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Life & Annuities



Lessons from Recent and Historical Epidemics: Bugs, Behavior, and Beyond!

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04 September 2019



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Outline

- I. Basic Definitions
- II. Historical Pandemics
- III. Influenza and Other Contemporary Epidemics
- IV. RGA approach to Epidemics, Pandemics and Infectious Disease monitoring



Disease X



- How do we gauge likelihood and impact of Disease X spread?
- To what extent does Disease X present a foreign travel risk?
- Which product lines will be impacted by Disease X?
- What will be our message to investors?
- Are there any risks to business continuity?

<https://pixabay.com/en/newspaper-paper-headline-brown-34126/> (CC) Creative commons

Definitions



endemic



Definitions

endemic

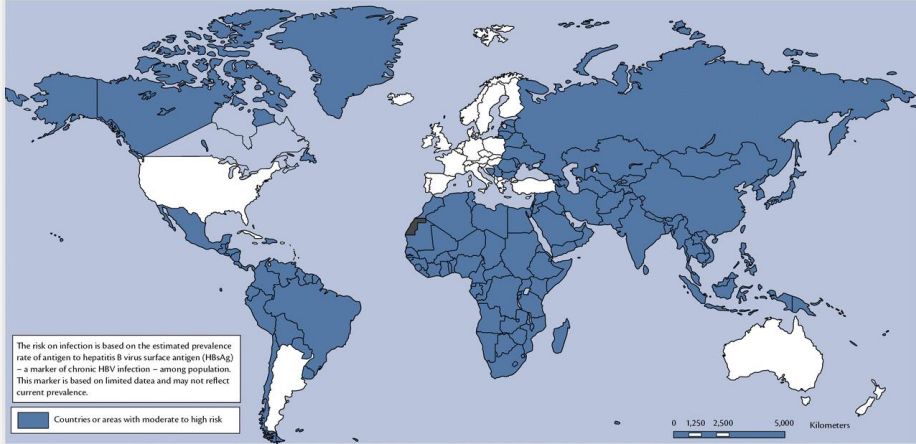
Habitual presence of disease
within a geographic areas

- “native”, “steady”, “permanent”
- Insurance implications – example pricing and underwriting hepatitis B

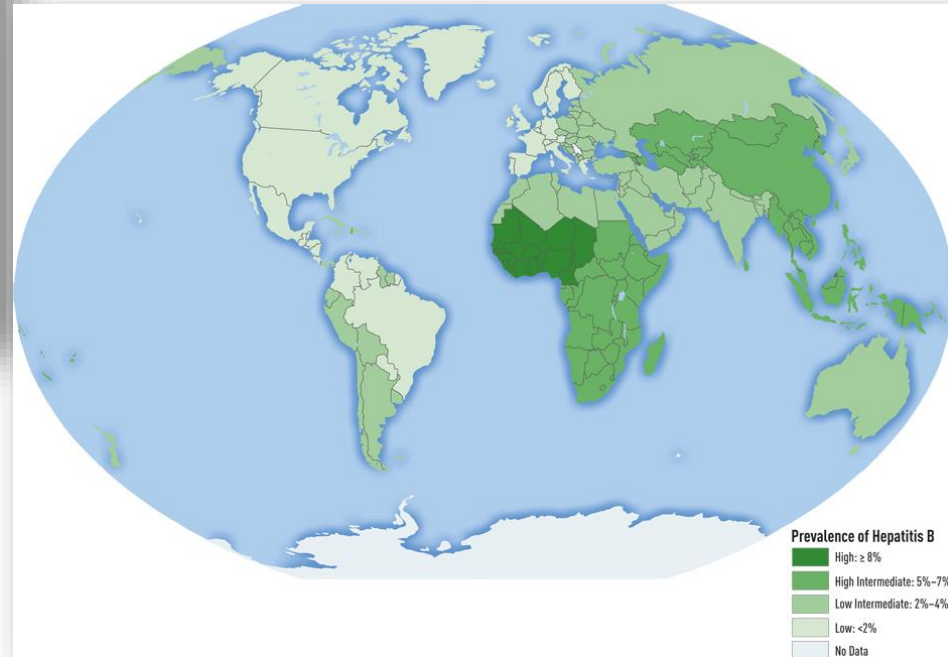


Endemic Hepatitis B

Hepatitis B, countries or areas at risk



<http://wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/hepatitis-b>
http://gamapserver.who.int/mapLibrary/Files/Maps/Global_HepB_ITHRiskMap.png





epidemic



Definitions

epidemic

The occurrence of more cases of disease than expected in a given area or among a specific group of people over a particular period of time

- Generally implies *relatively* rapid spread
- Not limited to infectious diseases

Epidemic

**Disease
Outbreak**

Cluster



pandemic



Definitions

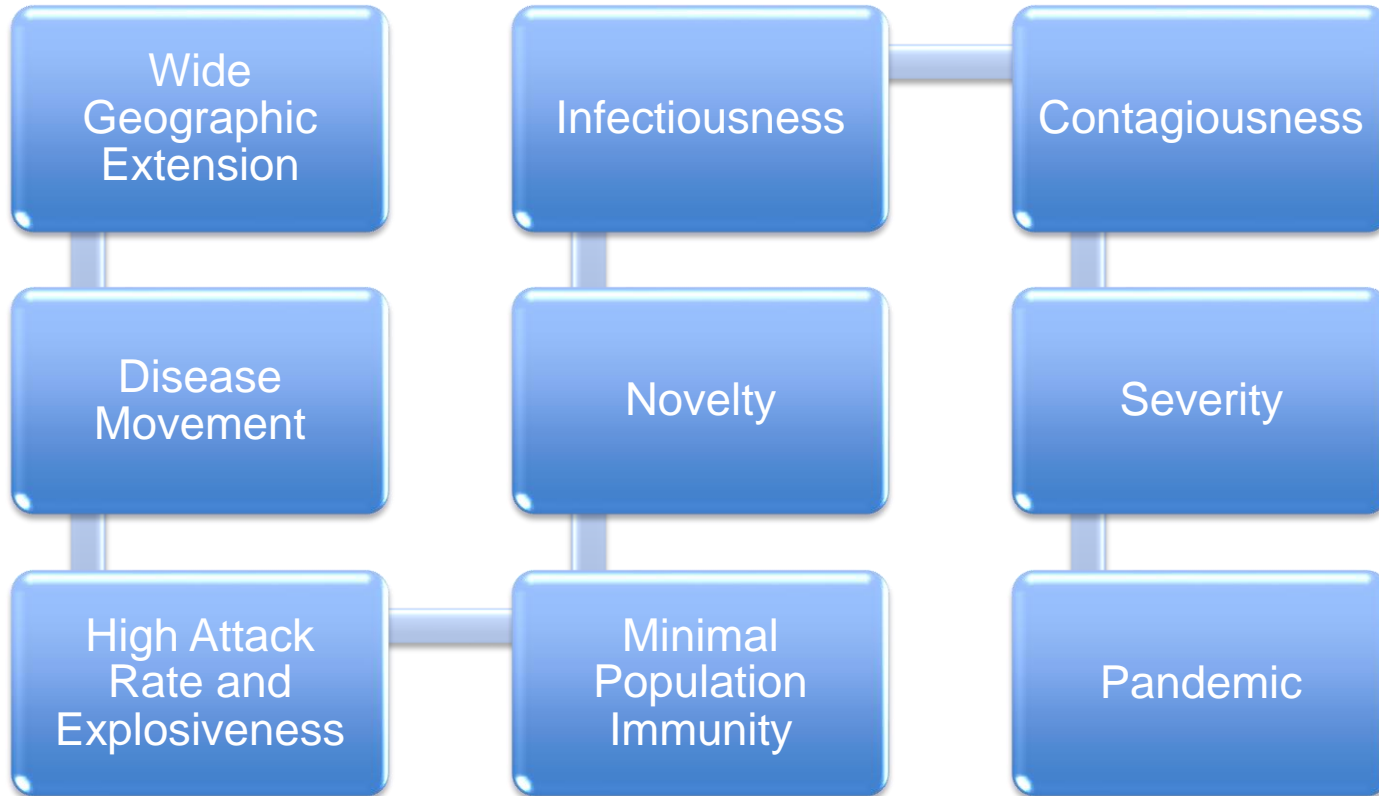
pandemic

When an infectious disease crosses international boundaries and affects a large number of individuals



Criteria for Pandemic

Morens et al.¹





Influence of Human Behavior

CDC – Factors in the Emergence of Infectious Diseases²

War

Sexual
Behaviors

IV Drug Use

Urban Decay

High Density
Facilities

Population Migration and Growth



Elimination vs eradication



Elimination versus Eradication

WHO Definitions

Elimination

- reduction to zero (or a very low rate) of new cases in a defined geographical area.

Eradiation

- complete and permanent worldwide reduction to zero new cases of the disease through deliberate efforts

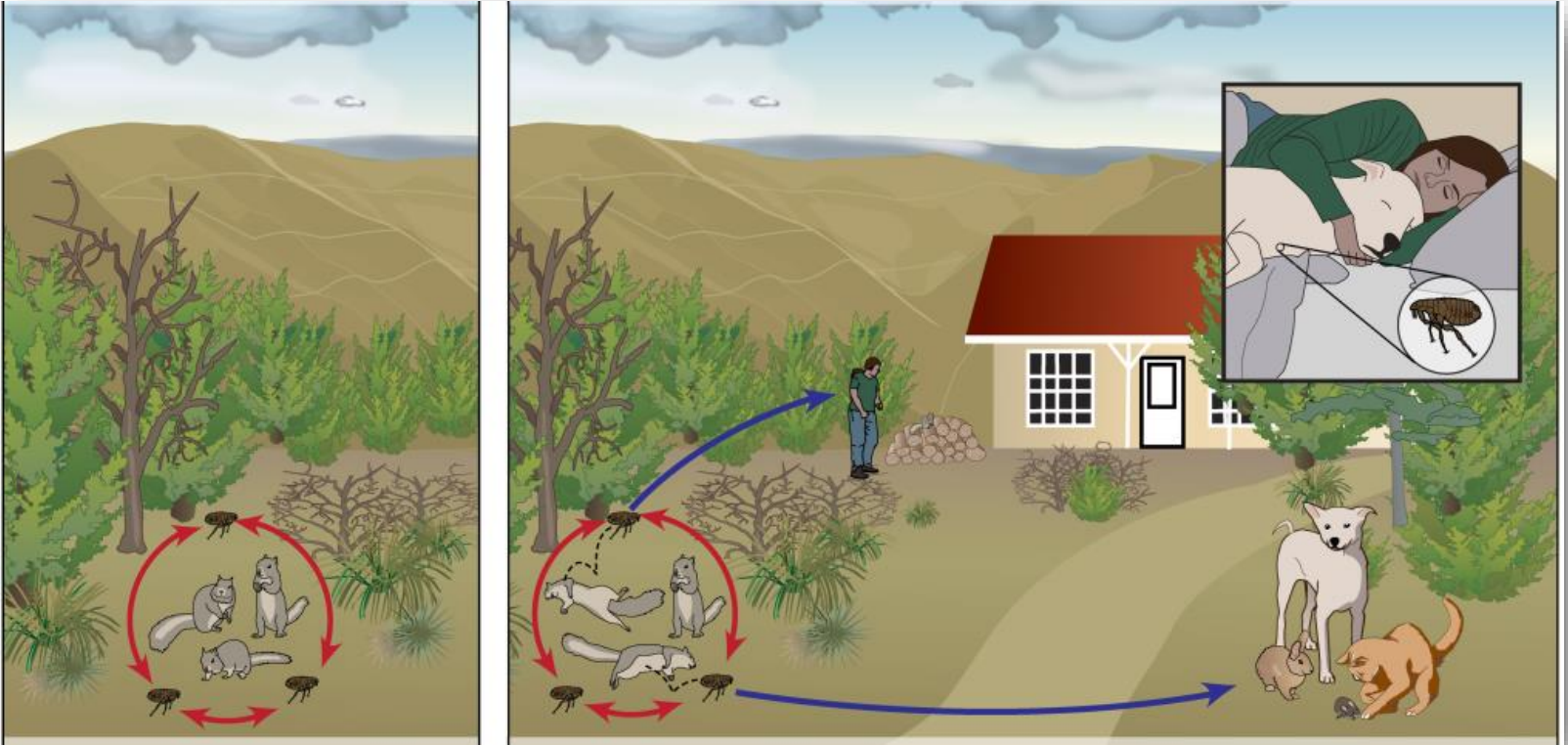
Historical Pandemics

Bubonic Plague/Black Death

- Began in China around 1334 and spread via new trade routes to Europe (Silk road)³
- Generally considered to be deadliest pandemic by proportion of population killed
- Estimated 60% of Europe's population decimated, and 75-200 million overall³
- 80% case fatality rate
- 3 basic clinical sequelae – lymphadenopathy (buboes), (gangrenous) septicemia, and pneumonia



By Unknown - <http://supotnitskiy.ru/stat/stat8.htm>, Public Domain, <https://commons.wikimedia.org/w/index.php?curid=18142655>



<http://www.cdc.gov/plague/resources/plagueecologyus.pdf>



Yersinia Pestis

Why so deadly?⁴

- Climate Change (prosperity, warmth, rain, and movement into cities)
- Broad temperature range of organism (less seasonal) with multiple hosts
- New transportation and trade routes
- New relation to animals
 - Tarbagan and black rats
 - *Most emerging infectious diseases are epi-zoonotic*
- Contagious (droplet spread)
- Importance of quarantine



[https://en.wikipedia.org/wiki/Tarbagan_marmot#/media/File:Marmota_sibirica_-_ \(Russia, Mongolia\) - Rochers-de-Naye, Switzerland, 2009.JPG](https://en.wikipedia.org/wiki/Tarbagan_marmot#/media/File:Marmota_sibirica_-_ (Russia, Mongolia) - Rochers-de-Naye, Switzerland, 2009.JPG) Creative Commons BY SA 3.0



Spanish Influenza (1918)

“The Mother of All Pandemics”

- Mortality estimates vary widely between 30-100 million
- 2.5% case fatality rate but infected 28% of all Americans
- Caused by H1N1 family of viruses
- Especially high relative virulence among those 15-34, enhanced by WWI living conditions⁵

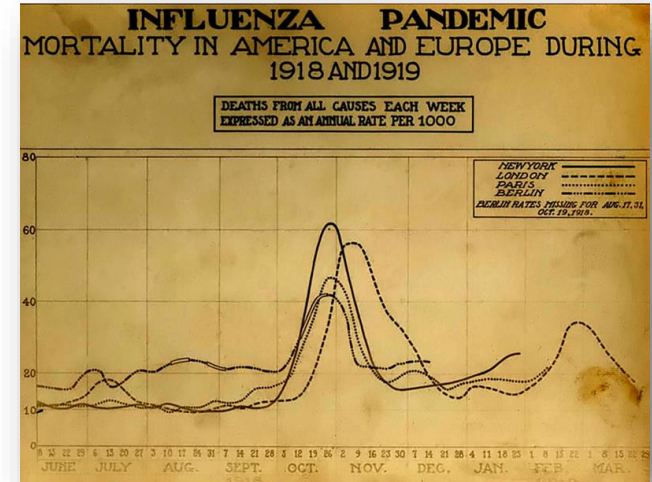


<https://commons.wikimedia.org/wiki/File:CampFunstonKS-InfluenzaHospital.jpg> Public Domain



Spanish Influenza

- Occurred in three waves the first of which was fairly mild
- By the end of the third wave, life expectancy decreased by estimated 10-12 years
- The mortality rate was 2.5% compared to 0.1% average for prior influenza strains⁶. Virus was reconstructed in 2005 and found to be an entirely novel variant (for humans). Avian mutation propagated in pigs (genetic variants still exist).



By (Image: courtesy of the National Museum of Health and Medicine) - Pandemic Influenza: The Inside Story. Nicholls H, PLoS Biology Vol. 4/2/2006, e50 <http://dx.doi.org/10.1371/journal.pbio.0040050>, Public Domain, <https://commons.wikimedia.org/w/index.php?curid=1441889>

Influenza and Other Contemporary Epidemics and Pandemics



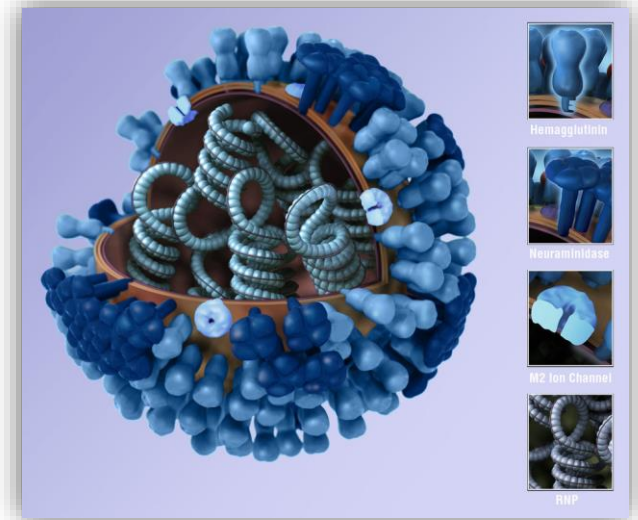
By Jpatokal - Own work, CC BY-SA 3.0, <https://commons.wikimedia.org/w/index.php?curid=7127535>



Influenza

The Basics

- Influenza are single-stranded RNA viruses in the Orthomyxoviridae family
- Influenza A and B strains cause the great majority of human infections
- The two major surface proteins for Influenza A are hemagglutinin (H) and neuraminidase (N)
 - These key determinants in
 - Antigenic Typing
 - Virulence
 - Vaccination Targets
 - Antiviral drugs inhibit neuraminidase
- 2009 – a new strain for humans emerged: a subtype of H1N1 (“swine flu”)





Influenza

Why so deadly?

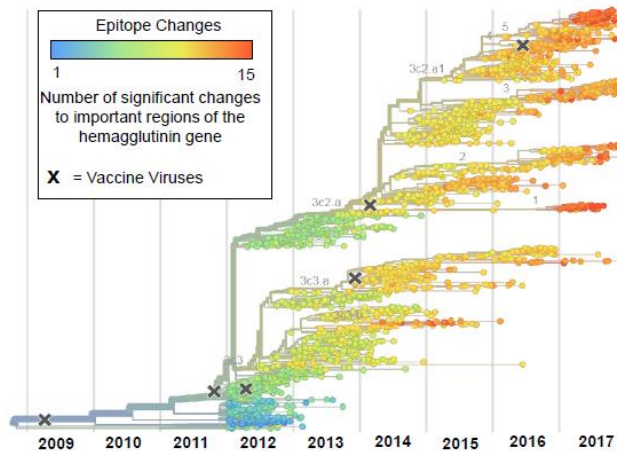
- High levels of “antigenic drift” – The virus lacks adequate error checking capabilities
 - Mutation rates 300 x similar viruses
 - Allows to escape environmental pressures through rapid evolutionary selection
 - Allows evasion from host immunity
- Antigenic “shift” – exchange of genetic material between two different strains of influenza (during coinfection of a host)
 - While these occur less often they can be quite virulent (responsible for the three major pandemic outbreaks)
- Infects as a population of viruses with minor variants (not a single virus)
- “If you have seen one influenza season, you have seen one influenza season”



Influenza

H3N2 virus

- 78% of positive influenza tests in US last flu season were H3N2 strain
- Higher mortality rates in young children and elderly
- Severe Australian season was a warning signal



- H3N2 Viruses Evolve More Rapidly than Other Influenza Viruses
- H3N2 has required twice the number of vaccine viruses changes than H1N1
- CDC surveillance shows several H3N2 genetic groups co-circulating this season

Source: CDC <https://www.cdc.gov/grand-rounds/pp/2018/20180116-severe-influenza.html>



SARS

Just the (bad) Facts

- Over 750 deaths (44 in Canada)
- 9% fatality rate if infected (but low R_0 of 4)
- Spread to five countries within 24 hours(!)⁷
- 6 continents, 30 countries with 6 months



SARS

The Canada Experience⁸

Date: 10 Feb 2003

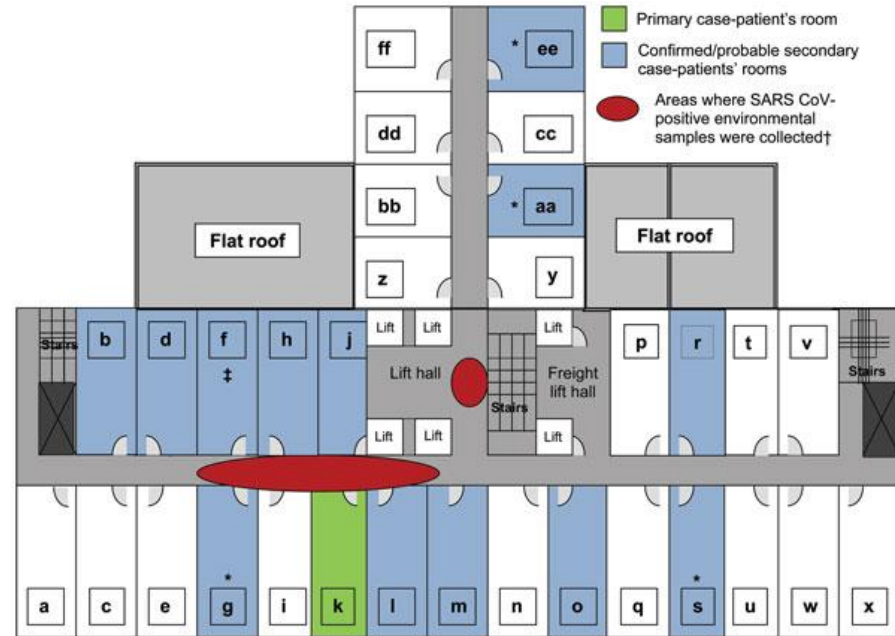
From: Stephen O. Cunnion, MD,

This morning I received this e-mail and then searched your archives and found nothing that pertained to it. Does anyone know anything about this problem?

"Have you heard of an epidemic in Guangzhou? An acquaintance of mine from a teacher's chat room lives there and reports that the hospitals there have been closed and people are dying."

--

Stephen O. Cunnion, MD, PhD, MPH



ProMED-mail. Pneumonia—China (Guangdong): RFI. ProMED-mail archive 20030210.0357. Brookline, MA, USA: International Society for Infectious Diseases; 2003 Feb 10. <http://www.promedmail.org>

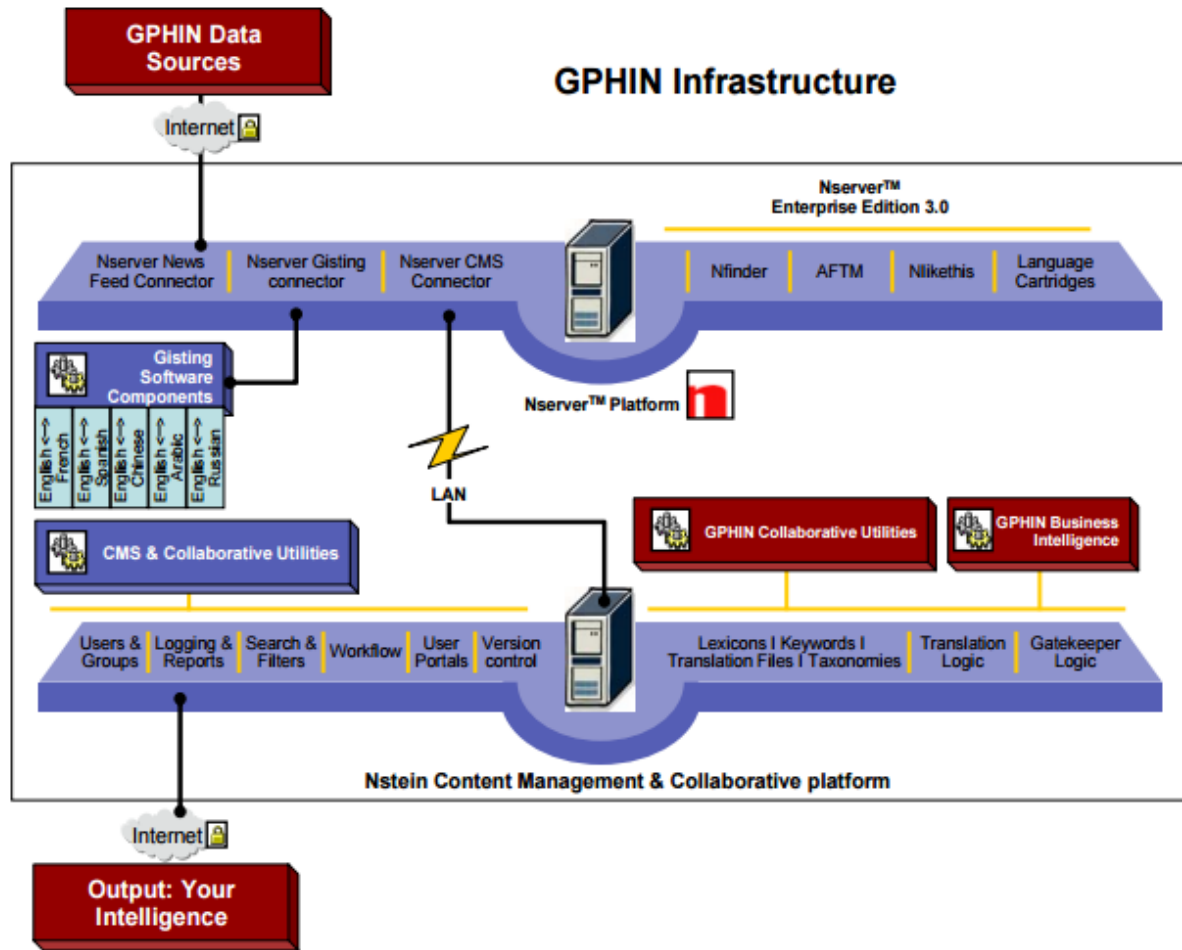
By Christopher R. Braden, Scott F. Dowell, Daniel B. Jernigan, and James M. Hughes - Emerging Infectious Diseases Journal, Volume 19, Number 6—June 2013, <http://wwwnc.cdc.gov/eid/article/19/6/13-0192-f1.htm>, Public Domain, <https://commons.wikimedia.org/w/index.php?curid=26334381>



SARS

Global Public Health

Intelligence Network (GPHIN)⁸





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ORIGINAL ARTICLE

Identification of Severe Acute Respiratory Syndrome in Canada

Susan M. Poutanen, M.D., M.P.H., Donald E. Low, M.D., Bonnie Henry, M.D., Sandy Finkelstein, M.D., David Rose, M.D., Karen Green, R.N., Raymond Tellier, M.D., Ryan Draker, B.Sc., Dena Adachi, M.Sc., Melissa Ayers, B.Sc., Adrienne K. Chan, M.D., Danuta M. Skowronski, M.D., M.H.Sc., Irving Salit, M.D., Andrew E. Simor, M.D., Arthur S. Slutsky, M.D., Patrick W. Doyle, M.D., M.H.Sc., Mel Krajden, M.D., Martin Petric, Ph.D., Robert C. Brunham, M.D., and Allison J. McGeer, M.D., for the National Microbiology Laboratory, Canada, and the Canadian Severe Acute Respiratory Syndrome Study Team*

N Engl J Med 2003; 348:1995-2005 | [May 15, 2003](#) | DOI: 10.1056/NEJMoa030634

Share:     



Middle East Respiratory Syndrome (MERS- CoV)



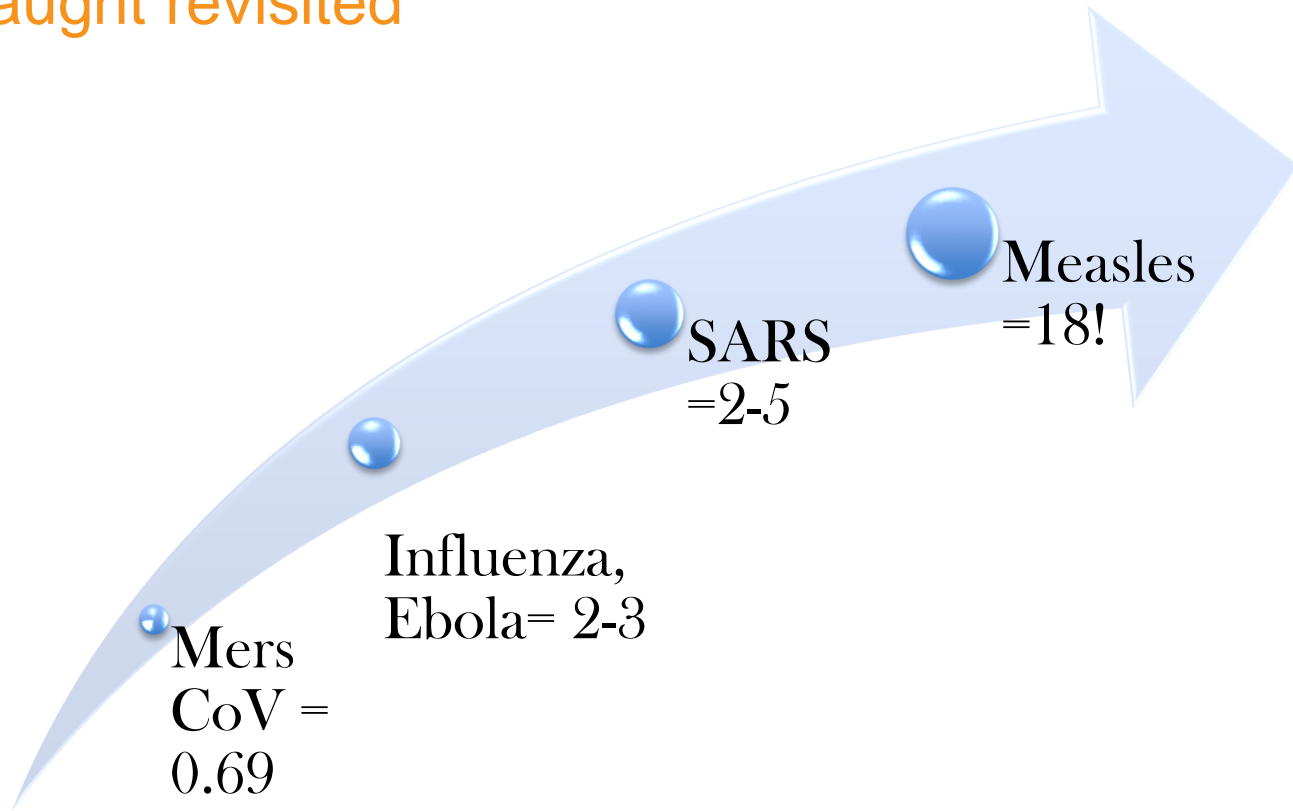
- Caused by coronavirus (similar to SARS)
- First case identified in 2012
- Mostly limited to the Arabian Peninsula
- Symptoms: fever, cough, shortness of breath, pneumonia
- Mortality rate 35+%
- Can be transmitted from person-to-person (not sustained)



https://upload.wikimedia.org/wikipedia/commons/4/44/Masjid_al-Haram_panorama.JPG



R naught revisited





Zika Virus – The New Kid on the Block (or not)

- Flavivirus first identified in Africa in 1947
- Transmitted by *Aedes* mosquitoes
- Sporadic outbreaks for 50 years
- Epidemics: 2007 in Micronesia and 2013 in French Polynesia
- Introduced to Brazil in 2014
- Only 20% of people with symptoms: fever, rash, fatigue
- Essentially a non-fatal disease in adults
- No specific treatment or vaccine available
- Mosquito control measures





Zika Virus – Areas with Active Transmission

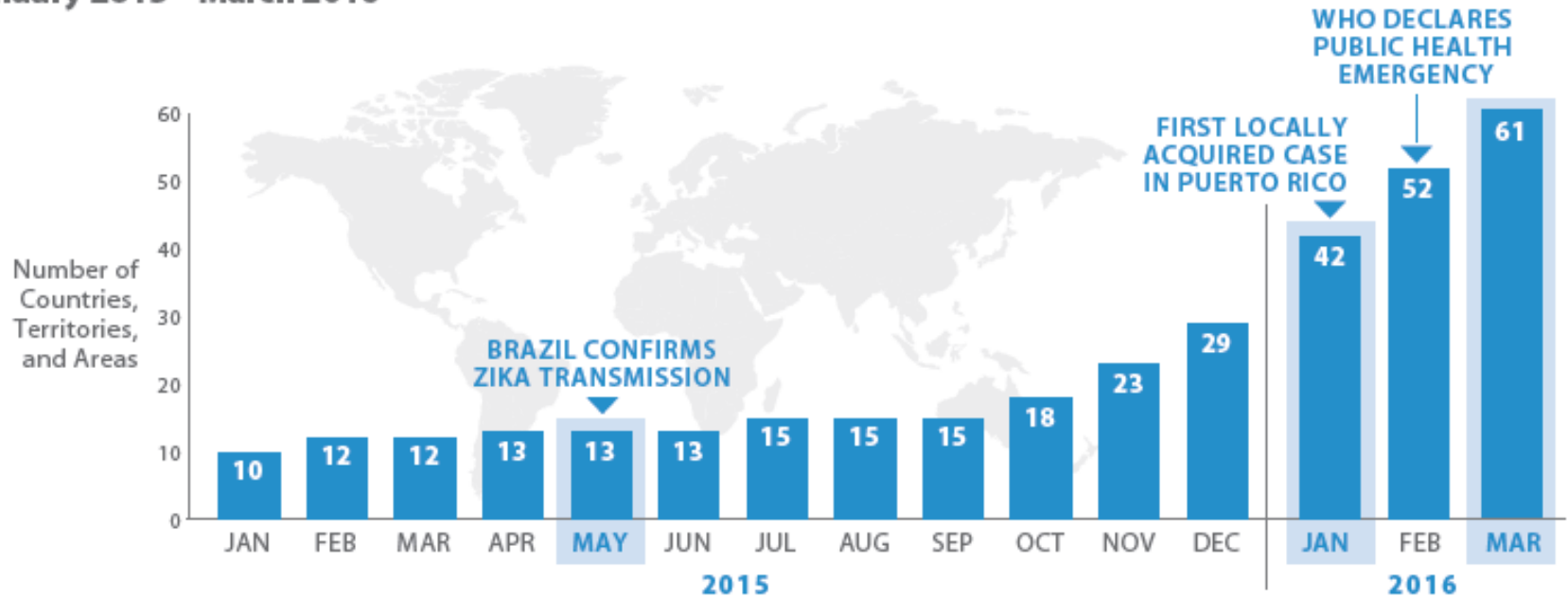


Sources: <http://www.cdc.gov/zika/geo/active-countries.html>



Zika Virus – Areas with Active Transmission

Cumulative Number of Countries, Territories and Areas Worldwide Reporting Local Zika Virus Transmission, January 2015 – March 2016



Sources: Kaiser Family Foundation



Zika Virus – What's the Risk?



**World Health
Organization**

**ZIKA VIRUS
MICROCEPHALY
AND GUILLAIN-BARRÉ SYNDROME**

**SITUATION REPORT
21 APRIL 2016**



<http://www.who.int/emergencies/zika-virus/situation-report/24-march-2016/en/>



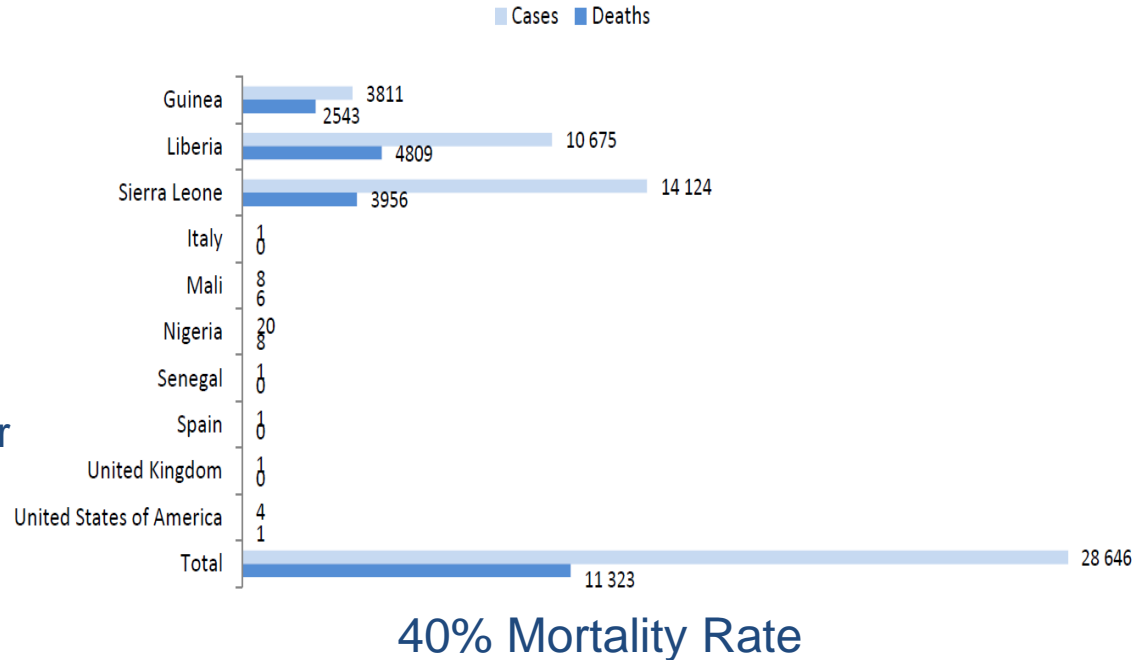
Zika and Microcephaly Risk⁹

Overall ZIKV infection rate	Estimated microcephaly risk (%)							
	Baseline		With 1 st trimester ZIKV infection		With 2 nd trimester ZIKV infection		With 3 rd trimester ZIKV infection	
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI
10%	0.021	(0.02, 0.024)	6.38	(5.75, 7.01)	0.025	(0.001, 0.092)	0.027	(0.001, 0.098)
20%	0.021	(0.02, 0.024)	3.23	(2.92, 3.56)	0.013	(0, 0.047)	0.014	(0, 0.052)
30%	0.021	(0.02, 0.024)	2.19	(1.98, 2.41)	0.009	(0, 0.031)	0.01	(0, 0.036)
40%	0.021	(0.02, 0.024)	1.66	(1.51, 1.83)	0.006	(0, 0.023)	0.008	(0, 0.028)
50%	0.021	(0.02, 0.024)	1.35	(1.22, 1.49)	0.005	(0, 0.018)	0.006	(0, 0.023)
60%	0.021	(0.02, 0.024)	1.14	(1.03, 1.25)	0.004	(0, 0.015)	0.006	(0, 0.021)
70%	0.021	(0.02, 0.024)	0.993	(0.899, 1.09)	0.004	(0, 0.013)	0.005	(0, 0.018)
80%	0.021	(0.02, 0.024)	0.883	(0.798, 0.971)	0.003	(0, 0.012)	0.005	(0, 0.017)



Ebola

- 20 significant outbreaks since 1976, previous largest was in 2000 in Uganda with 425 cases
- The recent outbreak is Zaire Ebola virus (deadliest type); started in Guinea, December 2013 and is the largest in history



Source: WHO – Ebola Situation Report – 30 Mar 2016



Ebola

- Natural reservoirs remain unknown – endemic in West Africa
- Spread by direct contact with blood or body fluids
- Average incubation period 11.4 days (2-21 days)
- Mean time to death after admission to hospital 4.2 ± 6.4 days
- Mean time to discharge 11.8 ± 6.1 days
- Case fatality rate 40+%
- No vaccine – multiple trials are underway

Source: WHO



Dengue Fever

- Flavivirus – 4 types – transmitted by *Aedes* mosquito
- Occurs in tropical and sub-tropical parts of the world
- 390 million + cases/year globally
- Pan American Health Organization: 2003 -> 2013 cases increased by a factor of 5
- Symptoms: asymptomatic infection -> hemorrhagic fever and shock
- 500,000 hospitalizations/year
- Overall mortality < 1%, but hemorrhagic fever mortality up to 50%



Source: <http://www.who.int/mediacentre/factsheets/fs117/en/>



Dengue – Vaccine Progress

The NEW ENGLAND
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ESTABLISHED IN 1812

JANUARY 8, 2015

VOL. 372 NO. 2

Efficacy of a Tetravalent Dengue Vaccine in Children
in Latin America

- Phase 3 trial in 5 Latin American countries
- Children 9 – 16 years, 3 injections
- Followed for 25 months
- Results:
 - Overall vaccine efficacy: 64.7%
 - Efficacy against hospitalization: 80.3%
 - Efficacy against severe disease: 95.5%
 - Safety profile same as placebo



Chikungunya

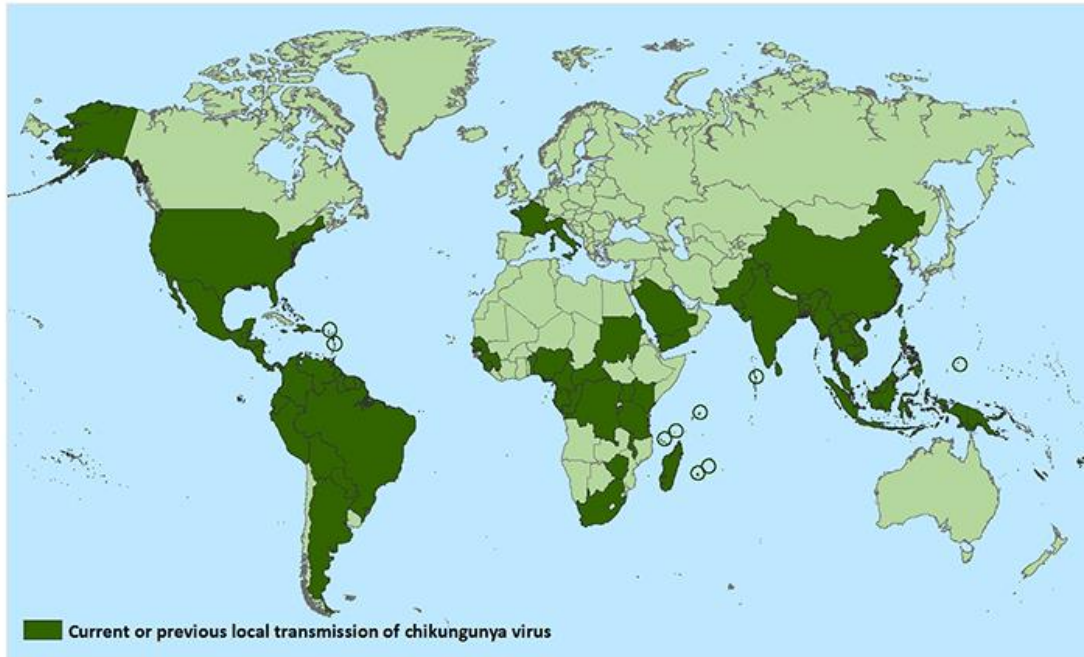
- Alphavirus causing an acute dengue-like disease – first identified in Africa in 1952
- Introduced to Caribbean and the Americas in 2013
- Transmitted by *Aedes* mosquitoes
- High fever, joint and muscle pain, headache (7 – 10 days)
- Usually not fatal
- No specific treatment or vaccine available
- Mosquito control measures
- Up to 60% have joint pain at 3 years and some have cognitive impairment



Sources: N ENGL J MED 2015;372;1231-9 / PLoS Negl Trop Dis 7(3): e2137

Chikungunya

Countries and territories where chikungunya cases have been reported* (*as of April 22, 2016*)



*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.

Source: CDC



Anti-microbial Resistance (AMR)

- **Anti-microbial:** a compound (naturally occurring or modified) with an ability to inhibit or kill micro-organisms which is made into medication for humans or animals to treat infections
- **Anti-biotic:** an antimicrobial specifically directed against bacterial infections
- Penicillin discovered by Fleming in 1928
- 20th century notable for discovery of many anti-microbials and significant success in clinical medicine
- **The Problem:** Micro-organisms have an ability to mutate and become *resistant* to anti-microbials



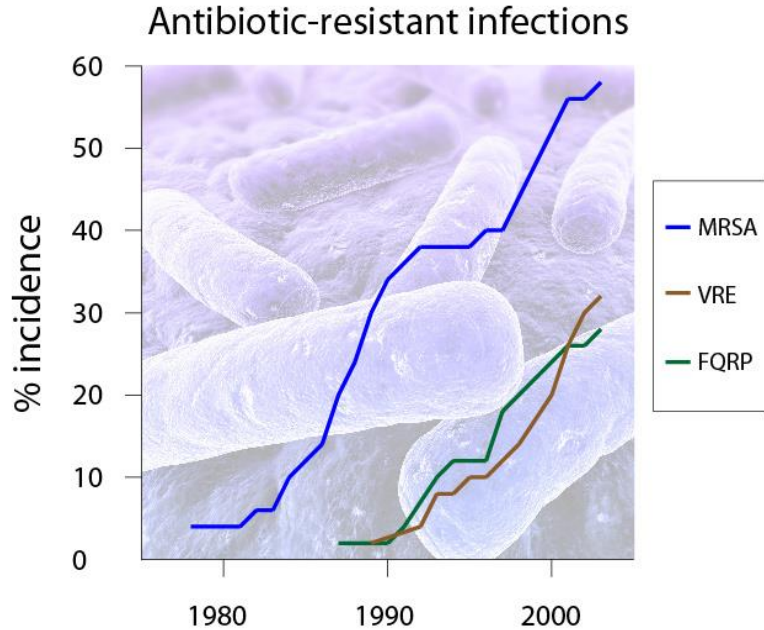


Era of “Superbugs”

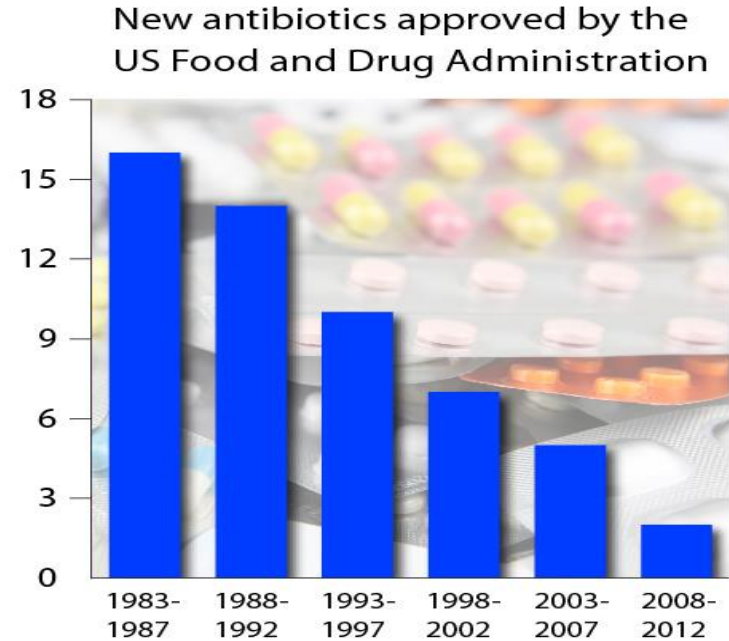
“The emergence of MCR-1 heralds the breach of the last group of antibiotics, polymyxins, by plasmid-mediated resistance.”¹⁰



Anti-microbial Resistance (AMR)



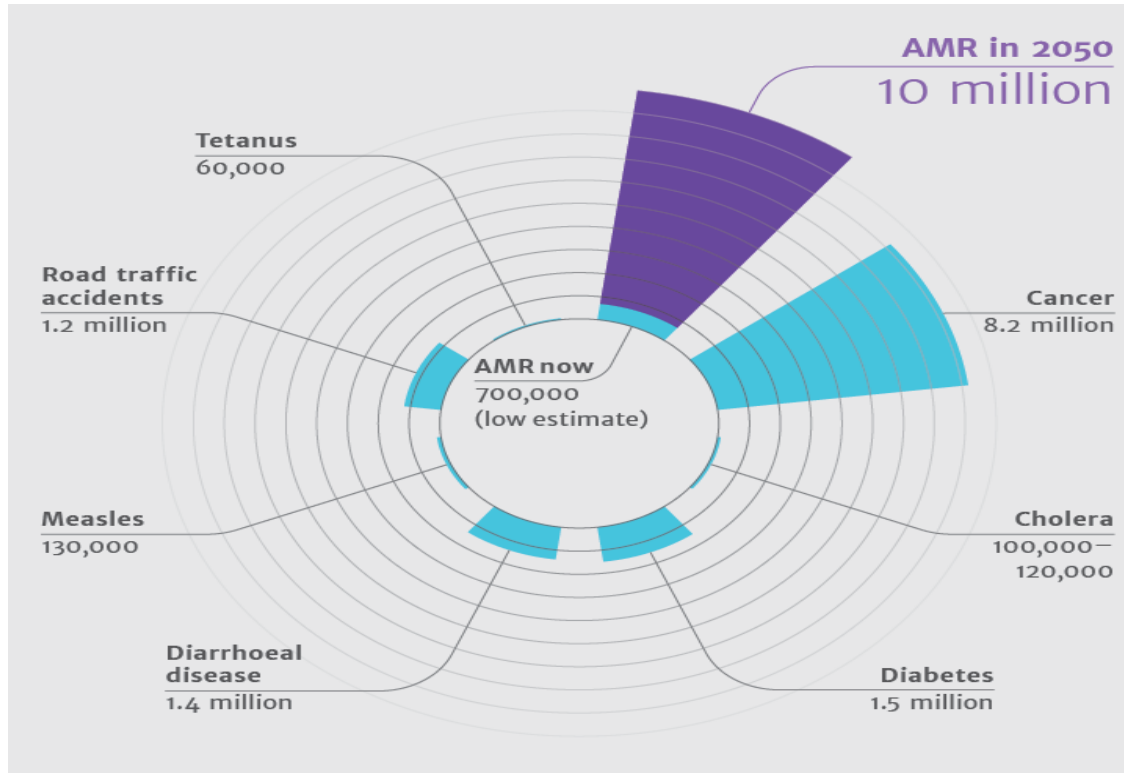
Source: Centers for Disease Control and Prevention



Source: Infectious Diseases Society of America



Anti-microbial Resistance (AMR)





Anti-microbial Resistance (AMR): Solutions

- International cooperation – governments and researchers
- Track anti-microbial resistance patterns, speed diagnosis
- Ensure appropriate use of anti-microbials by doctors and patients
- Increase development of new anti-microbials and streamline process
- Leverage technology to develop speed diagnosis, alternative treatments
 - Genetics, genomics, vaccines, and “big data”

RTGA approach to Epidemics, Pandemic and Infectious Disease Monitoring



RGA Epidemic/Pandemic Approach

- Pandemic Risk Governance Team
 - Ebola Guidance and update
 - First industry Zika white paper
- Longer Life Foundation
- Infectious Disease Consultation – CIDRAP, Bluedot
 - Flu Vaccine Effectiveness study





Longer Life Foundation



Identification of Human Genetic Variants for High Risk of Severe Influenza Disease

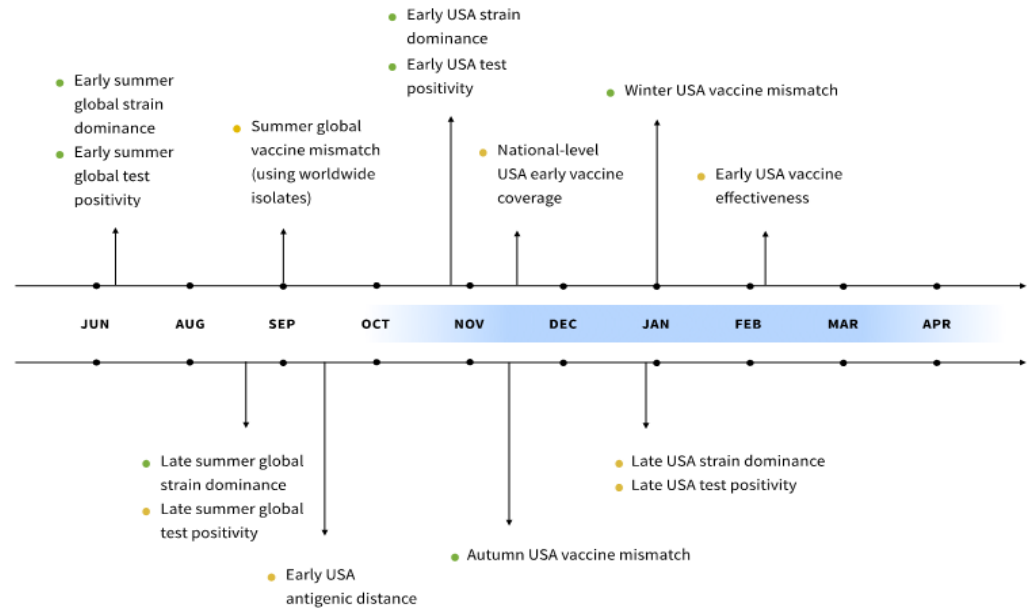
Adrianus Boon, Ph.D.

Project Overview:

Influenza virus kills nearly 500,000 individuals each year and this number can increase dramatically during a pandemic with a novel strain of influenza virus. Infections with influenza virus can be prevented by antiviral drugs like oseltamivir or vaccinations. However, antiviral drugs are not prescribed prophylactically and vaccination is not monitored for efficacy providing ample opportunity for influenza to infect and cause disease. If we can identify individuals that are at increased risk of severe influenza virus we can tailor our care to provide drugs prophylactically to improve health and longevity. The goal of our research is to define genetic biomarkers that predict susceptibility to influenza disease. The interferon pathway is very important for restricting influenza virus replication and therefore disease. Individuals with unique or rare polymorphisms in essential genes in this pathway are more susceptible to influenza virus and more likely to require hospital care or succumb to infection. Because of the importance of this pathway we want to study polymorphisms in two interferon pathway genes that have previously been shown to effect viral diseases and antiviral immunity. These polymorphisms are relatively common in the population with about 5-10% of all people carrying two copies of the minor allele. To test if these genetic differences between individuals predispose to more severe disease we will use cultured primary human airway epithelial cells as a model to look at the role of these polymorphisms on disease parameters. Airway epithelial cells are the primary target cell of influenza virus and we know that increased virus replication and attenuated antiviral immunity correlate with severe disease. We will determine virus replication and antiviral gene-expression in cells obtained from individuals with different IFN genotypes. Analysis of the data between cells containing the two alleles will reveal if this genetic marker can be used to identify individuals that are genetically susceptible to influenza virus. The identification of prognosticators of influenza disease and survival is of special interest to the Foundation and leads to fewer influenza associated deaths and hospitalizations.



Influenza Modeling



LEGEND - Colours represent strength of evidence for association with excess influenza mortality:

- Evidence in literature and models
- Evidence in literature but not models

■ Influenza Season (October to April)



Influenza Modeling

Early Results (15 years of data)

Influenza Test Positivity

- For every one percentage point increase in the proportion of positive tests for influenza globally in **June**, excess mortality in the upcoming influenza season increased by 3%

Dominant influenza subtype

- An H3 strain was dominant globally in June, a 52% increase in excess mortality due to influenza would have been expected in the upcoming influenza season.
- If an H3 strain was dominant in November, it would be associated with a 130% increase in excess mortality due to influenza.

Vaccine match

- The antigenic match over the summer reported by the CDC in September/October was not found to be statistically significantly predictive of reduced rates of excess mortality.
- If greater than 90% of the H3 isolates by the end of November matched the vaccine strain, mortality decreased by 45% compared to years where it did not match.



Center for Infectious Disease Research and Policy
University of Minnesota

- Led by Michael T. Osterholm, PhD, MPH, an international authority on emerging infectious diseases
- Emerging Situation Intelligence Calls
- Infectious Disease Briefings
- Decision-Point Dialogues
- Daily News Service
- Virtual Table Top Pandemic Simulation exercises



Questions?





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9. Johansson, Michael A., Luis Mier-y-Teran-Romero, Jennita Reefhuis, Suzanne M. Gilboa, and Susan L. Hills. 2016. "Zika and the Risk of Microcephaly." *New England Journal of Medicine* 375 (1): 1–4. doi:10.1056/NEJMp1605367.
10. Liu, Yi-Yun, Yang Wang, Timothy R. Walsh, Ling-Xian Yi, Rong Zhang, James Spencer, Yohei Doi, et al. 2016. "Emergence of Plasmid-Mediated Colistin Resistance Mechanism MCR-1 in Animals and Human Beings in China: A Microbiological and Molecular Biological Study." *The Lancet. Infectious Diseases* 16 (2): 161–68. doi:10.1016/S1473-3099(15)00424-7.

Thank you

