Fever and Rash: Infectious Diseases of Leisure: *Urgencies, Emergencies and Nuisances*

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Associate Hospital Epidemiologist

VCU Medical Center
Virginia Commonwealth University
When Mars Meets Venus....
Case 1

• 21 year old man complained of 3 days of flu-like illness with low grade fever, arthralgias and myalgias
• Over the past 24 hours he noted tender pustular lesions on his hands, feet, arms, legs and lower back.
• He denied headache, photophobia, meningismus, genital lesions and penile discharge
• The past medical history is significant for a history of genital HSV.
Case 1

- Physical examination:
  - Vitals: T 38.8C, P100, RR 14, BP 130/72
  - General: appears uncomfortable
  - HEENT/Chest/Abdomen: all WNL
  - Genitals: normal, no lesions, no penile discharge
Pustular, tender erythematous lesions
Pustular, tender erythematous lesions
Pustular, tender erythematous lesions
Swollen and tender PIP joint, 3rd digit of right hand
Extremities: swollen, tender, erythematous left knee
Gonococcemia
Gonococcus

- Gram negative diplococcus
- Humans are the only natural host
- Transmitted sexually by contact with an infected individual; may be transmitted from mother to baby during birth
Cases of *N. gonorrhea* in the United States, 1996-2003

<table>
<thead>
<tr>
<th>Year</th>
<th>Cases</th>
<th>Rate (per 100K)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1996</td>
<td>328,169</td>
<td>121.8</td>
</tr>
<tr>
<td>1997</td>
<td>327,665</td>
<td>120.2</td>
</tr>
<tr>
<td>1998</td>
<td>356,492</td>
<td>129.2</td>
</tr>
<tr>
<td>1999</td>
<td>360,813</td>
<td>129.3</td>
</tr>
<tr>
<td>2000</td>
<td>363,136</td>
<td>128.7</td>
</tr>
<tr>
<td>2001</td>
<td>361,705</td>
<td>126.8</td>
</tr>
<tr>
<td>2002</td>
<td>351,852</td>
<td>122.0</td>
</tr>
<tr>
<td>2003</td>
<td>335,104</td>
<td>116.2</td>
</tr>
</tbody>
</table>

Centers for Disease Control and Prevention. [Sexually Transmitted Disease Surveillance, 2003](https://www.cdc.gov/std/stats03/).
Richmond, Virginia: Gonorrhea Rate Tops US Chart

*Times-Dispatch (Richmond, Va.)*

03.06.02; Tammie Smith

Richmond, Va., had the **highest gonorrhea rate in 2000 among US cities**, even though the actual number of cases declined from 1999. In 1999, Richmond had the nation's second-highest gonorrhea rate, just below Baltimore's. Baltimore dropped to third place in the 2000 calculations.

*Richmond's gonorrhea rate was 923.6 cases per 100,000 residents in 2000; this is about seven times the national average* of 131.6 cases per 100,000 people. In raw numbers, Richmond recorded 1,752 cases of gonorrhea in 2000, down from 1,827 the year before; however, greater declines in other high-ranking cities put *Richmond in the top spot.*
Gonococcemia

Overt clinical signs of genital infection are frequently absent in disseminated gonococcemia.

*N. gonorrhoea* is cultured from a mucosal site in 80% of the cases.
The multiple potential paths of Gonococcal invasion
# Gonococcemia

<table>
<thead>
<tr>
<th>Mode of Transmission</th>
<th>Clinical Manifestations</th>
<th>Dermatologic Manifestations</th>
</tr>
</thead>
</table>
| Person to person via sexual contact | • Fever  
  • Chills, malaise  
  • Joint pain: either single or multiple joints (knee pain, wrist pain, ankle pain)  
  • Joint swelling (knees, wrists, ankles) | • Skin rash: begins as flat, pink-to-red macules that evolve into pustular papules and nodules  
  • Painful tendons of wrists, digits, heels  
  • A combination of skin rash and aching, swollen tendons |
## Gonococcemia

### Diagnostic Pearls

<table>
<thead>
<tr>
<th>Ask about sexual activity!</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Intercourse and oral sex</td>
</tr>
</tbody>
</table>

- Blood culture
- Skin lesion culture
- Culture of synovial fluid from joints
- Urethral discharge culture
- Culture from endocervix
- Throat culture
- Anal culture
- Cultures should be performed on *chocolate agar*

### Management

- Treatment is usually with intravenous antibiotics:
  - Ceftriaxone
  - Levofloxacin

- Concurrent treatment for chlamydia should be given:
  - Doxycycline
  - Azithromycin

Ask about sexual activity!
Crowded Environments
Case 2

- A 24 year old inmate from the Richmond City Jail with fever, headache and myalgias 24 hours prior to admission.
- Over the last 12 hours nuchal rigidity developed.
- He was found unconscious in his cell and immediately transferred to VCU.
Case 2

T:39.9°C, P=1118, BP=130/80, RR-20

Appears ill, uncooperative
Nuchal rigidity noted
Cardiac and respiratory exams normal
Abdomen soft and non-tender
Cutaneous exam: petechial rash - non blanching, with diffuse purpura on lower extremities
Case 2

WBC 17,000, 90%N
BUN/Creatinine- WNL
LFT: AST 55/ALT 45
CXR: clear
LP: increased pressure: cloudy; increased protein, decreased glucose

Gram stain
Meningococcal Disease

Inmate dies of meningitis

No other cases reported among other inmates, city jail staff

BY JIM MASON
Times-Dispatch Staff Writer

A Richmond City Jail inmate diagnosed with bacterial meningitis died yesterday morning in Medical College of Virginia Hospitals.

The Richmond Sheriff’s Office identified the inmate as Stephen Stevenson but provided no other details about him. A hospital spokesperson confirmed the death.

Sheriff Michelle B. Mitchell couldn’t be reached last night, but a news release from her office yesterday afternoon said there had been no other reported cases among inmates or jail staff.

Doctors at MCV’s Infectious Disease Clinic made the diagnosis and recommended treatment with an antibiotic for anyone who had had contact with the inmate, the release said.

The jail’s night watch commander, asked last night whether any jail inmates or staff had been treated, said he wasn’t authorized to give any information.

According to the news release, Stevenson entered the jail July 23.

Friday, he became ill with flu-like symptoms and was treated at the jail for pain and a fever.

A physician at the jail treated him Saturday morning for a viral infection and dehydration, the news release said.

Saturday evening, Stevenson’s condition deteriorated, and he was taken to MCV.

Meningitis is an infection of the fluid of a person’s spinal cord and fluid surrounding the brain. Viral meningitis is generally less severe, while bacterial meningitis may result in brain damage and is potentially fatal.

Infection is marked by high fever, headache and a stiff neck. Symptoms that can develop within hours or a few days. Other symptoms may include nausea, vomiting and sleepiness.

Medical authorities say early diagnosis and treatment with antibiotics are critical.

Contact Jim Mason at (804) 649-6451 or jmason@timesdispatch.com

MONDAY, SEPTEMBER 10, 2001

Meningitis hits VUU student

Bacterial version strikes freshman

BY SHAWN COX
Times-Dispatch Staff Writer

An 18-year-old freshman at Virginia Union University was in critical condition last night after contracting bacterial meningitis, a rare but contagious, and potentially fatal, infection.

The New York City native, whose identity is being withheld at the request of his family, was admitted to Virginia Commonwealth University’s Medical College of Virginia Hospitals about 3 a.m. yesterday after experiencing vomiting and other flu-like symptoms.

“The doctor said, if he had a crystal ball and could look in it and tell us that everything was going to be all right, he certainly would want to be able to do that,” VUU President Bernard W. Franklin said last night. “But at this point, the best that we can do is wait and pray.

“This has been a very sobering experience for our students, even though during our freshman orientation program we did emphasize the importance of getting a vaccination for meningitis. After the sobering effect, I...
### Meningococcal Disease: Recent Cases at MCVH

<table>
<thead>
<tr>
<th></th>
<th>Case #1</th>
<th>Case #2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admit date</td>
<td>August 11, 2001</td>
<td>September 8, 2001</td>
</tr>
<tr>
<td>Age/gender</td>
<td>24 year old male inmate</td>
<td>18 year old male college student</td>
</tr>
<tr>
<td>Residence</td>
<td>Richmond City Jail</td>
<td>Virginia Union U. dormitory</td>
</tr>
<tr>
<td>Presentation</td>
<td>1 day h/o headache, fever, myalgias; found unconscious</td>
<td>1 day h/o headache, nausea; seizure</td>
</tr>
<tr>
<td>PMH</td>
<td>GSW abdomen 1997→ asplenic</td>
<td>PMH: “meningitis” at age 9</td>
</tr>
<tr>
<td>Outcome</td>
<td>Died on hospital day #3</td>
<td>Discharged on hospital day #23</td>
</tr>
</tbody>
</table>
Microbiology

- Gram-negative, biscuit-shaped diplococci
- Usually found extracellularly & in PMNs
- Usually encapsulated & piliated
- Aerobic
- 13 serogroups based on capsular polysaccharide
- Humans are the only natural reservoir
Epidemiology of Meningococcal Disease

- 2,400-3,000 cases/year in the US
- 500,000 cases/year in the world
- 2nd most common cause of meningitis in the US (10-35% of cases)
- >90% of cases occur in pts <45 years old
- Numerous outbreaks on college campuses
- Meningitis belt: intense serogroup A epidemics in broad savannah region in Africa from Gambia to Ethiopia

Source: WHO, 1998
## Risk Factors for Meningococcal Disease in College Students

Matched (3:1) case control study; 96 cases; multivariate analysis

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freshman in dormitory</td>
<td>3.6 (1.6-8.5)</td>
<td>.003</td>
</tr>
<tr>
<td>White race</td>
<td>6.6 (1.2-38.0)</td>
<td>.03</td>
</tr>
<tr>
<td>Radiator heat</td>
<td>4.0 (1.4-11.0)</td>
<td>.008</td>
</tr>
<tr>
<td>URI in last month</td>
<td>2.3 (1.0-5.3)</td>
<td>.04</td>
</tr>
</tbody>
</table>

Bruce MG et al. JAMA 2001;286:688-693.
# Meningococcal Disease, US Army, World Wars

<table>
<thead>
<tr>
<th></th>
<th>Number of cases</th>
<th>Number of deaths</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>World War I</td>
<td>5,839</td>
<td>1,836</td>
<td>31.4%</td>
</tr>
<tr>
<td>World War II</td>
<td>13,922</td>
<td>559</td>
<td>4.0%</td>
</tr>
</tbody>
</table>

Host Response to Respiratory Infection with *N. meningitidis*

- Complete eradication of the organism
- Nasopharyngeal carrier state without systemic invasion
- Nasopharyngeal carrier state leads to systemic disease
Transmission

- Person to person by respiratory droplets or direct contact with secretions
- Since respiratory droplet susceptible to drying, close contact (<3 feet) is necessary for transmission
- Most pts have not had contact with a case, thus *asymptomatic carriers* are the source of transmission
- 300-1000 fold increased risk for invasive disease in household contacts of an index case (attack rate 0.3-1%)
- 1/1000-1/5000 colonized persons develops invasive disease
Colonization

- Site of colonization is the nasopharynx
- 5-10% of adults are asymptomatic carriers
- Median duration of carriage = 9-10 months
- Carriage rate increases under conditions where people from different regions are brought together (e.g., military recruits, pilgrims, colleges, jails)

Pathology

- Primary lesion: diffuse vascular damage & intravascular coagulation
- Blood vessels blocked by fibrin thrombi with trapping of WBCs & bacteria → tissue ischemia
- Sites: skin, serosal & mucosal surfaces, mediastinum, epicardium, endocardium, lungs, liver, kidneys, adrenals, intestines, spleen
<table>
<thead>
<tr>
<th>Clinical Syndromes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacteremia without sepsis</strong></td>
</tr>
<tr>
<td>(transient benign bacteremia)</td>
</tr>
<tr>
<td>Child presents with upper respiratory illness or viral</td>
</tr>
<tr>
<td>exanthem; blood cultures surprisingly grow NM but</td>
</tr>
<tr>
<td>repeat cultures negative; uncomplicated recovery</td>
</tr>
<tr>
<td>without antibiotics</td>
</tr>
<tr>
<td><strong>Meningococcemia without meningitis</strong></td>
</tr>
<tr>
<td>Septic picture; headache, fever, rash, malaise,</td>
</tr>
<tr>
<td>hypotension</td>
</tr>
<tr>
<td><strong>Meningitis + meningococcemia</strong></td>
</tr>
<tr>
<td>Headache, fever, meningeal signs, cloudy CSF; DTRs,</td>
</tr>
<tr>
<td>superficial reflexes present; no pathologic reflexes</td>
</tr>
<tr>
<td><strong>Meningoencephalitis</strong></td>
</tr>
<tr>
<td>Profoundly obtundated, meningeal signs, septic CSF;</td>
</tr>
<tr>
<td>DTRs, superficial reflexes altered; pathologic</td>
</tr>
<tr>
<td>reflexes frequently present</td>
</tr>
</tbody>
</table>

Acute Meningococcemia without Meningitis

• Presents with sudden onset of fever, chills, myalgias, weakness, nausea, vomiting, headache
• Leukocytosis with left shift
• Rash present or develops over next few hours
• Some develop hypotension or shock
• In fulminant cases, death can occur within 12 hours of symptom onset
Acute Meningococcemia: Rash

• Erythematous maculopapular rash
  – Light pink
  – Indistinct borders
  – Transient (half hour to 2 days)

• Purpuric rash
  – Occurs in 40-90%
  – Always accompanied by DIC
  – Petechiae, ecchymoses or gross intracutaneous hemorrhages
  – Purpura usually appear within 12-36 hours of disease onset
  – May lead to purpura fulminans
Meningococcemia Complications

- Purpura fulminans
- Autoimmune-like complications:
  - Synovitis
  - Serositis
- Neurologic sequelae (0-15%)
  - Deafness (4-6%)
  - CN VI, VII palsies (5-10%)
Meningococcemia Complications

- Bilateral adrenal hemorrhage (Waterhouse-Friderichsen Syndrome)
  - Found in 30% of patients with shock secondary to meningococcal disease
  - Found in 70% of cases at autopsy

Laboratory Studies

- CSF: gram stain positive in 75-80%; culture positive in 90%
- CSF latex agglutination: 70-80% sensitive
- Peripheral blood smear: organisms may be seen indicating high-grade bacteremia; suspect asplenic state
- Blood culture: positive in 40-75%
Chronic Meningococcemia

- Chronic meningococcemia is a rare (<200 documented cases) clinical presentation of *N. meningitidis* most often observed in adults.
- Clinically, it can be confused with the dermatitis-arthritis syndrome associated with subacute gonococcemia.
  - Recurrent attacks of fever associated with migratory arthralgias, arthritis, and leukocytosis.
  - Recur over a period of 6-8 months.
  - Cutaneous manifestations are variable
    - include rose-colored macules and papules
    - indurated nodules, petechiae, purpura, or large hemorrhagic areas.
Chronic Meningococcemia

• Chronic meningococcemia differs histopathologically from acute meningococcemia
  – no bacteria are present in the cutaneous lesions
  – thrombi do not occlude capillaries and venules, and endothelial swelling does not occur.
  – The most common finding in a person with chronic meningococcemia is a leukocytoclastic angiitis.
Management

- Early fluid resuscitation for patients in shock
- Inotropic support
- Alkalization for patients with rhabdomyolysis
- Maintain high suspicion for adrenal insufficiency
- Empiric corticosteroids for meningococcal meningitis controversial

Management: Antimicrobials

• Should not be delayed for diagnostic procedures
• Drug of choice: ceftriaxone 2 g IV q 12 hr
Prognosis

• “No other infection so quickly slays...”
  Herrick WW. Arch Intern Med 1919;23:409-418.

• Almost all deaths from meningococcal meningitis are due to cerebral edema and brainstem herniation

• Little improvement in outcome over the past few decades despite significant advances in critical care

• Meningitis: 10-15% mortality
• Meningococcemia: up to 40% mortality
• Sequelae (hearing loss, neurologic disability, limb loss) in 11-19%
The Great Outdoors
Case 3

• A 12 year old boy presents to the emergency department with a 2 day history of chills, fever and headache after a camping trip.
• These symptoms were preceded by nausea, vomiting and abdominal pain but no diarrhea.
• There was no dyspnea or chest pain.
Case 3

T = 40°C, P-110 RR20, 120/60
Ill appearing
Conjunctival suffusion with periorbital edema
Cardiac- unremarkable
Chest- unremarkable
Abdomen: generalized tenderness
Labs:
WBC-10,000, Plts-160,000
AST-85; Alp-WNL
Chemistries WNL
CXR- WNL
RMSF-*Rickettsia rickettsii*

- *Rickettsia rickettsii*, an intracellular pathogen
- Organisms range in size from 0.2 x 0.5 micrometers to 0.3 x 2.0 micrometers.
- They are not visualized by routine staining.

Gimenez stain of tick hemolymph cells infected with *R. rickettsii*
RMSF - *Rickettsia rickettsii*
RMSF

Rocky Mountain wood tick
(*Dermacentor andersoni*)

- Rickettsiae are transmitted to a vertebrate host through saliva while a tick is feeding.
- It usually takes several hours of attachment and feeding before the rickettsiae are transmitted to the host.
- About 1%-3% of the tick population carries *R. rickettsii*, even in highly endemic areas.

The American dog tick
(*Dermacentor variabilis*)
RMSF

- Rocky Mountain spotted fever has been a reportable disease in the United States since the 1920s.
- In the last 50 years, approximately 250-1200 cases of Rocky Mountain spotted fever have been reported annually.
- Over 90% of patients with Rocky Mountain spotted fever are infected during April through September. This period is the season for increased numbers of adult and nymphal *Dermacentor* ticks.
The rash involves the palms or soles in as many as 50% to 80% of patients. As many as 10% to 15% of patients may never develop a rash.
RMSF

Early (macular) rash on sole of foot

Late (petechial) rash on palm and forearm

Caveat: Approximately 10–15% of patients have Rocky Mountain spotless fever. This more often is reported in older patients and African American patients.
## RMSF

<table>
<thead>
<tr>
<th>Mode of Transmission</th>
<th>Clinical Manifestations</th>
<th>Dermatologic Manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initial symptoms:</td>
<td>• The rash first appears 2-5 days after the onset of fever</td>
</tr>
<tr>
<td></td>
<td>• fever</td>
<td>• Early- small, flat, pink, non-itchy macules on the wrists, forearms, and ankles.</td>
</tr>
<tr>
<td></td>
<td>• nausea</td>
<td>• The characteristic red, spotted (petechial) rash of typically on the sixth day or later after onset of symptoms</td>
</tr>
<tr>
<td></td>
<td>• vomiting</td>
<td>• This type of rash occurs in only 35% to 60% of patients</td>
</tr>
<tr>
<td></td>
<td>• severe headache</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• myalgias</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• anorexia</td>
<td></td>
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<tr>
<td></td>
<td>Late signs and symptoms</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• abdominal pain</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• arthragias</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• diarrhea</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 3-5% mortality due to myocarditis</td>
<td></td>
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</tbody>
</table>
RMSF

• The indirect immunofluorescence assay (IFA) is the reference standard in Rocky Mountain spotted fever serology and is the test currently used by CDC and most state public health laboratories.

• IFA has a sensitivity of 70% and a specificity of 100%.
### RMSF

<table>
<thead>
<tr>
<th>Diagnostic Pearls</th>
<th>Serology:</th>
</tr>
</thead>
</table>
| • Fever, rash, and history of tick bite.  
• *Treatment decisions should be based on epidemiologic and clinical clues, and should never be delayed while waiting for confirmation by laboratory results.* | • Most patients demonstrate increased IgM titers by the end of the first week of illness.  
• Diagnostic levels of IgG antibody generally do not appear until 7-10 days after the onset of illness. |
RMSF

Diagnostic Pearls

- Thrombocytopenia with normal WBC and petechial rash is suggestive of RMSF
- The rash of RMSF begins peripherally and then spreads centrally
- Edema of the hands and feet is common
- Abdominal symptoms and CNS symptoms may predominate in the early presentation
- Conjunctival suffusion and periorbital edema are important clues to RMSF
RMSF

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
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</table>
| **Antibiotic:**  
tetracyclines (doxycycline) for 7-14 days.  
**Supportive Care:**  
IV hydration for hypotension or prerenal azotemia  
Supplemental oxygen and endotracheal (ET) intubation  
Packed red blood cells (pRBCs) for anemia or severe life-threatening GI bleeding  
Platelet transfusion for severe thrombocytopenia with active bleeding  
Hemodialysis for acute tubular necrosis |
Case 4

- A 40 year old man has been vacationing with his family in the New England Coast. Two weeks later he complains of progressive fever and myalgias. He denies cough, chest pain, dyspnea, diarrhea, abdominal pain and night sweats.
Case 4

Physical Exam
T:102F, P118, BP170/90, R14
Sick appearing, uncomfortable
HEENT-WNL
Chest: clear
Cardiac: no murmurs
Abdomen: possible splenomegaly
Ext: no edema or clubbing
Labs:
WBC 4100, 5% atypical lymphocytes
Plts 75,000, ESR-44
Chemistries-WNL, CXR-WNL
Dr. Paul Ehrlich
(Immunologist)

Dr. Sigmund Freud
(Not an immunologist)

However, they look alike, dress alike, have similar haircuts and appear to be fond of cigars
Human monocytic ehrlichiosis (HME) is caused by *Ehrlichia chaffeensisis*. Lone-star tick (*Amblyomma americanum*), American dog tick (*Dermacentor variabilis*), Deer tick (*Ixodes scapularis*), American dog tick (*D variabilis*).

Human granulocytic ehrlichiosis (HGE) is caused by *Ehrlichia phagocytophilia*.
Man’s Best Friend

Animals such as dogs, deer, and goats are common natural hosts (or reservoirs) for *E. chaffeensis* (which causes HME)
Ehrlichiosis

Infected or Uninfected Adult Female
*Amblyomma americanum*

Secondary Route

Uninfected Eggs

Uninfected Larvae

1st Blood Meal

Infected Nymph

2nd Blood Meal

3rd Blood Meal
Adult Mating

Infected Adult

Primary Route

Infected Human
# Ehrlichiosis

<table>
<thead>
<tr>
<th>Clinical Manifestations</th>
<th>Dermatologic Manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tick bites or exposure (&gt;90% in 1 series) Fevers (&gt;90%)</td>
<td>Rash (10%): When present in <em>ehrlichiosis</em>, the rash is <em>maculopapular</em> and <em>not</em> petechial. Evidence for vasculitis is not observed in ehrlichiosis as it is in RMSF.</td>
</tr>
<tr>
<td>Headaches (&gt;85%)</td>
<td></td>
</tr>
<tr>
<td>Malaise (&gt;70%)</td>
<td></td>
</tr>
<tr>
<td>Myalgias (&gt;70%)</td>
<td></td>
</tr>
<tr>
<td>Rigors (60%)</td>
<td></td>
</tr>
<tr>
<td>Nausea (40%)</td>
<td></td>
</tr>
<tr>
<td>Vomiting (40%)</td>
<td></td>
</tr>
<tr>
<td>Anorexia (40%)</td>
<td></td>
</tr>
<tr>
<td>Confusion (20%)</td>
<td></td>
</tr>
</tbody>
</table>

*Maculopapular* refers to red blotches that are raised and smooth on the skin.
**Ehrlichiosis**
The hematopoietic system is the main organ system affected. Target cells for the pathogens are monocytes or granulocytes.

Photomicrograph of a granulocyte containing the *Ehrlichia* morula (arrow) of HGE. Stain is with *Wright’s-Giemsa.*

*E.chafeensis* causing HME
# Ehrlichiosis

**Laboratory**

- The diagnosis of HME or HGE suggested by a single elevated immunoglobulin G (IgG) immunofluorescent antibody (IFA) *Ehrlichia* titer or by demonstrating a 4-fold or greater increase between acute and convalescent IFA *Ehrlichia* titers.
- Alert the lab to look for cytoplasmic inclusions (morulae), which are diagnostic of ehrlichiosis.
- Morulae occur more frequently in HGE than HME.
- A complete blood count (CBC) should be obtained for possible neutropenia, lymphocytopenia, or thrombocytopenia.
- Serum transaminases are mildly elevated as in other tick-borne transmitted infectious diseases.
### Ehrlichioses

#### Clinical Course
- The HME mortality rate is reported to be 2-5%, while that for HGE is 7-10%.
- HME has a reported hospitalization rate as high as 60%, while that for HE is 28-54%.
- Death is due to DIC and hemorrhagic complications.

#### Management
- Doxycycline is the preferred antibiotic.
- Supportive care may be necessary if symptoms are severe and if there are hemorrhagic complications.
<table>
<thead>
<tr>
<th><strong>RMSF</strong></th>
<th><strong>Ehrlichiosis</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Tick borne</td>
<td>• Tick borne</td>
</tr>
<tr>
<td>• Fever, headaches, arthralgias, myalgias are common</td>
<td>• Fever, headaches, arthralgias, myalgias are common</td>
</tr>
<tr>
<td>• Rash common; petechial in nature</td>
<td>• Rash uncommon: lacy, maculopapular</td>
</tr>
<tr>
<td>• Conjunctival suffusion and periorbital edema is an important diagnostic clue.</td>
<td>• Conjunctival suffusion and periorbital edema is <strong>absent</strong></td>
</tr>
<tr>
<td>• Serology or skin biopsy with IFA may help confirm diagnosis</td>
<td>• Wright’s Giemsa stain of blood may be diagnostic (morulae)</td>
</tr>
<tr>
<td>• Rx: doxycycline</td>
<td>• Rx: doxycycline</td>
</tr>
</tbody>
</table>
And remember…..

Ticks can carry more than one infectious agent:

Co-infections have occurred with *Babesia microti*, RMSF and/or *Ehrlichia* species.
Dining
Case

• “An Anchorage woman reported that she and her husband had become ill about one-half hour after consuming a meal of marinated raw salmon. Illness consisted of generalized hives, a brassy taste, flushing, abdominal cramps, nausea, and vomiting without diarrhea. Symptoms persisted for four hours.”
Case

• “August 12th, a Valdez physician informed our office that three days previous she had treated nine Japanese sailors for an illness which began one hour after eating a meal of mixed raw cod, flounder and salmon.”
• “Illness was said to have affected most of the 23 man crew, but only nine were seen by the doctor. “
• “She found tachycardia in two, hives in four, nausea in eight, and vomiting in two. No respiratory difficulty was noted. Treatment included emetics, antihistamines, and epinephrine.”
• “Symptoms resolved by morning and the crew left for Japan with a cargo of refrigerated raw fish.”
Is this an allergic reaction to fish?
Scombroid

- Scombroid fish poisoning is a food-related illness typically associated with the consumption of fish.
  - Scombroidea fish
    - large dark meat marine tuna, albacore, mackerel, skipjack, bonito, marlin Mahi-Mahi
Scombroid

Symptoms are related to the ingestion of biogenic amines, especially histamine. Serum histamine levels and urinary histamine excretion are elevated in humans with acute illness. The result is a massive histamine like reaction. Cooking does not inactivate the toxin!
# Scombroid

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Dermatologic Manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>The onset of symptoms is usually 10-30 minutes after ingestion of the implicated fish, which is said to have a characteristic <em>peppery bitter</em> taste.</td>
<td>Nonspecific: diffuse, macular, blanching erythema and hives</td>
</tr>
</tbody>
</table>

- Flushing
- Palpitations
- Headache
- Nausea and Diarrhea
- Sense of anxiety
- Prostration or loss of vision (rare)
- Tachycardia and wheezing
- Hypotension or hypertension
## Scombroid

<table>
<thead>
<tr>
<th>Diagnostic Pearls</th>
<th>Management</th>
</tr>
</thead>
</table>
| • Disease of acute onset and short duration  
  • Generally, the diagnosis is clinical; no laboratory tests are necessary.  
  • If the diagnosis requires confirmation, histamine levels can be measured in a the suspect frozen fish. | • ECG, IV access, oxygen, and cardiac monitoring as needed.  
  • Treat bronchospasm as needed  
  • Serum histamine levels and urinary histamine excretion is elevated in acute illness. Treat with antihistamines: H1- and H2-blockers.  
  • Consider use of activated charcoal only if presentation is very early and a large amount of fish was ingested. |
Paradise
Case report

• A 51-year-old woman was brought to the hospital after a close friend found her semiconscious, obtunded, and listless.
• The woman, a native of Korea, was seen at church on a Sunday, where she appeared healthy, alert, and talkative, without any complaints or symptoms. The next morning, she began to experience episodic chills lasting 30 to 40 minutes.
• As the day progressed, her appetite waned as she became weaker. That evening, her lethargy was so pronounced that she could not get up from her couch.
• The patient had a medical history of chronic active hepatitis B virus (HBV) infection
Case report

- The patient was brought to the emergency department, where she was lethargic and diaphoretic.
- She was tachypneic (25-32 breaths/min) and mildly tachycardic (95-105 beats/min) with a temperature of 103°F and systolic blood pressure between 90 and 100 mm Hg.
- Physical examination revealed that she was obtunded and lethargic. Her sclera was icteric, and her skin was jaundiced with mild generalized edema.
- Auscultation of her abdomen revealed decreased bowel sounds.
- Palpation of the abdomen revealed diffuse tenderness, and a liver edge was noted 2 to 3 cm below the costodiaphragmatic angle.

http://www.residentandstaff.com/article.cfm?ID=281
Case report

• Edema of the legs was noted, with the right being more swollen than the left.
• The right leg was erythematous and exquisitely tender with any movement or palpation.
• Two prominent blisters, approximately 4 and 6 cm in diameter, soft and compressible and filled with serous fluid.
Case Report

• On the third day, the surgery and orthopedic specialists concurred that surgical debridement of the right leg was necessary.

• The surgical specimen taken from the right ankle grew a bacillus species later identified as Vibrio vulnificus.

• It was discovered that she had purchased a can of oysters but could not recall if she consumed it.

http://www.residentandstaff.com/article.cfm?ID=281
Vibrio vulnificus

June 04, 1993 / 42(21);405-407

July 26, 1996 / 45(29);621-624
Vibrio vulnificus Infections Associated with Eating Raw Oysters -- Los Angeles, 1996
Vibrio vulnificus

Vibrio vulnificus causes wound infections, gastroenteritis or a serious syndrome known as "primary septicema."
**Vibrio vulnificus**

<table>
<thead>
<tr>
<th>Mode of Transmission</th>
<th>Clinical Manifestations</th>
<th>Dermatologic Manifestations</th>
</tr>
</thead>
</table>
| Transmitted to humans through open wounds in contact with seawater or through consumption of certain improperly cooked or raw shellfish. **AVOID RAW CLAMS and OYSTERS!** | -Gastroenteritis: usually develops within 16 hours of eating the contaminated food  
-Sepsis: 60% case fatality  
Over 70 percent of infected individuals have distinctive bullous skin lesions. | From hematogenous spread or from direct inoculation  
**Bullous skin lesions** |
Vibrio vulnificus


Vibrio vulnificus

• High Risk Conditions Predisposing to Vibrio vulnificus infection:
  – Liver disease, either from excessive alcohol intake, viral hepatitis or other causes
  – Hemochromatosis, an iron disorder
  – Diabetes
  – Stomach problems, including previous stomach surgery and low stomach acid (for example, from antacid use)
  – Cancer
  – Immune disorders, including HIV infection
  – Long-term steroid use (as for asthma and arthritis).
# Vibrio vulnificus

## Diagnostic Pearls

- Consumption of shellfish, clams
- Exposure to seawater (bathing/swimming)
- Violaceous, large bullous lesions
- Sepsis

_A physician should suspect V. vulnificus if a patient has watery diarrhea and has eaten raw or undercooked oysters or when a wound infection occurs after exposure to seawater_

## Culture

Vibrio organisms can be isolated from cultures of stool, wound, or blood

*V. vulnificus* infection is diagnosed by routine stool, wound, or blood cultures

- The laboratory should be notified as a special growth medium is preferred

## RX:

Doxycycline or a third-generation cephalosporin (e.g., ceftazidime)
Hot tub party
Pseudomonas Dermatitis/Folliculitis Associated With Pools and Hot Tubs -- Colorado and Maine, 1999--2000

• The Colorado Department of Public Health and Environment (CDPHE) was notified of approximately 15 persons with folliculitis after they had used a hotel pool and hot tub.

• The Maine Bureau of Health (MBOH) was notified of several cases of dermatitis/folliculitis among persons who had stayed at Hotel A in Bangor, Maine, during February 18--27, 2000.

www.cdc.gov/mmwr/preview/mmwrhtml/mm4948a2.htm
*P. aeruginosa*, ubiquitous gram negative organism found in soil and fresh water.

Gains entry through hair follicles or via breaks in the skin.

Minor trauma from wax depilation or vigorous rubbing with sponges may facilitate the entry of organisms into the skin.

Hot water, high pH (>7.8), and low chlorine level (<0.5 mg/L) all predispose to infection.
The rash onset is usually 48 hours (range, 8 h to 5 d) after exposure to contaminated water, but it can occur as long as 14 days after exposure.
**Pseudomonas Dermatitis/Folliculitis**

- Lesions begin as pruritic, erythematous macules that progress to papules and pustules.
- Lesions involve exposed skin, but they usually spare the face, the neck, the soles, and the palms.
- The rash usually clears spontaneously in 2-10 days, rarely recurs, and heals without scarring.
Systemic symptoms have been reported

Number and percentage of case patients with *Pseudomonas* dermatitis/folliculitis* associated with hot tub use, by symptom - Colorado, 1999

<table>
<thead>
<tr>
<th>Symptom</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash</td>
<td>19</td>
<td>(100)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>11</td>
<td>(58)</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>10</td>
<td>(53)</td>
</tr>
<tr>
<td>Fever</td>
<td>8</td>
<td>(42)</td>
</tr>
<tr>
<td>Joint pain</td>
<td>7</td>
<td>(37)</td>
</tr>
<tr>
<td>Muscle aches</td>
<td>6</td>
<td>(32)</td>
</tr>
<tr>
<td>Nodules on feet</td>
<td>5</td>
<td>(26)</td>
</tr>
<tr>
<td>Nodules on hands</td>
<td>5</td>
<td>(26)</td>
</tr>
<tr>
<td>Chest pain</td>
<td>4</td>
<td>(21)</td>
</tr>
</tbody>
</table>

* n = 19
## Pseudomonas Dermatitis/Folliculitis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>•Clinical presentation and history</td>
<td>• <em>P aeruginosa</em> is usually a self-limited infection, clearing in 2-10 days. Despite the discomfort caused by the rash, no treatment is necessary.</td>
</tr>
<tr>
<td>•The diagnosis is best verified by results of bacterial culture growth from either a fresh pustule or a sample of contaminated water.</td>
<td>•For complicated cases: associated mastitis, persistent infections, immunosuppression a course of ciprofloxacin (500 or 750 mg PO bid) is advised.</td>
</tr>
<tr>
<td>•Gram stain of a pustule</td>
<td></td>
</tr>
</tbody>
</table>
Conclusion

• Although uncommon, leisurely activities can predispose to certain infections either by personal or environmental contact, tick arthropod vectors, or ingested.

• Fever and rash are important clinical presentations of infectious diseases including gonococcemia, meningococcemia, RMSF, *Ehrlichiosis*, scombroid, *V. vulnificus* and *Pseudomonas* follicultis.

• Although confirmatory diagnostic tests are available, history, clinical presentation and epidemiologic clues are essential for the making the diagnosis.