National Hospital for Infectious Disease
Lima, Peru
Viral Diseases
Case 1
Clinical Features of Dengue (Break-bone Fever)

- Rash - “white islands in sea of red”
- Sudden onset of:
  - fever
  - severe headache
  - myalgias and arthralgias
  - leukopenia/thrombocytopenia
- Shock and hemorrhage may lead to death
- Treatment focuses on supportive care
Dengue Fever

- AKA – “breakbone fever”
- Caused by 1 of 4 serotypes of Flavivirus
- *Aedes* mosquito
- Recognized as a disease in tropical areas for nearly 250 years
- Common throughout the tropical world
Dengue, countries or areas at risk, 2008*

The contour lines of the January and July isotherms indicate the potential geographical limits of the northern and southern hemispheres for year-round survival of Aedes aegypti, the principal mosquito vector of dengue viruses.

*As of 1 November 2008

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, 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.

Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS) World Health Organization

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Patient with DHF
Case 2

Peruvian woman
“Rash for years”
Sister with tropical spastic paraplegia
Adult T-cell Leukemia/Lymphoma (HTLV-1)

- Regional concern
- ATLL <5% of HTLV-1+
- Leukemia, LAD, and hypercalcemia
- Skin lesions in 50%
  - nodules or tumors (33%)
  - generalized papules (22%)
  - plaques (19%)
ATLL/HTLV-1
Histopathology

- Medium/large cells
- +/- epidermotropism
- CD3+, CD4+, CD8-
- +/- CD25 expression
- TCR analysis clonal
- HTLV-1 DNA (dx test)
Case 3
(adult)
Case 3
(Child)
Chronic Infective Dermatitis

- 1966 - relapsing “eczema” in Jamaican kids
- 1990 - association between CID and HTLV-1
- 1995 - additional patients in Colombia
- Common in children, rare in adults
- Scalp, face, axilla, groin
- *Staph* involved (?)
- Improves with antibiotics but recurs with d/c
Bacterial Diseases
Case 4

- 11 year-old boy
- Verrucous lesions
- Hemorrhagic, easily traumatized
- Outdoors in early evening
- “Silent” flying insects swarming at night
Verruga peruana

- Carrion’s disease
- Acute (hemorrhagic) & chronic (verrucous) forms
- *B. bacilliformis*
- *Lutzomyia* fly is vector
- Geographically constrained (800-3000 m)
Museo Nacional de Antropología
Lima, Peru

*Lutzomyia* - note the hairs on the wings.
Verruga Peruana

• Histology
  – Proliferative vessels, chronic inflammation
  – Mitotic figures
  – Organism RARELY visible
  – Rocha-Lima bodies are intracellular reddish granules in endothelial cells (Giemsa)
Acute Phase (Oroya Fever)

- Intracellular infection
- Hemolytic anemia
- Hepatosplenomegaly
- Myocarditis
- ↓ CD4 counts
- Opportunistic infections (salmonella)
Leprosy
The Biblical Scourge

- *Mycobacterium leprae*
- #2 mycobacterial disease worldwide
- Existed for millennia
- Continues to be a problem to this day
Leprosy in the Middle Ages

- Epidemic in 1300s
- Lepers considered “dead to the world”
- Often had to leave all they knew behind
- Entered “lazar-houses”
THE HAWAIIAN LEPER COLONY

MOLOKAI ISLAND AND ITS DISEASE-STRICKEN INHABITANTS.

Efforts of the Government to Stamp Out the Scourge by Segregation—More Virulent and Malignant in These Islands than Anywhere Else upon the Face of the Globe—What Father Damien Did to Improve the Condition of the Unfortunates.
Leprosy Enters Modern Age

Gerhard Henrick Armauer Hansen

1873 - “intracellular rods in tissues”

Wanted to fulfill Koch’s postulates:
- present in all persons with disease
- causes disease in healthy individual
- grown outside the body

1875 - injected into non-consenting woman

1892 - recognized as discoverer of AFB
Polymorphic Presentation

• HLA type & immune predisposition impacts
• “Indeterminate” – early, before declaration
• Ridley–Jopling classification system:
Tuberculoid Leprosy
TT Leprosy

- Nerve enlargement is common with TT
  - Great auricular
  - Ulnar
  - Common peroneal
Tuberculoid Leprosy
Borderline Leprosy
Borderline Leprosy
Lepromatous Leprosy
Lepromatous Histology
Treatment of Leprosy

• WHO guidelines:
  – Single lesion
    • OTD rifampin 600 mg, ofloxacin 400 mg, minocycline 100 mg
  – Paucibacillary disease
    • dapsone 100 mg qd & rifampin 600 mg qmo x 6 mos
  – Multibacillary disease
    • dapsone 100 mg qd, clofazimine 50 mg qd and 300 mg qmo, plus rifampin 600 mg qmo x 12 mos
Reversal Reactions

- Type I – Reversal Reaction
- Type II – ENL
Reactions to Therapy

- **Type I – Reversal Reaction**
  - Sudden & with treatment, neuritis predominates, tx with prednisone

- **Type II – ENL**
  - Later in course, skin predominates, “unwell”, tx with thalidomide

- **Lucio phenomenon**
Possible Reservoir in Americas
Case 8

- 27 year-old Bolivian
- 17 month history of non-healing leg ulcer
- No pain or symptoms
- Ulcer tremendously undermined upon exploration
Buruli Ulcer

- *M. ulcerans*
- #3 mycobacterial disease worldwide
- Large, *painless* ulcers
- Slow growth
- Difficult culture
- PCR available
- Mycolactone causes immunosuppression and cytotoxicity which perpetuates ulcer
Buruli ulcer

- Histology
  - Coagulation necrosis
  - Destruction of nerves, vessels, appendages
  - Necrosis extends beyond edges of ulcer
  - Clumps of acid-fast bacilli at base
  - Little inflammation in active lesions
  - Granulation or fibrosis in healing lesions
Case 9

- 43 year old man
- Long h/o of respiratory difficulty
- Trouble swallowing
- Plaques on face for last several years
Rhinoscleroma
(“Slavic leprosy”)

- Chronic granulomatous condition of aerorespiratory tract:
  - nasal cavity (>95%)
  - nasopharynx/larynx (>40%)
  - trachea (12%) & bronchi (2-7%)
  - rarely surrounding soft tissues

- Klebsiella rhinoscleromatosi

- Ciprofloxacin and extensive surgery
Jan Mikulicz-Radecki

Russell bodies

morula cells (of Mott)
Case 10

- 24 year-old “jungle worker”
- Multiple STDs in past
- “Jungle parties”
Secondary Syphilis

- Treponemia
- Usually 4-8 weeks after chancre
- “Boiled ham” or “copper penny” rash
- Often with palmoplantar involvement
- Partially treated cases with poor healthcare
- Sequelae not normally seen in US should be considered abroad
Syphilis in the United States
19 cases of secondary syphilis
- superficial and deep perivascular pattern (9)
- lichenoid pattern (4)
- combined pattern (6)

All cases demonstrated plasma cells
Sparse plasma cells in 4 cases
Granulomas noted in 53% of cases
Perineural infiltrate in 74% of cases
Variable acanthosis and dyskeratosis
Secondary Syphilis
Immunohistochemical Studies

Fig. 5. A) Steiner stain highlights both spirochetes (arrow) and melanin granules resulting in marked background artifacts. In contrast, spirochete immunostain highlights B) many organisms in the lower epidermis, C) occasional organisms in the dermis, and D) rare spirochetes within follicular epithelium.
Children of the partygoers...
Figure 5. Typical skin lesions in an infant with symptomatic congenital syphilis. Desquamating and exudative lesions around the toes are shown. These lesions are highly contagious by contact.

Table 1 - Frequency of the Common Early Manifestations of Congenital Syphilis Among 139 Symptomatic Infants

<table>
<thead>
<tr>
<th>Clinical findings</th>
<th>Percent Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash</td>
<td>68</td>
</tr>
<tr>
<td>Fever</td>
<td>42</td>
</tr>
<tr>
<td>Failure to thrive</td>
<td>33</td>
</tr>
<tr>
<td>Hepatosplenomegaly</td>
<td>71</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>14</td>
</tr>
<tr>
<td>Central nervous system involvement</td>
<td>23</td>
</tr>
<tr>
<td>Pseudoparalysis</td>
<td>15</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>17</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>14</td>
</tr>
<tr>
<td>Ascites</td>
<td>9</td>
</tr>
<tr>
<td>Laboratory abnormalities</td>
<td></td>
</tr>
<tr>
<td>Leukocytosis</td>
<td>72</td>
</tr>
<tr>
<td>Anemia (Coombs-negative hemolytic anemia)</td>
<td>58</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>40</td>
</tr>
<tr>
<td>Renal manifestation (e.g., proteinuria, hematuria)</td>
<td>16</td>
</tr>
<tr>
<td>Radiographic abnormalities</td>
<td></td>
</tr>
<tr>
<td>Periostitis or Osteochondritis</td>
<td>78</td>
</tr>
</tbody>
</table>
Case 11

- Prostitute S/P NSVD
- Plaque for 6 years
- Still working in the Callao
The Crush Prep

- Tissue “crushed” with second slide
- Useful for several diseases (molluscum)
- Actual crush prep from the previous case
Granuloma inguinale

- Donovanosis
- *Calymmatobacterium granulomatis*
- Intracellular GNB (*Klebsiella* spp.)
- Crush prep use Giemsa
- Histopath use Warthin-Starry
- Treat with long term doxycycline (also TMP/SMX, cipro, azithro, EES)
Modified Steiner Stain
Fungal Diseases
Cryptococcosis

- Classically *C. neoformans*
- Pigeon excrement
- Seen all over the world
- Opportunistic infection (HIV)
- Skin manifestations in 10-15%
- Cutaneous cryptococcosis often resembles molluscum (also common to HIV patients)
"Nodular and Diffuse" dermatitis

- Clear or mucinous areas apparent
- “Nodular and Diffuse” dermatitis
- Clear or mucinous areas apparent
Many yeast within mucoid areas...
Large & Pleomorphic Yeast with Surrounding Halo (the capsule)
PAS-D stains the fungal wall

mucin stains may highlight residual mucin capsule

PAS-D stains the fungal wall
Case 12

- 23 year-old man
- Works on oil rig in Amazon basin
- 10 year h/o of asymptomatic deformity of L ear
- Firm & densely keloidal lesion
(Elsayed S, et al. 2004.)
Lobomycosis

- *Lacazia loboii*
- Induced keloidal response
- Lemon-shaped yeast connected with “stalk”
- Also problem of dolphins (naval handlers)
- Surgical excision remains chief strategy
Case 13

Rural field worker from high jungle area.
Perioral and mucosal lesions for months.
Paracoccidioidomycosis

- South American blastomycosis
- Dimorphic yeast
- Forms “mariner’s wheel” in tissue
- Commonly involves mucosal tissue
- Men >> women
Paracoccidioidomycosis

- **Characteristic Histology**
  - Central cell surrounded by blastoconidia (Mariner’s wheel)

- **Treatment**
  - Lengthy regimens, frequent relapses
  - Unique sensitivity to sulfa
  - Ketoconazole, itraconazole, and fluconazole also used
  - Voriconazole may be alternative
Protozoal Disease
Cases 14 & 15

Young healthy adolescents.
From Nazca area of Peru.
Slowly expansive plaques of the central face.
Free Living Ameoba

- *Balamuthia mandrillaris*
  - emerging pathogen
  - derived from water
  - central facial involvement
  - fatal if it penetrates CNS
  - treat with albendazole and itraconazole, plus TMP/SMX or amphotericin
Success in Balamuthia is Highly Variable
Case 16

52 year-old man from Lima
Migratory urticarial plaques
Family of money and influence
Eats ceviche ≥ twice/week
Gnathostomiasis

- Fish nematode - *Gnathostoma spinigerum*
- “Emerging pathogen”
- Formerly of Thailand, now in Mexico & Peru
- Can cause of eosinophilic meningitis
- Anisakis more common illness from sushi (but requires a inept chef)
What has been will be again, what has been done will be done again; there is nothing new under the sun.

- Eccl. 1:9
Case 17

- 38 year-old woman
- Vacation property in the jungle
- Sleeps outdoors
- Itching nodule weeks
- “un choque que que mueve”
Myiasis

- Most common - human bot fly \textit{(Dermatobia hominis)}
- Life cycle utilizes mosquitoes
- Incubation period of 5-8 weeks
- Surgical removal
- “Bacon therapy”
- In Africa, tumbu fly is the most common cause (iron clothes!)
Case 18

- 53 year-old man
- From jungle area
- Slow healing ulcers on legs 14 years earlier
- Nasal stuffiness 5 years
Mucocutaneous Leishmaniasis
Espundia

- Leishmania braziliensis
  - Intracellular protozoa
  - Spread by bite of Lutzomyia fly
  - Mucosal lesions decades after skin lesions

Use amphotericin for failures
“Touch Prep”

- Method of rapid diagnosis for leishmaniasis
- Amastigotes with nucleus **AND** kinetoplast
Leishmaniasis

• Diagnosis
  – Amastigotes within macrophages
  – Kinetoplast is key to identification
  – Peripheralized in histiocytes (“Ferris-wheel”)
  – Chronicity yields lower level of organisms
  – Culture (NNN media) or PCR (too sensitive)
Old World Leishmaniasis: An Emerging Infection among Deployed US Military and Civilian Workers

Peter J. Weina,1 Ronald C. Neafie,2 Glenn Wortmann,4 Mark Polhemus,4 and Naomi E. Aronson2,4,5

1674 • CID 2004:39 (1 December) • EMERGING INFECTIONS
Unknown Etiology
Case 20

- Woman from low jungle
- 3 weeks of burning skin
- Fever, chills, unwell
- Clearing-burning jungle prior to illness
- Others in community with similar affliction
Fogo selvagem  
(“wild fire”)  

- Endemic and epidemic pemphigus foliaceus  
- Particularly in Amazon basin (Brazil & Peru)  
- Often affect many in village at same time  
- ? bite of black fly  
  \((Simulium\ damnosum)\)
Fogo Selvagem

• Clinically and histologically identical to pemphigus foliaceus:
  – Immunofluorescence results similar
  – Treat with prednisone, possibly dapsone as steroid sparing agent (widely available)
  – Course/outcome highly variable
Thanks!