ID Alert!
recognizing rapidly fatal infections
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Fever and…. 
- Rash and altered mental status
- Rash
- Muscle pain
- Lymphadenopathy
- Hypotension
- Shortness of breath
- Recent travel
- Abdominal pain and diarrhea

Case 1. The cross-country trucker
- A 30 year-old trucker driving from Oklahoma to California is hospitalized in Deming with fever and headache

- He is treated with broad-spectrum antibiotics, but deteriorates with obtundation, low platelet count, and a centrifugal petechial rash and is transferred to UNMH
What is your diagnosis?

What is the differential diagnosis of fever and headache with *petechial* rash? (in the US)
- Tickborne rickettsioses
  - RMSF
- Bacteria
  - Neisseria meningitidis

Key diagnosis in this case:
“doxycycline deficiency”
- Key vector-borne rickettsioses treated with doxycycline:
  - **RMSF**-case-fatality 5-10%
    - Fever, nausea, vomiting, myalgia, anorexia and headache
    - Maculopapular rash progresses to petechial after 2-4 days of fever
    - Occasionally without rash
- **Human granulocytotropic anaplasmosis (HGA)**: case-fatality<1%
- **Human monocytotropic ehrlichiosis (HME)**: case fatality 2-3%
Lab clues in rickettsioses

- The total white blood cell (WBC) count is typically normal in patients with RMSF, but increased numbers of immature bands are generally observed.

- Thrombocytopenia, mild elevations in hepatic transaminases, and hyponatremia might be observed with RMSF whereas leukopenia (up to 53% of patients), thrombocytopenia (up to 94% of patients), and modest elevations of liver transaminase levels are particularly suggestive of HME and HGA.

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**FIGURE 5.** Average reported annual incidence* of Rocky Mountain spotted fever, by state — United States, 1997-2002

* Per 1,000,000 persons per year.

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**FIGURE 12.** Comparison of mosquito (Aedes aegypti) and tick vectors, *A. americanum* (deer tick) and *D. variabilis* (brown dog tick), by the vector.
Meningococcal disease-skin lesions

Meningococcal lesions: back
Case #2 fever and rash

- Circa 1973, a sailor is seen in Seattle with a fever and rash, attempts are made to detain him, but he sails to San Francisco and is finally examined by public health authorities in Los Angeles.
- He has vesicular lesions
- Why was the sailor detained?

Smallpox: Rash Progression

- Day 4
- Day 5
- Day 7
- Days 8-9
Smallpox: Rash Distribution

Varicella in a Healthy Adult

Smallpox Vs. Chickenpox

<table>
<thead>
<tr>
<th></th>
<th>Variola</th>
<th>Varicella</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incubation</td>
<td>7-17 days</td>
<td>14-21 days</td>
</tr>
<tr>
<td>Fever prodrome</td>
<td>2-4 days</td>
<td>minimal/none</td>
</tr>
<tr>
<td>Distribution</td>
<td>face/extremities</td>
<td>trunk/clusters</td>
</tr>
<tr>
<td>Progression</td>
<td>synchronous</td>
<td>synchronous</td>
</tr>
<tr>
<td>Scab formation</td>
<td>10-14 d p rash</td>
<td>4-7 d p rash</td>
</tr>
<tr>
<td>Scab separation</td>
<td>14-28 d p rash</td>
<td>&lt;14 d p rash</td>
</tr>
<tr>
<td>Lesions soles/palms</td>
<td>yes</td>
<td>no</td>
</tr>
</tbody>
</table>
ID alert: Rash and fever
Reportable illnesses to DOH
• All vaccine-preventable illnesses
• Measles—eliminated from Western Hemisphere, but, of the vaccine-preventable diseases, measles is the leading killer of children accounting for nearly 800,000 deaths each year. Over half of global measles deaths occur in African infants and children.
• Mumps
• Rubella
• Chickenpox
• If any of the above is suspected in a healthcare worker, that raises the level of urgency and need for contact investigation even higher.
  - Call 505-827-0006

Case #3 Fever and muscle pain
• A young man presents to an emergency room complaining of severe leg pain
• He has been taking ibuprofen, but states he has been feeling chilled and has had some subjective low grade temperatures

By the time he is transferred, the patient develops a cellulitis
Which progresses to…..

Classification of rapidly fatal skin and soft tissue infections

<table>
<thead>
<tr>
<th>Classification</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Necrotizing fasciitis</td>
<td>Acute, rapidly developing infection of deep fascia; marked pain, tenderness, swelling, and often crepitus; bullae and necrosis of underlying skin</td>
</tr>
<tr>
<td>Type I (mixed infection of anaerobes and facultative species such as streptococci or gram-negatives, CA-MRSA also associated)</td>
<td></td>
</tr>
<tr>
<td>Type II (infection with group A streptococci)</td>
<td>Acute infection, often accompanied by toxic shock syndrome; rapid progression of marked edema to violaceous bullae and necrosis of subcutaneous tissue; absence of crepitus</td>
</tr>
<tr>
<td>Anaerobic myonecrosis (gas gangrene, due to Clostridium perfringens)</td>
<td>Rapidly progressive toxemic infection of previously injured muscle, producing marked edema, crepitus, and brown bullae (showing large, gram-positive bacilli with scavenging polymorphonuclear neutrophils); brown bullae on radiography extensive gaseous dissolution of muscle and fascial planes; bacteremic spread of C. septicum from occult colonic cancer can produce myonecrosis without penetrating trauma</td>
</tr>
<tr>
<td>Cutaneous anthrax</td>
<td>Gelatinous eschar surrounding an anthrax lesion may be mistaken for cellulitis; anthrax lesion is painless or pruritic; epidemiologic factors are of paramount importance</td>
</tr>
</tbody>
</table>

Key features of necrotizing fasciitis

<table>
<thead>
<tr>
<th>Feature</th>
<th>Percentage of Patients (%)</th>
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</thead>
<tbody>
<tr>
<td>Fever</td>
<td>95</td>
</tr>
<tr>
<td>Hypotension</td>
<td>80</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>80</td>
</tr>
<tr>
<td>Tachypnea</td>
<td>75</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>60</td>
</tr>
<tr>
<td>Diaphoresis</td>
<td>50</td>
</tr>
<tr>
<td>Epigastrium</td>
<td>45</td>
</tr>
<tr>
<td>Hyperreflexia</td>
<td>40</td>
</tr>
<tr>
<td>Edema</td>
<td>35</td>
</tr>
<tr>
<td>Necrosis</td>
<td>30</td>
</tr>
<tr>
<td>Tenderness</td>
<td>25</td>
</tr>
<tr>
<td>Crepitus</td>
<td>20</td>
</tr>
</tbody>
</table>

Variables Associated with Mortality in Necrotizing Soft Tissue Infection

- Timing to operative intervention*
- Age older than 60 years
- Number of comorbidities
- Diabetes mellitus
- Shock on admission
- Acute renal failure
- Coagulopathy or acidosis on admission
- Clostridial or group A streptococcal infection
- *Vibrio vulnificus* infection
- Admission white blood cell count 30 cells/mm³
- Admission serum creatinine 2 mg/dL.

*Only variable that has been shown to be predictive of survival in all studies*

Fournier gangrene and debridement

Antibiotic management

- Blood and tissue cultures
- Tissue gram stain
- Vancomycin, piperacillin-tazobactam and clindamycin pending results
- Clindamycin may be helpful in turning off toxin production
- Piperacillin-tazobactam is needed for gram-negative and streptococcal coverage
- Vancomycin is needed for MRSA coverage
Case #4

- A 16-year-old boy was hospitalized at the VA hospital with headache, nausea and vomiting, and fever and chills
- He lived in the East Mountain area near Albuquerque and had noticed two insect bites on his legs two weeks prior to admission
- Exam was significant for temp 101.3 (39) and a 2cm diameter lymph node in the groin which was firm, mobile, and extremely tender

Lab examination

- CSF was normal
- WBC was 6.2 k
- Node aspirate showed some WBCs, negative gram stain
- The patient was treated with doxycycline, piperacillin/tazobactam and gentamicin

Lab results

- Node cultures and blood cultures were positive for Yersinia pestis
- The patient required two courses of therapy after his initial course for persistent inguinal lymphadenopathy with necrosis, also packing of the inguinal area
What to do for suspected plague

- Call DOH 505-827-0006
- Obtain labs, blood cultures, and bubo aspirate
- Submit to State Laboratory Division for rapid testing
- Maintain patient in droplet precautions until pneumonic plague has been excluded by chest X-ray

Antimicrobial therapy

- Streptomycin not readily available
- A retrospective analysis of 75 plague patients treated in New Mexico between 1985 and 1999 suggests that gentamicin, or a combination of gentamicin and doxycycline, is at least as efficacious as streptomycin.

Differential diagnosis

- Staphylococcal or streptococcal lymphadenitis
- Tularemia
- Combination therapy eg cefazolin, gentamicin and doxycycline, will cover the above pending culture results. A serology may be used for diagnosis of tularemia (also flea and tick-borne in the West, inhalational via rabbits-Franciscella tularensis)
- Stable patients may be streamlined to doxycycline alone.
Case #5 Fever and hypotension

- Septic shock: may progress to refractory shock and multiorgan system failure
- Remember that hypotension may be relative
- Culture and administer the antibiotic regimen indicated by your facility's antibiogram
- At UNMH: vancomycin and piperacillin-tazobactam.

Rapid administration of Abx in septic shock is critical

- Multivariate analysis of 2731 adults with septic shock
- Overall mortality was 56.2%, 78% had documented infection
- Median time to initiation of effective therapy was 6 hours
- Each hour of delay reduced survival by 7.6%
- First doses within one hour of hypotension had 79.9% survival; delay to the second hour, 70.5%; delay of 9-12 hours had 23.4% survival
- Antibiotic timing accounted for 28.1% of variance, APACHE II score explained 24.6% of the variance and volume of fluid administered in the first hour explained <2% of the variance
- Kumar. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med 2006; 34: 1589-96

#6 Fever and shortness of breath

- Sampling of differential diagnoses:
  - A patient with HIV risk factors
  - A patient who cleaned out an old shed two weeks ago
  - A patient who imports hides from Africa to make drums
  - A patient who presents with pleuritic chest pain and cough during influenza season
Chest Radiograph
Note:
• widened mediastinum
• increased interstitial markings
• pleural effusions

The ecology of anthrax
• Disease in cattle has been linked with endemic soil environments since antiquity
• Spores contaminate wool, hair, skins, bone meal
• Animal management: vaccination, quarantine, identify incubator areas
Risks in the US

- GI anthrax from eating contaminated meat
- Inhalational anthrax from spores aerosolized from imported hides or other products with animal skins.
- Cutaneous: working directly with animal hides.
- Bioterrorism

Cutaneous anthrax
#7 Fever and recent travel

- A hunting guide who has just returned from Africa sees his primary care provider with fever, chills, headache, and diarrhea

- He does not routinely take malaria prophylaxis
Malaria:

2008 report from CDC: 1,298 cases of malaria with an onset of symptoms among patients in the United States. These cases included one transfusion-related case, one congenital case, and two fatal cases. Plasmodium falciparum, P. vivax, P. malariae, and P. ovale were identified in 40.6%, 14.6%, 1.5%, and 1.4% of cases, respectively. Based on estimated volume of travel from the World Tourism Organization, the highest estimated relative case rates of malaria among travelers occurred among those returning from countries in West Africa. A total of 508 U.S. civilians acquired malaria abroad among the 800 civilians for whom chemoprophylaxis information was known. 344 (71.7%) reported that they had not followed a chemoprophylactic drug regimen recommended by CDC for the area to which they had traveled. Fourteen cases were reported in pregnant women, among whom none adhered to a complete prevention drug regimen.

Salmonella typhi

Dengue fever

Differential diagnoses in returning travelers

- Malaria
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- Salmonella typhi
- Dengue fever

Diagnosis of malaria

- Thick and thin blood smears
- Suggestive labs: anemia, thrombocytopenia, elevated LDH
- The patient should be hospitalized with access to ICU
- Serial smears should be performed to make diagnosis and monitor response, plus CBC, chemistries
- For help: call CDC malaria hotline 1-770-488-7788

Typical first-line therapies

- P. falciparum or Species not identified (PCR is available to distinguish species if lab unable)
- Chloroquine-resistant or unknown resistance
- A. quinacrine-proguanil (Malarone™): Adult tab = 150 mg quinacrine/100 mg proguanil 2 tabs qid x 1 day
- B. Atovaquone-proguanil (Malarone™): Adult tab = 250 mg atovaquone/100 mg proguanil 4 adult tabs qd x 3 days
- C. Quinine sulfate plus one of the following: Doxycycline, Tetracycline, or Clindamycin
- Quinine sulfate 642 mg base (=750 mg salt) po tid x 3 or 7 days
- Doxycycline 100 mg po bid x 7 days
- Tetracycline 250 mg po qid x 7 days
- Clindamycin 90 mg base/day po divided tid x 7 days
- D. Mefloquine (Lariam™ and generics)
- 400 mg base (=500 mg salt) as initial dose, followed by 250 mg base (=300 mg salt) po given 6-12 hours after initial dose Total dose = 1200 mg salt

http://www.cdc.gov/malaria/
Fever, diarrhea and abdominal pain

Is there a trend?

Numbers of death certificates per year listing C. difficile (ICD10 code A04.7) as the primary cause of death 1999-2009, New Mexico

The organism

- *Clostridium difficile* is an anaerobic spore-forming gram-positive rod
- This organism cannot be cultured from stool in commercial laboratories
Epidemic (BI/NAP1/027) Strain


Complicated and recurrent Clostridium difficile infection - expert opinion on Rx

<table>
<thead>
<tr>
<th>Initial episode:</th>
<th>Hypotension, shock, ileus, megacolon</th>
</tr>
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<tbody>
<tr>
<td>Severe, complicated</td>
<td>Vancomycin 500mg po qid and consider adding Metronidazole 500mg iv q8. For ileus consider adding rectal vancomycin 500mg qid (mixed in 100cc NS). Surgical consultation may be indicated.</td>
</tr>
<tr>
<td>WBC over 15k, creatinine &gt;1.5, low albumin</td>
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First recurrence: Same as above, based on severity

Metronidazole for mild to moderate disease, vancomycin 1.25mg po qid for severe disease

Second recurrence: Infectious Diseases consult recommended

*Do not use metronidazole beyond 2nd recurrence due to risk of neurotoxicity

Vancomycin taper:
125mg po qid for 10-14d then 125mg po bid for 7d then 125mg po qid for 7d then 125mg po qod for 2-4 wks
### Key tips in “ID alert” conditions

- History of exposures
- Full skin exam
- Review medications for intake of OTC antipyretics and NSAIDs
- History of travel
- Patient not responding to “broad-spectrum antimicrobials”
- Know when to call: ID Pals, DOH, a surgeon, CDC