BUGS IN THE BLOOD

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Hematopathology
Victoria, BC

Morphology of Microbes

- VIRUSES
- BACTERIA
- PARASITES

- RBC
- WBC
- BLOOD

<table>
<thead>
<tr>
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- Morphologic detection of “bugs in the blood”

- “Bugs” also affect the “blood”:
  - “Responses” = leukocytosis, cytopenias versus
  - “Pathologies” = Hemolysis

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**INFECTIONOUS DISEASE LAB TESTING:**

- GRAM STAIN
- CULTURE & SENSITIVITY
- SEROLOGY (IgM, IgG) --- ex. ELISA
- MOLECULAR ------ ex. PCR
- CBC
- MORPHOLOGY --- Peripheral smear, marrow Bx
INFECTIOUS MONONUCLEOSIS

• Etiology = EBV virus
• Pathology = Infects B-cells, T-cells are reactive
  Autoanti-i cold agglutinin
• Clinical = 10-25 yo
  Fever, sore throat, fatigue
  Lymphadenopathy
  Splenomegally (50%)
• Lab =

MONONUCLEOSIS

INFECTIOUS MONONUCLEOSIS: TONSILLITIS
MONONUCLEOSIS

- **Etiology:** EBV virus
- **Pathology:** Infects B-cells, T-cells are reactive
  Autoanti-i cold agglutinin
- **Clinical:** 10-25 yo
  Fever, sore throat, fatigue
  Lymphadenopathy
  Splenomegally (50%)
- **Lab:** CBC
  Morphology
  Monospot test → False negatives
  EBV serology → IgM VCA

*What Is The Monospot Test?*

Direct solid-phase immunoassay
To detect Heterophile Antibodies

**HANTAVIRUS INFECTION**

1) Thrombocytopenia
2) Plasma cells and immunoblasts
3) Left-shifted, non-toxic neutrophilia
HANTAVIRUS

- Transmission:
  - Rodents, eg. Deer mice
  - Airborne

- Pathology:
  - Increase pulmonary capillary permeability?

- Clinical:
  - Flu-like
  - Hantavirus Pulmonary Syndrome (Rare but severe)

- Lab:
  - Serology – via ELISA
  - CBC
  - Morphology

Rat Temple, India
• **Transmission**= Blood, Air, Vertical
• **Pathology**= - ss DNA virus  
  - Replicate in dividing cells
• **Diseases**=  
  Erythema infectiosum (5th Disease)  
  Fetal infection  
  Pure red cell aplasia – Transient  
  - Chronic
• **Lab**=  
  - 5th Disease = Clinical +/- Serology  
  - PRCA = morphology + PCR

5th Disease Rash: Slapped Cheek  
And Glove & Stocking Appearance
HEMOLYSIS DUE TO C.WELCHII (PERFRINGENS) TOXIN

CLOSTRIDIUM WELCHII

- What: gm + bacilli, spore, anaerobe
- Transmission: Spores into damaged tissue
  - Fecal-oral
- Pathology:
  - Exotoxins
  - Hemolytic anemia
  - Gas gangrene
  - Necrosis
  - GI ulcers/perforation
  - N/V/D/ abdominal pain
- Lab:
  - Hemolytic tests = retic, LDH, bilirubin
  - Haptoglobin, DAT, CBC.
  - C & S

GAS GANGRENE DUE TO C.WELCHII
SPIROCHETE: BORRELIA RECURRENTIS

SPIROCHETES

• Borrelia recurrentis
• Borrelia burgdorferi
• Leptospira
• Treponema pallidum

• Length
• Width
• Number of spirals
<table>
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<td>3 Stages:</td>
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<td><strong>B. Burgdor.</strong></td>
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### LEPTOSPIRAE

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### TREPONEMA PALLIDUM
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**3 Stages/Lesions of Syphilis:**

1. Painless ulcer/chancre, lasts 1 to 2 months
2. Maculopapular rash, can be on palms/soles
3. 1/3 of untreated go on to tertiary syphilis years later
   - “Gummas”
   - eyes, brain, bone, etc.

**BORRELIA BURGDORFERI**
### Transmission Clinical

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### 3 Stages of Lyme’s Disease:
1. Erythema Migrans – diagnostic but rarely present.
2. Flu-like, facial palsies, heart palpitations, joint swelling/pain, etc.
3. Arthritis + cardiovascular and neurological systems may be affected.

### First Line Tests for Spirochetes:
- **B. Recurrentis**: Serology (ELISA), PCR
- **Leptospirae**: Serology (ELISA), Cultures of blood and urine
- **Syphilis**: RPR screen, TP-PA (particle agglutination), DFA or PCR of lesions
- **B. Burgdorferi**: Serology as screen (ELISA), Western Blot, PCR of fluids
EHRLICHIOSIS

- What = Gram neg, Obligate intracellular rickettsiae
- Transmission = Ticks
- Pathology = Infect circulating WBC
- Clinical = Flu-like signs & symptoms
- Lab = Morphology, PCR, Serology neg in 85% within first 7 – 10 days of infection
**BARTONELLA BACILLIFORMIS**

- **What**: Gram neg. aerobic, flagellated, rod
- **Epidemiology**: Peru, Equador, Colombia
- **Transmission**: Sandfly
- **Pathology**:
- **Clinical**:
- **Lab**:

---

**Sandfly: Carrier of Disease**
BARTONELLA BACILLIFORMIS

• What= Gram neg. aerobic, flagellated, rod

• Epidemiology= Peru, Equador, Colombia

• Transmission= Sandfly

• Pathology= Invade RBC → IV hemolysis ♣
   Endothelium → Vascular Tumor ♦

• Clinical= ♣ Oroya Fever
   ♦ Verruga Peruana

• Lab= -Morphology: Blood and Skin Bx + silver stain
   -Blood C&S, Serology, PCR

VERRUGA PERUANA DUE TO BARTONELLA

MAHA “Triad”
MAHA Triad =
- Schistocytes
- Anemia
- Thrombocytopenia

MAHA Types =
- HUS
- TTP
- Severe DIC
- HELLP Syndrome

ABOUT MAHAs…

MAHA “Triad”:
HUS DUE TO E.COLI TOXIN

E.coli O:157 H7
Verotoxin
Meat, milk, Juice, etc
Bloody diarrhea

HUS MECHANISM??

Renal Insufficiency
Micro-thrombosis
MAHA
Lab Tests To Assess HUS

- CBC (~ mins)
- Peripheral smear (~ mins)
- Stool C&S (~ 24 hrs)
- Stool PCR for shigatoxin (~ 48 hrs)
- Ideally need a rapid test to differentiate HUS from TTP

TOXOPLASMOsis gondii
(Parasitic protozoa)

TOXOPLASMOsis: life cycle

Cat Feces

Pregnant Mom

• Invade parenchyma, monocyte/macrophage
• Acute phase --------- Tachyzoites
• Chronic phase ------ Bradyzoites form cysts

Baby
TOXOPLASMOSIS

• Clinical=
  -Adults: asymptomatic to mild unless immunocompromised (reactivation)
  -Baby: more severe the earlier in gestation the infection occurs

• Involvment =
  -Fluid: blood, sputum, CSF
  -Tissue: marrow, lymph node, spleen, eyes, ears, liver, heart, brain

• Tests=
  -Serology
  -Morphology

BABESIOSIS
(Parasitic Protozoa)

To differentiate from malaria:

• Extracellular forms
• Tetrads, dyads
• No pigment
**BABESIOSIS**

- **Morphologic Differential**: P. falciparum
- **Transmission**: Tick
  - Also carrier for Lyme’s
  - Ehrlichiosis
- **Clinical**: Asymptomatic to mild
  - Severe hemolysis is rare
- **Tests**: Morphology
  - Serology (1st 7 days false-neg can occur)
  - Tests for co-infections

---

**Malaria:**

*Plasmodium falciparum*

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**About “Bad Air” Malaria:**

- **What**: Parasite, 4 species
  - P. falciparum
  - P. vivax
  - P. ovale
  - P. malariae
- **Transmission**: Female anopheles mosquito
- **Clinical**: Uncomplicated: fever, chills, may be cyclic
  - Severe: CNS, respiratory, renal, metabolic
- **Epidemiology**=
- **Tests**=
Mosquito: Carrier of Malaria

**About “Bad Air” Malaria:**

- **What:** Parasite, 4 species - P. falciparum, P. vivax, P. ovale, P. malariae
- **Transmission:** Female anopheles mosquito
- **Clinical:**
  - Uncomplicated: fever, chills, may be cyclic
  - Severe: CNS, respiratory, renal, metabolic
- **Epidemiology:** ~1 million deaths in those < 5 yo
  - Africa, Asia, S. America, Central America, Caribbean, Middle east…
- **Tests:**

Geographical Distribution of Malaria, WHO
About “Bad Air” Malaria:

• What = - Parasite, 4 species - P. falciparum - P. vivax - P. ovale - P. malariae

• Transmission = - Female anopheles mosquito

• Clinical = - Uncomplicated: fever, chills, may be cyclic - Severe: CNS, respiratory, renal, metabolic

• Epidemiology = - ~ 1 million deaths in those < 5 yo - Africa, Asia, S. America, Central America, Caribbean, Middle east…

• Tests = - Morphology + rapid diagnostic test (RDT) - PCR

Malaria Rapid Diagnostic Test

What = - Adjunct test to confirm morphology - Not for monitoring therapy

Principle = - Immunochromatography to detect: - HRP-2 = detects only P.falciparum - LDH - Aldolase

Pros = - Quick, easy, presence/absence of falciparum

Cons = - False positives (RF, heterophile Ab) - False negatives (gametocytes, prozone effect) - Inaccurate if any change in temp, humidity, etc. - Proteins can persist for 2 weeks post-therapy although asexual stages are eradicated

Morphology: still the gold standard

1. Degree of Parasitemia
2. Speciation
Hypnozoites
- Vivax
- Ovale

MALARIA

- P. falciparum
- P. vivax
- P. ovale
- P. malariae

- Trophozoite size, number
- Schizont merozoite number
- Gametocyte shape
- RBC size
- Pigment present

P. FALCIPARUM:
TROPHOZOITE & GAMETOCYTE
P. VIVAX: TROPHOZOITE & SCHIZONT

P. MALARIAE TROPHOZOITE

P. OVALE TROPHOZOITE
LEISHMANIA DONOVANI

LEISHMANIA

- **What**: Blood / tissue parasitic protozoa
- **Epidemiology**: Tropics / Subtropics
- **Transmission**: Sandfly
- **Clinical**
  - Visceral—— *L. donovani* (can be lethal)
  - Cutaneous ulcers (milder)
  - Mucocutaneous (severe)
- **Lab**
  - Morphology: blood, marrow or skin
  - C & S of punch biopsy

VISCERAL LEISHMANIASIS
CUTANEOUS LEISHMANIASIS

TRYPANOSOMA CRUZI

About Trypanosoma...

What = - A parasitic protozoa
Pathologic species = - T. gambiense
- T. rhodesiense
- T. cruzi
Tests = - Serologic screen
- Morphologic diagnosis
<table>
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<th>Disease</th>
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<td>T. gambiense</td>
<td>African Sleeping Sickness</td>
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<tr>
<td>T. rhodesiense</td>
<td>-1st phase = flu-like</td>
</tr>
<tr>
<td>T. cruzi</td>
<td>Chaga’s Disease</td>
</tr>
<tr>
<td>T. rangeli</td>
<td>Non-pathogenic</td>
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- **1st phase** = flu-like
- **2nd** = can be lethal
- Acute = swelling
- Chronic = dormant,
  - ~25% get enlarged heart, colon, esophagus

**CHAGAS DISEASE: ROMAÑA’S SIGN**
• Overall Relative Length
  • Anterior= Flagellum length
  • Membrane= Degree of undulation
  • Posterior= Kinetoplast size

• T. rhodesiense/
  T. gambiense

• T. cruzi

• T. rangeli

T. GAMBIENSE & T. CRUZI
**WUCHERERIA BANCROFTI**
(Parasitic Nematode)

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<td>W. Bancrofti</td>
<td>Mosquito</td>
<td>- Elephantiasis (Lymphedema)</td>
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<tr>
<td>(S.E. Asia, Africa)</td>
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<tr>
<td>B. Malayi</td>
<td>Mosquito</td>
<td>- Lymphadenitis,</td>
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<td>Loa Loa</td>
<td>Deer fly</td>
<td>- Conjunctiva,</td>
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<tr>
<td>(W &amp; C Africa)</td>
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<td>- Skin (Calabar swellings)</td>
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<td>M. Perstans</td>
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<td>- Non-pathogenic</td>
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**ELEPHANTIASIS**
Loa Loa: The “Eye Worm”

- SHEATH
- Nuclei at tip
- Shape of tip

Other than Loa Loa, which other microfilariae involves the skin and eyes?

Onchocerca volvulus
Oncocerca Volvulus:

- No sheath
- No nuclei at tip
- Longer

- Skin nodules
- “River blindness”

- No sheath yet pathogenic?
- Pathogenesis due to dead worms releasing the endosymbiotic bacteria Wolbachia species.

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Textbooks

Websites
2. BCCDC – BC Center for Disease Control: http://www.bccdc.ca/default.htm

Experts
Discussions with Dr. Pamela Kibsey, Medical Microbiology, Victoria BC