world's population – are at risk from dengue.
- WHO estimates ~ 50 million dengue infections worldwide every year
- In 2014 there were more than 1,173,000 reported cases in the Americas
- Endemic in more than 100 countries
- Explosive outbreaks occur – In 2013, Brazil reported over 205,000 cases, in 7 weeks

Pan American Health Organization

World Health Organization

Dengue, countries or areas at risk, 2013

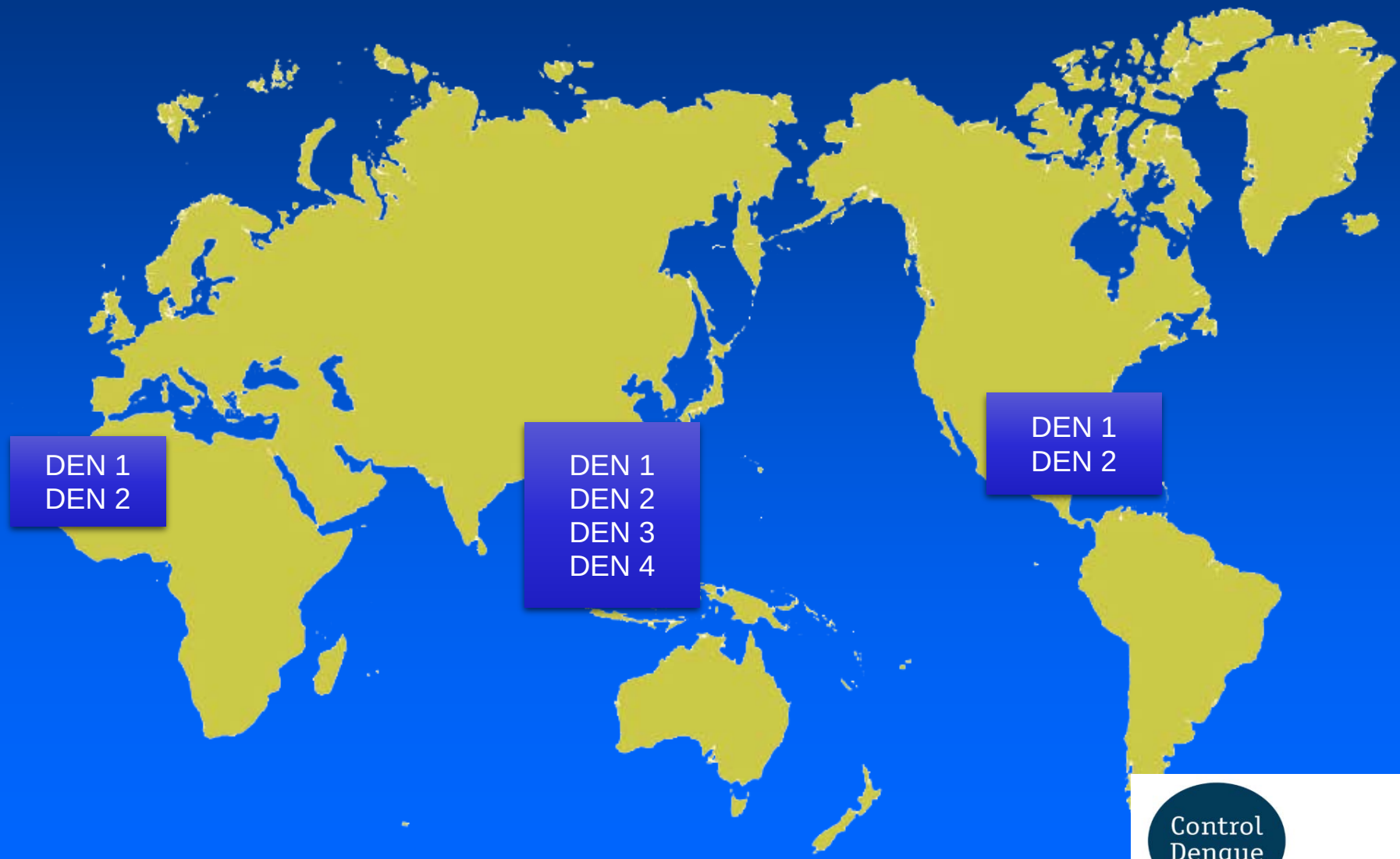


The contour lines of the January and July isotherms indicate areas at risk, defined by the geographical limits of the northern and southern hemispheres for year-round survival of Aedes aegypti, the principal mosquito vector of dengue viruses.

Data Source: World Health Organization
Map Production: Health Statistics and Information Systems (HSI)
World Health Organization

World Health Organization

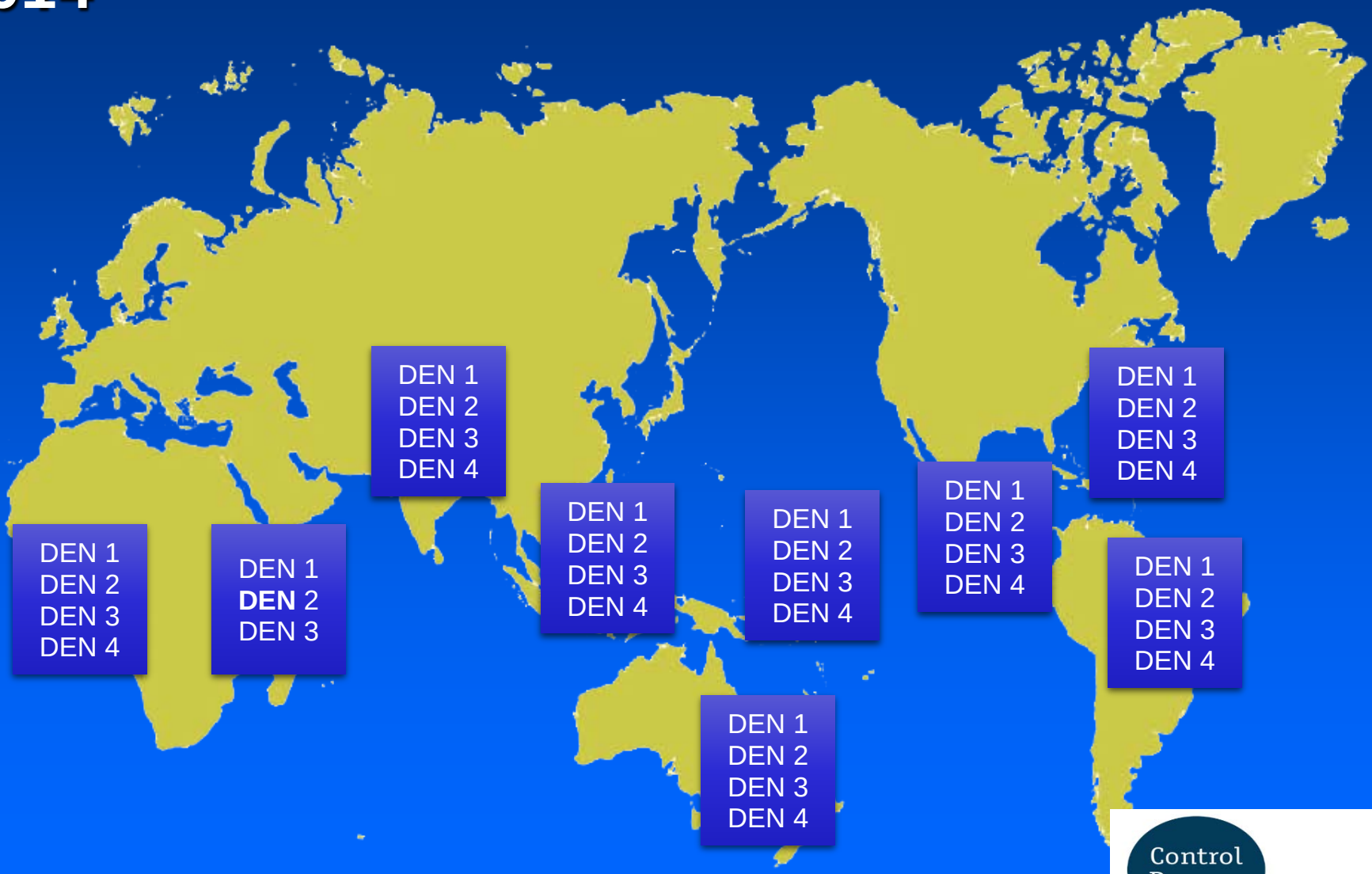
Global distribution of dengue virus serotypes, 1970



Control Dengue

PDC Partnership

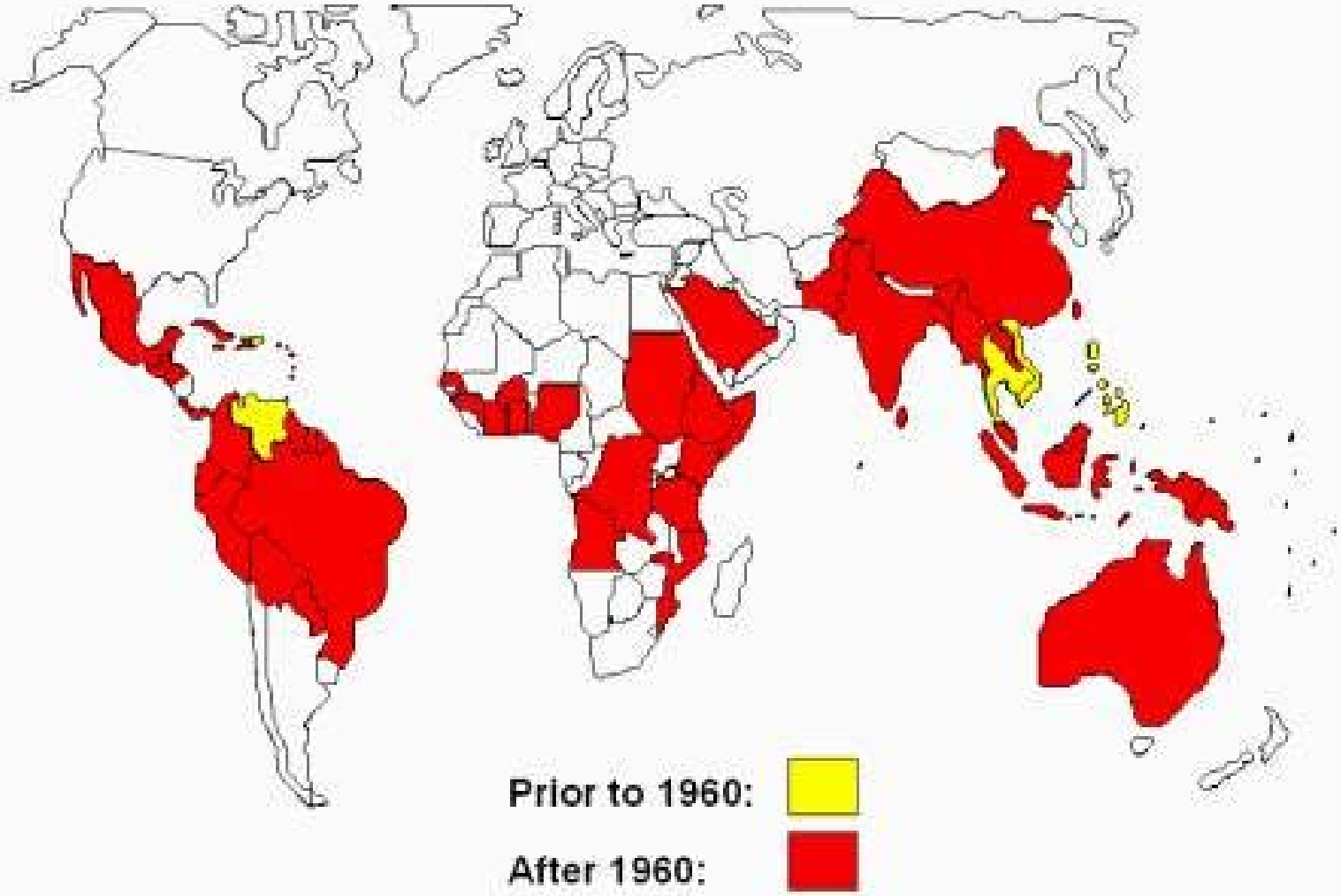
Global distribution of dengue virus serotypes, 2014



Control Dengue

PDC Partnership

Emergence of Dengue and Dengue Hemorrhagic Fever



Published Date: 2013-12-09 12:31:29
Subject: PRO/EDR> Chikungunya (52): Caribbean (St Martin) alert
Archive Number: 20131209.2099940

CHIKUNGUNYA (52): CARIBBEAN (SAINT MARTIN) ALERT

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A ProMED-mail post
http://www.promedmail.org
ProMED-mail is a program of the
International Society for Infectious Diseases
http://www.isid.org

Date: Fri 6 Dec 2013
Source: The Daily Herald [edited]
http://www.thedailyherald.com/index.php?option=com_content&view=article&id=44572

In St Martin, 2 cases of chikungunya [virus infection], a dengue-like sickness, have been confirmed following testing at the specialist laboratory in Marseille that returned positive results to Agence Regional de Sante (ARS [Regional Health Agency]) on 5 Dec 2013.

The disclosure was made by ARS Director-General Patrice Richard on Friday [6 Dec 2013] at a press conference in the Prefecture attended by Prefet Philippe Chopin, President of the Collectivity Aline Hanson, Dutch-side [St Maarten] Minister of Public Health Cornelius de Weever and specialist epidemiologists.

Richard said family doctors, for about 2 weeks, have been reporting cases of people showing suspected signs of chikungunya, and not dengue [virus infections]. There is no current evidence that chikungunya is on the Dutch side [of the island]. The virus can be imported by travelling from a risk country.

The 2 confirmed cases originated in French Quarter. In addition, there are currently 4 "probable" cases and 30 "suspected" cases, 15 of which are in the Oyster Pond area. In technical terms, "suspected" means just the signs are manifested while "probable" is a diagnostic test that calculates the likelihood that chikungunya [virus] has been contracted, according to epidemiologists.

ARS is awaiting more results of other cases from the Marseille laboratory.

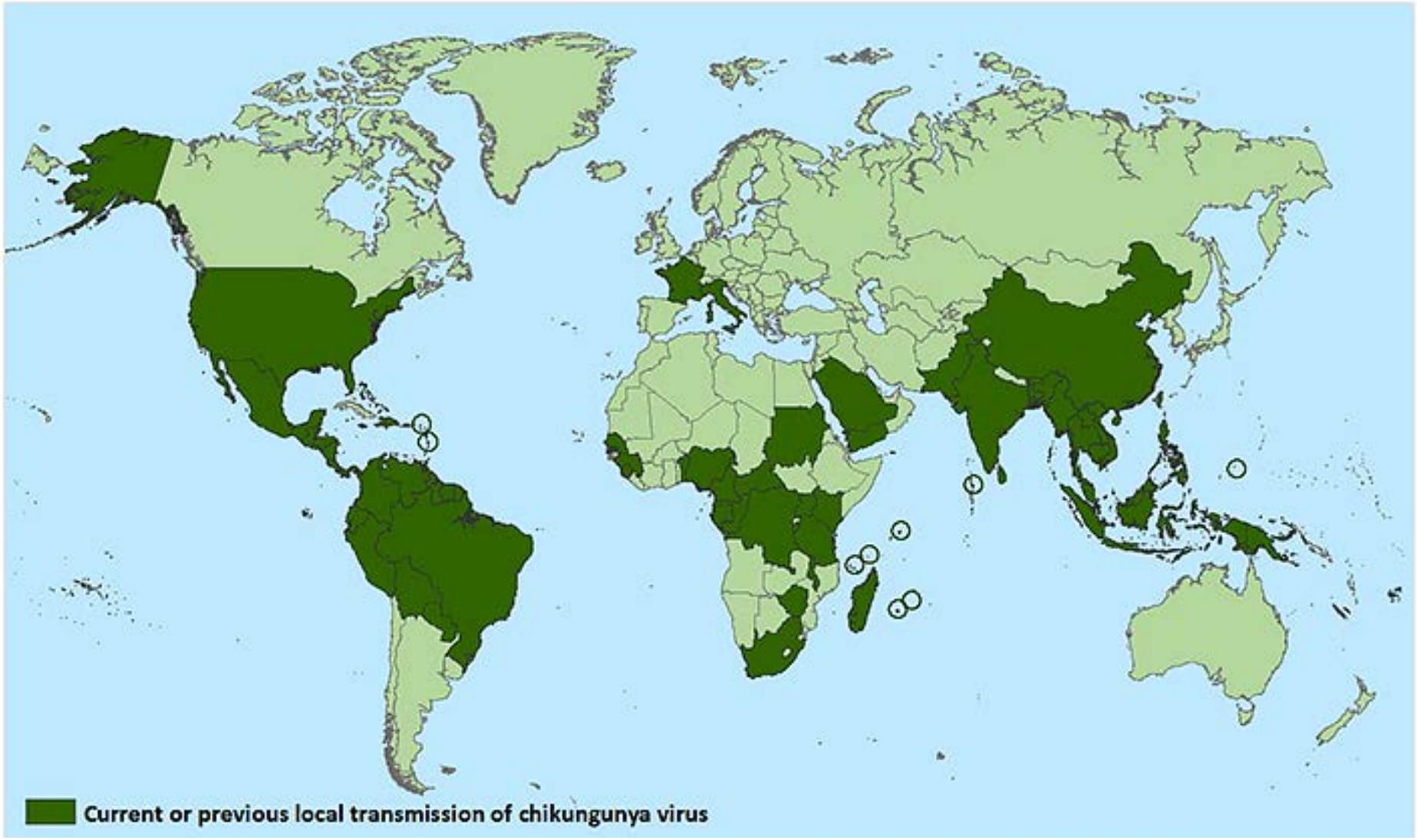
"Chikungunya is in the Pacific islands, in Asia, in India, but never until now in the Caribbean islands," noted epidemiologist Marion Petit-Sinturel. "It's the 1st time we have located transmission here in St Martin."

ARS Director Pascal Godefroy said the situation is likely to change quickly as results come in. "This could be the beginning of an epidemic since we are already in a dengue epidemic," he said.

Minister de Weever acknowledged that "mosquitoes don't stop at the border," and assured the full cooperation of Dutch-side health authorities.

Countries and territories where chikungunya cases have been reported*

(as of October 20, 2015)



*Does not include countries or territories where only imported cases have been documented. This map is updated weekly if there are new countries or territories that report local chikungunya virus transmission.

Pan American Health Organization

World Health Organization Americas

Countries/territories with autochthonous transmission or imported cases of Chikungunya in the Americas, EW 49, 2013 - EW 5, 2016

Data source:
PAHO/WHO. Number of reported cases of Chikungunya Fever in the Americas

http://www.paho.org/chikungunya

Map production:
PAHO-WHO AD CHA IR ARO

* Note: Entire countries have been shaded on the map though there is no evidence of country-wide virus presence.

Pan American Health Organization
World Health Organization
Americas

Number of Reported Cases of Chikungunya Fever in the Americas, by Country or Territory
2016 (to week noted)
Cumulative cases
Epidemiological Week / EW1 (Updated as of 8 January 2016)

Country/Territory	Epidemiological Week[a]	Autochthonous transmission cases[b]		Imported cases	Incidence Rate[c]	Deaths[d]	Population[e] X 1000
		Suspected	Confirmed				
North America							
Bermuda	Week 17			3			70
Canada	Week 36			85			35,871
Mexico	Week 51		11,468	20	9.2		125,235
United States of America[f]	Week 50			653			325,127
Subtotal		*0*	*11,468*	*761*	*2.4*	*0*	*486,303*
Central American Isthmus							
Belize	Week				0.0		347
Costa Rica	Week 20		142		2.8		5,001
El Salvador	Week 35	39,704	17		618.1	0	6,426
Guatemala	Week 48	27,759	1,998		183.1	5	16,255
Honduras	Week 45	82,003	5		973.6	1	8,423
Nicaragua	Week 51	68,945	5,117		1,183.9	1	6,256
Panama	Week 51	123	36	19			3,987
Subtotal		*218,534*	*7,315*	*19*	*483.7*	*7*	*46,695*
Latin Caribbean							
Cuba	Week				0.0		11,248
Dominican Republic	Week 28	67			0.6		10,652
French Guiana	Week 47	6,960	1,759		3,340.6	2	261
Guadaloupe	Week 46	157			33.4		470
Haiti	Week						10,603
Martinique	Week 46	341			84.2		405
Puerto Rico[f]	Week 51	801	214		27.6	1	3,680
Saint Barthelemy	Week 18	317			3,561.8		9
Saint Martin (French part)	Week 46	602			1,686.7		36
Subtotal		*9,245*	*1,973*	*0*	*30.0*	*3*	*37,364*
Andean Area							
Bolivia	Week 13	143	916	1	9.6		11,024
Colombia	Week 51	355,175	3,192		723.5	70	49,529
Ecuador	Week 51	29,350	4,173	21	206.6	2	16,225
Peru	Week 48	85	100	77	0.6		31,161
Venezuela	Week 51	15,839	355	0	51.8	0	31,292
Subtotal		*400.592*	*8.736*	*99*	*294.0*	*72*	*139.231*
TOTAL		653,249	31,543	935	69.1	82	991,134

THE TICO TIMES News

MOSQUITO-BORNE VIRUSES

Dengue, chikungunya cases in Costa Rica up by over 600 percent

Although most of the interest these days is focused on the arrival in the country of the Zika virus, there's been a staggering rise in other — and in many cases more serious — mosquito-borne diseases in the first months of the year.

The Health Ministry reported last week that the number of people in Costa Rica who have tested positive for dengue or chikungunya during the first five weeks of 2016 jumped more than 600 percent for both viruses compared to the same period last year.

A total of 3,253 people here have been diagnosed with dengue since January, while another 850 have tested positive for chikungunya. Both viruses cause fever, headaches, joint pain, extreme fatigue and rashes. Chikungunya can also lead to encephalitis, a potentially fatal brain inflammation.

Dengue is now present in 73 of the country's 81 cantons, while chikungunya — which arrived in the country just two years ago — is present in 45.

Roberto Castro, director of the ministry's health analysis unit, said the sharp increase in patients with the two viruses is at least partially due to unusual weather. Dengue and chikungunya cases usually peak here in the last few months of the year, during the transition from the rainy season to the dry season. That transition usually ends in December, but this year the rainy season ended late, thanks in part to the effects of *El Niño* and climate change

Chikungunya virus–associated encephalitis

A cohort study on La Réunion Island, 2005–2009

Patrick Gérardin, MD, PhD
Thérèse Couderc, PhD
Marc Bintner, MD
Patrice Tournebize, MD
Michel Renouil, MD
Jérome Lémant, MD
Véronique Boisson, MD
Gianandrea Borgherini, MD
Frédérik Staikowsky, MD, PhD
Frédéric Schramm, MD, PhD
Marc Lecuit, MD, PhD
Alain Michault, PharmD†
On behalf of the Encephalchik Study Group

Correspondence to Dr. Gérardin: patrick.gerardin@chu-reunion.fr

ABSTRACT

Objective: To estimate the cumulative incidence rate (CIR) of Chikungunya virus (CHIKV)-associated CNS disease during the La Réunion outbreak, and assess the disease burden and patient outcome after 3 years.

Methods: CHIKV-associated CNS disease was characterized retrospectively in a cohort of patients with positive CHIKV reverse transcriptase PCR or anti-CHIKV immunoglobulin M antibodies in the CSF and fulfilling International Encephalitis Consortium criteria for encephalitis or encephalopathy. Neurologic sequelae were assessed after 3 years.

Results: Between September 2005 and June 2006, 57 patients were diagnosed with CHIKV-associated CNS disease, including 24 with CHIKV-associated encephalitis, the latter corresponding to a CIR of 8.6 per 100,000 persons. Patients with encephalitis were observed at both extremes of age categories. CIR per 100,000 persons were 187 and 37 in patients below 1 year and over 65 years, respectively, both far superior to those of cumulated causes of encephalitis in the United States in these age categories. The case-fatality rate of CHIKV-associated encephalitis was 16.6% and the proportion of children discharged with persistent disabilities estimated between 30% and 45%. Beyond the neonatal period, the clinical presentation and outcomes were less severe in infants than in adults.

Conclusions: In the context of a large outbreak, CHIKV is a significant cause of CNS disease. As with other etiologies, CHIKV-associated encephalitis case distribution by age follows a U-shaped parabolic curve. *Neurology*® 2016;86:94–102

GLOSSARY

ADEM = acute disseminated encephalomyelitis; **CHIKV** = Chikungunya virus; **CFR** = case-fatality rate; **CIR** = cumulative incidence rate; **DQ** = development quotient; **DWI** = diffusion-weighted imaging; **ECSA** = East Central South African; **IEC** = International Encephalitis Consortium; **IgM** = immunoglobulin M; **LP** = lumbar puncture; **NECACD** = nonencephalitic Chikungunya virus–associated CNS disease; **WNV** = West Nile virus.

Chikungunya virus (CHIKV) is a re-emerging alphavirus.[1] Alphaviruses are divided into arthritogenic viruses (old world) and encephalitogenic viruses (new world) including equine encephalitis viruses.[2]

Until its reemergence in the Indian Ocean in 2004 and the worldwide spread that followed, beyond the burden of arthritis, known for lasting weeks to years,[3] Chikungunya was considered as a nonfatal disease with spontaneous resolution, not causing lifelong disabilities, even though rare cases of CNS disease had been reported.[4,5]

The major outbreaks that have occurred since 2005 in the Indian Ocean islands were attributable to a new Indian Ocean lineage that evolved from the East Central South African (ECSA) lineage and selected the mutation E1-A226V, which favors transmission by *Aedes albopictus*.[6,7]

Supplemental data at Neurology.org

RAPID RISK ASSESSMENT

Zika virus infection outbreak, French Polynesia

14 February 2014

Main conclusions and options for mitigation

- This is the first documented outbreak of Zika virus (ZIKAV) infection in French Polynesia and New Caledonia.
- During the course of the ZIKAV outbreak, neurological and auto-immune complications have been reported in a context of concurrent circulation of two dengue serotypes (dengue 1 and 3) since February 2013.
- Vigilance must be enhanced towards imported cases of ZIKAV infection in the EU Member States and EU overseas countries and territories and outermost regions, in particular where effective vectors are present; early detection of cases is essential to reduce the risk of autochthonous transmission.
- Clinicians and travel medicine clinics should be aware of the situation in the Pacific islands and include ZIKAV infection in their differential diagnosis. An isolated positive result for dengue IgM antibodies among travellers returning from areas affected by Zika should prompt a possible investigation for another flavivirus aetiology.
- The potential neurological and auto-immune complications might require specific healthcare capabilities and treatment (ICU) which need to be taken into account in an insular context facing a large-scale Zika outbreak.
- As an emerging pathogen, the laboratory capacity to confirm suspected Zika cases should be strengthened in the region as well as in Europe to differentiate ZIKAV infections from other arboviral dengue-like illnesses. Regional reference laboratories could provide support to confirm suspect cases.
- As many unanswered questions remain, further epidemiological and laboratory investigations could be conducted to establish:
  - evidence about eco-epidemiology of ZIKAV (viral strain genetic characteristics, transmission cycle(s), vectors and reservoir hosts) to assess its implications for public health;
  - the relationship between neurological and auto-immune complications and ZIKAV infection, notably with other aetiologies, previous infection with other infectious agents and human risk factors;
  - the performance of Zika serology and its cross-reactivity with other flaviviral infections;
  - the possibility of using urine samples for detection of the ZIKAV genome as well as other flaviviral infections.
- Blood safety authorities need to be vigilant regarding the epidemiological situation and should consider deferral of donors with travel history in line with measures defined for West Nile virus. Blood safety procedures are already in place in the Pacific region in the context of the ongoing outbreak of dengue and chikungunya and have included ZIKAV nucleic acid testing since early January 2014 in French Polynesia.

Suggested citation: European Centre for Disease Prevention and Control. Rapid risk assessment: Zika virus infection outbreak, French Polynesia. 14 February 2014. Stockholm: ECDC; 2014.

Stockholm, February 2014

Pan American Health Organization
World Health Organization
Americas

Epidemiological Alert

Zika virus infection

7 May 2015

The Pan American Health Organization (PAHO) / World Health Organization (WHO) recommends its Member States establish and maintain the capacity for Zika virus infection detection, clinical management and an effective public communication strategy to reduce the presence of the mosquito that transmits this disease, particularly in areas where the vector is present.

Situation summary

The Zika virus was first isolated in 1947 in Zika Forest (Uganda), in a Rhesus monkey during a study of the transmission of wild yellow fever. It was first isolated in humans in 1952 (Uganda, Tanzania).[1,2] In 1968 the virus was detected in human samples in Nigeria. [3,4]

In 2007 the first major outbreak of Zika virus fever occurred on the island of Yap (Micronesia) where 185 suspected cases were reported, of which 49 were confirmed and 59 were considered probable. The outbreak lasted 13 weeks (April to July). The probable vector was identified as being *Aedes hensilli*, however the presence of the virus in the mosquito could not be determined.

Subsequently an outbreak in French Polynesia, which began at the end of October 2013. Around 10,000 cases were registered, of which approximately 70 were severe cases, including neurological (Guillain Barré syndrome, meningoencephalitis) or autoimmune (thrombocytopenic purpura, leukopenia) complications. An investigation was carried out to determine the association between these complications and primary or secondary co-infection with other flaviviruses, especially dengue virus[5,6] The vectors responsible for transmission were *Aedes aegypti* and *Aedes polynesiensis*. In 2014, cases were also recorded in New Caledonia and in the Cook Islands.

To date, no death attributed to Zika virus infection has been reported in any of the outbreaks.

Zika virus infection

This is a disease caused by the Zika virus (ZIKAV), an arbovirus the flavivirus genus (family Flaviviridae), very close phylogenetically to viruses such as dengue, yellow fever, Japanese encephalitis, or West Nile virus.

The Zika virus is transmitted by mosquitoes of the genus Aedes, in urban areas (*A. aegypti*) as well as in the wild.

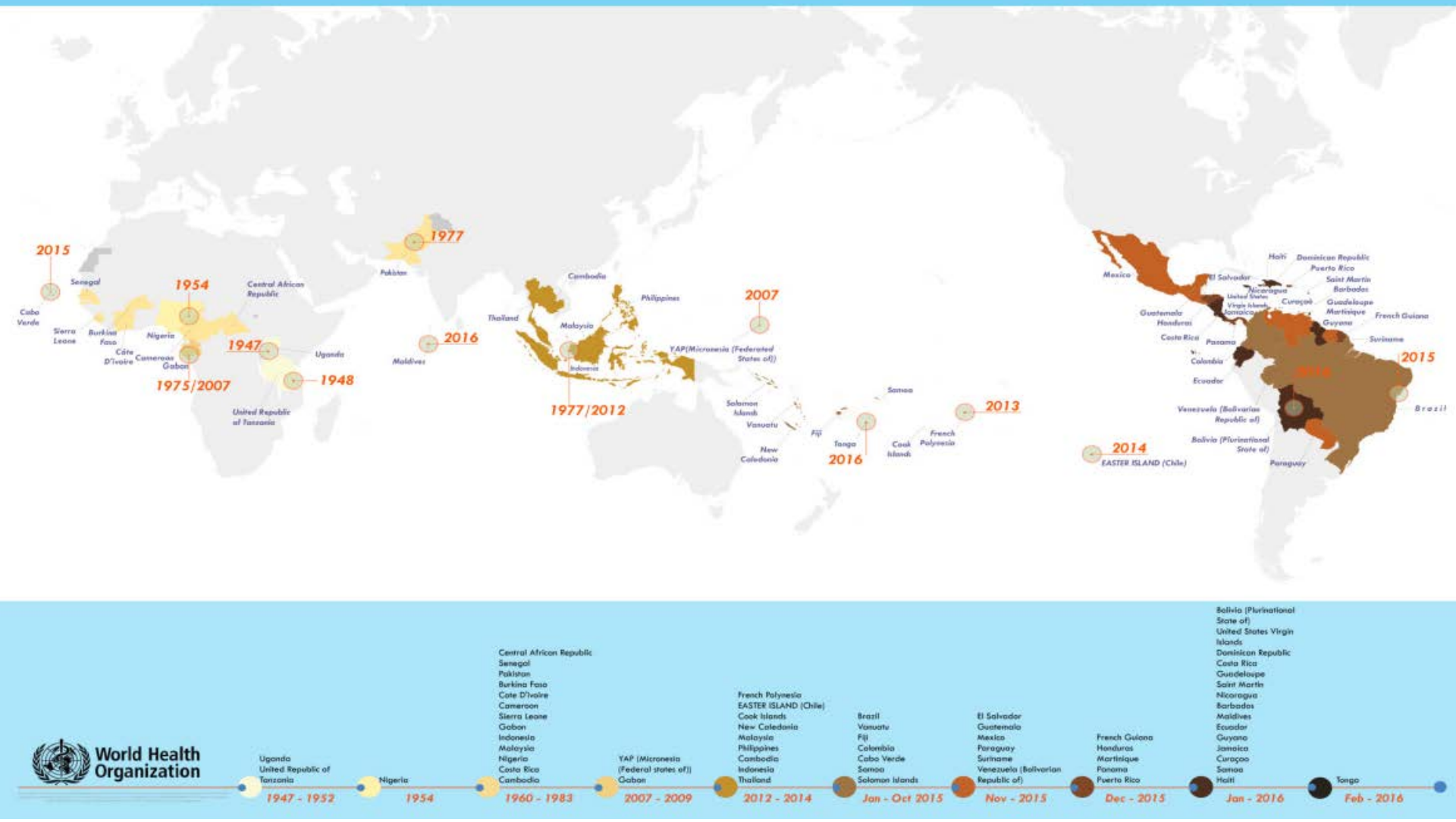
After an infected mosquito bite, the disease symptoms usually appear following an incubation period of three to twelve days.

The infection may present itself as asymptomatic or with a moderate clinical picture; no fatal cases have been detected to date.

In symptomatic cases, with **moderate disease**, the symptoms appear acutely and include fever, non-purulent conjunctivitis, headache, myalgia and arthralgia, asthenia, maculopapular rash, edema in the lower limbs and less frequently, retro-orbital pain, anorexia, vomiting, diarrhea, or abdominal pain. The symptoms last for 4-7 days and are self-limiting. Complications (neurological, autoimmune) are rare and have only been identified in the epidemic in French Polynesia.

World Health Organization

Countries and territories showing historical time-line of Zika virus spread (1947 - 2016)



Pan American Health Organization

World Health Organization
REGIONAL OFFICE FOR THE Americas

Countries and territories with autochthonous transmission in the Americas reported in 2015-2016

Epidemiological Week (EW) 17 of 2015 to EW 6 of 2016

UNIVERSITY OF MINNESOTA

CIDRAP Center for Infectious Disease Research and Policy

CDC notes Zika-microcephaly link, ponders travel alert

Filed Under: Chikungunya; Dengue; Meningitis; Zika

Jim Wappes | Editorial Director | CIDRAP News | Jan 14, 2016

The US Centers for Disease Control and Prevention (CDC) yesterday presented perhaps its most compelling evidence for a link between Zika virus infection and microcephaly, a condition of small heads and brains that has risen 10-fold in Brazil as Zika infections there have spiked, according to media reports.

CDC / James Gathany

The CDC is also considering warning pregnant women not to travel to Zika-affected countries, officials said.

And in related news, two National Institutes of Health (NIH) experts wrote in the *New England Journal of Medicine* (*NEJM*) yesterday that the disease presents yet another facet of the growing threat of mosquito-borne diseases to North America.

Zika detection in infants, moms

Lyle Peterson, MD, MPH, the director of the CDC's Division of Vector-Borne Diseases, said yesterday that CDC lab tests have confirmed Zika virus in the brains of two Brazilian newborns who died and in the placentas of two women who miscarried, the Associated Press (AP) reported today. All four cases involved microcephaly.

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

CDC adds countries to interim travel guidance related to Zika virus

Media Statement

For Immediate Release: Friday, January 22, 2016

Contact: Media Relations,
(404) 639-3286

CDC is working with other public health officials to monitor for ongoing Zika virus transmission. Today, CDC added the following destinations to the Zika virus travel alerts: Barbados, Bolivia, Ecuador, Guadeloupe, Saint Martin, Guyana, Cape Verde, and Samoa. On January 15, CDC issued a travel alert (Level 2-Practice Enhanced Precautions) for people traveling to regions and certain countries where Zika virus transmission is ongoing: the Commonwealth of Puerto Rico, a U.S. territory; Brazil; Colombia; El Salvador; French Guiana; Guatemala; Haiti; Honduras; Martinique; Mexico; Panama; Paraguay; Suriname; and Venezuela. Specific areas where Zika virus transmission is ongoing are often difficult to determine and are likely to continue to change over time.

As more information becomes available, CDC travel alerts will be updated. Travelers to areas where cases of Zika virus infection have been recently confirmed are at risk of being infected with the Zika virus. Travelers to these areas may also be at risk of being infected with dengue or chikungunya viruses. Mosquitoes that spread Zika, chikungunya, and dengue are aggressive daytime biters, prefer to bite people, and live indoors and outdoors near people. There is no vaccine or medicine available for Zika virus. The best way to avoid Zika virus infection is to prevent mosquito bites.

Some travelers to areas with ongoing Zika virus transmission will become infected while traveling but will not become sick until they return home. Symptoms include fever, rash, joint pain, and red eyes. Other commonly reported symptoms include muscle pain, headache, and pain behind the eyes. The illness is usually mild with symptoms lasting from several days to a week. Severe disease requiring hospitalization is uncommon and case fatality is low. Travelers to these areas should monitor for symptoms or illness upon return. If they become ill, they should tell their healthcare professional where they have traveled and when.

REUTERS

Business | Wed Feb 24, 2016 6:16am EST

Related: U.S., AEROSPACE & DEFENSE

Exclusive: U.S. airfares to Puerto Rico slide; debt crisis, Zika weigh

NEW YORK/SAN JUAN | BY JEFFREY DASTIN AND NICK BROWN

U.S. airlines have slashed leisure fares to Puerto Rico in recent months to lure travelers to the debt-strapped island, hit by economic turmoil and lately the arrival of the mosquito-borne Zika virus.

The lowest fares to San Juan, Puerto Rico, have fallen 22 percent on average from a year ago, according to an early February analysis of six of the busiest U.S. domestic routes to the island's capital by Harrell Associates, shared exclusively with Reuters.

The drop outpaced an 18 percent fall nationwide in the high-restriction fares during that time, according to the travel consultancy's analysis.

"It's a combination of slack demand in both directions," said Robert Mann, an airline industry consultant.

"Leisure travelers going to Puerto Rico are concerned both about the state of the economy and the extent to which leisure resort facilities are going to be properly maintained," he said. "If you're a Puerto Rican resident, the buying power just isn't there."

With a stagnating economy and an exodus of its population to the mainland, the U.S. territory has defaulted on part of its $70 billion in debt and asked its creditors to renegotiate the borrowing terms to slash its debt burden.

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 65
February 10, 2016

Notes from the Field

Evidence of Zika Virus Infection in Brain and Placental Tissues from Two Congenitally Infected Newborns and Two Fetal Losses — Brazil, 2015

Roosecelis Brasil Martines, MD, PhD[1]; Julu Bhatnagar, PhD[1]; M. Kelly Keating, DVM[1]; Luciana Silva-Flannery, PhD[1]; Atis Muehlenbachs, MD, PhD[1]; Joy Gary, DVM, PhD[1]; Cynthia Goldsmith, MS[1]; Gillian Hale, MD[1]; Jana Ritter, DVM[1]; Dominique Rollin, MD[1]; Wun-Ju Shieh, MD, PhD[1]; Kleber G. Luz, MD, PhD[2]; Ana Maria de Oliveira Ramos, MD, PhD[3]; Helaine Pompeia Freire Davi, MD, PhD[4]; Wanderson Kleber de Oliveria, MD[5]; Robert Lanciotti, PhD[6]; Amy Lambert, PhD[6]; Sherif Zaki, MD, PhD[1]

Zika virus is a mosquito-borne flavivirus that is related to dengue virus and transmitted primarily by *Aedes aegypti* mosquitoes, with humans acting as the principal amplifying host during outbreaks. Zika virus was first reported in Brazil in May 2015 (*1*). By February 9, 2016, local transmission of infection had been reported in 26 countries or territories in the Americas.* Infection is usually asymptomatic, and, when symptoms are present, typically results in mild and self-limited illness with symptoms including fever, rash, arthralgia, and conjunctivitis. However, a surge in the number of children born with microcephaly was noted in regions of Brazil with a high prevalence of suspected Zika virus disease cases. More than 4,700 suspected cases of microcephaly were reported from mid-2015 through January 2016, although additional investigations might eventually result in a revised lower number (*2*). In response, the Brazil Ministry of Health established a task force to further investigate possible connections between the virus and brain anomalies in infants (*3*).

Since November 2015, CDC has been developing assays for Zika virus testing in formalin-fixed, paraffin-embedded (FFPE) tissue samples. In December 2015, FFPE tissues samples from two newborns (born at 36 and 38 weeks gestation) with microcephaly who died within 20 hours of birth and two miscarriages (fetal losses at 11 and 13 weeks) were submitted to CDC, from the state of Rio Grande do Norte in Brazil, for histopathologic evaluation and laboratory testing for suspected Zika virus infection. All four mothers had clinical signs of Zika virus infection, including fever and rash, during the first trimester of pregnancy, but did not have clinical signs of active infection at the time of delivery or miscarriage. The mothers were not tested for antibodies to Zika virus. Samples included brain and other autopsy tissues from the two newborns, a placenta from one of the newborns, and products of conception from the two miscarriages.

FFPE tissues were tested by Zika virus reverse transcription-polymerase chain reaction (RT-PCR) targeting the nonstructural protein 5 and envelope genes using general methods for RT-PCR (*4*), and by immunohistochemistry using a mouse polyclonal anti-Zika virus antibody, using methods previously described (*5*). Specific specimens from all four cases were positive by RT-PCR, and sequence analysis provided further evidence of Zika virus infection, revealing highest identities with Zika virus strains isolated from Brazil during 2015. In the newborns, only brain tissue was positive by RT-PCR assays. Specimens from two of the four cases were positive by immunohistochemistry: viral antigen was noted in mononuclear cells (presumed to be glial cells and neurons within the brain) of one newborn, and within the chorionic villi from one of the miscarriages. Testing for dengue virus was negative by RT-PCR in specimens from all cases.

For both newborns, significant histopathologic changes were limited to the brain, and included parenchymal calcification, microglial nodules, gliosis, and cell degeneration and necrosis. Other autopsy tissues and placenta had no significant findings. Tests for toxoplasmosis, rubella, cytomegalovirus, herpes simplex, and HIV were negative in the two mothers who experienced miscarriages. Placental tissue from one miscarriage showed heterogeneous chorionic villi with calcification, fibrosis, perivillous fibrin deposition, and patchy intervillositis and focal villitis, while tissue from the other miscarriage had sparsely sampled normal-appearing chorionic villi.

* Updated information about local transmission of Zika virus is available online (http://www.cdc.gov/zika/geo/index.html).

BRIEF REPORT

Zika Virus Associated with Microcephaly

Jernej Mlakar, M.D., Misa Korva, Ph.D., Nataša Tul, M.D., Ph.D., Mara Popović, M.D., Ph.D., Mateja Poljšak-Prijatelj, Ph.D., Jerica Mraz, M.Sc., Marko Kolenc, M.Sc., Katarina Resman Rus, M.Sc., Tina Vesnaver Vipotnik, M.D., Vesna Fabjan Vodušek, M.D., Alenka Vizjak, Ph.D., Jože Pižem, M.D., Ph.D., Miroslav Petrovec, M.D., Ph.D., and Tatjana Avšič Županc, Ph.D.

SUMMARY

A widespread epidemic of Zika virus (ZIKV) infection was reported in 2015 in South and Central America and the Caribbean. A major concern associated with this infection is the apparent increased incidence of microcephaly in fetuses born to mothers infected with ZIKV. In this report, we describe the case of an expectant mother who had a febrile illness with rash at the end of the first trimester of pregnancy while she was living in Brazil. Ultrasonography performed at 29 weeks of gestation revealed microcephaly with calcifications in the fetal brain and placenta. After the mother requested termination of the pregnancy, a fetal autopsy was performed. Micrencephaly (an abnormally small brain) was observed, with almost complete agyria, hydrocephalus, and multifocal dystrophic calcifications in the cortex and subcortical white matter, with associated cortical displacement and mild focal inflammation. ZIKV was found in the fetal brain tissue on reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assay, with consistent findings on electron microscopy. The complete genome of ZIKV was recovered from the fetal brain.

ZIKV, AN EMERGING MOSQUITO-BORNE FLAVIVIRUS, WAS INITIALLY ISOlated from a rhesus monkey in the Zika forest in Uganda in 1947.[1] It is transmitted by various species of aedes mosquitoes. After the first human ZIKV infection, sporadic cases were reported in Southeast Asia and sub-Saharan Africa.[2] ZIKV was responsible for the outbreak in Yap Island of Micronesia in 2007 and for major epidemics in French Polynesia, New Caledonia, the Cook Islands, and Easter Island in 2013 and 2014.[3,4] In 2015, there was a dramatic increase in reports of ZIKV infection in the Americas. Brazil is the most affected country, with preliminary estimates of 440,000 to 1.3 million cases of autochthonous ZIKV infection reported through December 2015.[5]

The classic clinical picture of ZIKV infection resembles that of dengue fever and chikungunya and is manifested by fever, headache, arthralgia, myalgia, and maculopapular rash, a complex of symptoms that hampers differential diagnosis. Although the disease is self-limiting, cases of neurologic manifestations and the Guillain–Barré syndrome were described in French Polynesia and in Brazil during ZIKV epidemics.[5,6] Recent reports from the Ministry of Health of Brazil suggest that cases of microcephaly have increased by a factor of approximately 20 among newborns in the northeast region of the country, which indicates a possible association between ZIKV infection in pregnancy and fetal malformations.[5]

We present a case of vertical transmission of ZIKV in a woman who was prob-

From the Institute of Pathology, Faculty of Medicine (J. Mlakar, M. Popović, J. Mraz, A.V., J.P.), and the Institute of Microbiology and Immunology, Faculty of Medicine (M. Korva, M.P.-P., M. Kolenc, K.R.R., M. Petrovec, T.A.Z.), University of Ljubljana, and the Department of Perinatology, Division of Gynecology and Obstetrics (N.T., V.F.V.), and the Institute of Radiology (T.V.V.), University Medical Center Ljubljana — all in Ljubljana, Slovenia. Address reprint requests to Dr. Avšič Županc at the Institute of Microbiology and Immunology, Faculty of Medicine, University of Ljubljana, Zaloška 4, Ljubljana 1000, Slovenia, or at tatjana.avsic@mf.uni-lj.si.

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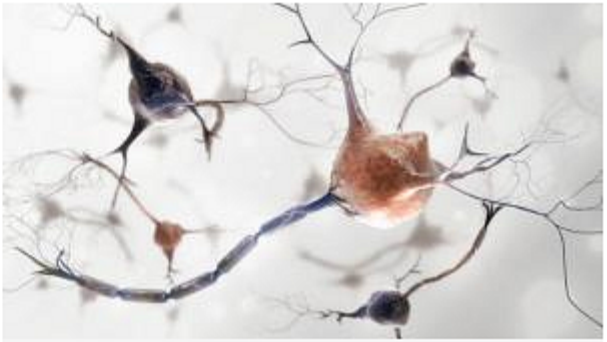
WHO reports more local Zika confirmations, GBS spike

Filed Under: Zika

Lisa Schnirring | News Editor | CIDRAP News | Jan 21, 2016

In Zika virus developments today, the World Health Organization (WHO) said El Salvador is investigating an unusual spike in Guillain-Barre syndrome (GBS) that may be linked its recent surge of infections and confirmed the first locally transmitted cases in two French Caribbean territories, St. Martin and Guadeloupe.

Also, Brazilian scientists reported Zika virus in placental tissue, shedding a little more light on the possible link between maternal infections and microcephaly—or smaller-than-normal heads—in babies.



muzon / iStock

Thought to be an autoimmune disorder that damages nerve cells, GBS causes muscle weakness and sometimes paralysis.

GBS reports hint at acute illness complications

Though the main threat surrounding the Zika virus epidemic has been a heart-wrenching rise in microcephaly cases, new questions are swirling about other complications in what is typically a fairly mild illness. Thought to be an autoimmune disorder that damages nerve cells, GBS causes muscle weakness and sometimes paralysis. Most people recover, but some have lingering nerve damage.

Spread of the pandemic Zika virus lineage is associated with NS1 codon usage adaptation in humans

Caio César de Melo Freire[1], Atila Iamarino[1], Daniel Ferreira de Lima Neto[1], Amadou Alpha Sall[2], and Paolo Marinho de Andrade Zanotto[1*]

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ABSTRACT

Zika virus (ZIKV) infections were more common in the zoonotic cycle until the end of the 20th century with few human cases in Africa and Southeastern Asia. Recently, the Asian lineage of ZIKV is spreading along human-to-human chains of transmission in the Pacific Islands and in South America. To better understand its recent urban expansion, we compared genetic differences among the lineages. Herein we show that the recent Asian lineage spread is associated with significant NS1 codon usage adaptation to human housekeeping genes, which could facilitate viral replication and increase viral titers. These findings were supported by a significant correlation with growth in Malthusian fitness. Furthermore, we predicted several epitopes in the NS1 protein that are shared between ZIKV and Dengue. Our results imply in a significant dependence of the recent human ZIKV spread on NS1 translational selection.

Keywords: Zika virus, emerging diseases, molecular evolution, codon usage adaptation, NS1

telesur

Zika Virus: Despite Lack of Evidence, El Salvador Warns Against Pregnancy for 2 Years

A man carries his son as health workers fumigates the Altos del Cerro neighbourhood to combat the Zika virus in Soyapango, El Salvador Jan. 21, 2016. | Photo: Reuters

Published 22 January 2016

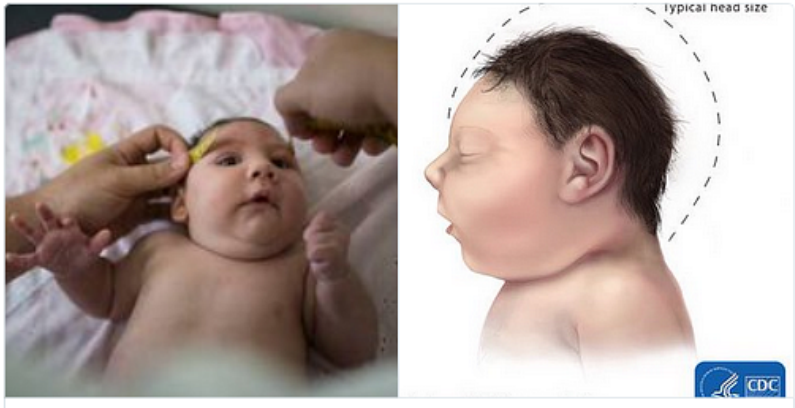
Although there is still no evidence that the Zika virus is responsible for microcephaly in babies, health officials in the Central American nation have warned women against falling pregnant.

Health officials in El Salvador have advised women to delay pregnancy until 2018 amid fears that the spreading Zika virus causes birth defects in newborns.

The mosquito-borne virus is suspected to cause a rare brain defect in babies, known as microcephaly, which causes abnormally small heads, leading to severe developmental issues, brain damage and sometimes death.

Speaking Thursday, El Salvador's vice minister for public health, Eduardo Espinoza, warned women from the central American country to avoid having babies for the next two years to avoid passing on potential negative effects of the Zika virus.

"We'd like to suggest to all the women of fertile age that they take steps to plan their pregnancies, and avoid getting pregnant between this year and next," he said.



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CDC advises on Zika-related sexual spread, pregnancy care

Filed Under: Guillain-Barre Syndrome; Zika

Lisa Schnirring | News Editor | CIDRAP News | Feb 05, 2016

EmiliaU/ iStock

Just days after Dallas officials announced a sexually transmitted Zika virus case, the Centers for Disease Control and Prevention (CDC) today released interim guidance on preventing such cases and at the same time updated its guidance for health providers caring for pregnant women who may have been exposed.

Both sets of advice focus tightly on the threat to pregnant women and their babies, given the suspected link between Zika virus and microcephaly, which the CDC said is becoming stronger. The CDC published both documents as early reports on its *Morbidity and Mortality Weekly Report (MMWR)* portal.

At a media briefing today, CDC Director Tom Frieden, MD, MPH, said mosquito bites are still the primary way Zika virus transmits, but he also fielded questions about two more routes revealed by Brazilian scientists today: saliva and urine. He said so far the CDC has no data on the virus in saliva and urine, so the risk of transmission through those routes isn't clear.

"We're quite literally discovering more about it each and every day," he said, also acknowledging reports this week of blood-transfusion transmission. "We take all reports seriously, but back to the bottom line: This is a mosquito-borne disease."

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CDC probes 14 more Zika cases possibly spread via sex

Filed Under: Zika

Lisa Schnirring | News Editor | CIDRAP News | Feb 23, 2016

In a sign that sexual transmission of Zika virus may occur more often than currently thought, the US Centers for Disease Control and Prevention (CDC) said today it is investigating 14 new reports of possible transmission through that route.

Manuel Faba Ortega / iStock

The development underscores earlier advice that people returning from outbreak areas take strict safe-sex precautions, the CDC said.

Zika confirmed in 2 cases

The CDC said that several of the possible sexual transmission cases it and state health department partners are investigating involve pregnant women, the group at highest risk in the outbreak.

Investigations into the 14 possible cases are at various stages. In two instances, Zika infections have been confirmed in women whose only known exposure was sexual contact with a sick man who had recently traveled to an area where the virus is circulating. Tests results on their male partners are pending.

Prevention of potential sexual transmission of Zika virus

Interim guidance

18 February 2016

WHO/ZIKV/MOC/16.1

World Health Organization

1. Introduction

1.1 Background

This guidance has been developed to provide advice on the prevention of potential sexual transmission of Zika virus. The primary transmission route of Zika virus is via the *Aedes* mosquito. However, sexual transmission of Zika virus may also be possible, with limited evidence recorded in a few cases. This is of concern due to an association between Zika virus infection and potential complications, including microcephaly and Guillain-Barré syndrome.

The current evidence base on Zika virus remains extremely limited. This guidance will be reviewed and the recommendations updated as new evidence emerges.

1.2 Target audience

This document is intended to inform the general public, and to be used by health care workers and policy makers to provide guidance on appropriate sexual practices in the context of Zika virus.

2. Potential sexual transmission of Zika virus

2.1 Current evidence

hematospermia during a Zika virus outbreak in French Polynesia in December 2013 [3]. He had previously experienced symptoms of Zika virus infection twice: two weeks and ten weeks before presentation with hematospermia. Zika virus was isolated from semen samples taken at presentation and also three days later. The observation of Zika virus in semen supports the possibility that the virus could be sexually transmitted.

2.2 Interim recommendations

Based on precautionary principles, WHO recommends that:

1. All patients (male and female) with Zika virus infection and their sexual partners (particularly pregnant women) should receive information about the potential risks of sexual transmission of Zika virus, contraceptive measures and safer sexual practices[1], and should be provided with condoms when feasible. Women who have had unprotected sex and do not wish to become pregnant because of concern with infection with Zika virus should also have ready access to emergency contraceptive services and counselling [4].
2. Sexual partners of pregnant women, living in or returning from areas where local transmission of Zika virus is known to occur, should use safer sexual

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Pope signals contraceptives may be OK in light of Zika

Filed Under: Zika

Lisa Schnirring | News Editor | CIDRAP News | Feb 18, 2016

While on his way home from Mexico and Cuba, Pope Francis today hinted that women in Zika-affected countries could use artificial contraception to avoid pregnancy even though Catholic Church teaching generally forbids it, and his comments coincided with guidance from the World Health Organization (WHO) on preventing sexual transmission of the disease.

Marko Vombergar / Aleteia / Flickr cc

Pope Francis during his recent visit to Mexico.

Contraception considered, but not abortion

The world's largest share of Catholics live in Latin America and the Caribbean, with Brazil as the nation with the largest number, according to a 2013 demographic analysis by the Pew Research Center. Countries where local transmission is occurring and health organizations have urged women to consider postponing pregnancy until the Zika-linked microcephaly threat virus fades, a difficult prospect in areas where contraceptives aren't readily available.

In response to a question about whether abortion or birth control would be considered a "lesser evil" in the

World Health Organization

Information for travellers visiting Zika affected countries

Updated
12 February 2016

Travellers should stay informed about Zika virus and other mosquito-borne diseases and consult their local health or travel authorities if they are concerned.

Based on available evidence, WHO is not recommending any travel or trade restrictions related to Zika virus disease. Countries reporting sporadic Zika infections in travellers arriving from affected countries pose little, if any, risk of onward transmission.

As a precautionary measure, some national governments may make public health and travel recommendations to their own populations, based on their assessment of the available evidence and local risk factors.

Precautionary measures for pregnant women and women considering pregnancy

Based on the latest evidence that Zika virus infection during pregnancy may be linked to microcephaly in newborns, WHO is issuing further precautionary travel advice to women who are pregnant and their sexual partners.

Women who are pregnant should discuss their travel plans with their health care provider and consider delaying travel to any area where locally acquired Zika infection is occurring.

Zika virus is spread by mosquitoes, and not by person-to-person contact, though a small number of cases of sexual transmission have been documented.

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WHO stiffens Zika travel advice for women, airs countermeasure efforts

Filed Under: Zika

Lisa Schnirring | News Editor | CIDRAP News | Feb 12, 2016

In the wake of mounting evidence connecting maternal Zika virus infections to microcephaly in babies, the World Health Organization (WHO) today strengthened its travel advice for pregnant women, and also offered new projections about the development of tools such as vaccines to battle the outbreak.

In other developments, the WHO also provided new details about recently reported Zika-related findings in several countries, including Guillain-Barre syndrome cases in South America, a sexual transmission case in Texas, and a microcephaly case in Hawaii.

quintanilla / iStock

Maintaining a safe and adequate blood supply during Zika virus outbreaks

Interim guidance

February 2016

WHO/ZIKV/HS/16.1

World Health Organization

1. Introduction

1.1 Background

These guidelines have been developed in recognition that infection with Zika virus may present a risk to blood safety, and in consideration of the declaration on 1 February 2016 by the WHO Director-General of a Public Health Emergency of International Concern with regard to clusters of microcephaly and other neurological disorders, potentially associated with Zika virus. Currently there is limited knowledge of Zika virus biology and lack of definitive evidence of a link between infection and potential complications. These guidelines will be regularly reviewed and updated as new information becomes available.

Zika virus is a mosquito-borne flavivirus, related to dengue. It is transmitted to humans through the bite of an infected mosquito from the *Aedes* genus. This mosquito also transmits dengue, chikungunya and yellow fever viruses [23].

Zika virus infection is followed by an incubation period prior to the development of clinical symptoms, which occur in only a minority of infected individuals. Asymptomatic infections are common, as described for other flaviviral infections such as dengue and West Nile other autoimmune neurological complications was suspected during a 2013–2014 outbreak in French Polynesia and remains under investigation [6, 16].

During the Zika virus outbreak in French Polynesia between November 2013 and February 2014, a total of 1,505 healthy blood donors were tested by nucleic acid amplification technology (NAT) -based assays, with 42 (2.8 %) confirmed positive for Zika virus RNA. Blood donors positive for Zika virus RNA were contacted retrospectively to investigate the occurrence of 'Zika fever-like syndrome' (rash and/or conjunctivitis and/or arthralgia) after their blood donation. Of the 42 donors that tested positive, 11 declared that they had a Zika fever-like syndrome from 3–10 days after they gave blood. No transmission of Zika virus through transfusion was documented in this study [3, 13]. However, transmission of related flaviviruses (dengue and West Nile viruses) by blood transfusion has been documented [2, 18, 22]. Recently two probable cases of Zika virus transmission by blood transfusion have been reported from Campinas, Brazil [19].

1.2 Target audience

This guidance is intended for use by national health

U.S. Department of Health and Human Services

U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

FDA News Release

FDA issues recommendations to reduce the risk for Zika virus blood transmission in the United States

As a safety measure against the emerging Zika virus outbreak, today the U.S. Food and Drug Administration issued a new guidance recommending the deferral of individuals from donating blood if they have been to areas with active Zika virus transmission, potentially have been exposed to the virus, or have had a confirmed Zika virus infection.

"The FDA has critical responsibilities in outbreak situations and has been working rapidly to take important steps to respond to the emerging Zika virus outbreak," said Luciana Borio, M.D., the FDA's acting chief scientist. "We are issuing this guidance for immediate implementation in order to better protect the U.S. blood supply."

While there have been no reports to date of Zika virus entering the U.S. blood supply, the risk of blood transmission is considered likely based on the most current scientific evidence of how Zika virus and similar viruses (flaviviruses) are spread and recent reports of transfusion-associated infection outside of the U.S. Furthermore, about 4 out of 5 of those infected with Zika virus do not become symptomatic. For these reasons, the FDA is recommending that blood establishments defer blood donations from individuals in accordance with the new guidance.

In areas without active Zika virus transmission, the FDA recommends that donors at risk for Zika virus infection be deferred for four weeks. Individuals considered to be at risk include: those who have had symptoms suggestive of Zika virus infection during the past four weeks, those who have had sexual contact with a person who has traveled to, or resided in, an area with active Zika virus transmission during the prior three months, and those who have traveled to areas with active transmission of Zika virus during the past four weeks.

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WHO unveils Zika game plan, mosquito-control assessment

Filed Under: Dengue; Zika

Lisa Schnirring | News Editor | CIDRAP News | Feb 16, 2016

The World Health Organization (WHO) today released the details of a joint strategy to battle Zika virus, which will cost $56 million to implement, and weighed in on mosquito control, a complex challenge that might get a boost from new techniques.

The WHO spelled out the strategy in a 32-page report, with the main steps through June focusing on coordinating experts and resources to help countries with surveillance for the virus and disorders that may be linked to it, mosquito control, risk communication, guidance, medical care, and countermeasure research and development.

Dean Calma-IAEA/ Flickr cc

Release of sterilized male insects has been useful in agriculture pest control settings.

Plan outlines steps for next 5 months

In a statement, the WHO said that of the $56 million for implementation, $25 million would go toward response actions based out of the regional office for the Americas and $31 million is earmarked to support the work of its 23 key partners. The agency added that it would draw from its new emergency contingency fund—established in the wake of West Africa's Ebola outbreak—to pay for initial operations.

STAT | Reporting from the frontiers of health and medicine

After the Ebola crisis, can the WHO rise to the challenge of Zika?

By HELEN BRANSWELL *@HelenBranswell*

FEBRUARY 24, 2016

The fast-spreading Zika virus outbreak has presented much of the world with a public health crisis. It may also have presented the World Health Organization with a shot at redemption.

The global health agency is still bruised from harsh criticism over its handling of two recent crises. Its response to the mild 2009 H1N1 flu pandemic was seen as an expensive overreaction in some quarters. Five years later, instead of overreacting, the WHO was faulted for not responding urgently enough to the West Africa Ebola outbreak.

For the WHO and its director-general, Dr. Margaret Chan, Zika could be a chance to get it right.

"She has to be a leader," said Lawrence Gostin, a global health law expert who has been critical of Chan. "Epidemics are health events, but they're also political events."

Read more: International panel calls for overhaul of WHO following Ebola crisis

REUTERS

Life | Mon Feb 8, 2016 12:11pm EST

Related: HEALTH

Race to fast-track Zika trials as 12 groups seek vaccine

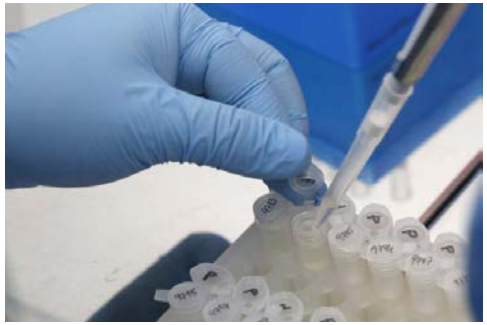
LONDON | BY BEN HIRSCHLER

At least 12 groups are now working to develop a Zika vaccine and health authorities said on Monday they were working to ensure development proceeded as rapidly as possible.

The World Health Organization said it was important to establish speedy regulatory pathways, although all the vaccines remained in early-stage development and licensed products would take "a few years" to reach the market.

With no approved Zika vaccines or medicines and none even undergoing clinical studies, scientists and drugmakers are on the starting-block in fighting the mosquito-borne disease suspected of causing a spike in birth defects in Brazil.

However, Zika is similar to dengue, yellow fever and West Nile virus, for which vaccines exist or are being developed, and the hope is to try similar approaches against the latest hazard.



The London-based European Medicines Agency (EMA) said it had established an expert task force on Zika to advise companies working on vaccines and medicines, mirroring similar action during Ebola and pandemic flu outbreak in 2009.

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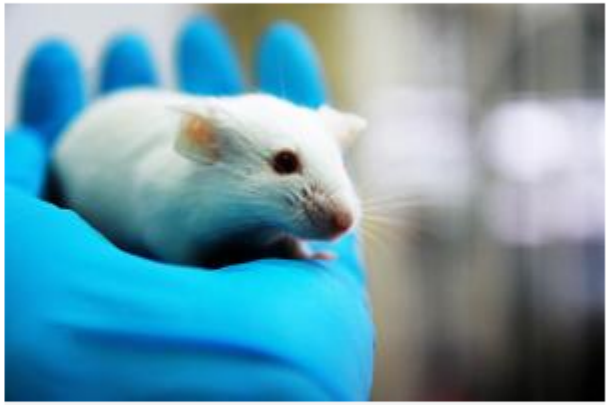
Inovio reports promising Zika vaccine results in mice

Filed Under: Zika

Lisa Schnirring | News Editor | CIDRAP News | Feb 17, 2016

Vaccine developer Inovio today reported promising results of a preclinical trial of its DNA-based Zika virus vaccine in mice.



Mycroyance / Flickr cc

The vaccine prompted a robust immune response in laboratory mice, clearing the way for the vaccine to be tested next in nonhuman primates, Inovio Pharmaceuticals, based in Plymouth Reading, Pa., said in a news release. The company is developing the vaccine with partners at GeneOne Life Sciences and academic institutions.

J. Joseph Kim, PhD, Inovio's president and CEO, said that, following nonhuman primate tests, it plans to start phase 1 human trials by the end of 2016.

Inovio's vaccine targets multiple Zika virus antigens with DNA constructs generated by its proprietary SynCon vaccine technology. The vaccine was given to mice with its electroporation delivery system. All vaccinated mice showed evidence of seroconversion as well as robust and broad T-cell response.

Brazil and US university reach deal on Zika vaccine

By JOSHUA GOODMAN Feb. 11, 2016 11:50 AM EST

BRASILIA, Brazil (AP) — Brazil has signed an agreement with the University of Texas Medical Branch to develop a vaccine against the Zika virus, adding the goal is for the vaccine to be ready for clinical testing within 12 months.

Health Minister Marcelo Castro said at a news conference that the government will invest $1.9 million in the research, which will be jointly conducted by the University of Texas Medical Branch in Galveston and the Evandro Chagas Institute in the Amazonian city of Belem.

He said the Health Ministry also has reached vaccine partnerships with the U.S. Centers for Disease Control and Prevention and is looking to work with pharmaceutical giant GlaxoSmithKline because of its role developing a vaccine against Ebola after a deadly outbreak in West Africa in 2014.

Brazil's Zika outbreak has become a public health crisis since researchers here linked the mosquito-borne virus to a surge in a rare birth defects compromising infants' brains. The connection has yet to be scientifically proven, but the CDC has pointed to strong evidence of a link between the two and called on pregnant women to avoid travel to 22 countries and territories in the Americas with active outbreaks.

Inovio Pharmaceutical's DNA Vaccine for Zika Virus Induces Robust Immune Responses in Preclinical Study

Biotech begins clinical manufacturing; expects to test Zika vaccine in humans in 2016

PLYMOUTH MEETING, Pa., Feb. 17, 2016 (GLOBE NEWSWIRE) -- Inovio Pharmaceuticals, Inc. (NASDAQ:INO) announced today that preclinical testing of its synthetic vaccine for the Zika virus induced robust and durable immune responses, demonstrating the potential for a SynCon® vaccine to prevent and treat infections from this harmful pathogen. Health authorities have observed neurological and autoimmune complications potentially associated with Zika virus, including microcephaly in newborns and Guillain-Barre syndrome. Inovio is developing its Zika vaccine with GeneOne Life Sciences (KSE:011000) and academic collaborators.

Dr. J. Joseph Kim, Inovio's President and CEO, said, "Using our SynCon® technology we rapidly generated a synthetic vaccine candidate that shows promise as a preventive and treatment. With robust antibody and killer T cell responses generated by our vaccine in mice, we will next test the vaccine in non-human primates and initiate clinical product manufacturing. We plan to initiate phase I human testing of our Zika vaccine before the end of 2016."

University of Minnesota

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Obama seeks $1.8 billion for Zika response; CDC ups emergency level

Filed Under: Zika

Lisa Schnirring | News Editor | CIDRAP News | Feb 08, 2016

The Obama administration announced today that it will ask Congress for $1.8 billion in emergency funding to help prepare for and respond to the Zika virus threat, as the US Centers for Disease Control and Prevention (CDC) stepped up its emergency response to its highest level.

Greg Knobloch / CDC

In a White House statement today the Obama administration said it has been aggressively working on Zika virus response since late 2015 and that it would make a formal request for the $1.8 billion in emergency funding shortly.

"As spring and summer approach, bringing with them larger and more active mosquito populations, we must be fully prepared to mitigate and quickly address local transmission within the continental U.S., particularly in the Southern United States," the statement said.

Proposed funding breakdown

The largest chunk of the funds—$1.48 billion—would go to the Department of Health and Human Services (HHS), and within it, the CDC. Funding is targeted, for example, to improving mosquito control efforts, improving surveillance, boosting lab capacity and infrastructure, establishing rapid response teams if clusters are detected in the United States, and monitoring for pregnancy and Guillain-Barre syndrome (GBS) risks.

STAT | Reporting from the frontiers of health and medicine

POLITICS

Abortion politics threatens to derail Zika funding in Congress

By SHEILA KAPLAN *@bySheilaKaplan*

FEBRUARY 10, 2016

WASHINGTON — Two Republican lawmakers leading a congressional hearing on the Zika virus Wednesday said they hope pregnant women who become infected will not have abortions to avoid giving birth to children with a birth defect.

By linking abortion politics to the Zika virus, Representatives Jeff Duncan of South Carolina and Christopher Smith of New Jersey raised a prospect that worries public health advocates: that President Barack Obama's request for $1.8 billion in emergency funds to fight the virus could get derailed by battles over whether the money could be used for abortions.

CDC Director Dr. Thomas Frieden assured Congress that Obama's Zika budget request doesn't include money for abortions.

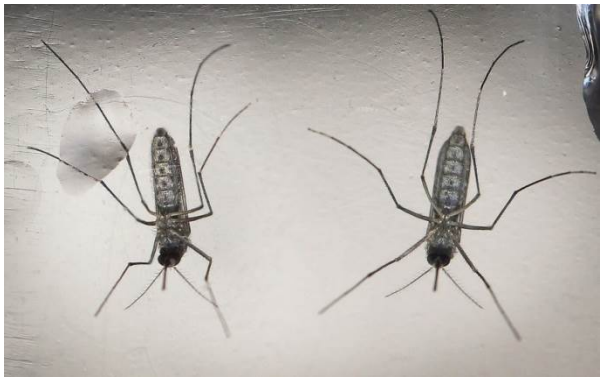
According to the Centers for Disease Control and Prevention, the mosquito-borne virus is strongly associated with microcephaly, a congenital abnormality in which babies are born with undersized heads, and sometimes, small brains and a range of of health and cognitive difficulties.

Testifying at the hearing, CDC Director Dr. Thomas Frieden said new research has provided more evidence of a link between Zika and microcephaly, but said it is still not definitive. The hearing was held by two subcommittees of the House Foreign Affairs Committee.

The Washington Post

Energy and Environment

A shocking one-third of Americans believe this Zika conspiracy theory



Fear and misinformation about the Zika virus still abound, according to a new survey just released by the University of Pennsylvania's Annenberg Public Policy Center. Most notably, the survey finds that more than a third of respondents incorrectly believe that genetically modified mosquitoes have caused the spread of the disease.

The survey, which was conducted this month by telephone, included 1,014 respondents in the U.S. It included eight questions probing participants' knowledge about the disease and its transmission and their level of concern about it. Some questions suggested a high level of knowledge about the disease on certain fronts. Ninety-one percent of respondents were aware that mosquitoes transmit the virus, for instance, and two-thirds of respondents said they were familiar with news reports about Zika.

On the other hand, fewer than half of the participants correctly identified Brazil as the country with the largest current Zika outbreak. Nearly 20 percent of respondents incorrectly believe that it's possible to contract the virus by sitting next to an infected person. In fact, Zika is primarily transmitted by infected mosquitoes, although it could also be contracted by blood or sexual contact with an infected person.

Zika

Resources

Jump to Selected Reading

Last updated Feb 23, 2016

Latest Cases & General Information

Zika virus (CDC landing page)
Zika situation report (WHO, Feb 19, 2016)
Zika virus (WHO fact sheet, January 2016)
Zika virus infections and complications called Public Health Emergency of International Concern (WHO, Feb 1, 2016)
Zika virus disease, frequently asked questions about Zika virus (WHO Emergencies Preparedness, Response)
Zika virus infection (PAHO/WHO landing page)

Maps

2016 Zika outbreak timeline map (HealthMap)
Pregnant? The CDC says these are the Zika-affected areas to avoid (STAT map, Feb 2, 2016)
Here are all the known cases of Zika virus in the world (*Popular Science* map)

The New York Times

SundayReview | OPINION

How Scared Should You Be About Zika?

By MICHAEL T. OSTERHOLM JAN. 29, 2016

Every time there is a major infectious disease outbreak that scares us — Ebola in West Africa in 2014, Middle East Respiratory Syndrome (MERS) on the Arabian Peninsula in 2012 and in South Korea in 2015, and now the Zika virus in South and Central America and the Caribbean — government leaders, the public and the news media demand explanations, guidance and predictions, and often express indignation that not enough was done to prevent it. Today everyone is asking about Zika: How did this crisis happen, and what do we need to do to make it go away? We immediately forget about the outbreak that came before it, and don't plan for the ones we know are on the horizon. Almost no one wants to talk about Ebola or MERS now, or what we have or haven't done to try to prevent an ugly recurrence.

When it comes to diseases, we have a very short attention span, and we tend to be reactive, rather than proactive. Instead of devoting ourselves to a comprehensive plan to combat microbial threats, we scramble to respond to the latest one in the headlines. There are lessons from previous infectious disease outbreaks that could and should have left us much better prepared than we are.

1. **Mosquito-borne diseases**
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   - HPV

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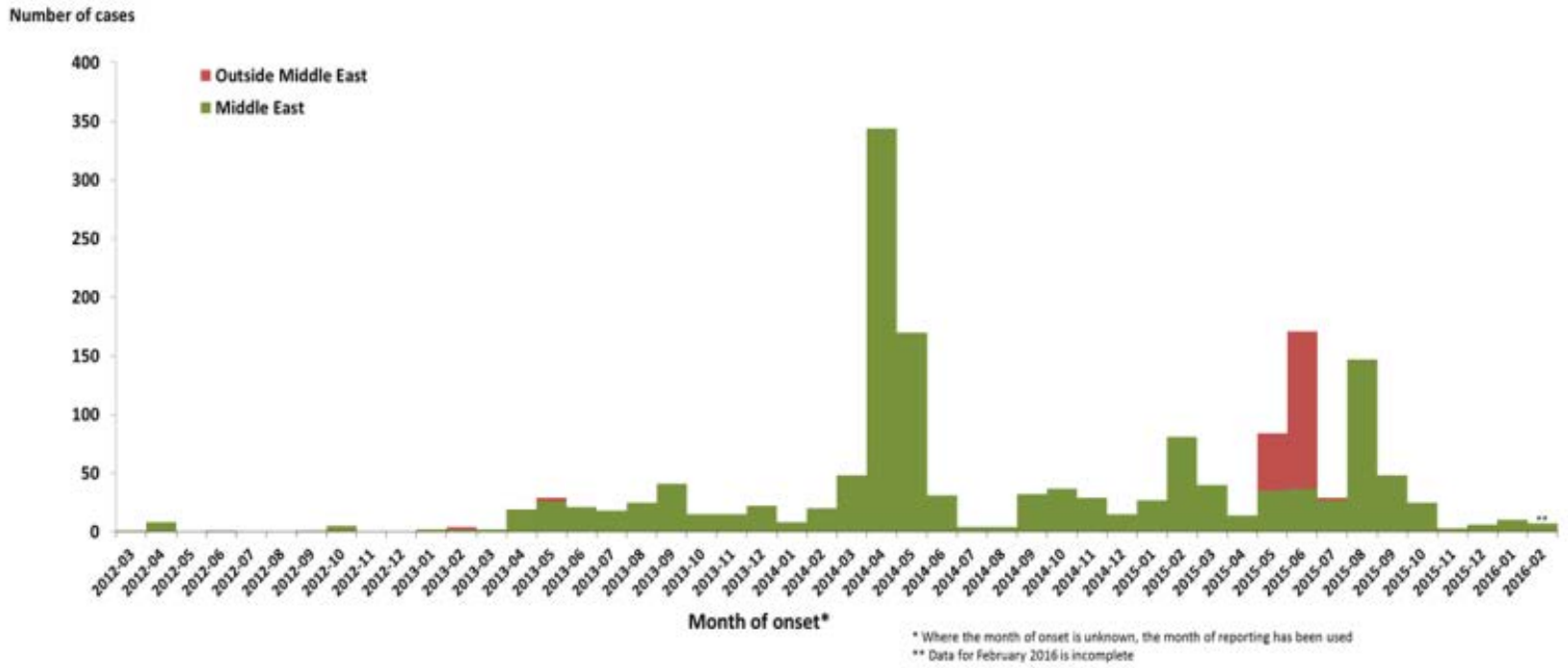
University of Minnesota

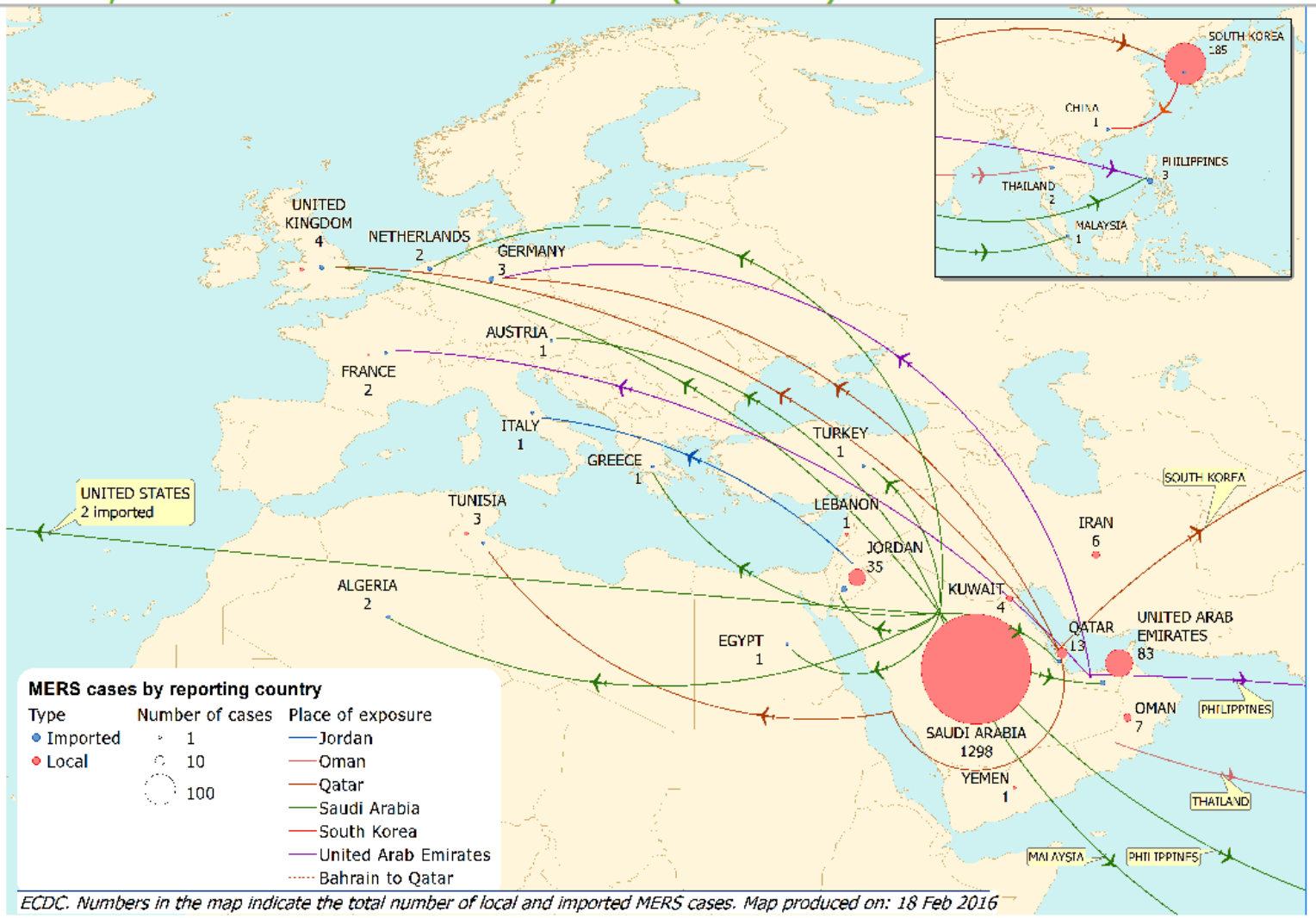
European Centre for Disease Prevention and Control

Cases of MERS-CoV by place of reporting, March 2012 – 18 February 2016 (n=1 663)



European Centre for Disease Prevention and Control

Distribution of confirmed cases of MERS-CoV by first available date, and probable place of infection, March 2012 – 18 February 2016 (n=1 663)



ECDC. Numbers in the map indicate the total number of local and imported MERS cases. Map produced on: 18 Feb 2016

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CIDRAP Center for Infectious Disease Research and Policy

Studies uncover MERS patterns in camels, vaccine potential

Filed Under: MERS-CoV

Lisa Schnirring | News Editor | CIDRAP News | Dec 17, 2015

A large Saudi Arabian camel sampling study published today revealed several new clues about MERS-CoV, building a strong case for the animals' role as the source of human infections, while a second study detailed early results for a camel vaccine.

Isabell Schulz / Flickr cc

Both studies were published today in *Science*. The camel MERS-CoV (Middle East respiratory syndrome coronavirus) sampling study was led by a team from Hong Kong and also included researchers from Saudi Arabia, Australia, and Egypt. The vaccine study was based at Erasmus Medical Center in the Netherlands and included scientists from Germany and Spain.

Samples yield MERS-CoV prevalence, lineages

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News Scan for Feb 16, 2016

Saudi Arabia reports two fatal MERS cases in Al-Kharj

Saudi Arabia today reported two fatal MERS-CoV cases in elderly men in the same city, Al-Kharj in the central part of the country, where two other cases were reported in recent weeks.

The two latest victims were 75 and 80 years old and were not healthcare workers, the Saudi Ministry of Health (MOH) said. The younger man had contact with camels, but the older one did not, and the source of his infection is under investigation.

With the two deaths, Saudi Arabia has had three fatal MERS cases this month; the previous one involved a 34-year-old man in the southern city of Najran.

Last week the MOH reported MERS-CoV (Middle East respiratory syndrome coronavirus) in a 41-year-old man in Al-Kharj who had household contact with another MERS patient and indirect contact with camels, a known source of the virus. He was in stable condition on Feb 12.

In addition, a 47-year-old Al-Kharj man who had frequent contact with camels contracted MERS in late January, according to earlier reports. He was in stable condition when the World Health Organization noted his case on Feb 2.

The MOH's cumulative count of MERS cases in Saudi Arabia has reached 1,296, including 554 deaths, 740 recoveries, and 2 patients still under treatment.

PUBLIC RELEASE: 16-FEB-2016

First-in-man trial of MERS vaccine begins at Walter Reed Army Institute of Research

THE U.S. MILITARY HIV RESEARCH PROGRAM (MHRP)

SILVER SPRING, Md. - The Walter Reed Army Institute of Research (WRAIR) began vaccinations today in a Phase 1 clinical trial to evaluate the safety and immune response of a vaccine candidate to prevent Middle East Respiratory Syndrome (MERS).

Though other vaccine candidates have previously been tested for use in camels, which are the suspected source of the coronavirus which causes MERS (MERS-CoV), this vaccine is the first to be tested in humans. Seventy-five participants will receive the vaccine at WRAIR's Clinical Trial Center in Silver Spring, Md. The vaccine (GLS-5300) is being co-developed by Inovio Pharmaceuticals and GeneOne Life Science Inc.

IMAGE: THE DANIEL K. INOUYE BUILDING ON THE WALTER REED ARMY INSTITUTE OF RESEARCH CAMPUS. view more ›

CREDIT: WRAIR

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   - HPV

World Health Organization

Influenza

Risk Assessment - Seasonal Influenza A(H1N1)pdm09

8 February 2016

Compared to previous years, northern hemisphere seasonal influenza activity commenced late in some countries in western Europe, North America and eastern Asia. Transmission, as demonstrated by influenza-like illness (ILI) rates, has started to exceed country-specific baseline rates, but is still relatively low in general with the exception of some eastern European countries where a sharp increase of ILI rates has been observed and countries in western Asia where influenza activity may have already peaked.

Among the currently circulating seasonal influenza viruses in the temperate zone, influenza A(H1N1)pdm09 virus is predominating, except in northern China where influenza A(H3N2) and influenza B viruses are widely co-circulating though the proportion of A(H1N1)pdm09 virus is increasing. In a few European countries, influenza A(H3N2) and influenza B viruses are also circulating.

In some countries there have been reports of hospitalizations with severe disease associated with influenza A(H1N1)pdm09 virus infections. Based on the WHO global influenza surveillance, in countries with influenza A(H1N1)pdm09 virus predominating, the hospitalization and intensive care unit (ICU) admission patterns seem to be

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Late start to Northern Hemisphere flu season feels strong H1N1 impact

Filed Under: Influenza, General

Lisa Schnirring | News Editor | CIDRAP News | Feb 09, 2016

After a slow start to the flu season in many Northern Hemisphere countries, activity is starting to pick up, much of it led by the 2009 H1N1 virus, known to cause severe illnesses even in younger healthy people, the World Health Organization (WHO) said yesterday in a pair of updates.

Leituvis1/ iStock

The WHO also addressed genetic changes in the former pandemic strain, but said so far evidence suggests the circulating strains are similar enough to the one in the vaccine to trigger protection.

Activity high in some locations

Parts of the Middle East have been the main hot spots this winter, but activity may have peaked in locations such as Iran, Jordan, and Oman, the WHO said. However, flu activity is climbing in Europe, especially northern and eastern countries where flulike illnesses and severe infections from 2009 H1N1 are up sharply.

theguardian

Swine flu spreading across eastern Europe and Middle East

3,000 people a day in Ukraine are being hospitalised with H1N1 virus as scientists investigate why flu strain is hitting those in younger age groups hardest

Maxim Tucker in Kiev

Tuesday 9 February 2016 06.00 EST

Swine flu has killed 183 people in Ukraine this winter and is spreading rapidly across eastern Europe and the Middle East. At least 107 people have died in Russia after contracting the disease, 18 in Armenia and 10 in Georgia, according to government figures.

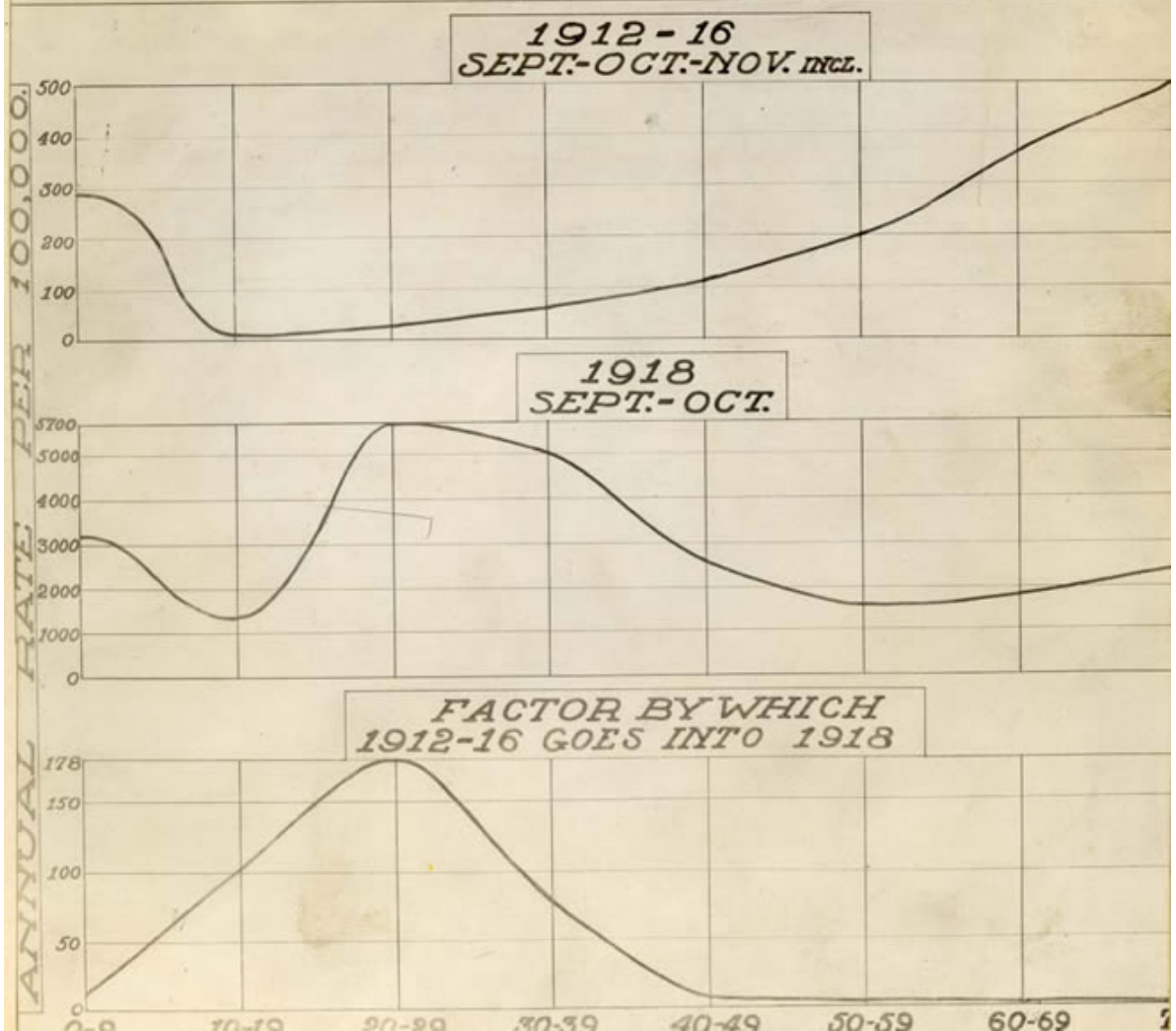
In the Middle East, 112 deaths from the virus have been reported in Iran and there are unconfirmed reports of dozens more deaths in areas of Syria and Iraq occupied by Islamic State.

Rates of severe H1N1 infection have spiked within the EU. Hospitals in eight countries have recorded an increase in the number of cases requiring intensive care over the past three weeks, according to the World Health Organisation (WHO).

"Western European countries are also reporting severe cases associated with H1N1," said Dr Caroline Brown, programme manager for influenza at the WHO in Europe. "It's all over the region at the moment."

Unlike other strains of the flu virus, which are most dangerous for older people, H1N1 can be life-threatening for healthy people under the age of 65. Symptoms can appear similar to the common cold and include fever, fatigue, coughing and a sore throat - but the disease can quickly lead to pneumonia if left untreated. The US Centers for Disease Control and Prevention estimates that the 2009-10 global H1N1 pandemic caused an estimated 284,000 deaths worldwide.

AGE DISTRIBUTION OF DEATHS FROM INFLUENZA AND PNEUMONIA AT BOSTON



PLoS Currents Beta Influenza
Rapid Access to Research in Progress Home

Preliminary Estimates of Mortality and Years of Life Lost Associated With the 2009 A/H1N1 Pandemic In the US and Comparison With Past Influenza Seasons

Viboud C, Miller M, Olson D, Osterholm M, Simonsen L.

March 20,2010

Estimates of Number of Deaths, Mean Age of Deaths, and Years of Life Lost Attributable to the 2009 Pandemic In the US.

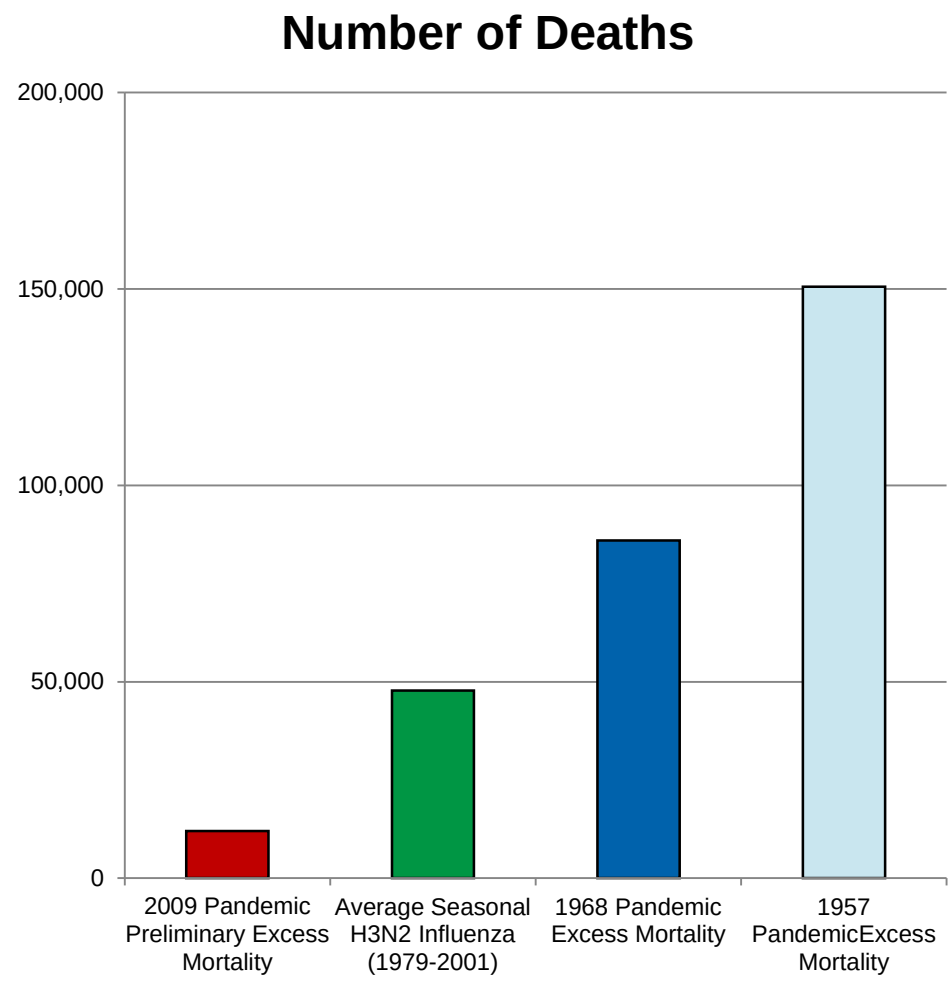
	Number of deaths (adjusted to 2000 pop.)	Mean age of deaths (yrs)	Years of life lost (adjusted to 2000 pop.)
2009 Pandemic	7,500-44,100 *	37.4	334,000-1,973,000
	12,000 (8,500-17600) **		463,300 (328,900 – 680,300)
1968 Pandemic	86,000 ***	62.2	1,693,000
1957 Pandemic	150,600 ***	64.6	2,698,000
1918 Pandemic	1,272,300 ***	27.2	63,718,000
Average A/H3N2 season, 1979-2001	47,800 ***	75.7	594,000

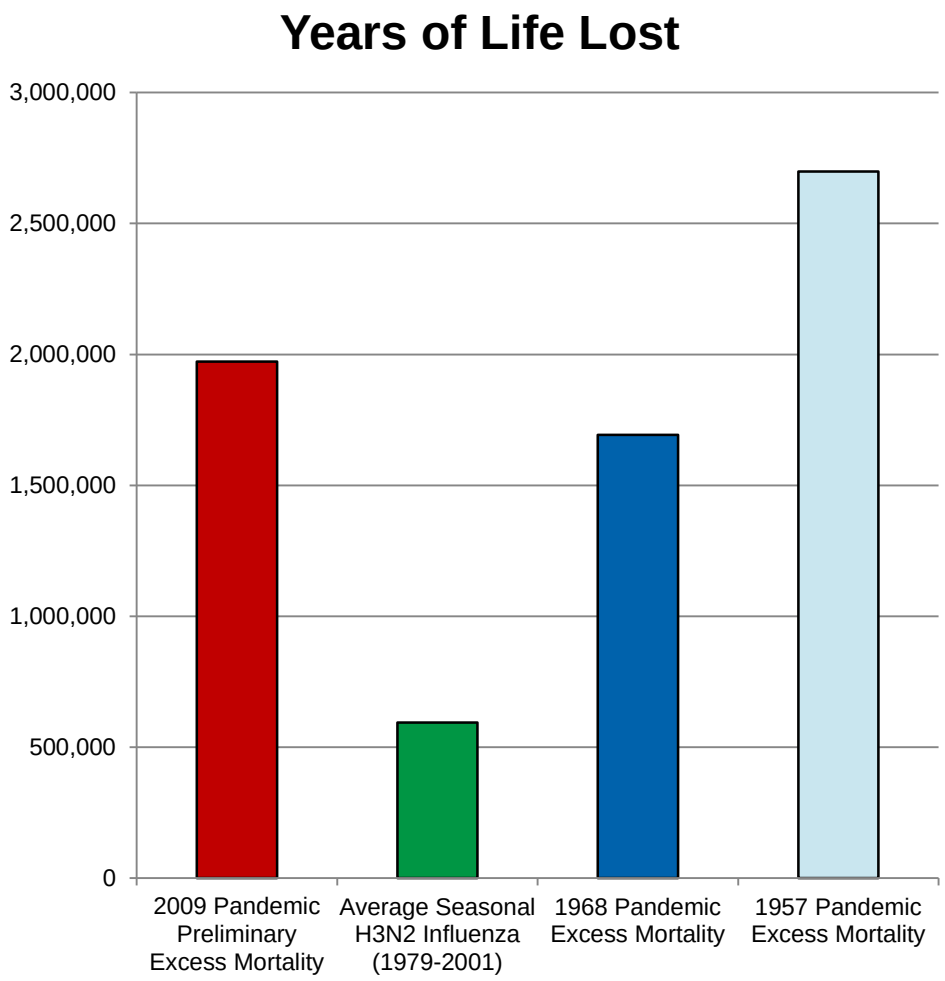
* Range is based on estimates of excess P&I deaths (lower) and all-cause deaths (upper), based on projections from the 122 cities mortality surveillance

** Estimates based on CDC's probabilistic estimates, using 2009 pandemic survey data (different from CDC's excess mortality method for measuring seasonal influenza burden)

*** Estimates based on excess mortality approach applied to final national vital statistics and adjusted to the 2000 population age structure

Death and Years of Life Lost From Influenza





Viboud C, Miller M, Olson D, Osterholm M, Simonsen L. 2010 March 20

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Flu Scan for Feb 11, 2016

Early European flu vaccine estimate finds lower protection against H1N1

European investigators who track the effectiveness of seasonal flu vaccines released their early findings today, showing a drop in protection against the 2009 H1N1 virus. However, they warned that the late start of Europe's flu season reduced the sample size, which makes their predictions less precise.

Members of the Influenza Monitoring Vaccine Effectiveness in Europe (I-MOVE) network published their findings today on the group's Web site and in a brief report in the latest issue of *Eurosurveillance*.

Earlier this week European health officials signaled that an influenza B strain mismatch had the potential to hurt the vaccine's effectiveness and they wondered if the emergence of new 2009 H1N1 subgroups would also dampen the impact of this season's vaccine.

The I-MOVE findings are based on case-control studies involving lab-confirmed flu at 10 study sites in Germany, France, Hungary, Ireland, Italy, Poland, Portugal, Spain, Sweden, and the Netherlands. Their early results put overall vaccine effectiveness (VE) for all ages at 46.3% (95% confidence interval [CI], 4.9% to 69.7%). For adults ages 18 to 64 the adjusted VE was slightly lower at 45.2% (95% CI, –12.5% to 73.3%). Assessing overall VE for seniors was hampered by only 14 flu cases in the study.

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Lactating mothers infected with Ebola virus: EBOV RT-PCR of blood only may be insufficient

M Moreau (mil.moreau@gmail.com)[1,2], C Spencer[2,3], J G Gozalbes[2], R Colebunders[4,5], A Lefevre[2,6], S Gryseels[7,8], B Borremans[7,8], S Gunther[7,9], D Becker[7,10], J A Bore[7], F R Koundouno[7], A Di Caro[7,11], R Wölfel[7,12], T Decroo[13], M Van Herp[13], L Peetermans[14], A M Camara[15]

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Article submitted on 1 January 2015 / published on 22 January 2015

We describe two Ebola virus (EBOV) RT-PCR discordant mother–child pairs. In the first, blood from the breastfeeding mother, recovering from EBOV infection, tested negative twice but her urine tested positive. Her child became infected by EBOV and died. In the second, the breastfed child remained EBOV-negative, although the mother's blood tested positive. We highlight possible benefits of EBOV RT-PCR testing in urine and breast milk and the need for hygiene counselling when those fluids are EBOV-positive.

We report two Ebola virus (EBOV) RT-PCR discordant mother-child pairs that illustrate that EBOV RT-PCR testing of relevant fluids in addition to blood, such as urine and breast milk, may be useful, in certain instances.

report of two EBOV RT-PCR discordant mother-child pairs illustrates possible benefits of EBOV RT-PCR testing in urine and breast milk, not just in blood.

Case 1: mother-child pair

In early October 2014, a woman in her late 30s was referred to the Ebola Treatment Centre (ETC) of Médecins Sans Frontières (MSF) in Guéckédou, Guinea because of general malaise and myalgia. She was accompanied by her asymptomatic, almost exclusively breastfed, six-month-old infant.

The patient had taken care of a relative who had developed symptoms compatible with EBOV in early September and had died 12 days after symptom onset. The patient had also organised the funeral. Two days

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CDC to end Ebola-related screening of travelers from Guinea

Filed Under: Ebola; Polio; VHF

Robert Roos | News Writer | CIDRAP News | Feb 18, 2016

Starting tomorrow, travelers from Guinea to the United States will no longer have to fly to designated airports and undergo special screening for Ebola virus disease (EVD), signaling the end of enhanced US screening prompted by West Africa's Ebola epidemic, the Centers for Disease Control and Prevention (CDC) announced today.

Thomas Lillis IV / Flickr cc

In other Ebola news, the availability of skilled personnel, expertise, and organizational structures from Nigeria's polio control program played a critical role in stopping Ebola when it spilled into the country from Liberia in 2014, according to a Feb 16 report in the *Journal of Infectious Diseases* (*JID*).

End to screening

Enhanced screening for travelers from Liberia and Sierra Leone, the other two countries hit by major Ebola epidemics, ended last September and December, respectively.

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News Scan for Feb 15, 2016

Ebola vaccine looks promising in monkey study

An experimental Ebola virus vaccine based on a cytomegalovirus (CMV) provided some protection to rhesus macaques in a lab experiment, according to a report published today in *Scientific Reports*, a *Nature* publication.

To make the vaccine, researchers from Plymouth University in the United Kingdom, the US National Institutes of Health, and the University of California, Riverside, engineered a macaque CMV to express the Ebola virus glycoprotein, according to the report.

Four macaques were injected with the vaccine and two with a control vaccine before they were exposed to a normally lethal dose of Ebola virus. Three of the four vaccinated macaques survived; the two controls and one vaccinated animal became ill and were euthanized when they reached a "predetermined humane endpoint." Two of the three surviving macaques had a transient fever, and one had Ebola virus in its blood for a short time.

In a Plymouth University press release, the investigators said CMV-based vaccines can be made to produce the target protein at different intervals after vaccination, and this vaccine was designed to make the Ebola glycoprotein at later times.

YAHOO! NEWS

Russia says its Ebola vaccine 'effective' in initial tests

AFP February 15, 2016 12:22 PM

Geneva (AFP) - Russia's health minister said Monday that an Ebola vaccine developed by the country over the last 15 months had shown encouraging results and would undergo further testing in West Africa.

"Phases one and two of testing were managed in Russia with volunteers and showed that the vaccine was very effective," health minister Veronika Skovortsova told reporters in Geneva.

Skovortsova said the vaccine GamEvac-Combi, developed at a government vaccine research institute, would now be put to additional tests in Guinea.

The West African countries of Guinea, Liberia and Sierra Leone have been hardest-hit by the worst-ever Ebola outbreak which has killed more than 11,300 people since December 2013.

The Russian minister made the comments ahead of a meeting Tuesday with the UN's World Health Organization chief Margaret Chan.

The WHO is hoping to study the Russian findings before giving an opinion on the new vaccine.

February 2015

Recommendations for Accelerating the Development of Ebola Vaccines

REPORT & ANALYSIS

wellcome trust

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The New York Times

LIVE

Why Pertussis is Making a Comeback

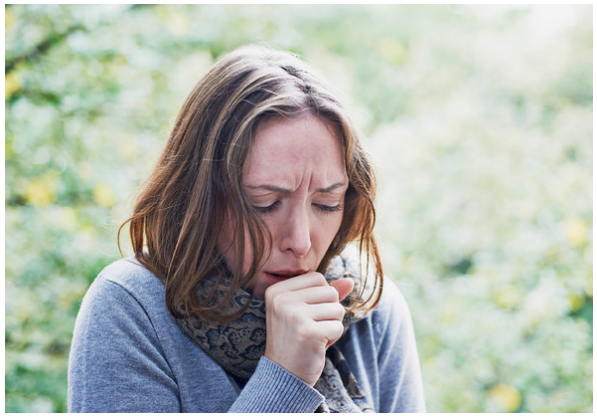
By RONI CARYN RABIN FEBRUARY 22, 2016 1:10 PM Comment

Whooping cough, a potentially life-threatening childhood illness, all but disappeared in the 1940s after a vaccine was developed. Why is it making a comeback now, when most children are vaccinated?

In recent years, there have been several outbreaks reaching numbers not seen since the 1950s. A spike in 2012 sickened 48,277 Americans, and 20 died, most of them infants. There were 13 deaths in 2013 and again in 2014, the last year for which statistics are available.

The respiratory illness induces such powerful, uncontrollable fits of coughing — the medical term is paroxysmal coughing — that older patients may break a rib or burst capillaries in the eyes. Children may have seizures. Babies, who cannot cough that hard, can stop breathing and die.

A recent study from California confirms what earlier reports have suggested: that the newer pertussis vaccine, reformulated to be safer and have fewer side effects than the older version, just isn't as effective.



Whooping cough protection fades fast after Tdap booster, study finds

By Carina Storrs, Special to CNN

Updated 7:47 AM ET, Fri February 5, 2016

Story highlights

A new study of Tdap in California finds it only gives adolescents good protection from whooping cough for two years

Many states require Tdap for children in middle school

The DTaP vaccine, part of routine childhood immunization, offers similarly short-lived protection from pertussis

(CNN)—A booster vaccine for whooping cough, which many states require for middle school-aged children, does not provide long-lasting protection, a study finds.

The Tdap booster is meant to protect against pertussis, or whooping cough, tetanus and diphtheria. The study found it protected about 69% of adolescents against whooping cough in the first year after vaccination, but protection dropped to 57% of adolescents in the second year, then 25% and 9% in the third and fourth years after vaccination, respectively.

Researchers looked at diagnosed pertussis infections in about 280,000 children from 2009, when the children were 10 years old, until 2015. Nearly everyone received Tdap by the time they were 11 or 12 because California mandated the booster for seventh graders starting in 2011.

"It provides moderate protection during the first year but years two and three after vaccination, there is not that much protection left," said Dr. Nicola P. Klein, co-director of the Kaiser Permanente Vaccine Study Center in Northern California, and lead author of the study, which was published on Friday in the journal Pediatrics.

USA TODAY
A GANNETT COMPANY

Study: Fewer young women infected with HPV, thanks to vaccines

Kim Painter, Special for USA TODAY 12:01 a.m. EST February 22, 2016

(Photo: Joe Raedle, Getty Images)

Thanks to a vaccination program that began a decade ago, fewer U.S. women are entering adulthood infected with a sexually transmitted virus that can cause cancer, new research shows.

The study, published Monday in *Pediatrics*, is the first to show falling levels of dangerous strains of the human papillomavirus (HPV) among women in their early 20s. Researchers believe those women are the leading edge of a generation that should see fewer cases of cervical, vaginal, anal and throat cancers in the decades ahead.

Health officials have recommended vaccines against HPV for girls and young women since 2006 and for boys and young men since 2011.

Earlier reports showed infections starting to drop among teen girls, despite fairly low vaccination rates. The new report, from researchers at the federal Centers for Disease Control and Prevention, shows rates dropping in girls and women ages 14 to 24. Similar data on boys and young men are not yet available.

“We are seeing exactly what we would expect — that the first impact would be seen in the youngest age groups and, then as they age into the older age groups, we would see an impact on young women,” lead researcher Lauri Markowitz said. “But we would see greater impact with greater vaccine coverage.”

The study is based on interviews and medical tests conducted during the federal government’s National Health and Nutrition Examination Surveys in 2003-2006 (before the vaccines) and 2009-2012 (the most recent data available).

Prevalence of HPV After Introduction of the Vaccination Program in the United States

Lauri E. Markowitz, MD,[a] Gui Liu, MPH,[a] Susan Hariri, PhD,[a] Martin Steinau, PhD,[b] Eileen F. Dunne, MD, MPH,[a] Elizabeth R. Unger, MD, PhD[b]

abstract

BACKGROUND: Since mid-2006, human papillomavirus (HPV) vaccination has been recommended for females aged 11 to 12 years and through 26 years if not previously vaccinated.

METHODS: HPV DNA prevalence was analyzed in cervicovaginal specimens from females aged 14 to 34 years in NHANES in the prevaccine era (2003–2006) and 4 years of the vaccine era (2009–2012) according to age group. Prevalence of quadrivalent HPV vaccine (4vHPV) types (HPV-6, -11, -16, and -18) and other HPV type categories were compared between eras. Prevalence among sexually active females aged 14 to 24 years was also analyzed according to vaccination history.

RESULTS: Between the prevacccine and vaccine eras, 4vHPV type prevalence declined from 11.5% to 4.3% (adjusted prevalence ratio [aPR]: 0.36 [95% confidence interval (CI): 0.21–0.61]) among females aged 14 to 19 years and from 18.5% to 12.1% (aPR: 0.66 [95% CI: 0.47–0.93]) among females aged 20 to 24 years. There was no decrease in 4vHPV type prevalence in older age groups. Within the vaccine era, among sexually active females aged 14 to 24 years, 4vHPV type prevalence was lower in vaccinated (≥1 dose) compared with unvaccinated females: 2.1% vs 16.9% (aPR: 0.11 [95% CI: 0.05–0.24]). There were no statistically significant changes in other HPV type categories that indicate cross-protection.

CONCLUSIONS: Within 6 years of vaccine introduction, there was a 64% decrease in 4vHPV type prevalence among females aged 14 to 19 years and a 34% decrease among those aged 20 to 24 years. This finding extends previous observations of population impact in the United States and demonstrates the first national evidence of impact among females in their 20s.

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Dr Markowitz conceptualized and designed the analyses and drafted the manuscript; Ms Liu conducted the data analyses and reviewed and revised the manuscript; Dr Hariri assisted with study design and data analyses and reviewed and revised the manuscript; Dr Steinau supervised laboratory testing and reviewed and revised the manuscript; Dr Dunne assisted with study design and data collection and reviewed and revised the manuscript; and Dr Unger assisted with study design, supervised laboratory testing, and reviewed and revised the manuscript. All authors approved the final manuscript as submitted.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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WHAT'S KNOWN ON THIS SUBJECT: Previous studies have found declines in vaccine type human papillomavirus (HPV) prevalence and genital warts among young females in the United States after introduction of the HPV vaccination program.

WHAT THIS STUDY ADDS: This study extends previous observations of quadrivalent HPV vaccine impact and examines cross-protection. Within 6 years of vaccine introduction, there were decreases in national vaccine type HPV prevalence of 64% and 34% among females aged 14 to 19 years and 20 to 24 years, respectively.

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Questions, Comments and Discussion

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