Emerging infections in the US

Martin Rodriguez
Roadmap

✧ Introduction
✧ Review of some emerging and reemerging infections in the US
✧ Concerns for the future
Introduction
Infectious diseases in humans

- Over a thousand human pathogens
- Tremendous impact in humans in history

<table>
<thead>
<tr>
<th>Era</th>
<th>Life Expectancy at Birth (years)</th>
<th>Life Expectancy at Older Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper Paleolithic</td>
<td>33</td>
<td>At age 15, life expectancy an additional 39 years (total age 54).¹⁹¹⁰</td>
</tr>
<tr>
<td>Neolithic¹¹</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Bronze Age and Iron Age¹²</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Classical Greece¹³</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Classical Rome¹³</td>
<td>28</td>
<td>At age 15, life expectancy an additional 37 years (total age 52).¹²¹³</td>
</tr>
<tr>
<td>Pre-Columbian North America¹⁴</td>
<td>25-30</td>
<td></td>
</tr>
<tr>
<td>Medieval Islamic Caliphate¹⁵</td>
<td>35+</td>
<td></td>
</tr>
<tr>
<td>Medieval Britain¹⁶¹⁷</td>
<td>30</td>
<td>At age 21, life expectancy an additional 43 years (total age 64).¹⁸¹⁷</td>
</tr>
<tr>
<td>Early Modern Britain¹²¹⁰¹⁹</td>
<td>25-40</td>
<td></td>
</tr>
<tr>
<td>Early 20th Century²⁰²¹</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>2010 world average²²</td>
<td>67.2</td>
<td></td>
</tr>
</tbody>
</table>
Top causes of death, 1900 vs 2010

Some important epidemics in history

✧ “Plague”
  ➢ Europe, 541-542 CE, 40% of Constantinople population died, bubonic plague
  ➢ Europe and Asia, 1347-1351 CE, killed more than 70 million people, bubonic plague

✧ Measles and smallpox
  ➢ Conquest of America, up to 10 million people

✧ Flu
  ➢ 1918-19, 30-50 million deaths (World war I, about 37 million)
Definitions

✧ Emerging infectious disease
  ➢ An infectious disease that has newly appeared in a population, or that has been known previously but is rapidly increasing in incidence or geographic range

✧ Reemerging infectious disease
  ➢ An infectious disease that had been present at the location in the past and was considered eradicated or controlled, but now is coming back
Emerging and reemerging infections

Where did HIV come from?

- Zoonosis
- HIV-1
  - From chimpanzee simian immunodeficiency virus (SIV) in the early 1900s, in the DRC
What has happened since then?

Probable Routes of Initial Global Spread of HIV-1 in the 1960s and 1970s

Exponential Epidemic Growth

WHO: 40 M infected 2000
Adults and children estimated to be living with HIV | 2013

Total: 35.0 million [33.2 million – 37.2 million]
Emerging and re-emerging infectious diseases
2 yo boy develops red eyes, runny nose, fever, followed by rash after visiting Disneyland

Family opted to not vaccinate him
What is the diagnosis?

a) Enterovirus
b) Adenovirus
c) Measles
d) Rubella
e) Kawasaki syndrome
Epidemiology of measles

✧ In the world
  ➢ 20 million cases worldwide per year, 146000 deaths

✧ In Europe
  ➢ Ongoing outbreaks in many countries, 30000 in France
  ➢ Many unvaccinated

✧ In the US
  ➢ In 2000, measles was declared eliminated from the US
  ➢ Cases and outbreaks still occur, imported
  ➢ Most cases occur in unvaccinated people
U.S. Measles Cases by Year

*Provisional data reported to CDC’s National Center for Immunization and Respiratory Diseases*
2015 Measles Cases in the U.S.
January 1 to March 20, 2015

Cases*:
- 0
- 1-4
- 5-9
- 10-19
- 20+

*Provisional data reported to CDC’s National Center for Immunization and Respiratory Diseases

† CDC will update these data weekly on Mondays.
Number of Reported Measles Cases with onset date from Jan 2012 to Jul 2012

Data source: surveillance DEF file
Data in HQ as of 8 August 2012

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.
Measles

✧ Fever, runny nose, cough, conjunctivitis, malaise
  ➢ Koplik’s spots: "grains of salt on a red background"

✧ Maculopapular rash
  ➢ Starts on face, spreads distally
  ➢ Darkens after 3-4 days

✧ Complications
  ➢ Transient immunosuppression
  ➢ Pneumonia, encephalitis
What measures do you need to implement if the patient is admitted?

a) Contact precautions
b) Droplet precautions
c) Airborne precautions
d) Make sure all involved healthcare workers have had 1 MMR vaccine
Measles

- Highly contagious (90% if unvaccinated)
  - Incubation 6-19 days
  - Contagious 5 days before rash - 4 days after it appears
- Infection control
  - Airborne, communicate with HD within 24 hours
- Laboratory confirmation
  - Measles-specific IgM
  - RNA by RT-PCR (throat or nasopharyngeal swab)
- Evidence of immunity
  - 2 doses of MMR (97% vs 93%), birth before 1957
Other “old infections” in the US

- **Mumps**
  - 1151 cases in 2014

- **Pertussis**
  - 28660 cases in 2014, 279 in AL

*Data from CDC National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System.*
38 yo man, 3 day of fever, joint pains, headache
On day 2 developed a rash, and on day 3 swollen joints
WBC 4.2 (%: 80N, 10L, 5M, 1B), normal Hct and plt
Came back 1 week ago from the Dominican Republic
What is the most likely diagnosis?

a) Meningococcemia
b) West Nile virus
c) Chikungunya
d) Dengue
e) Malaria
Chikungunya fever

✧ Vector: *Aedes aegypti* and *A. albopictus*
✧ Described in Africa
  - Makonde language, “that which bends up”
✧ Epidemiology
  - Africa
  - Asia, large outbreak in Indian Ocean in early 2000s, later in SE Asia
  - Latin America and Caribbean: large outbreak since 2013
Countries and territories where chikungunya cases have been reported*
(as of March 10, 2015)

Current or previous local transmission of chikungunya virus
In 2014, 2492 were reported to in the US
Chikungunya fever

- Incubation: 1-12 days (mean 3)
- Most are symptomatic
  - Fever, chills, headache, nausea, vomiting, photophobia
  - Arthralgias: polyarticular, migratory
  - Can evolve to arthritis, similar to RA, large and small joints
  - Rash: flushing then maculopapular rash, < 50% of cases
  - Lymphopenia is common
  - Rare complications: encephalitis, myocarditis
Chikungunya arthritis

Simon et al. Medicine 2007; 86 (3)
Chikungunya fever

 diagnoses

 ➢ Chikungunya-specific IgM detectable at 5-7 days
 ➢ RT-PCR within 1st 5 days

 treatment

 ➢ Supportive care, NSAIDS
 ➢ Referral to rheumatologist if symptoms persist

 prevention

 ➢ Insect repellant
 ➢ Vaccine in development
27 yo woman with 3 days of fevers, headache, muscle aches and a rash
Came from Honduras 4 days ago
WBC 2.31, HCT 40.3, plt 116
UA 3+blood, 60-70 RBC
What is the most likely diagnosis?

a) Dengue
b) Leptospirosis
c) Acute HIV
d) Hantavirus
e) SLE
Dengue

- The most important arthropod-borne viral disease
- Dramatic increase in recent years, 100 countries
- Estimates of up to 390 million infections per year, almost 100 million symptomatic
- In Latin America, 66K cases in 1980, 700K in 2000
- In the US mostly seen in travelers
  - Endemic disease reported from FL, TX, over 1000 cases from Puerto Rico

Dengue

- Transmitted by *Aedes aegypti* and *A. albopictus*
- Predominantly in urban areas
Dengue, geographic distribution

Dengue cases reported to WHO
Dengue

- Incubation 3-14 days
- Most asymptomatic or nonspecific illness
- Fever, headache, retroorbital pain, muscle and joint pains
- Maculopapular rash, 2-5 days after fever, seen in 50%, “white islands in a sea of red”
- Leukopenia, thrombocytopenia, elevated LFTs, abnormal coags

Complications of dengue

✧ Shock
  ➢ Capillary leak
  ➢ Hemoconcentration

✧ Hemorrhage
  ➢ Thombocytopenia
  ➢ Prolonged coags

✧ Encephalitis, hepatitis, myocarditis
Dengue

診断
- Dengue-specific IgM detectable at 5-7 days
- RT-PCR within 1st 5 days

治療
- Supportive care, blood products if needed
- Volume status (shock or edema)

予防
- Insect repellent
- Vaccines being developed
56 year-old man from Montgomery comes in with fever, confusion, and leg weakness for 4 days (August)

Temp 104, confused, strength 5/5 in the arms, 3/5 in the lower extremities, decreased DTR in legs, tremors

CSF: WBC 1351, 70% polys, 30% lympho/monos, culture negative
What is the most likely diagnosis?

a) Eastern equine encephalitis
b) West Nile encephalitis
c) Enterovirus D68 encephalitis
d) Pneumococcal meningitis
e) Meningococcal meningitis
West Nile virus (WNV)

- Became famous in 1999 after outbreak in NYC
- Spread to the rest of continental US
- Transmitted by Culex mosquitoes, summer or fall
Global distribution of West Nile virus
Spread of WNV in US

- 62 cases in 1999, 2469 in 2013
- 39,557 cases between 1999 and 2013, 1554 deaths

West Nile virus

- Asymptomatic, 80%
- Nonspecific febrile illness, about 20%
  - Rash, malaise, fatigue, fever, myalgias
- Neuroinvasive disease, 1/150
  - Encephalitis, meningoencephalitis, meningitis
  - Poliomyelitis (acute flaccid paralysis)
- Case fatality rate in neuroinvasive disease 2-12%
- Some left with persistent fatigue, weakness
You suspect West Nile virus, how would you confirm the diagnosis?

a) Serum PCR for WNV
b) CSF PCR for WNV
c) CSF viral culture
d) WNV serologies from CSF and/or serum
West Nile virus

診断

- WNV IgM in CSF or serum
- WNV IgG fourfold increase
- PCR and culture low sensitivity

治療

- Supportive care

防止

- Insect repellent
42 yo man with a new skin lesion
Fatigue, arthralgia, and headache for 2 days
Few days ago visited Connecticut and went hiking (Summer)
What would you do next?

a) Start amoxicillin, no need for serology
b) Check Lyme IgM
c) Check Lyme IgG
d) Check Lyme IgM and IgG
e) Check Lyme Western Blot
Lyme disease

- Most common arthropod-borne illness in the US
  - 1000 cases in 1990, now 30000 per year
  - In the NE, mid Atlantic and mid Western states
- Caused by *Borrelia burgdorferi*
- Transmitted by *Ixodes* ticks
  - Infected from animals and pass to humans (nymphs)
  - Spring and Summer
  - Tick has to be attached to human for 36-48 hours
- Incubation time 1-2 weeks
Reported Cases of Lyme Disease by Year, United States, 1995-2013

- Confirmed cases
- Probable cases*

Cases

Confirmed cases in 2013

1 dot placed randomly within county of residence for each confirmed case

Erythema chronicum migrans

✧ Small papule or macule, site of the tick bite, enlarges
  ➢ Common in groin, axilla, legs
  ➢ 2/3 classic bull’s-eye
  ➢ 20% have multiple lesions
✧ No need for confirmatory test if right presentation and epi
✧ Fatigue, headache, arthralgia, myalgia, and, less often, fever
Classic EM—Circular red rash with central clearing that slowly expands

Bluish hue without central clearing

Red, expanding lesion with central crust

Red, oval-shaped plaque on trunk

Red-blue lesion with central clearing on back of knee

Early disseminated Lyme disease—multiple red lesions with dusky centers
Lyme disease

✧ Early disseminated disease weeks to months after bite
  ➢ Neurological
    ✓ CN palsy, meningoencephalitis, radiculitis, neuropathy
  ➢ Cardiac
    ✓ Myopericarditis, AV heart block
✧ Late disease: months to years after bite
  ➢ Arthritis
    ✓ Large joints, mostly knees
  ➢ Encephalopathy, polyneuropathy
Two-Tiered Testing for Lyme Disease

First Test

- Enzyme Immunoassay (EIA)
- OR
- Immunofluorescence Assay (IFA)

Positive or Equivocal Result

Negative Result

Consider alternative diagnosis

OR

If patient with signs/symptoms consistent with Lyme disease for ≤ 30 days, consider obtaining a convalescent serum

Second Test

- Signs or symptoms ≤ 30 days
  - IgM and IgG Western Blot
- Signs or symptoms > 30 days
  - IgG Western Blot ONLY
<table>
<thead>
<tr>
<th>Condition and Recommended Drug</th>
<th>Dose(^a)</th>
<th>Duration(^\dagger) days</th>
<th>Comments(^g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythema migrans</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doxycycline (for patients ≥8 yr of age)</td>
<td>200 mg/day (pediatric dose, 4 mg/kg/day) orally, divided into two doses per day</td>
<td>14 (range, 10–21)</td>
<td>Do not use to treat children &lt;8 yr of age or women who are pregnant or lactating; warn patient about exposure to sun, since photosensitivity rash occurs in 20–30% of patients; drug has good penetration into the central nervous system; patient should take drug with fluids to minimize nausea and gastrointestinal irritation; also effective against granulocytic anaplasmosis but not against babesiosis</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>1500 mg/day (pediatric dose, 50 mg/kg/day) orally, divided into three doses per day</td>
<td>14 (range, 14–21)</td>
<td>This agent is not effective against granulocytic anaplasmosis or babesiosis</td>
</tr>
<tr>
<td>Cefuroxime axetil</td>
<td>1000 mg/day (pediatric dose, 30 mg/kg/day) orally, divided into two doses per day</td>
<td>14 (range, 14–21)</td>
<td>This agent is not effective against granulocytic anaplasmosis or babesiosis</td>
</tr>
<tr>
<td>Meningitis(\S)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>2 g/day (pediatric dose, 50–75 mg/kg/day) intravenously once per day</td>
<td>14 (range, 10–28)</td>
<td>Treatment has risks associated with indwelling catheters, including infection, and can cause pseudolithiasis in the gallbladder</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>6 g/day (pediatric dose, 150–200 mg/kg/day) intravenously, divided into doses administered every 8 hr</td>
<td>14 (range, 10–28)</td>
<td>Treatment has risks associated with indwelling catheters, including infection</td>
</tr>
<tr>
<td>Cranial-nerve palsy without clinical evidence of meningitis(\S)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doxycycline (for patients ≥8 yr of age)</td>
<td>200 mg/day (pediatric dose, 4 mg/kg/day) orally, divided into two doses per day</td>
<td>14 (range, 14–21)</td>
<td>See comments for drugs used to treat erythema migrans; there is not good evidence that treatment changes the outcome of facial palsy, but it does prevent additional sequelae of infection</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>1500 mg/day (pediatric dose, 50 mg/kg/day) orally, divided into three doses per day</td>
<td>14 (range, 14–21)</td>
<td></td>
</tr>
<tr>
<td>Cefuroxime axetil</td>
<td>1000 mg/day (pediatric dose, 30 mg/kg/day) orally, divided into two doses per day</td>
<td>14 (range, 14–21)</td>
<td></td>
</tr>
<tr>
<td>Carditis</td>
<td>Same oral agents as for erythema migrans; same parenteral agents as for meningitis</td>
<td>Same doses as for oral and parenteral agents used to treat erythema migrans</td>
<td>14 (range, 14–21)</td>
</tr>
<tr>
<td>Arthritis</td>
<td>Same oral agents as for erythema migrans; same parenteral agents as for meningitis</td>
<td>Same doses as for oral and parenteral agents used to treat erythema migrans</td>
<td>28</td>
</tr>
</tbody>
</table>
Post treatment Lyme syndrome

✧ 10-20% appropriately treated patients with confirmed Lyme disease may have chronic symptoms
  ➢ Fatigue, myalgias, arthralgias
✧ Cause unknown
✧ Placebo-controlled randomized trials have not shown benefits of more treatment
Lyme disease

✿ Prevention

- Awareness, check for ticks, insect repellent
- Removal of tick
- Vaccine withdrawn from market
- Doxycycline 200 mg within 72 hours after tick removal, consider if engorged nymphal tick
✧ 63 yo lady comes in with 3 days of fever, chills, headache, sweats, diarrhea
✧ Lives in rural AL, around woods, recent tick bites
✧ Summer time
✧ On exam febrile, has faint rash in trunk
✧ WBC 1.7 (80%PMN, 15% L), plt 40000, AST 150, ALT 214
How would you manage this patient while awaiting test results?

a) Observe for now awaiting results of tests
b) Start vancomycin and piperacillin/tazobactam
c) Start linezolid
d) Start ceftriaxone
e) Start doxycycline
Ehrlichiosis

- Transmitted by Lone Star ticks
  - Most recall bites
- *Ehrlichia chaffeensis*
- *Anaplasma phagocytophilum*
Ehrlichiosis

- Fever, headache, malaise, myalgias
- Nausea vomiting
- Confusion
- Leukopenia, lymphopenia, thrombocytopenia
- Hepatitis
Ehrlichiosis

診断

- Serology, 可能在第一周時為陰性，康復期 titre
- PCR
- Morulae
  - 20% in HME, up to 80% in HGA
Ehrlichiosis

✧ Treatment
  - Doxycycline, start empirically, serologies take time
  - Occasional mortality

✧ Prevention
  - Awareness of ticks
  - Insect repellent
Rickettsia parkeri
Many other tickborne illnesses in the US

✧ Viral: Powassan, Colorado tick bite fever
✧ Presumed bacteria: STARI, relapsing fever, tularemia
✧ Protozoan: Babesia
✧ Recently described infections
  ➢ *Borrelia miyamotoi* in the NE
  ➢ Heartland virus in Missouri and Tennessee
  ➢ Bourbon virus
Concerns for the future
Dr. William H. Stewart,
US Surgeon General
1965-1969

“It is time to close the book on infectious diseases, and declare the war against pestilence won”
Concerns for the future

✧ Old pathogens
  ➢ Increasing incidence, resistance
  ➢ Few new antimicrobials in the pipeline
  ➢ Anti vaccine movement

✧ New pathogens
  ➢ Zoonosis
  ➢ Vector borne illnesses

✧ Expansion into new territories
  ➢ Animal and human migration
  ➢ Travel
Vaccines

PRE-VACCINE ERA ESTIMATED ANNUAL MORBIDITY IN THE U.S.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Percentage Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>100%</td>
</tr>
<tr>
<td>H. Influenza</td>
<td>99%</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>91%</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>83%</td>
</tr>
<tr>
<td>Measles</td>
<td>99%</td>
</tr>
<tr>
<td>Mumps</td>
<td>99%</td>
</tr>
<tr>
<td>Pertussis</td>
<td>93%</td>
</tr>
<tr>
<td>Pneumococcal Disease</td>
<td>74%</td>
</tr>
<tr>
<td>Polio</td>
<td>100%</td>
</tr>
<tr>
<td>Rubella</td>
<td>99%</td>
</tr>
<tr>
<td>Congenital Rubella</td>
<td>99%</td>
</tr>
<tr>
<td>Smallpox</td>
<td>100%</td>
</tr>
<tr>
<td>Tetanus</td>
<td>98%</td>
</tr>
<tr>
<td>Varicella</td>
<td>89%</td>
</tr>
</tbody>
</table>

MOST RECENT REPORTS OF CASES IN THE U.S.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Cases in the U.S.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>0</td>
</tr>
<tr>
<td>H. Influenza</td>
<td>243</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>11,049</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>11,267</td>
</tr>
<tr>
<td>Measles</td>
<td>61</td>
</tr>
<tr>
<td>Mumps</td>
<td>982</td>
</tr>
<tr>
<td>Pertussis</td>
<td>13,506</td>
</tr>
<tr>
<td>Pneumococcal Disease</td>
<td>4,167</td>
</tr>
<tr>
<td>Polio</td>
<td>0</td>
</tr>
<tr>
<td>Rubella</td>
<td>4</td>
</tr>
<tr>
<td>Congenital Rubella</td>
<td>1</td>
</tr>
<tr>
<td>Smallpox</td>
<td>0</td>
</tr>
<tr>
<td>Tetanus</td>
<td>14</td>
</tr>
<tr>
<td>Varicella</td>
<td>449,363</td>
</tr>
</tbody>
</table>
In 2010, over 940 million international tourist arrivals

8% of Americans travel to developing world per year

1-5% become ill
Global hot spots for emerging zoonosis

Figure 1: Global hotspots for emerging infectious diseases that originate in wildlife

Questions