



The Year in Review: Highlights in Pediatric Infectious Diseases 2015



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OUTBREAK/HIGHLIGHTS 2015

Local

- EREID
- Food Poisoning
- Dengue
- tOPV-bOPV Switch

International

- Ebola
- MERS-CoV
- Zika Virus





EMERGING AND REEMERGING INFECTIOUS DISEASES





The threat of Imported EREID is real!

- The pandemic will most likely be a respiratory infection...
 - Emergence of SARS-CoV in 2003,
 - The highly pathogenic Avian Influenza in 2004,
 - The pandemic influenza A (H1N1) of 2009, and
 - The very recent MERS-CoV (2013)





The threat of Imported EREID is real!

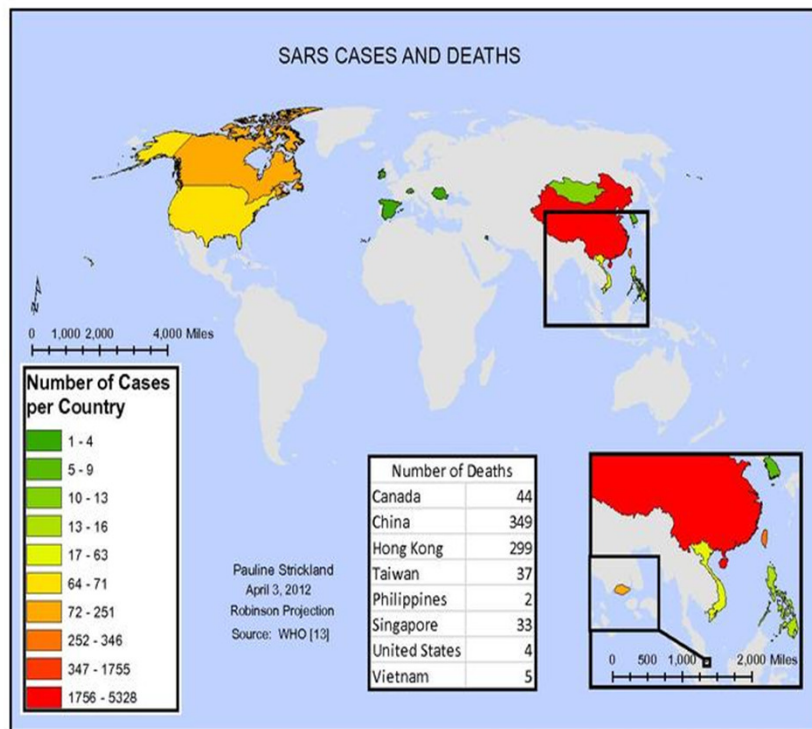
- Pathogens may be imported or exported out of the country to cause outbreaks.
 - 4.3 million foreign tourists annually from 2011-2013
 - 12 million Filipinos live overseas, and an annual average of 1-1.5 million are deployed abroad as overseas workers. Most of these overseas workers return to the Philippines for vacation or during contract breaks.
 - Participation in the annual Hajj pilgrimage, where millions of pilgrims from all over the world converge to visit holy sites in western Saudi Arabia.





2003 SARS Outbreak in the Philippines

- 92 suspect SARS cases admitted to RITM, San Lazaro Hospital or the regional hospitals in the provinces.
- 12 probable cases:
 - 2 were confirmed and died (the imported case and her father).
 - 6 cases were part of a chain of transmission linked to a single imported case who returned to the Philippines from Toronto, Canada - relatives of the two fatal cases or health workers that had been inadvertently infected.
 - 4 were imported cases from SARS affected areas – Hong Kong, Singapore and Taiwan.



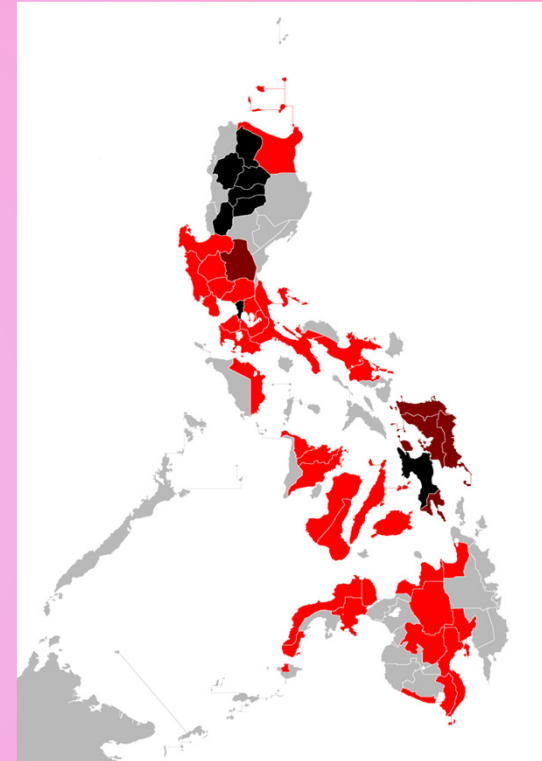


2009 flu pandemic in the Philippines

- 10 year old Filipina girl contracted A (H1N1) while **vacationing in Houston, Texas**
- Arrived on May 18, hospitalized at RITM, later lab confirmed as the 1st Philippine swine flu case
- Several local cases after contact with 2 infected Taiwanese women attending a wedding in Zambales

Major issues

- School opening in June 2009
- Around 10,000 samples received and half were lab-confirmed by RITM.
- National Influenza Surveillance Network in place
- 9 deaths

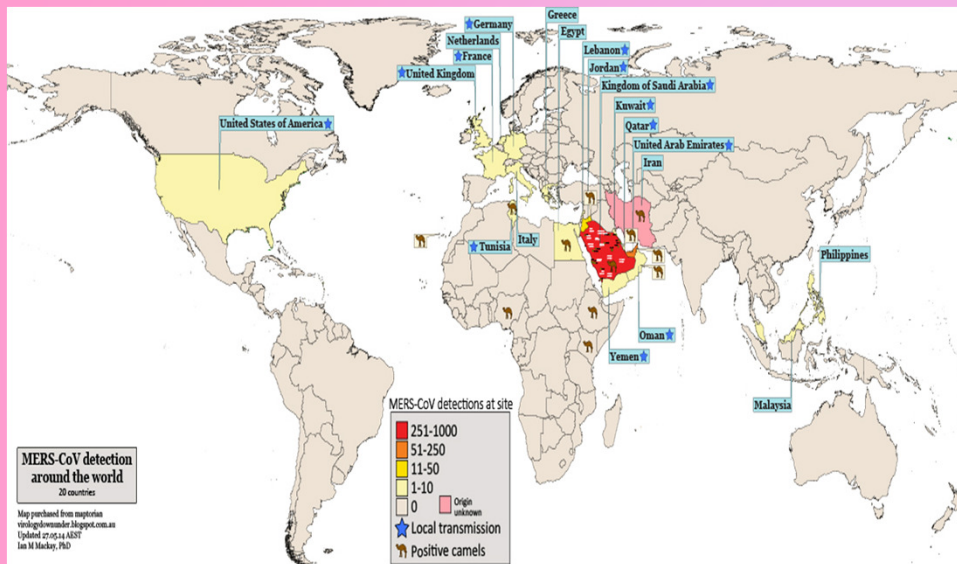




A country at risk for MERS

* Number of Deployed Overseas Filipino Workers by Top 10 Destinations

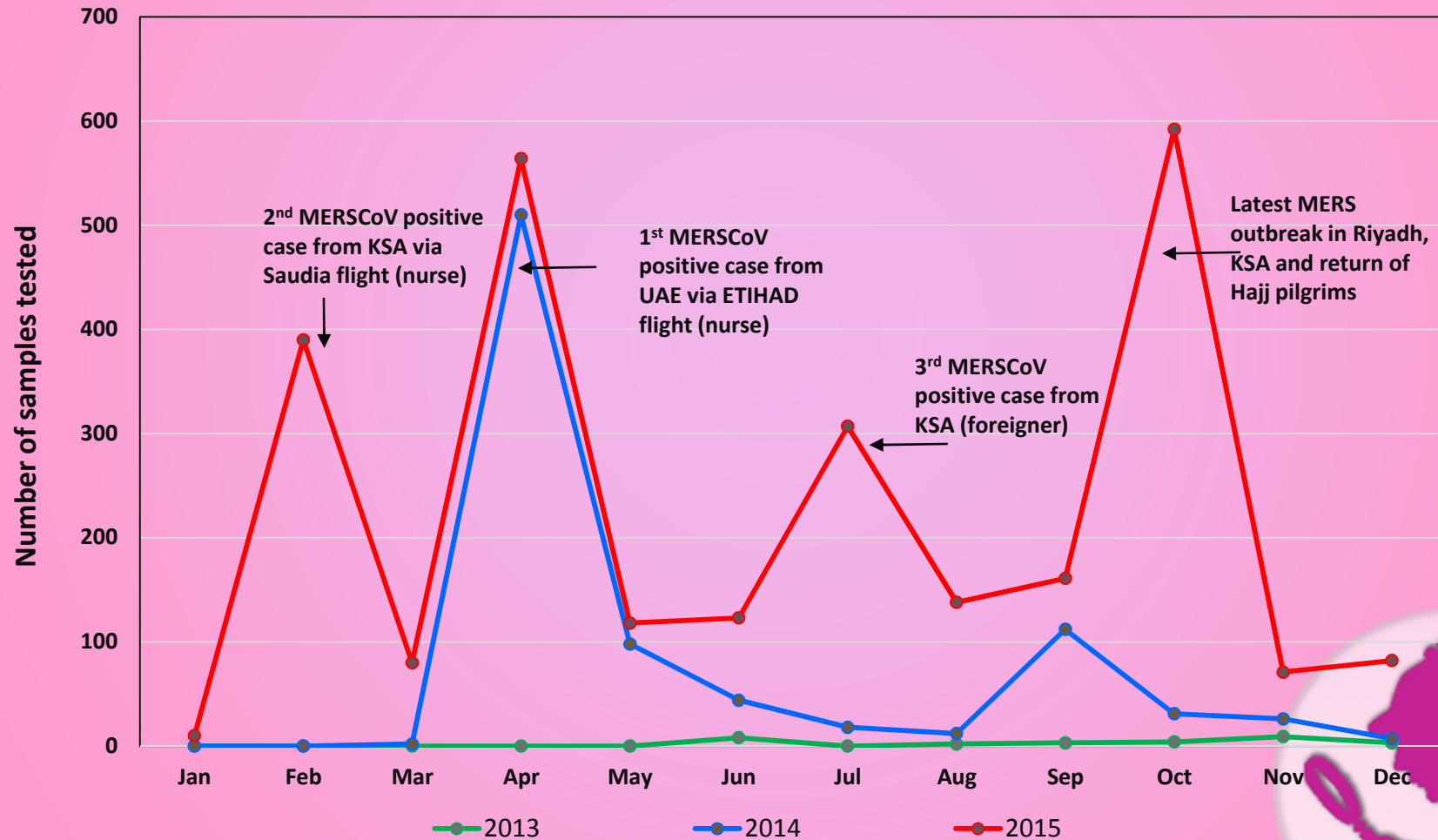
Destination	2012
All Destinations	1,436,166
Saudi Arabia	330,040
United Arab Emirates	259,546
Singapore	172,690
Hong Kong	131,680
Qatar	104,622
Kuwait	75,286
Taiwan	41,492
Malaysia	38,407
Italy	25,261
Bahrain	22,271



*2012 Annual Report, Philippine Overseas Employment Agency (POEA).



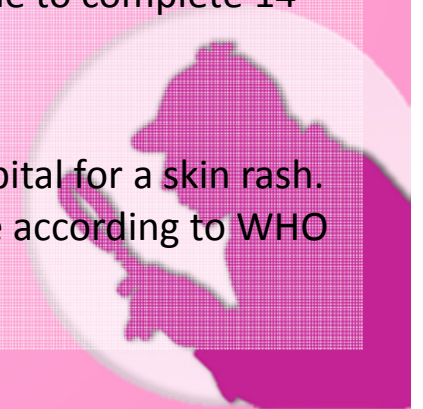
Distribution of Laboratory Samples Tested for MERS CoV in RITM, June 2013 to Dec. 2015 (N=2636)





MERS CoV Threat...

- Suspected cases of MERS-CoV infections have been referred and tested at RITM since 2013 when WHO declared MERS-CoV as a “threat to the entire world.”
- April 2014
 - An overseas Filipino healthcare worker who was reported to be positive for MERS-CoV came home from UAE.
 - 386 out of 414 passengers on the same flight were tested at RITM following the “No Regrets Policy” of the Philippine Government. All tested negative including the reported +case.
- February 2015
 - A Filipino nurse supervisor from Saudi, who claimed no patient exposure, was the first RITM NRL confirmed MERS case. She was first admitted to a private hospital.
 - Lab findings confirmed by HK Reference Lab. Patient sent home after 2 negative tests.
 - All contacts were quarantined, screened, sent home for continued quarantine to complete 14 days from onset of symptoms, after 2 negative lab tests.
- July 2015
 - A foreign national travelling from the Middle East consulted at a private hospital for a skin rash. Assessed as a PUI, samples were collected and sent to RITM. Tested positive according to WHO criteria, he was admitted to RITM. All contacts traced and tested negative.





RESTV (EBOLA RESTON)

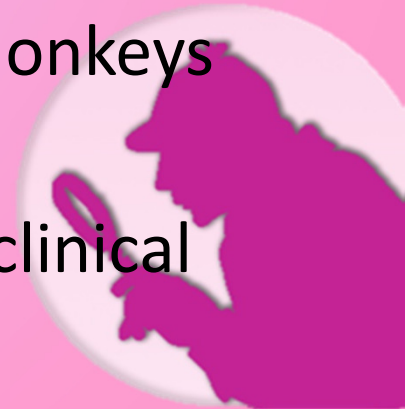




RESTV



- The only known Ebola of Asian origin with genetic characteristics similar to the virus first identified in Zaire.
- Crab-eating macaques (*Macaca fascicularis*) – imported from the Philippines.
- Causes a lower fatality rate in monkeys vs. African Ebola viruses.
- Can infect humans but with no clinical illness.





3 known, documented RESTV outbreaks in nonhuman primates (NHPs) in the world, all traced back to a single source in the Philippines

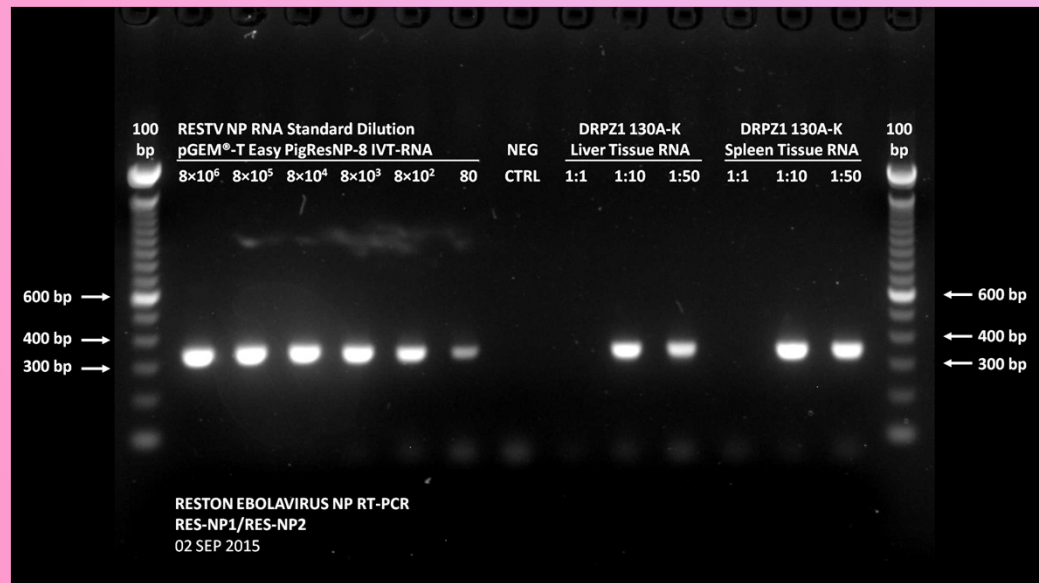


Year	Where	What	Surveillance at source facility
1989-1990	Reston, Virginia, USA/ Texas	1 st ever ebolavirus that emerged outside of Africa	RESTV Ag+ in 53% of 161 monkey deaths
		1 st known natural infection of ebolavirus in NHPs traced to the Philippines	
1992-1993	Sienna, Italy	Same Philippine source	2 Humans +IgG
1996	Texas	Same Philippine source	3 of 1732 monkeys Ab+, and 132 of 1011 dead, dying, or sick monkeys Ag+
1997-2008	RITM NRL - 11,295 primate sera had been screened for RESTV antibody and none was serologically positive		



2015 Ebola Reston in monkeys

- August 2015
- 35/381 monkeys for export were found (+) Ebola IgG/IgM ELISA
- 14 monkey deaths were reported – liver and spleen from 4 monkeys PCR+



Amplification of Reston ebolavirus nucleoprotein gene (NP) by one step RT PCR

RESTON SPECIFIC:337 bp





NOVEL PATHOGENS WITH OUTBREAK POTENTIAL





Novel respiratory viruses in children with severe pneumonia

Human metapneumovirus, human coronavirus NL63, human bocavirus, human polyomaviruses WU and KI

Suzuki, et al Respiratory viruses from hospitalized children with severe pneumonia in the Philippines. BMC Infectious Diseases 2012, 12:267

EV68 was detected in 21 (2.6%) of 816 samples by molecular methods. Since then, the detection frequency of EV-D68 has increased in different parts of the world, and EV-D68 is now recognized as a reemerging pathogen

Imamura et al. Enterovirus 68 among Children with Severe Acute Respiratory Infection, the Philippines. Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 17, No. 8, August 2011

Imamura T, Oshitani H. Global reemergence of enterovirus D68 as an important pathogen for acute respiratory infections. Rev. Med. Virol. 2015; 25: 102–114.

HRVC may have a different pathogenicity and can more commonly cause viremia than HRVA and HRVB.

N Fuji et al. Detection of Human Rhinovirus C Viral Genome in Blood among Children with Severe Respiratory Infections in the Philippines. Plos ONE November 2011 | Volume 6 | Issue 11

From November 2009 to December 2013 in the Philippines, 15 influenza C viruses were isolated, using MDCK cells, from specimens obtained from children with severe pneumonia and influenza-like illness (ILI) - First report of influenza C virus isolation in the Philippines.

Odagiri et al. Isolation and Characterization of Influenza C Viruses in the Philippines and Japan. Journal of Clinical Microbiology March 2015 Volume 53 Number 3



Hepatitis E virus

Hepatitis E virus is the causative agent of acute or fulminant hepatitis E, primarily transmitted by the fecal–oral route.

HE virus has been reported for the first time, and showed that Genotype 3 HEV in particular is circulating in the rivers of Manila City. G3 HEV can be isolated not only from infected humans but is known to be zoonotic.

Tian-Cheng Li et al. Short Report: Molecular Detection of Hepatitis E Virus in Rivers in the Philippines. Am. J. Trop. Med. Hyg., 90(4), 2014, pp. 764–766

A high prevalence of HEV antibodies in the household-raised pig population in rural areas of the Philippines was observed. This indicates the potential risk of HEV infection among local residents. Only genotype 3 of HEV was observed

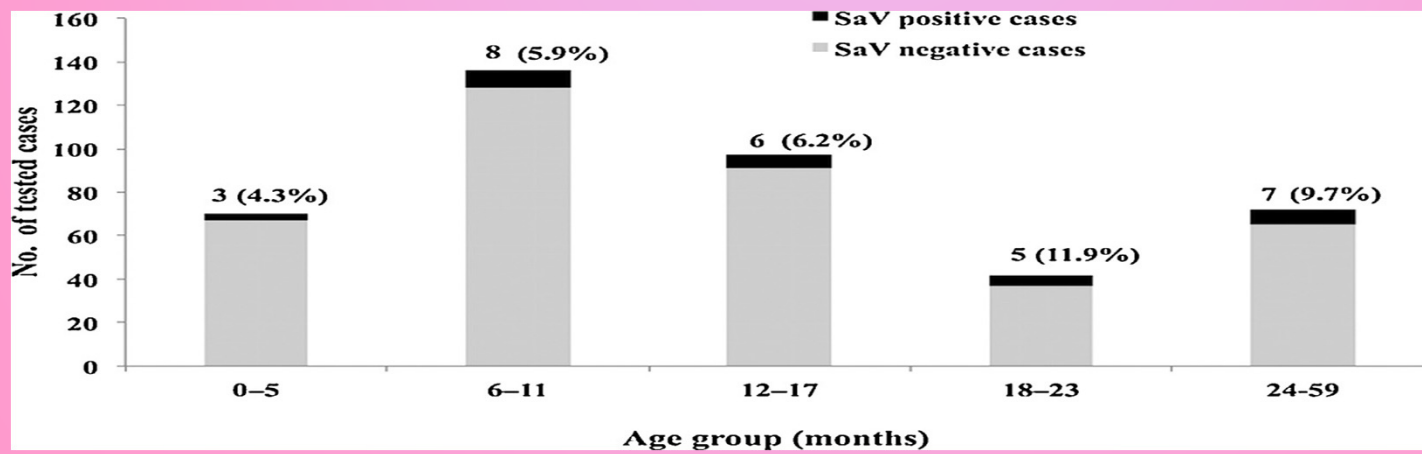
Liu et al. Seroprevalence and molecular characteristics of hepatitis E virus in household-raised pig population in the Philippines. BMC Veterinary Research (2015) 11:11



Sapovirus

SaV GII.1/GII.4 recombinant strains were detected in two distant islands in the Philippines, i.e., Leyte and Palawan Islands, which suggest that these recombinant strains were widely circulating in the Philippines.

Liu et al. Molecular detection and characterization of sapovirus in hospitalized children with acute gastroenteritis in the Philippines. Journal of Clinical Virology July 2015 V 68: 83-88





Summary EREID

- The Philippines is a hotspot for emerging and reemerging infections.
 - Overseas Filipinos
 - Tourist arrivals
 - Natural habitats of animals being encroached
- Addressing them by
 - National pandemic preparedness plan
 - Surveillance for emerging and reemerging infections including zoonoses; One Health Approach
 - Training of Health Providers in Clinical Management
 - Continuing research activities with new diagnostic tests





Distribution of Received Human Samples Implicated in Outbreak, RITM, Jan to Dec 2015 (N=9550)

Type of Disease Under Investigation	Number of Samples
Dengue	6679
Food Poisoning	1798
HFMD	461
Leptospirosis	283
Ebola Reston	99
Meningitis/Encephalitis	67
Chikungunya	49
Pertussis	43
Cholera	18
Diphtheria	14
Adverse Event Following Immunization	14
Diarrhea	9
AGE	7
Rotavirus	7
Meningococemia	1
Schistosomiasis	1
TOTAL:	9550





PHILIPPINES DENGUE UPDATE

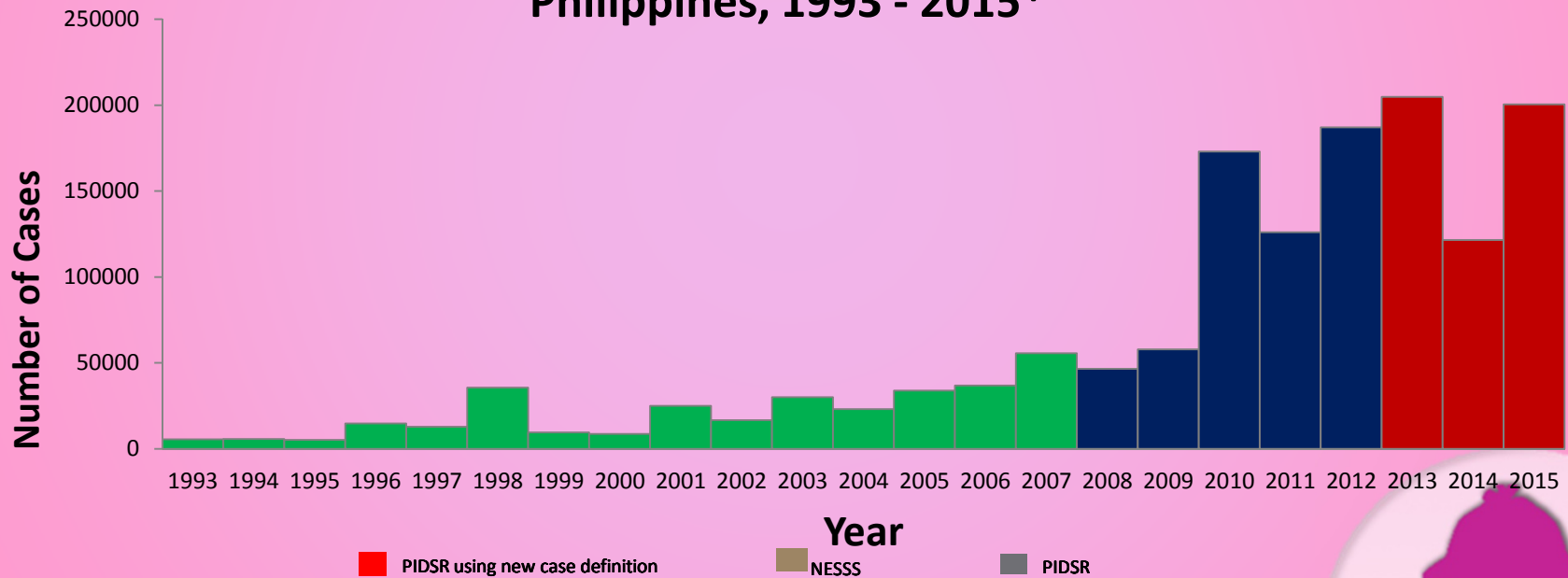
AS OF JANUARY 1 TO DECEMBER 31, 2015





Trend of Dengue Cases in the Philippines

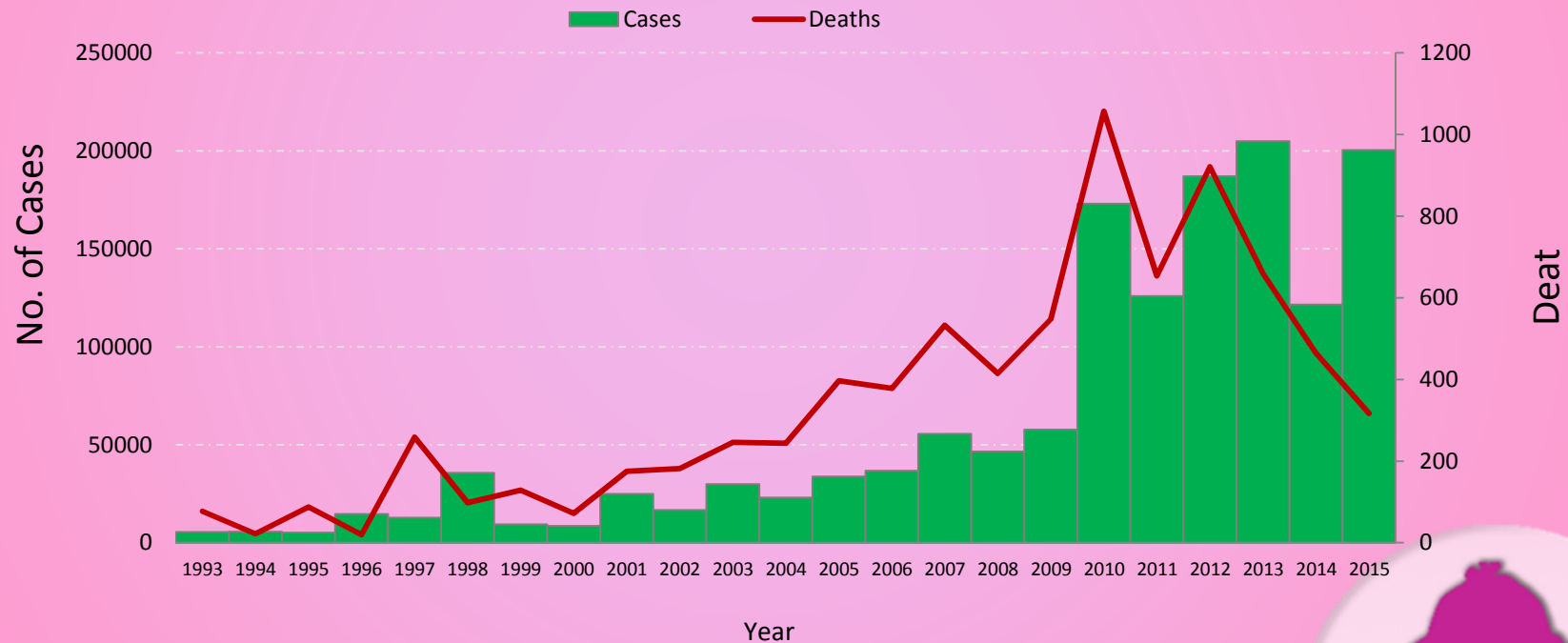
Number of Suspected Dengue Cases Reported per Year
Philippines, 1993 - 2015*





Trend of Dengue Cases in the Philippines

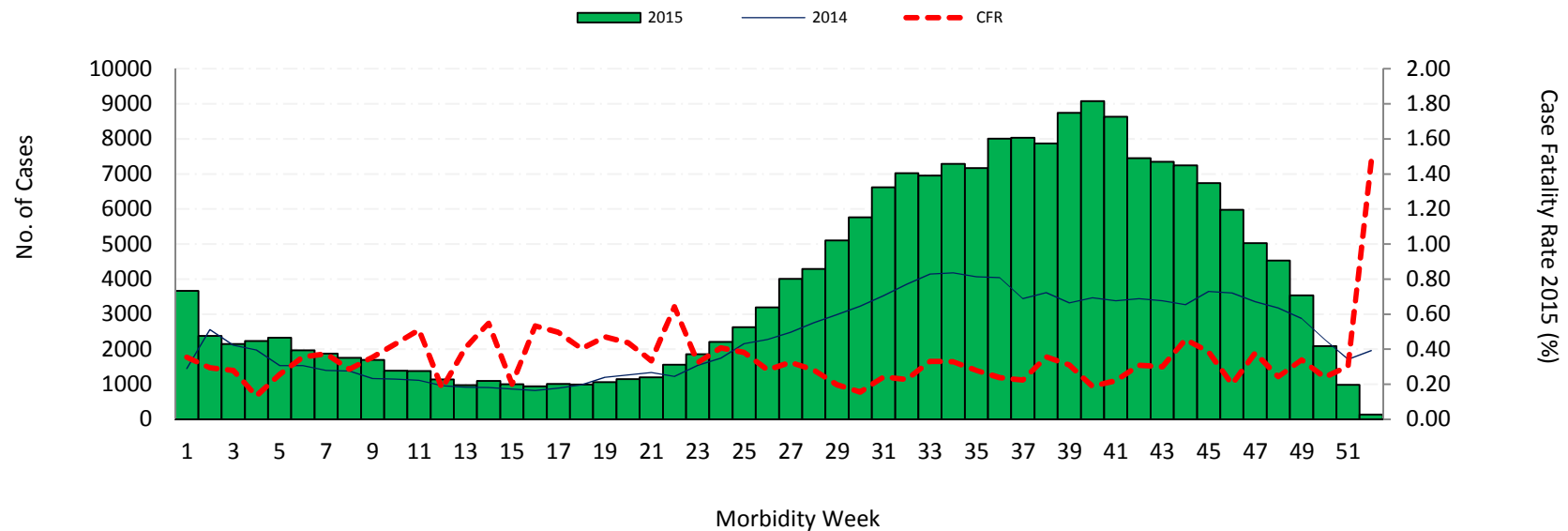
**Number of Suspected Dengue Cases and Deaths per Year
Philippines, Year 1993-2015**





Suspect Dengue Cases (January 1 – December 31, 2015)

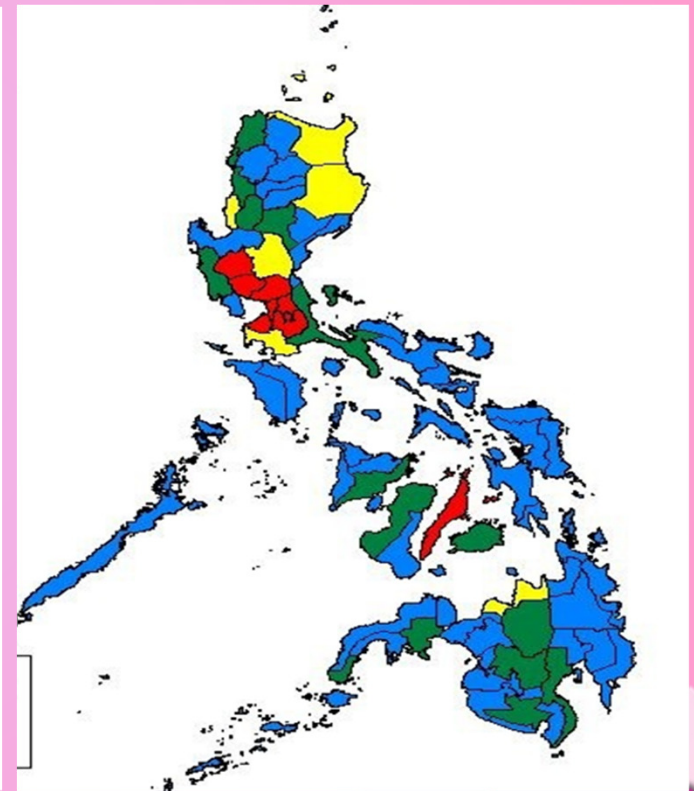
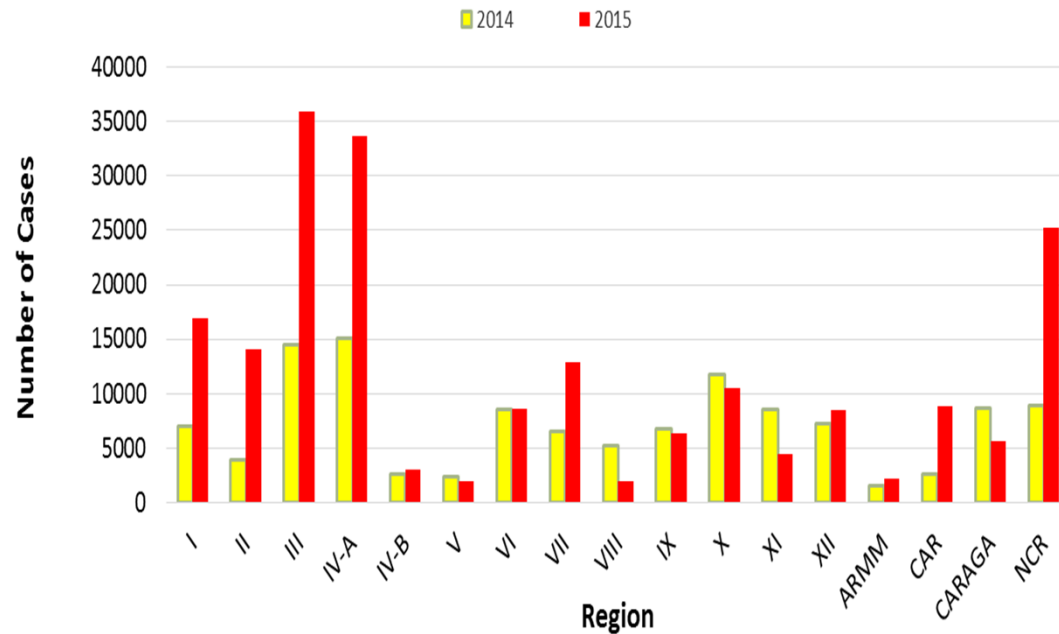
**Fig. 2 Suspect Dengue Cases by Morbidity Week, Philippines, as of December 31, 2015
2015* vs 2014 (N=200,415)**





Suspect Dengue Cases (January 1 – December 31, 2015)

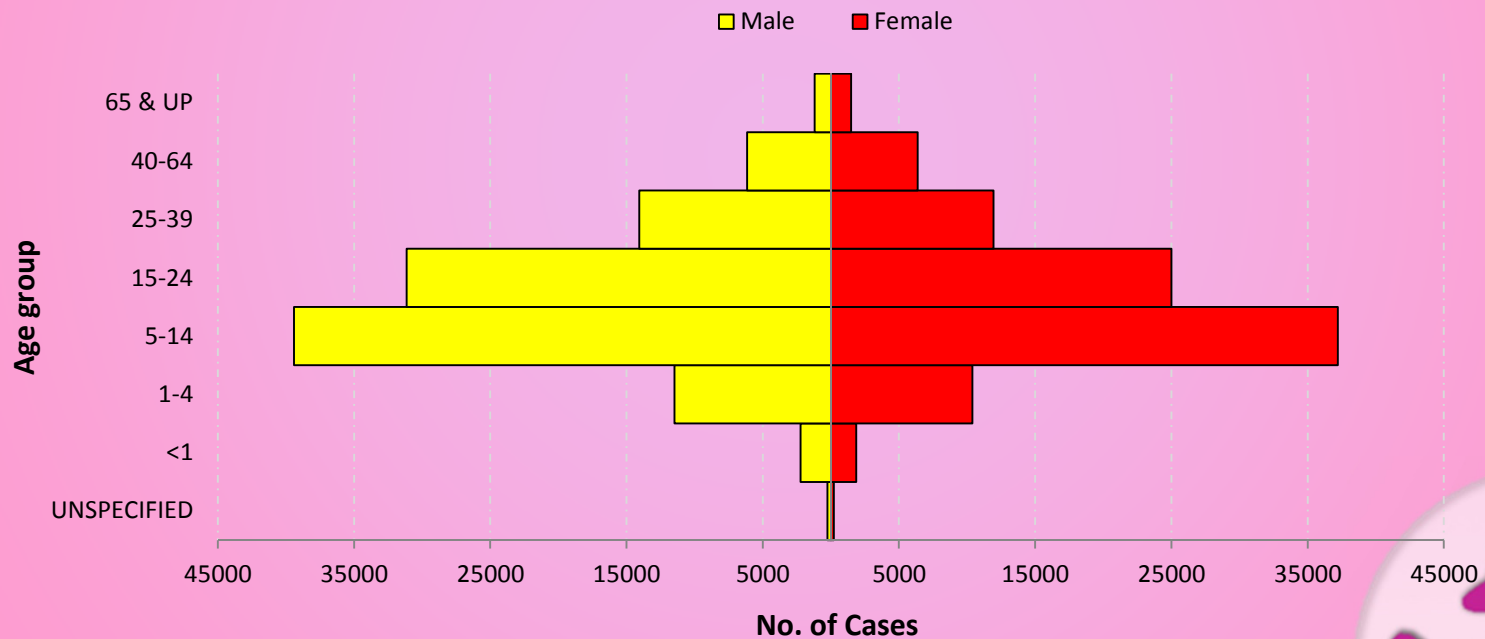
**Fig. 3 Suspect Dengue Cases by Region
Philippines, 2015 vs 2014 (N=200,415)**





Suspect Dengue Cases (January 1 – December 31, 2015)

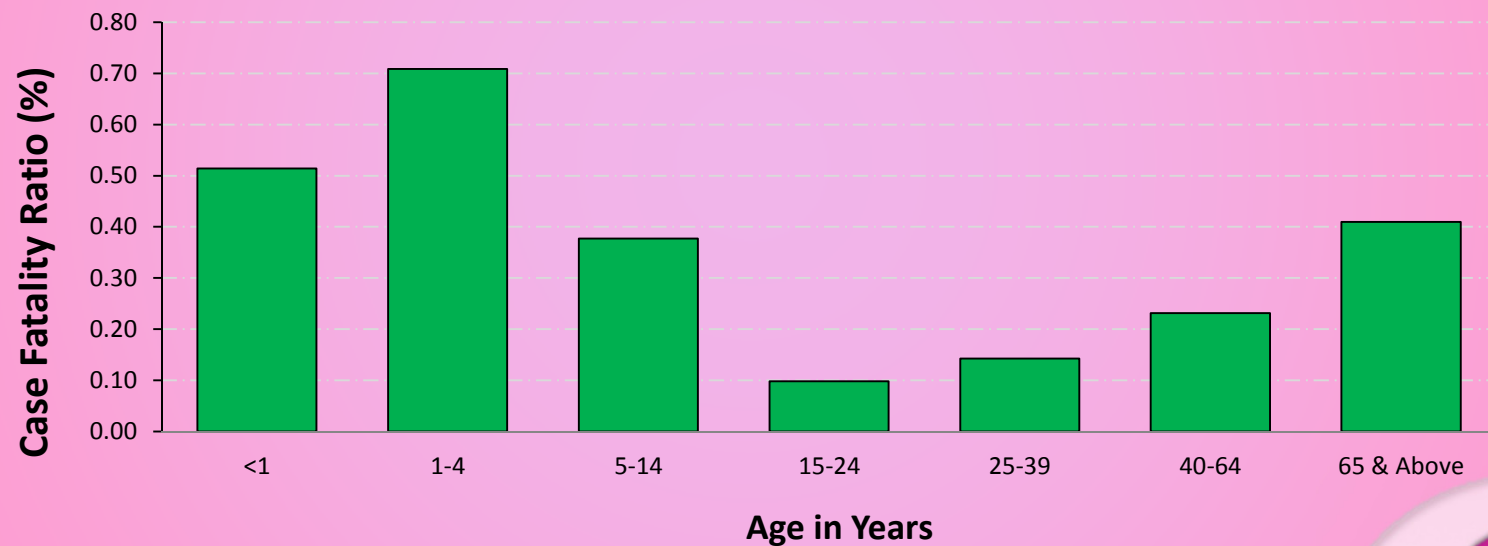
**Fig.4 Suspect Dengue Cases by Agegroup and Sex
Philippines, as of December 31, 2015 (N= 200,415)**





Suspect Dengue Cases (January 1 – December 31, 2015)

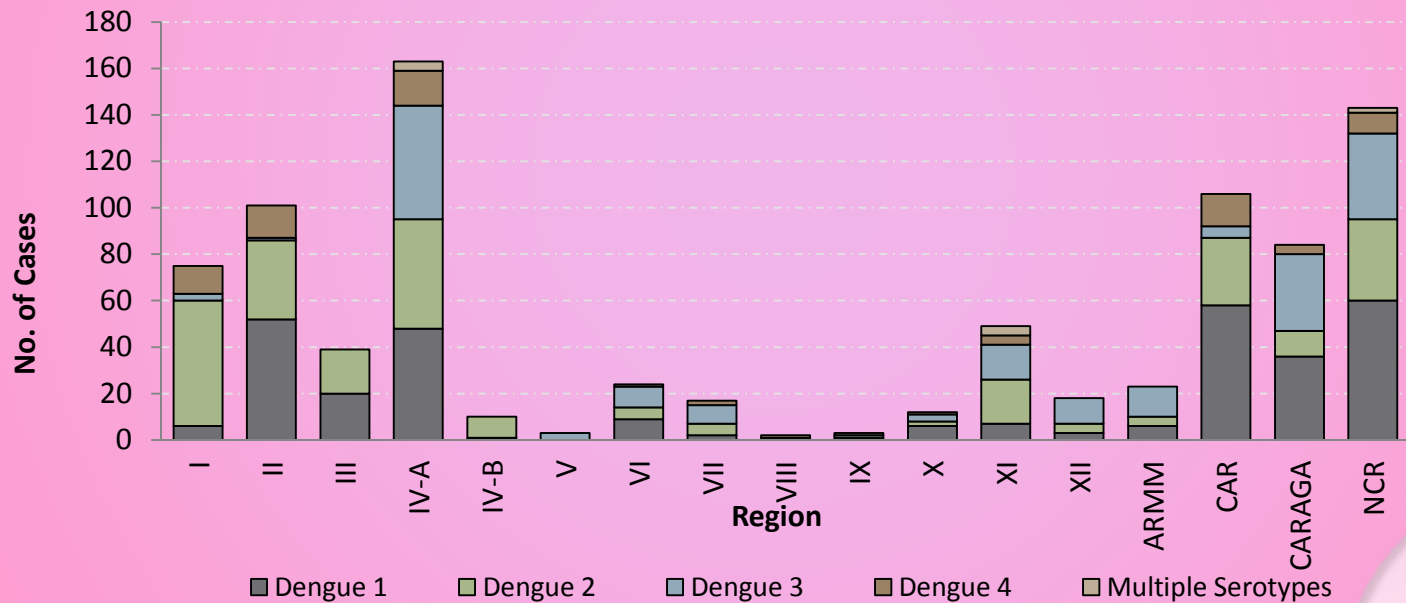
Fig. 5 Suspect Dengue Case Fatality Rate (CFR) by Age Group, Philippines, as of December 31, 2015





Suspect Dengue Cases (January 1 – October 3, 2015)

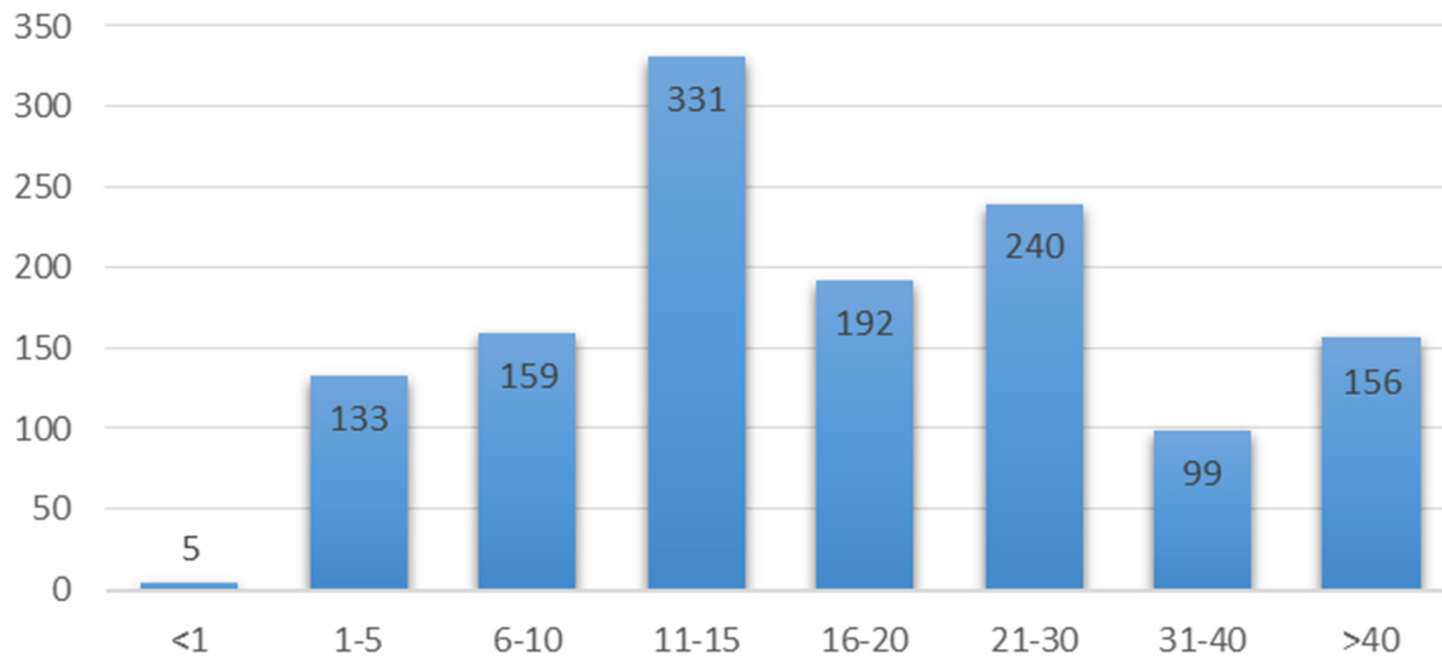
Fig. 6 Dengue Virus Serotype by Region





Food Poisoning Outbreak

Distribution of Food Poisoning Outbreak Samples by Age, RITM, Jan.-Dec. 2015





OTHER HIGHLIGHTS FOR 2015





New Antibiotics

- Paucity of new antibiotics
- FDA – approved antibiotics declining
 - Developing low-priced antibiotics
 - 1983-1987 16 new antibiotics approved
 - 2008-2012 1 antibiotic only
 - 2013-2015 6 new antibiotics approved
 - 3 Anti-staphylococcal (tedizolid, dalbavancin, oritavancin)
 - 2 for resistant Gram (-) bacilli (ceftazidime/avibactam, ceftolozane/tazobactam)
 - 1 for *C. difficile* (fidaxomicin)





New Antibiotics

- Ceftolozane/tazobactam
 - Treats highly resistant *P. aeruginosa* infections
 - Fewer toxicities
- Isavuconazonium sulfate
 - Active vs. molds and *Aspergillus*
 - Lesser side effects than Voriconazole
- Peramivir
 - Injectable neuraminidase inhibitor
 - For uncomplicated influenza
 - Limited evidence from H1N1 pandemic





New Antibiotics

- Cidofovir
 - Viral infections and transplant infections (adenovirus)
 - Toxic with minimal improvement
- Brincidofovir
 - Not FDA-approved
 - Promising, more efficacious vs. adenovirus, double-stranded DNA
 - Less toxic
 - Available in oral formulations





New Antibiotics in the pipeline

- Minocycline
- New polymyxins
- Meropenem/RPX7009
- Plazomicin





C. difficile INFECTION (CDI)

- Highest priority for CDC
- 354,000 cases and 29,000 deaths in US
 - \$1,200,000,000.00 cost
- PCR most sensitive
- Evidence of infection and need for treatment requires clinical correlations
 - Due to high carrier rates in hospitalized patients
 - 75% colonized at admission
 - Not all candidates for treatment unless with unexplained diarrhea





C. difficile INFECTION (CDI)

- In UK, reduced rates by 80%
 - Antibiotic control (fluoroquinolones & cephalosporins)
 - Gene sequencing
 - Inform Infection Control
- Patient to patient transmission in only 23% of cases





Molecular Diagnostics in Infectious Disease

- New tests and new data
- Gene sequencing
 - Current concepts about *C. difficile* and *S. aureus* transmission are wrong
- Detect pathogens with accuracy and speed
- Used in disease outbreaks to link cases and sources
- Trace transmission routes of carbapenemase-producing gram (-) bacilli





Molecular Diagnostics in Infectious Disease

- Used in Sexually transmitted diseases clinics
 - Detect *N. gonorrhoea* and *C. trachomatis*
- Detect influenza in offices and emergency departments
- Rapid PCR-based blood culture test successful in rapid identification of blood culture isolates
 - Required 24/7 decision management
 - Concurrent traditional blood cultures
 - Limits in identification
 - Concern about cost
 - Lack of sensitivity data
 - Inability to identify all pathogens
 - Difficulty in distinguishing pathogen from contaminants





Other Breaking News in 2015

- Medical Management with antibiotics for acute appendicitis works as well or better than surgery
- Varicella zoster implicated in giant cell arteritis with response to acyclovir (anecdotal)
- *Fusobacterium necrophorum* implicated as an important possible cause of pharyngitis





tOPV-bOPV SWITCH

- SAGE reaffirmed April 2016 as definitive date for globally synchronized withdrawal of type 2 OPV
 - Preparedness criteria for switch are met
 - Public health risks associated with continued use of type 2 component far outweigh the risk of new VDPV2 emergence after OPV 2 is stopped





tOPV-bOPV SWITCH

Risk Management Rationale

- IPV w/limited role in preventing VDPV2 emergence
 - Main role is minimizing occurrence of paralytic disease in any VDPV2 outbreak after switch
- Risk of VDPV2 emergence being reduced by extensive calendar of tOPV supplementary immunization activities before switch
- Highest risk countries will introduce IPV before switch
- Countries affected by delay are in lower risk
 - Population immunity vs. type 2 is high
 - Risk of VDPV2 emergence and spread is minimal





tOPV-bOPV SWITCH

Risk Management Rationale

- All countries will receive IPV supplies w/in ~ 3 months of switch
 - Catch-up vaccination will be conducted when sufficient supply available
- Global stock of mOPV2 and IPV is available for outbreak response if w/VDPV2 detected any country after tOPV-bOPV switch





2016 and BEYOND BIGGEST THREAT

- Antibiotic resistance is probably the biggest threat to Infectious disease Practice
 - Worldwide issue leading to:
 - Illnesses
 - Death
 - Prohibitive cost
 - Poor health outcomes
 - Need to use more toxic treatments





2016 and BEYOND BIGGEST THREAT

- CDC divides antimicrobial resistance into 3 levels:
 - Urgent threats – carbapenem-resistant *Enterobacteriaceae*. *N. gonorrhoea*
 - Serious threats – multidrug-resistant *Pseudomonas*, drug-resistant *Shigella* and *Salmonella*, MRSA
 - Concerning threats – vancomycin-resistant *S. aureus*, erythromycin-resistant group A *Streptococcus*, and clindamycin-resistant group B *Streptococcus*





2016 and BEYOND BIGGEST THREAT

Causes of antibiotic resistance

- Organisms developed evolutionary mechanisms
- Use of antibiotics in food-producing animals
- Prescriber issues
- Inappropriate use
- Unnecessary use
- Patient demand
- Person-to-person transmission





2016 and BEYOND BIGGEST THREAT

Prevention

- How do we prevent infections?
 - Promote vaccines
 - Prevent transmission of resistant infections via hand-washing campaigns
- Improve antibiotic prescribing
 - We need to know how to stop inappropriate and unnecessary prescribing
 - Need to ask :
 - “ Does patient really need this?”
 - “ Am I prescribing the right antibiotic?”
 - “ Is this the narrowest spectrum possible?”
 - “ Am I giving the shortest possible duration?”
 - “ Am I giving the right dose?”



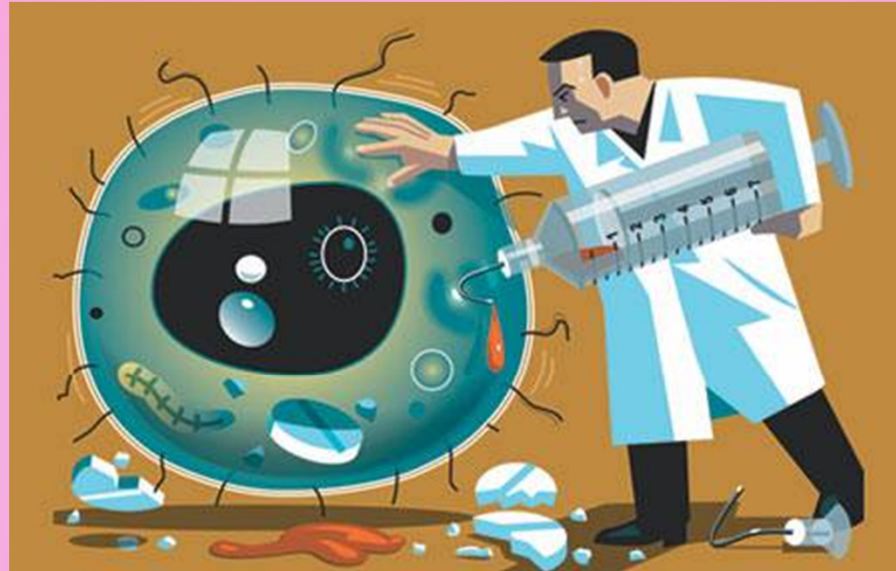


2016 and BEYOND BIGGEST THREAT

Prevention

- Teach medical students and residents
- Educate patients about when antibiotic is needed
 - Beneficial in changing behavior and patient understanding
- Antibiotic Stewardship
 - Limit abuse of antibiotics





THANK YOU

