EMERGING INFECTIONS AND ISSUES

INFECTIONS:
- AVIAN FLU
- SARS
- DHF
- XDR-TB

ISSUES:
- ANTIBIOTIC RESISTANCE
- STOCKPILING OF DRUGS/VACCINES
- NEW APPROACHES TO THERAPY
- GENETIC SUSCEPTIBILITY
“The global future of mankind will probably unfold as episodes of a suspense thriller that could be entitled, “Our Wits Versus Their Genes.”

- Joshua Lederberg
EMERGING INFECTIONS IN PEDIATRICS: PHILIPPINE EXPERIENCE

PROF LULU C BRAVO, MD
UNIVERSITY OF THE PHILIPPINES
MANILA
EMERGING DISEASES: DEFINITIONS

• Has increased in the past 20 years
• Comprise at least 12% of infections

• Types are:
  - newly identified organism or a new strain
    eg. SARS, AIDS
  - change due to evolution
    eg. Influenza H1N1
- Known infection identified in a new location
  eg. Japanese B encephalitis
- New infection in an area undergoing ecologic transformation
  eg. Lyme disease
- Pre-existing disease re-emerging as drug-resistant
  eg. MDRTB
MECHANISMS OF EMERGENCE AND RE-EMERGENCE

• Microbial adaption; e.g. genetic drift and genetic shift in Influenza A
• Changing human susceptibility; e.g. mass immunocompromisation with HIV/AIDS
• Climate and weather; e.g. diseases with zoonotic vectors such as Dengue (transmitted by mosquitoes) are moving further from the tropics as the climate warms
• Change in human demographics and trade; e.g. rapid travel enabled SARS to rapidly propagate around the globe
• Economic development; e.g. use of antibiotics to increase meat yield of farmed cows leads to antibiotic resistance
• Breakdown of public health; e.g. the current situation with Measles
• Poverty and social inequality; e.g. tuberculosis is primarily a problem in low-income areas
• War and famine
• Bioterrorism; e.g. 2001 Anthrax attacks
• Dam and irrigation system construction; e.g. malaria and other mosquito borne diseases
THE GLOBAL CHALLENGE

The Global Village

Global “microbial traffic”

GLOBALIZATION OF HEALTH / DISEASE
Global Burden of Infectious Diseases

Leading cause of death worldwide: About 15 million (>25%) of 57 million worldwide are the direct result of infectious diseases

-WHO Report 2004

Figure from Morrens et al, Nature Vol 430 July 2004
Global examples of emerging and re-emerging infectious diseases. Red represents newly emerging diseases; Blue, re-emerging diseases; Black, a ‘deliberately emerging’ disease.
THE PHILIPPINE SITUATION

... THE VIRUSES

....THE BACTERIA

.... THE PARASITES

AND OTHERS...
Japanese B Encephalitis

SENTINEL SURVEILLANCE ON ETIOLOGY OF MENINGITIS ENCEPHALITIS AND MENINGO-ENCEPHALITIS IN THE PHILIPPINES

A TECHNICAL PROGRESS REPORT
SEPTEMBER TO DECEMBER 2010

ESPINO, FE et al...
Research Institute of Tropical Medicine
### Distribution of Japanese B Encephalitis by age group (January to December 2010)

From sentinel hospitals during a 22 month period

<table>
<thead>
<tr>
<th>Age Group in Years</th>
<th>Total Number of specimens</th>
<th>Japanese Encephalitis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonate-&lt; 2 months</td>
<td>31</td>
<td>0</td>
</tr>
<tr>
<td>2 months-&lt;2 years</td>
<td>41</td>
<td>0</td>
</tr>
<tr>
<td>2-5 years</td>
<td>18</td>
<td>7 (38.9)</td>
</tr>
<tr>
<td>5-10 years</td>
<td>30</td>
<td>13 (43.3)</td>
</tr>
<tr>
<td>10-&lt;15 years</td>
<td>28</td>
<td>9 (32.1)</td>
</tr>
<tr>
<td>15 years and above</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Data not Available</td>
<td>16</td>
<td>3 (18.8)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>167</strong></td>
<td><strong>32 (19.2)</strong></td>
</tr>
</tbody>
</table>
Distribution of Japanese B Encephalitis by Age Group (January to December 2010)- From sentinel hospitals during a 22-month period
Frequency of Japanese B Encephalitis cases by Hospital (January to December 2010)

<table>
<thead>
<tr>
<th>Results</th>
<th>BuMC (%) (n=49)</th>
<th>BiMC (%) (n=37)</th>
<th>WVMC (%) (n=50)</th>
<th>TPH (%) (n=30)</th>
<th>PCMC (%) (n=1)</th>
<th>Total (%) (n=167)</th>
</tr>
</thead>
<tbody>
<tr>
<td>JE Positive</td>
<td>6 (12.2%)</td>
<td>14 (37.8%)</td>
<td>5 (10%)</td>
<td>7 (23.3%)</td>
<td>0</td>
<td>32 (19.2%)</td>
</tr>
</tbody>
</table>

1 Bulacan Medical Center  
2 Bicol Medical Center  
3 Western Visayas Medical Center  
4 Tarlac Provincial Hospital  
5 Philippine Children’s Medical Center
Distribution of Sentinel Hospitals for Japanese Encephalitis
1991

1. Dagupan City (Luzon) reported 4 deaths from encephalitis

13 hospitalized cases identified as encephalitis

$\rightarrow$ 5 deaths confirmed (45% fatality rate)

$\rightarrow$ 5 from different barangays discharged & improved at time of investigation
Japanese Encephalitis in the Philippines

2. *Pigcawayan at North Cotabato*
   Review of Records Jun-July 1991 at Cotabato Regional Hospital
   • 40 CNS infections identified
     → 8 JE cases suspected from Pigcawayan (confirmation not reported)
Japanese Encephalitis in the Philippines

**Characteristic neurologic features for JEV**

- Abulia with masked facies
- Variable changes in mentation
- Relative absence of cranial nerve involvement
- Lack of gross sensory deficit
- Asymmetric and irregular distribution of motor and tone abnormality
Japanese Encephalitis in the Philippines

Among Clinically Diagnosed Dengue Cases in 1999

- 6% (46/770) were positive for JE
- 0.8% (6/770) had co-infections of Chikungunya & JE
Japanese Encephalitis in the Philippines

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Japanese Encephalitis in the Philippines

<table>
<thead>
<tr>
<th>NOTIFIABLE DISEASES, 2001</th>
<th>No.</th>
<th>Rate/100,000 pop</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalitis / Meningitis</td>
<td>207</td>
<td>0.3</td>
</tr>
<tr>
<td>Meningococccemia</td>
<td>57</td>
<td>0.1</td>
</tr>
<tr>
<td>Dengue</td>
<td>23,235</td>
<td>29.8</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>845,526</td>
<td>1085.0</td>
</tr>
</tbody>
</table>
## Japanese Encephalitis in the Philippines

<table>
<thead>
<tr>
<th>NOTIFIABLE DISEASES, 2008</th>
<th>No.</th>
<th>Rate/100,000 pop</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalitis / Meningitis</td>
<td>788</td>
<td>0.9</td>
</tr>
<tr>
<td>Meningococcemia</td>
<td>17</td>
<td>0.0</td>
</tr>
<tr>
<td>Dengue</td>
<td>13,014</td>
<td>14.5</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>434,445</td>
<td>485.4</td>
</tr>
</tbody>
</table>
DENGUE

• Number of cases nationwide from January to Dec 2010 → 135,355
  – 134.84% higher compared to the same period last year (57,636)
• Patients’ ages ranged between less than 1 month - 95 years old
  – 78% belong to the 1-20 years age group
  – More deaths recorded in those below one year and in the 1-10 years age groups
  – Males comprised 52%

www.doh.gov.ph
Fig. 2 DENGUE Cases by Month, Philippines, 2010 vs 2009
DENGUE

• Total of 793 deaths recorded for the period → case fatality rate of 0.59% which decreased by 40% from 2009
• Reported cases with highest CFR are in region IX and ARMM
• Lowest CFR was found in CAR
# MENINGOCOCCAL DISEASE

<table>
<thead>
<tr>
<th>Region</th>
<th>Meningococcal Disease</th>
<th>MW 1 - 51 (Jan. 1 - Dec. 25)</th>
<th>MW 52 (Dec. 26 - Dec. 31)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Deaths</td>
<td>Cases</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>4A</td>
<td>15</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>4B</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>9</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>11</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>12</td>
<td>9</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>ARMM</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>CAR</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>CARAGA</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>NCR</td>
<td>28</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal</td>
<td>102</td>
<td>21</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>102</td>
<td>21</td>
<td>0</td>
</tr>
</tbody>
</table>
### Table 1. Quick Facts

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Reported Cases</td>
<td>112</td>
<td>1,417</td>
<td>5,841</td>
</tr>
<tr>
<td>Asymptomatic Cases</td>
<td>110</td>
<td>1,400</td>
<td>4,987</td>
</tr>
<tr>
<td>AIDS Cases</td>
<td>2</td>
<td>17</td>
<td>854</td>
</tr>
<tr>
<td>Males</td>
<td>103</td>
<td>1,300</td>
<td>4,532*</td>
</tr>
<tr>
<td>Females</td>
<td>9</td>
<td>117</td>
<td>1,298*</td>
</tr>
<tr>
<td>Youth 15-24yo</td>
<td>31</td>
<td>430</td>
<td>1,154</td>
</tr>
<tr>
<td>Children &lt;15yo</td>
<td>0</td>
<td>3</td>
<td>55</td>
</tr>
<tr>
<td>Reported Deaths due to AIDS</td>
<td>0</td>
<td>2</td>
<td>323</td>
</tr>
</tbody>
</table>

*Note: No data available on sex for eleven (11) cases.*
Figure 3. Number of HIV/AIDS Cases Reported in the Philippines by Year, Jan 1984 to November 2010 (N=5,841)

*Five initially asymptomatic cases reported in 2008, died due AIDS that same year.*
Tuberculosis, 2001

- <10 cases per 100,000
- 10-50 cases per 100,000
- 50-100 cases per 100,000
- >300 cases per 100,000
- 100-300 cases per 100,000
- <10 cases per 100,000

Source: WHO, 2002
<table>
<thead>
<tr>
<th>WHO REGIONS</th>
<th>Number of cases (thousands)</th>
<th>Cases per 100,000 population</th>
<th>Deaths from TB (including TB deaths in people infected with HIV)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Forms (%)</td>
<td>Smear-positive</td>
<td>All forms</td>
</tr>
<tr>
<td>Africa</td>
<td>2354 (26)</td>
<td>1000</td>
<td>350</td>
</tr>
<tr>
<td>The Americas</td>
<td>370 (4)</td>
<td>165</td>
<td>43</td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
<td>622 (7)</td>
<td>279</td>
<td>124</td>
</tr>
<tr>
<td>Europe</td>
<td>472 (5)</td>
<td>211</td>
<td>54</td>
</tr>
<tr>
<td>South-East Asia</td>
<td>2890 (33)</td>
<td>1294</td>
<td>182</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>2090 (24)</td>
<td>939</td>
<td>122</td>
</tr>
<tr>
<td>Global</td>
<td>8797 (100)</td>
<td>3887</td>
<td>141</td>
</tr>
</tbody>
</table>
High impact on countries with HIV infections due to considerable overlap between clinical pictures caused by TB and HIV-related lung disease.
HIV status often “unknown” in children suspected with TB

Thus:

important to do HIV testing for more appropriate treatment and prophylaxis
Multidrug-Resistant (MDR) TB

• MDR-TB is as infectious as drug susceptible TB
• Diagnosis is confused by lack of culture and susceptibility testing
• Suspected if:
  – an adult index case has MDR-TB
  – child is a treatment failure despite compliant therapy
  – the adult index case has unknown susceptible testing and with treatment failure or a retreatment case
NEGLECTED FOOD-BORNE DISEASES
<table>
<thead>
<tr>
<th></th>
<th>Philippines</th>
<th>Bangladesh</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cryptosporidium</strong></td>
<td>8.9%</td>
<td>8.4%</td>
</tr>
<tr>
<td><strong>G. lamblia</strong></td>
<td>2.5%</td>
<td>11%</td>
</tr>
<tr>
<td><strong>E. histolytica</strong></td>
<td>0.6%</td>
<td>8%</td>
</tr>
<tr>
<td></td>
<td>Adkins HJ, et al., JCM 1987, Method (?)</td>
<td>Haque, R et al. AJTMH 2003</td>
</tr>
</tbody>
</table>
Disruption of intestinal barrier function in HIV-infected patients with and without diarrhea in Fortaleza, Brazil

Lactulose / Mannitol Ratio

Healthy Controls (n = 13)  HIV+ Non-diarrhea (n = 19)  HIV+ Diarrhea (n = 19)

Lima et al. AJGastro. 92:1861, 1997
Disruption of Intestinal Barrier Function in Children with Cryptosporidial and non-Cryptosporidial Diarrhea in Fortaleza, Brazil

[vs controls: *p=0.001; **p<0.01]

Intestinal Barrier Disruption in HIV-infected patients with cryptosporidial, non-cryptosporidial, and microsporidial diarrhea

Cryptosporidiosis

- Causal Agent
  - Many species of Cryptosporidium exist that infect humans and a wide range of animals
  - C. parvum and C. hominis (formerly known as C. parvum anthroponotic genotype or genotype 1) are the most prevalent species causing disease in humans
Clinical Features

• Wide range of manifestation
  – Asymptomatic to severe life-threatening illness
  – Watery diarrhea is the most frequent symptoms
  – Dehydration, weight loss, abdominal pain
  – Fever
  – Nausea
  – Vomiting
Cyclosporiasis

- Recently identified as a unicellular coccidian parasite
- Causal agent: *Cyclospora cayetanensis*
- Designation given in 1994 to Peruvian isolates of human-associated Cyclospora
-Appears that all human cases are caused by this species
Clinical Features

• Incubation period: 1 week
• Symptomatic infections
  – Watery diarrhea, which can be severe
  – Anorexia
  – Weight loss
  – Abdominal pain
  – Nausea and vomiting
• Untreated infections typically lasts for 10-12 weeks and may follow a relapsing course
Laboratory Diagnosis

Specimen processing

- Fixed in 10% formalin
  - Direct microscopy
  - Concentration procedure
  - Preparation of stained smears
- Fixed in 2.5% potassium dichromate
  - For sporulation assay and molecular diagnosis
- Frozen without fixation
  - For molecular diagnosis
Microsporidiosis

- **Causal agents**
  - 14 microsporidian species
    - **Enterocytozoon bieneusi**
    - **Encephalitozoon intestinalis**
    - **Encephalitozoon hellem**
    - **Encephalitozoon cuniculi**
    - **Pleistophora sp.**
    - **Trachipleistophora hominis**
    - **T. anthropophteria**
    - **Nosema ocularum**
    - **N. algerae**
    - **Vittaforma corneae**
    - **Microsporidium ceylonensis**
    - **M. africanum**
    - **Brachiola vesicularum**
    - **B. connori**

- Increasingly recognized as opportunistic infectious agent worldwide.
Clinical Features

• Represents an important and rapidly emerging opportunistic disease
• Occurring mainly, but not exclusively, in severely immunocompromised patients with AIDS
• Cases of microsporidiosis in immunocompromised persons not infected with HIV as well as in immunocompetent persons also have been reported
Laboratory Diagnosis

• Light Microscopy
  – Chromotrope 2R method
• Transmission electron Microscopy
• Immunofluorescence Assay
• Molecular Methods
THE CHALLENGE FOR EMERGING DISEASES

• Need for Surveillance and Accurate Reporting
• Appropriate Laboratory procedures for Identification
• Networking
• Rapid Response In Outbreak Situations
• Control Measures in Place
REMAINING CHALLENGES AND ISSUES

VECTOR CONTROL
- MALARIA
- JAP B ENCEPHALITIS
- DENGUE

MASS DRUG ADMINISTRATION
- SCHISTOSOMIASIS
- FILARIASIS
- OTHER NEGLECTED DISEASES
InterAcademy Network for Emerging Infections (IANEI)

• UP MANILA- NIH AND NAST ENDEAVOR TO ESTABLISH A NETWORK FOR EMERGING INFECTIONS IN THE PHILIPPINES AND ASIA.
The IANEI aims to achieve the following objectives

1. To facilitate communication between academies of medicine and medical sciences on issues related to emerging infections

2. To develop and maintain a database of researches and programmes on the emerging infections
Objectives

IANEI

3. To provide evidence-based recommendations for health policy development for the control of emerging infections

4. To encourage collaboration between academies of medicine and medical sciences on researches and programmes on the control of emerging infections

5. To mobilize support for researches that would provide new knowledge crucial to increasing the effectiveness of control programmes for emerging infections
“If history is our guide, we can assume that the battle between the intellect and will of the human species and the extraordinary adaptability of microbes will be never-ending. To successfully fight our microbial foes, we must continue to vigorously pursue research on the basic mechanisms that underlie microbial pathogenesis and develop novel strategies to outwit these ingenious opponents. The past 10 years have been challenging but no more so than will be the future.”

- Steven A Fauci, EID 2005