Emerging Infectious Diseases

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Factors leading to disease emergence

- Resistance
  - Non-adherence
  - Overuse or misuse of antibiotics
  - Resistance to insecticidés (insect vectors)
- Population expansion and migration
  - Urbanization
  - Poverty
- Increased travel
- Lifestyle
- Agricultural practices
  - Large scale, few suppliers
Tuberculosis

- 2 billion people worldwide
- 10-15 million in US
- leading cause of death from one infectious organism
- kills more adults annually than AIDS & malaria combined
Disease development

- *Mycobacterium tuberculosis*
- Spread through air
  - active pulmonary TB
  - how long do droplets stay in the air?
  - Each person with active TB infects an average of 10-15 people per year
- Infected individuals may be asymptomatic
  - bacillus is walled off in the lungs
  - immunocompromise leads to development of pulmonary TB
What is causing this resurgence?

- Non-adherence
- Limited pharmaceutical arsenal
- Vaccine has limited efficacy
- Combination of AIDS & TB
How drug resistance develops

To control TB, patients must take antibiotics daily for 6 months.

When patients begin to feel better, they stop taking their antibiotics.

When they are placed on antibiotics again, the TB will be resistant and the medication will have no effect.
MDR-TB

• Every country has reported strains that are resistant to at least one drug
• MDR-TB is tuberculosis that is resistant to both rifampin and isoniazid, the two most powerful anti-TB drugs
• Global threat due to travel
• In US, has been reported in NY, SFO
• Increased incidence of MDR-TB in HIV co-infected patients
• WHO report 2010
  - 150,000 died of MDR-TB in 2008
  - Between 400,000 and 500,000 infected globally (3.6% of incident cases)
  - Major foci
    • Russia
    • Tajikistan
    • China & India (50% of cases)

Cost of treating MDR-TB is 10X higher than drug-susceptible TB; Drugs alone can cost 50-200x’s more!
XDR-TB

• Extensively drug resistant tuberculosis
• Resistant to isoniazid and rifampin + any fluoroquinolones and any of 3 anti-TB injectible drugs (capreomycin, kanamycin, amikacin)
• Difficult to determine incidence because few countries have ability to diagnose this
• May be linked to indiscriminate DOTS without susceptibility testing
• **Totally drug resistant TB**
• Resistant to every anti-tb drug
• 1\(^{st}\) reported in 2 HIV-neg, Italian women in 2003
• **Cause:** medical mismanagement, inappropriate therapy
• 1\(^{st}\) case in US in 19yo HIV-neg student from Peru
  - Hospitalized for 1 ½ years in last TB sanitarium in US (A.G. Holley State Hospital, Florida), 12/07
  - RX: 3 IV drugs per day, 30 pills per day
  - Released this year
Congenital Tuberculosis

• Fetus acquires TB from infected mother in utero
  - Nonspecific signs and symptoms
  - Infant with pneumonia, no response to conventional treatment
  - Rare
  - Always fatal

• Two methods of acquisition
  - Hematogenous acquisition through congenital vein with lesions in liver
  - Prenatal ingestion of infected fluid resulting in pulmonary and gastrointestinal dz

• Patients should be evaluated if at risk
  - TB endemic country
Figure 2. Image exams made during treatment of a two-three month-old congenital tuberculosis patient.
The Global Plan to Combat TB 2011-2015

• New effort by WHO

• Combination of improved testing, diagnosis, drugs
  – Most cases in Asia and Africa
  – 35% in China and India

• Goals
  – 90% treatment success by 2015
  – Mandatory HIV testing for all TB+ patients
Mycobacterium bovis

- TB in cattle
- Transmitted to humans through the consumption of unpasteurized dairy products
- Increasing cause of TB in California and other countries with large Hispanic populations of Mexican heritage
  - Queso fresco (fresh cheese), etc.
- This organism is universally resistant to pyrazinamide (PZA)!
  - Necessitates treatment with multiple drugs
  - Increased treatment duration (9 mo vs 6 mo)
- Higher mortality rate than MTB

EID, vol 14, No.6, June 2008
**Mycobacterium ulcerans**

- **Disease:** Buruli ulcer
- **Association with aquatic environments**
  - Natural reservoirs unknown
  - Insect vectors suspected, but unknown
- **Mostly in children <15yo**
- **40,000 currently reported (9/08) from W. Africa**
  - Also SE Asia, Australia (Bairnsdale Ulcer) + 28 other countries
  - Unexplained increase in last 10 years in Benin, Cote d’Ivoire, Gana

http://www.who.int/mediacentre/factsheets/fs199/en/
Buruli ulcer

- Extensive destruction of soft tissues and skin
- Formation of large ulcers and lesions predominately on legs
- No pain or fever
- Untreated lesions cause extensive scaring that impairs movement
- Permanent disabilities
Buruli ulcer

• Treatment:
  - Rifampin + streptomycin/amikacin x8wks for active disease, uncomplicated cases
  - Surgery to remove necrotic tissues or cover + correct skin deformities
  - Amputation and interventions to prevent disabilities
Buruli Ulcer in West Africa
Buruli Ulcer
Hepatitis C

- Approx. 3.2 million people in US are living with HCV
- HCV is responsible for:
  - 40% of chronic liver disease
  - 20-30% of all liver transplants
  - 8-10,000 deaths annually
  - Increasing evidence of link to hepatocellular carcinoma
Hepatitis C

Pamela Anderson

Mickey Mantel and Allen Ginsberg: Both died of hepatocellular carcinoma due to Hepatitis C infection.
Who is at risk?

• 40% injectable drug users
• 5% from transfusions
  - HCV was not recognized until 1989
  - current risk is 1/400,000 transfused units
• 5% in health care workers
  - from needle stick
  - risk: 3-10%
• 3% sexual contact
• 40% no obvious transmission
  - possible role of mother to infant
  - one report by human bite!
How bad is it?

- CDC shows 3.9 million people infected, 25,000 chronically infected
- This is expected to triple in next 20 years because no effective treatment
- Best suggestions
  - Avoid use of blood products
  - Autologous blood for elective surgery
Malaria

• 300-500 million new cases per year
• 2-3 million deaths annually
• US (1997): 1800 cases reported to CDC
  - represents only 25-30% of actual infected individuals
  - travel abroad, but many are autochthonous
    • “airport malaria”
    • Endogenous vectors
• Resistance
  - to anti-malarials
  - to pesticides
Worldwide distribution of malaria
Zoonotic malaria

• 26 species of plasmodium in primates
• Some of these implicated in human disease in increasing numbers
  - *Plasmodium knowlesi* infections in Thailand and Malaysia
    • 24 hour replication cycle
    • Potentially life threatening

*CID, 2008; 46:165-171*
Plasmodium knowlesi

- *Macaca fascicularis* is host in nature
- **Vector:** *Anopholes latens* (in Malaysia)
- **Question:** is this transmitted to people from other humans?
  - Analyses of blood from pts with *P. malariae*
    - Molecular methods
  - If so, will become 5th human malaria pathogen
Prevention

• Most of the cases occur in 3rd World

• Strategies
  - Eliminate mosquitoes
  - Prevent mosquitoes from biting
  - Treat those with malaria to reduce reservoirs

• Campaign to reduce disease by using bednets treated with natural pesticides

• Vaccine under development...why did it take so long?
Dengue

- Increased spread due to climactic changes, global urbanization, increased air travel
  - Previously confined to tropical areas
  - Increased incidence in Texas
- Among most important reemerging ID
- Vector: *Aedes albopictus* and *A. aegypti*
- Agent: Dengue viruses
  - Flavivirus
  - Den-1, 2, 3, 4

JAMA, Jan 2008
Dengue Fever & DHF

• Epidemiology
  - 50-100 million annual cases worldwide
  - 22,000 deaths

• Clinical
  - Sudden onset fever, severe headache
  - Myalgias and arthralgias = break bone fever
  - Sometimes shock, hemorrhage, death
Treatment & Prevention

- Fluid management
- Avoid aspirin and non-steroidal anti-inflammatory medications
  - Exacerbate bleeding
  - Reyes syndrome in children
- Acetaminophen for pain
- Prevention: Mosquito control measures
Dengue

- **Areas infested with *Aedes aegypti***
- **Areas infested with *Aedes aegypti* and dengue epidemic activity**

(based on CDC data)

Molecular Virology University of Heidelberg
Hantavirus Pulmonary Syndrome

- Outbreak in 1993 in Four Corners Region
- Cause: previously unrecognized strain of hantavirus
- Causes a severe respiratory infection with a 38% case fatality rate
- 336 cases in 31 states as of May 2003
Ebola

Ongoing battle in the Democratic Republic of Congo.
Issues: Bush meat consumption, burial practices, political unrest.
Hand, Foot, and Mouth Disease
Enterovirus 71
EV71: Clinical course

- Starts with slight fever
- Blisters and ulcers form in mouth
- Rashes on hands and feet
- Sequelae include:
  - meningitis,
  - Encephalitis
  - Pulmonary edema
  - Paralysis
• As of May 30, 2008
  - 10,696 cases successfully treated and 42 deaths in Anhui Province, China
    • Reporting over 1000 cases per day
    • 734 still hospitalized
    • 10 in critical condition
  - 283 cases in Macao
  - Kindergartens and primary schools in effected region have been closed.
West Nile Virus

West Nile Virus, 1999

Location with at Least One Positive Horse
Positive Humans and Wild Birds
Positive Wild Birds
One Positive Wild Bird

0 20 40 60 80 Miles
0 30 60 90 120 Kilometers
West Nile Virus

- Outbreak in New York 9/14/99
- Arboviral encephalitis first believed to be SLE
- Several elderly individuals died
- Virus was previously unknown in the U.S.
- 4156 cases with 284 deaths (4/15/03)
- Surveillance of human cases, mosquitoes, and birds
West Nile Virus: 2004
• First identified as atypical pneumonia in Guangdong province, China in Nov 2002
• Currently 8398 cases, 772 deaths reported from 29 countries (6/4/03)
• Causative agent: Novel coronavirus
• Acquired by close contact with infected patient
All of the cases in Canada were traced to one Dr. who spent one night in this hotel.
SARS: etiology

New Coronavirus isolated from patients with SARS
Where did SARS come from?

- Possible zoonosis....

Palm civets:  
used as source of musk and eaten as delicacy in China!

Horseshoe bat:  
Also sold as delicacy, Believed to be source
Monkeypox virus

- 81 cases reported by 7/2/03 from 6 states
- 19 patients required hospitalization
- Source: Shipment of animals from Ghana to US 4/19/03
  - Source animal: Gambian giant rat
  - Infected prairie dogs, rope squirrels, dormice
Sources

Gambian giant-pouched rat (*C. gambianus*)

[Image: courtesy Utah Hogle Zoo]

African Dwarf Dormouse (*Graphiurus murinus*)

[Image: courtesy rodentfancy.org]
FIGURE 2. Movement of imported African rodents to animal distributors and distribution of prairie dogs from an animal distributor associated with human cases of monkeypox — 11 states*, 2003†§

Rodent shipment from Accra, Ghana

- 50 Gambian giant rats (GR)
- 53 rope squirrels (RS)
- Two brush-tailed porcupines (BP)
- 47 tree squirrels (TS)
- 100 striped mice (SM)
- ~510 dormice (DM)

TX-1**: 4/9/03
TX-2 GR
TX-3 RS, SM DM
TX-4 DM
TX-5 DM
TX-6 TS, SM DM
TX-7 DM
TX-8 DM
TX-9 DM
TX-10 DM

NJ
RS, BP TS, SM

IL
Human cases: 17 confirmed 22 probable/suspect
24 PD traced
14 PD traced

IN
Human cases: seven confirmed nine probable/suspect

MO
Human cases: two confirmed

SC
No human cases

MI
No human cases

KS
Human cases: one confirmed

MN DM

WI DM

4/9/03 4/11/03 4/16/03 4/17/03 4/21/03 4/26/03 4/28/03 5/12/03 6/1/03 6/5/03

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* Illinois (IL), Indiana (IN), Iowa (IA), Kansas (KS), Michigan (MI), Minnesota (MN), Missouri (MO), New Jersey (NJ), South Carolina (SC), Texas (TX), and Wisconsin (WI). Japan is included among sites having received shipment of rodents implicated in this outbreak.
† As of July 8, 2003.
‡ Does not include one probable human case from Ohio; investigation is ongoing.
§ Date of shipment unknown.
** Identified as distributor C in MMWR 2003;52:561-4.
*** Identified as distributor D in MMWR 2003;52:561-4.
‡‡ Includes two persons who were employees at IL-1.
H1N1 Influenza
“Swine Flu”

• Initial cases in Mexico
  - Earliest known case from 5yo male in La Gloria, Mexico (Feb 2009)
  - Area used for commercial pig fattening, but no virus detected in any of pigs

• 1st detected mid-April 2009 in US
  - 4/15/09-7/24/09=43,771 cases
  - 5,011 hospitalized, 302 deaths

• Resembles a swine flu virus that emerged about time of 1918 human pandemic and circulated until 1957
H1N1 Influenza

- Reassortant virus with at least 3 “parents”
  - 6 genes from H1N2 virus in pigs in North America 1999-2000
- Closest related viruses isolated from cases that occurred over 10 years ago
- Where did it come from?
H1N1 Influenza

• Hypotheses
  - 1) Natural reassortant
    • Most likely occurred in birds, but association with pig viruses makes this unlikely
  - 2) Produced in laboratory
    • Virus sharing among research labs
    • Escaped viruses
    • Vaccine production
How new versions of flu viruses arise in nature
H1N1 Influenza

- Evidence for laboratory source
  - H1N1 that was involved in outbreak in 1977 was most like the virus that circulated after 1918 pandemic, then disappeared after 1957
  - Suggests that there was no viral replication in between....probably in a lab freezer and “escaped” when passaged in lab
H1N1 Influenza

• Evidence
  - Closest virus to current H1N1 is “2000 Indiana strain” that is used in commercial vaccines in N America
  - Few outbreaks in pigs in US and Mexico, probably due to the vaccine and cross immunity
  - 1st cases in Mexico in remote village where there was no international pig trade and none of the pigs were ill
**H1N1 Influenza**

**Global update**
- 206 countries, 6770 deaths
- Difficulty in assessing true numbers due to lack of testing in many countries

**US (cumulative 8/30-11/24/09)**
- 46,920 confirmed cases in US
- 138 pediatric deaths
- H1N1 activity appears to be declining
Pathogens newly recognized in the past two decades

- Acanthamebiasis
- Australian bat lyssavirus
- Atypical Babesia
- Bartonella henselae
- Ehrlichiosis
- Encephalitozoon cuniculi, hellem, bieneusi
- H. pylori
- Hendra virus
- Hep C & E
- HHV 8
- HHV 6
- Lyme borreliosis
- Parvovirus B19
- Enterovirus 71
- Clostridium difficile
- Mumps virus
- Streptococcus, Group A
- Staphylococcus aureus