

Infectious Diseases Emergencies

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Disclosures

- Research Grant: Astellas Pharmaceuticals
- I will not discuss off-label use and/or investigational use in my presentation

Learning Objectives

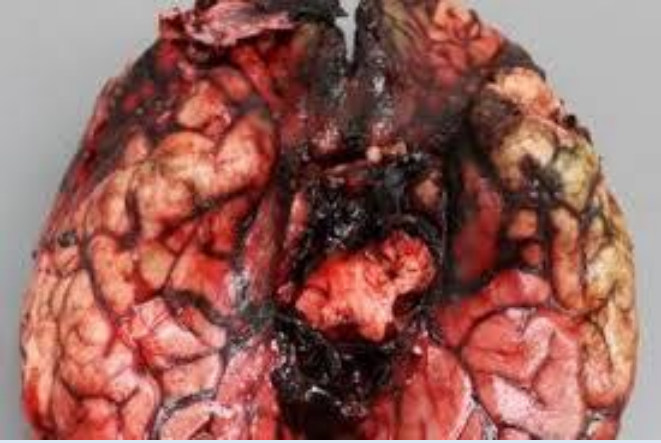
- Review principles of recognition and management of a selection of commonly encountered infectious disease emergencies in the primary care setting
- Identify strategies to diagnose, treat, and prevent life threatening infectious diseases commonly encountered by primary care providers
- Discuss effective management strategies when working with infectious disease consultants/specialists

“ I Have a Bad Headache”

- A 55 year old healthy woman complains of severe headache for 3 days which is associated with fever, nausea, and vomiting
- She self-diagnosed herself with a migraine headache
- 24 hours later she experienced photophobia and neck stiffness
- The following day her family called emergency services when she became disoriented

What is the most likely cause of her headache?

- A. Meningitis
- B. Sinusitis
- C. Mastoiditis
- D. Spinal Epidural Abscess
- E. Lemierre's Syndrome



Meningoencephalitis



A Continuum of Syndromes

- Meningitis
 - Acute: Fever, headache, +/- altered mental status
 - Chronic: Gradual and indolent onset of symptoms
 - Infection of central nervous system (CNS) for at least 4 weeks
- Encephalitis
 - Fever, headache, and altered mental status is common
 - Mental status changes occur early and progress to obtundation or coma
 - The most common focal neurological signs include:
 - Hemiparesis,
 - Aphasia, ataxia, cranial nerve palsies, myoclonus
 - Seizures

Characteristic Features of Common Causes of Meningitis

Organism	Site of Entry	Age Range	Predisposing Conditions
<i>Neisseria meningitidis</i>	Nasopharynx	All ages	Complement deficiency
<i>S. pneumoniae</i>	Nasopharynx, skull fracture, contiguous or distant foci of infection	All ages	Bacteremia, cribriform plate fracture, cochlear implants, cerebrospinal fluid otorrhea, defects of the ear ossicle
<i>Listeria monocytogenes</i>	Gastrointestinal tract, placenta	Elderly, Neonates	Defects in cell-mediated immunity, pregnancy, liver disease, alcoholism
CoN staphylococci <i>S. aureus</i>	Foreign body, Skin, Bacteremia	All ages	Surgery and foreign body, especially ventricular drains, endocarditis, skin
Gram-negative bacilli	Various	Elderly, Neonates	Advanced medical illness, neurosurgery, ventricular drains, strongyloidiasis
<i>Haemophilus influenzae</i>	Nasopharynx, contiguous spread from local infection	Adults; infants and children if not vaccinated	Diminished humoral immunity

Analyzing the Cerebrospinal Fluid (CSF)

The CSF formula

- Opening pressure
- Cell count and differential
- Protein
- Glucose
- Gram stain and culture

Normal Values

- Pressure 9 – 18 cm H₂O
- WBC/mm³ 0 – 5
- Protein mg/dL 15 – 40
- Glucose mg/dL 50 – 75
- Appearance - Clear

**Do not “waste” CSF on unnecessary tests;
it is difficult to get more!**

Differential Diagnosis: CSF Examination

50-100 WBC, 90% mononuclear
Normal glucose
Mildly elevated protein
Normal opening pressure

Viral or “Aseptic”
Neurosyphilis

Enteroviral PCR
West Nile IgM
HSV PCR
VDRL

1000 – 5000 WBC, 80% neutrophils
Glucose < 10
Elevated protein
60 -90% positive gram stain
70 -80% positive culture
Elevated opening pressure

Bacterial

Gram stain and culture
Blood cultures
Multiplex PCR assays

20-200 WBC, 90% mononuclear
Glucose < 40
Very elevated protein
Elevated opening pressure

Fungal
Tuberculosis

Fungal culture
Cryptococcal Antigen
Coccidioides
Antibody/antigen
AFB smear/culture

Management

Suspicion for bacterial meningitis

Yes

Immunocompromise,* history of CNS disease,[†] new-onset seizure, papilledema, altered consciousness, or focal neurologic deficit; or delay in performance of diagnostic lumbar puncture

No

Yes

Blood cultures and lumbar puncture STAT

Blood cultures STAT

Dexamethasone[‡] + empirical antimicrobial therapy[§]

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CSF findings c/w bacterial meningitis

Negative CT scan of the head

Positive CSF Gram stain

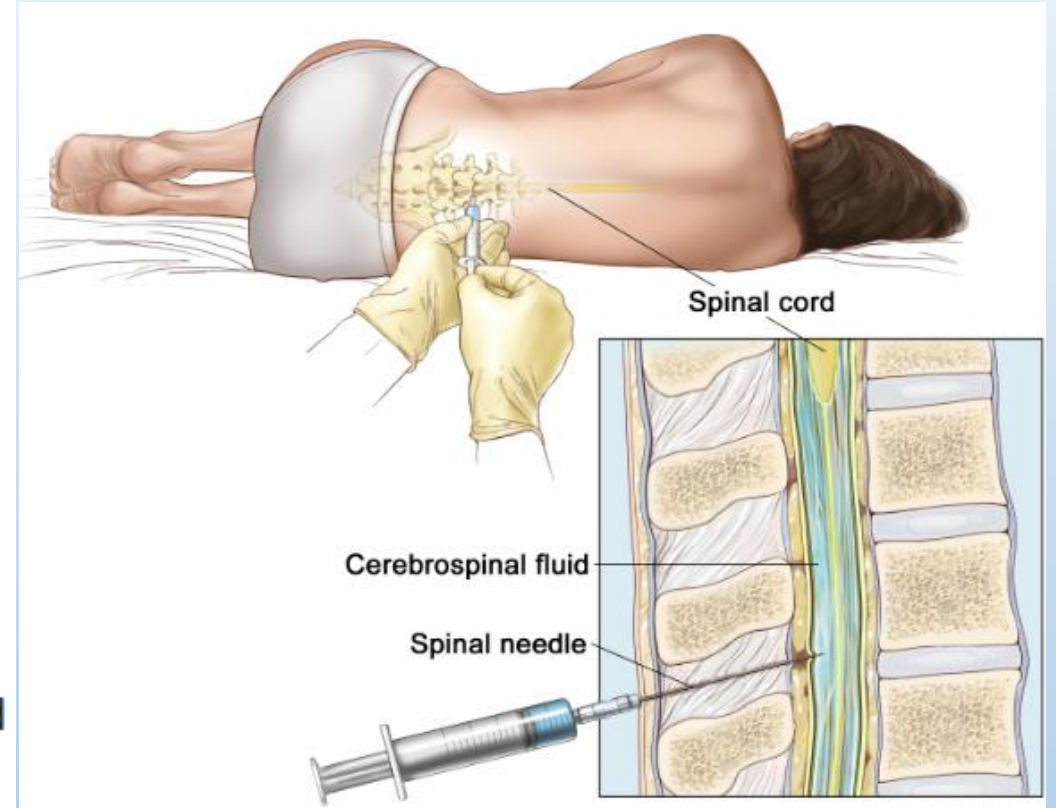
Yes

Perform lumbar puncture

No

Dexamethasone[‡] + empirical antimicrobial therapy[§]

Dexamethasone[‡] + targeted antimicrobial therapy^{||}



Treatment

Microorganism	Recommended therapy	Alternative therapies
<i>Streptococcus pneumoniae</i>	Vancomycin plus a third-generation cephalosporin ^{a,b}	Meropenem (C-III), fluoroquinolone ^c (B-II)
<i>Neisseria meningitidis</i>	Third-generation cephalosporin ^a	Penicillin G, ampicillin, chloramphenicol, fluoroquinolone, aztreonam
<i>Listeria monocytogenes</i>	Ampicillin ^d or penicillin G ^d	Trimethoprim-sulfamethoxazole, meropenem (B-III)
<i>Streptococcus agalactiae</i>	Ampicillin ^d or penicillin G ^d	Third-generation cephalosporin ^a (B-III)
<i>Haemophilus influenzae</i>	Third-generation cephalosporin ^a (A-I)	Chloramphenicol, cefepime (A-I), meropenem (A-I), fluoroquinolone
<i>Escherichia coli</i>	Third-generation cephalosporin ^a (A-II)	Cefepime, meropenem, aztreonam, fluoroquinolone, trimethoprim-sulfamethoxazole

- Penicillin resistance is increasing and antibiotic levels in CSF reach only 2-10% of serum levels
- PCN CSF breakpoints for *S. pneumoniae*:
 - <0.1 ug/ml
 - 0.1 – 1.0 ug/ml
 - ≥ 2.0 ug/ml

“My Father is Acting Strange”

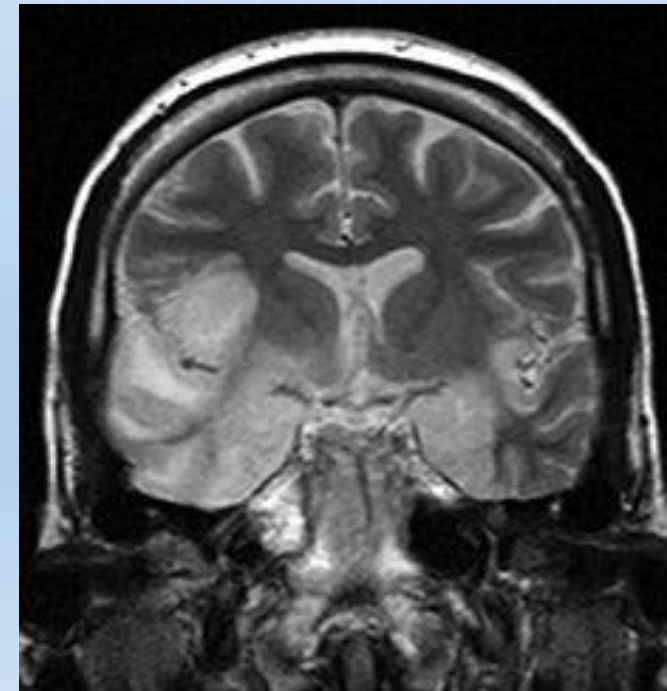
- A 82 year old man presented to the clinic with fever, fatigue, urinary incontinence, confusion, and had been walking naked in the house
- Urinalysis showed bacteriuria and pyuria and he was diagnosed with an urinary tract infection (UTI); he was prescribed Levofloxacin
- The following day he continued to have fever and worsening confusion
- He was admitted that evening after developing aphasia, ataxia, and seizures

What is his working diagnosis?

- A. Cystitis
- B. Prostatitis
- C. Influenza
- D. Herpes Encephalitis
- E. Community acquired pneumonia

Herpes Simplex Virus (HSV) Encephalitis

- Reactivation in cranial nerve ganglia and retrograde spread along axons
- Involvement of temporal lobe with personality changes, seizures, and focal neurologic findings
- Diagnosis: HSV 1/2 CSF PCR
- Intravenous Acyclovir is the recommended therapy



Herpes Simplex Virus (HSV) Encephalitis

Meningitis

HSV 2 >> 1

Associated with primary infection

Normal mental status

Can be recurrent (Mollaret)

Benign

Encephalitis

HSV 1 >> 2

Usually not primary in adults

Abnormal mental status

Usually no oral lesions

Acyclovir decreases mortality

“My Foot is Killing Me”

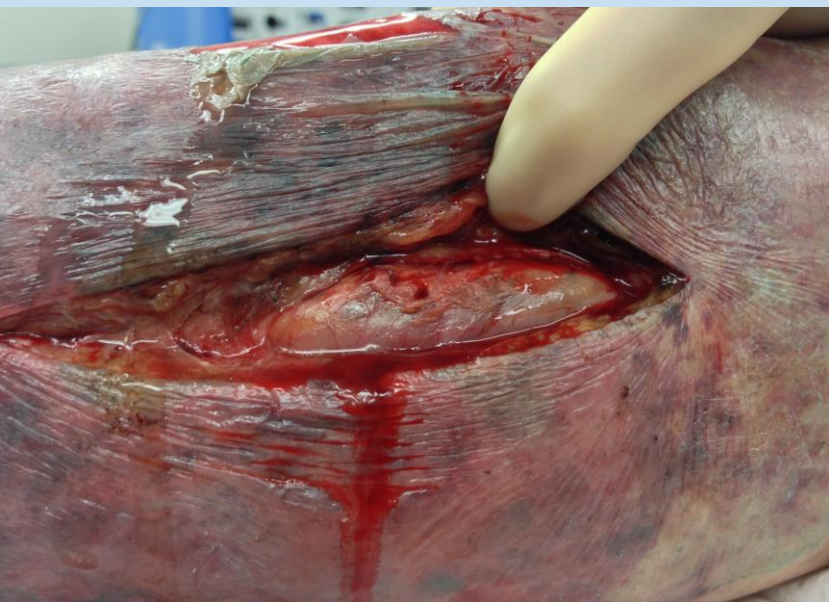
- A 50 year old woman presented to the clinic because of severe pain and swelling of her left foot
- She had been well until 2 days earlier when she noticed a lesion on her foot, thought to be an insect bite
- The next day, her foot became swollen and painful, she felt ill and febrile, and on the way to the ED she became confused and hypotensive
- Her skin appeared cyanotic and cool. The foot was mottled with a black eschar; the swelling extended up the thigh

What is the most likely diagnosis?

- A. Cellulitis
- B. Deep venous thrombosis
- C. Heart failure with lower extremity edema
- D. Necrotizing Fasciitis
- E. Erysipelas



Necrotizing Fasciitis



Necrotizing Fasciitis

- Necrotizing soft tissue infections include necrotizing forms of cellulitis, myositis, and fasciitis
- Type I necrotizing fasciitis, at least one anaerobic species is isolated in combination with one or more facultative anaerobic species such as streptococci (other than group A) and members of the Enterobacteriaceae
- Type II, group A streptococci are isolated alone or in combination with other species, most commonly *S. aureus*

Clinical Presentation

- Necrotizing fasciitis can affect any part of the body but is most common on the extremities
- Other sites of predilection are the abdominal wall, perianal and groin areas, and postoperative wounds
- The portal of entry is usually a site of trauma, post-surgical procedure, perirectal abscess, decubitus ulcer, or intestinal perforation



Clinical Features

- Severe, constant pain
- Bullae (occlusion of deep blood vessels that traverse the fascia)
- Skin necrosis or ecchymosis that precedes skin necrosis
- Gas in the soft tissues, detected by palpation or imaging
- Edema that extends beyond the margin of erythema
- Cutaneous anesthesia
- Systemic toxicity (fever, leukocytosis, delirium, and renal failure)
- Rapid spread, especially during antibiotic therapy

Diagnosis

- Prompt diagnosis is crucial because of the rapidity with which the process can progress and a mortality rate of 24% to 34%
- The most expeditious route to diagnosis is through surgical exploration without delay for imaging studies
- CT scanning and magnetic resonance imaging (MRI) can demonstrate subcutaneous and fascial edema and tissue gas
- Frozen section examination of biopsy specimens is helpful for early diagnosis

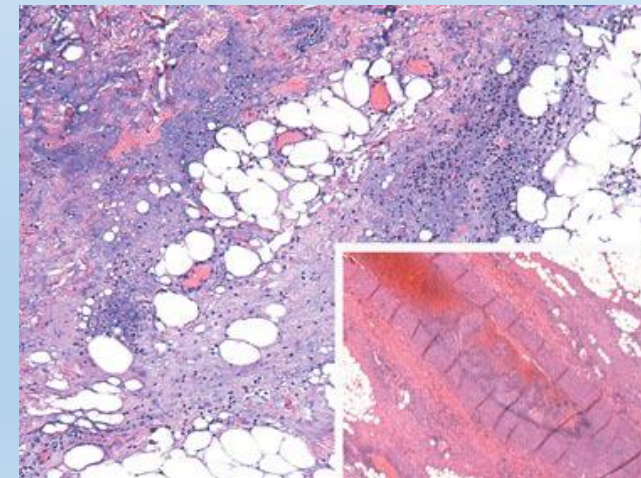
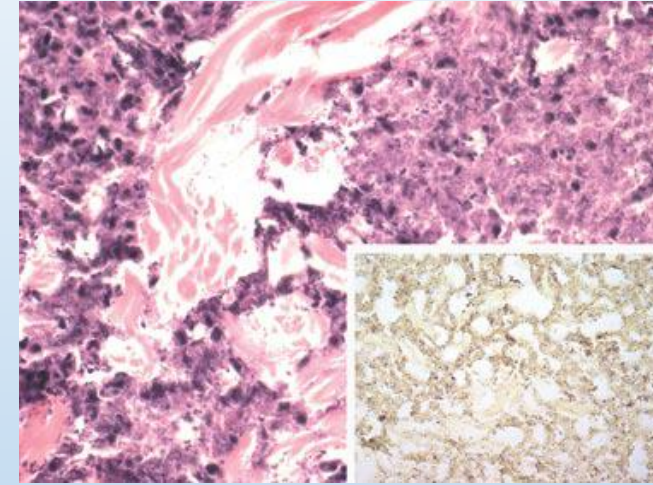


Table 1. Factors Conferring a Predisposition to Specific Necrotizing Soft-Tissue Infections.*

Predisposing Factor	Clinical Syndrome	Etiologic Agent
Major penetrating trauma: crush or deeply penetrating wound	Gas gangrene	<i>Clostridium perfringens</i> , <i>C. histolyticum</i> , or <i>C. novyi</i>
Minor penetrating trauma	NF type II	
Freshwater laceration		<i>Aeromonas hydrophila</i>
Saltwater laceration		<i>Vibrio vulnificus</i>
Minor nonpenetrating trauma: muscle strain, sprain, or contusion	NF type II or streptococcal myonecrosis	<i>Streptococcus pyogenes</i>
Mucosal breach: mucosal tear (rectal, vaginal, urethral); gastrointestinal, genitourinary or gynecologic surgery	NF type I	Mixed aerobic and anaerobic organisms
Skin breach		
Varicella lesions	NF type II or streptococcal myonecrosis	<i>S. pyogenes</i>
Insect bites	NF type II or streptococcal myonecrosis	<i>S. pyogenes</i>
Injection drugs	Gas gangrene	<i>C. perfringens</i> , <i>C. histolyticum</i> , <i>C. novyi</i> , or <i>C. sordellii</i>
Immunocompromised state		
Diabetes with peripheral vascular disease	NF type I	Mixed aerobic and anaerobic organisms
Cirrhosis and ingestion of raw oysters	NF type II	<i>V. vulnificus</i>
Neutropenia	Gas gangrene	<i>C. septicum</i>
In women: pregnancy, childbirth, abortion (spontaneous or medically induced), gynecologic procedures or surgery	NF type II, streptococcal myonecrosis, or clostridial myonecrosis	<i>S. pyogenes</i> , <i>C. perfringens</i> , or <i>C. sordellii</i>
Occult factors: colonic lesions, including carcinoma	Spontaneous gas gangrene	<i>C. septicum</i>

* Gas gangrene is also known as clostridial myonecrosis.

Treatment

Type of Infection	First-line Antimicrobial Agent	Adult Dosage	Pediatric Dosage Beyond the Neonatal Period
Mixed infections	Piperacillin-tazobactam plus vancomycin	3.37 g every 6–8 h IV 30 mg/kg/d in 2 divided doses	60–75 mg/kg/dose of the piperacillin component every 6 h IV 10–13 mg/kg/dose every 8 h IV
	Imipenem-cilastatin	1 g every 6–8 h IV	N/A
	Meropenem	1 g every 8 h IV	20 mg/kg/dose every 8 h IV
	Ertapenem	1 g daily IV	15 mg/kg/dose every 12 h IV for children 3 mo–12 y
	Cefotaxime plus metronidazole or clindamycin	2 g every 6 h IV 500 mg every 6 h IV 600–900 mg every 8 h IV	50 mg/kg/dose every 6 h IV 7.5 mg/kg/dose every 6 h IV 10–13 mg/kg/dose every 8 h IV
<i>Streptococcus</i>	Penicillin plus clindamycin	2–4 million units every 4–6 h IV (adult) 600–900 mg every 8 h IV	60 000–100 000 units/kg/dose every 6 h IV 10–13 mg/kg/dose every 8 h IV

Treatment

<i>Staphylococcus aureus</i>	Nafcillin	1–2 g every 4 h IV	50 mg/kg/dose every 6 h IV
	Oxacillin	1–2 g every 4 h IV	50 mg/kg/dose every 6 h IV
	Cefazolin	1 g every 8 h IV	33 mg/kg/dose every 8 h IV
	Vancomycin (for resistant strains)	30 mg/kg/d in 2 divided doses IV	15 mg/kg/dose every 6 h IV
	Clindamycin	600–900 mg every 8 h IV	10–13 mg/kg/dose every 8 h IV
<i>Clostridium</i> species	Clindamycin plus penicillin	600–900 mg every 8 h IV 2–4 million units every 4–6 h IV (adult)	10–13 mg/kg/dose every 8 h IV 60 000–100 000 units/kg/dose every 6 h IV
<i>Aeromonas hydrophila</i>	Doxycycline plus ciprofloxacin or ceftriaxone	100 mg every 12 h IV 500 mg every 12 h IV 1 to 2 g every 24 h IV	Not recommended for children but may need to use in life-threatening situations
<i>Vibrio vulnificus</i>	Doxycycline plus ceftriaxone or cefotaxime	100 mg every 12 h IV 1 g qid IV 2 g tid IV	Not recommended for children but may need to use in life-threatening situations

“My back is killing me”

- A 24 year old woman presents to the clinic with complains of fever, severe back pain described as "shooting" and stabbing in nature for 48 hours
- She was prescribed analgesics and heating pads
- The following day she developed lower extremity weakness with decreased sensation, difficulty walking, and bladder dysfunction
- That evening she was admitted to the ICU with sepsis

What is the most likely diagnosis?

- A. Disc with degenerative bone disease
- B. Metastatic tumor
- C. Vertebral discitis with osteomyelitis
- D. Spinal epidural abscess
- E. Herpes zoster, prior to the appearance of rash

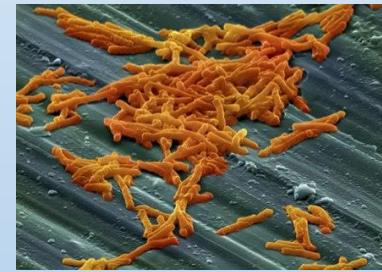
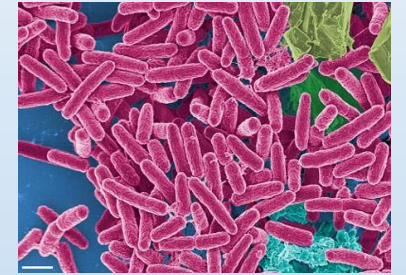
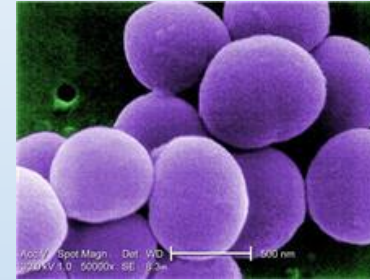
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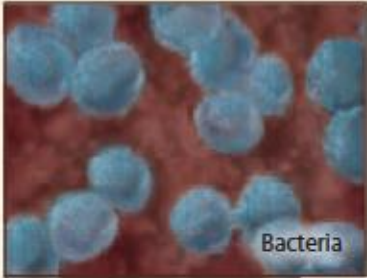
- Epidural abscess extending from the L4-S1 levels causing severe thecal sac stenosis with cauda equina impingement
- 2 out 2 blood cultures grew Methicillin-resistant *Staphylococcus aureus* (MRSA)

Microbiology

- *S. aureus* (Over 60% of cases)
- Gram-negative bacilli
- Streptococci
- Coagulase-negative staphylococci
- Anaerobes
- Others (fungi, tuberculosis, parasites)



Common Sources of Infection



Bacteria

Bloodstream infection associated with a central venous catheter

Intravenous drug use

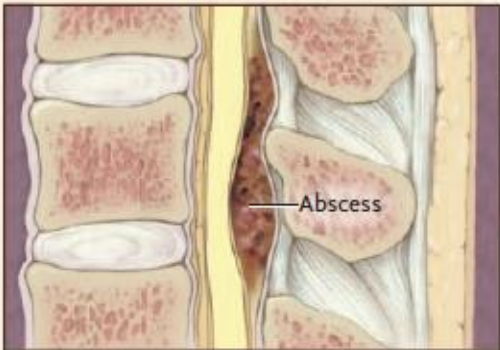
Catheter-related urinary tract infection

Vertebral osteomyelitis

Spinal catheter for analgesia or stimulation

Infected pressure sore

Spinal Epidural Abscess



Infectious Complications of Spinal Abscess



Endocarditis



Vertebral osteomyelitis

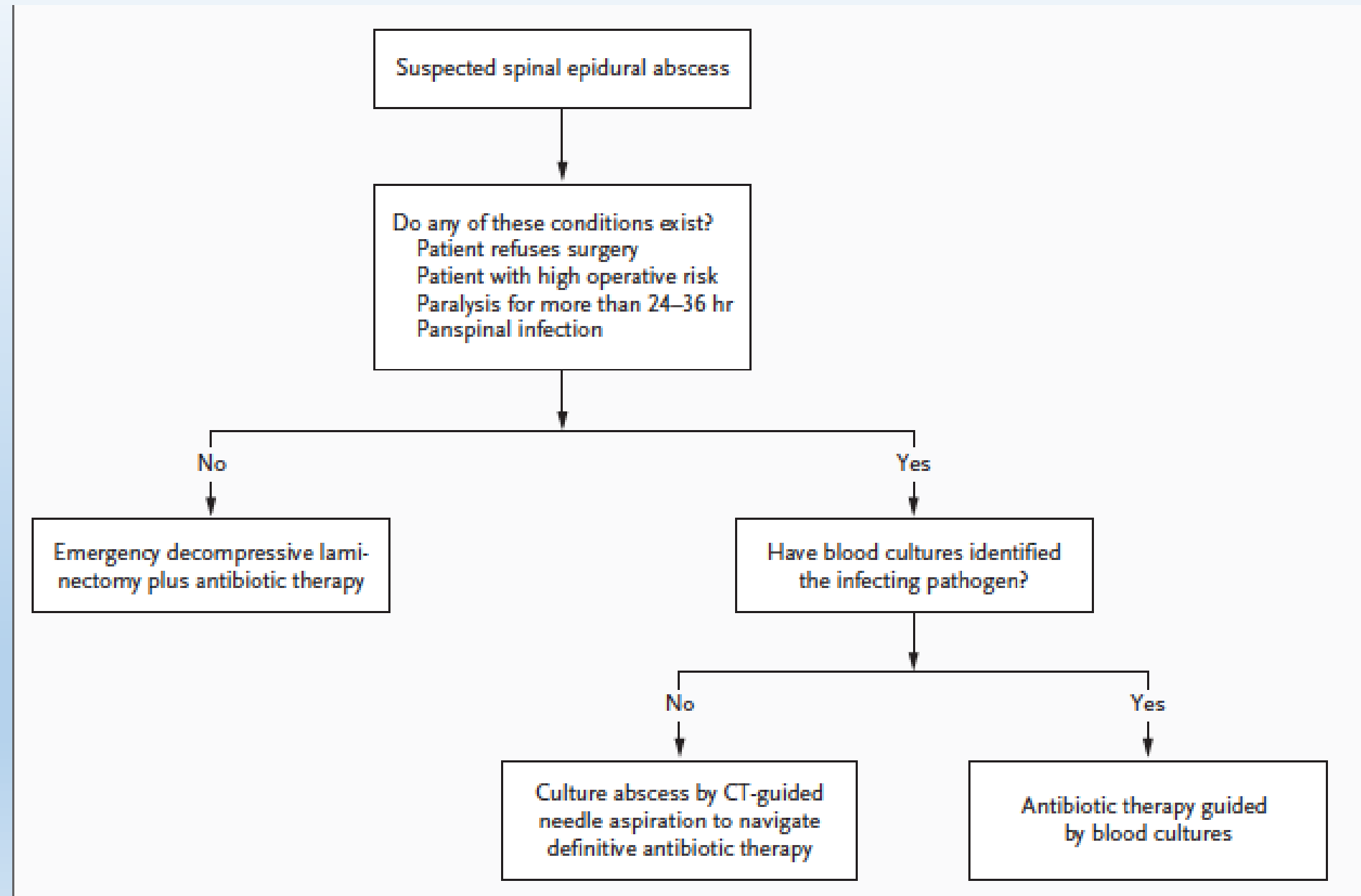


Psoas muscle abscess

Pathogenesis

- Abscesses are more likely to develop in larger epidural spaces that contain infection-prone fat

Management of Spinal Epidural Abscess



“I feel like I am going to die”

- A 23 year old Native American man presents to the clinic with complains of fever, chills, headaches, malaise, myalgia, nausea, and vomiting for 48 hours
- He reported visiting family on the reservation three days prior to his presentation
- His Labs revealed hyponatremia, thrombocytopenia, and elevated liver enzymes
- His family owns three outdoor dogs, two cats, and several horses

What is his likely diagnosis?

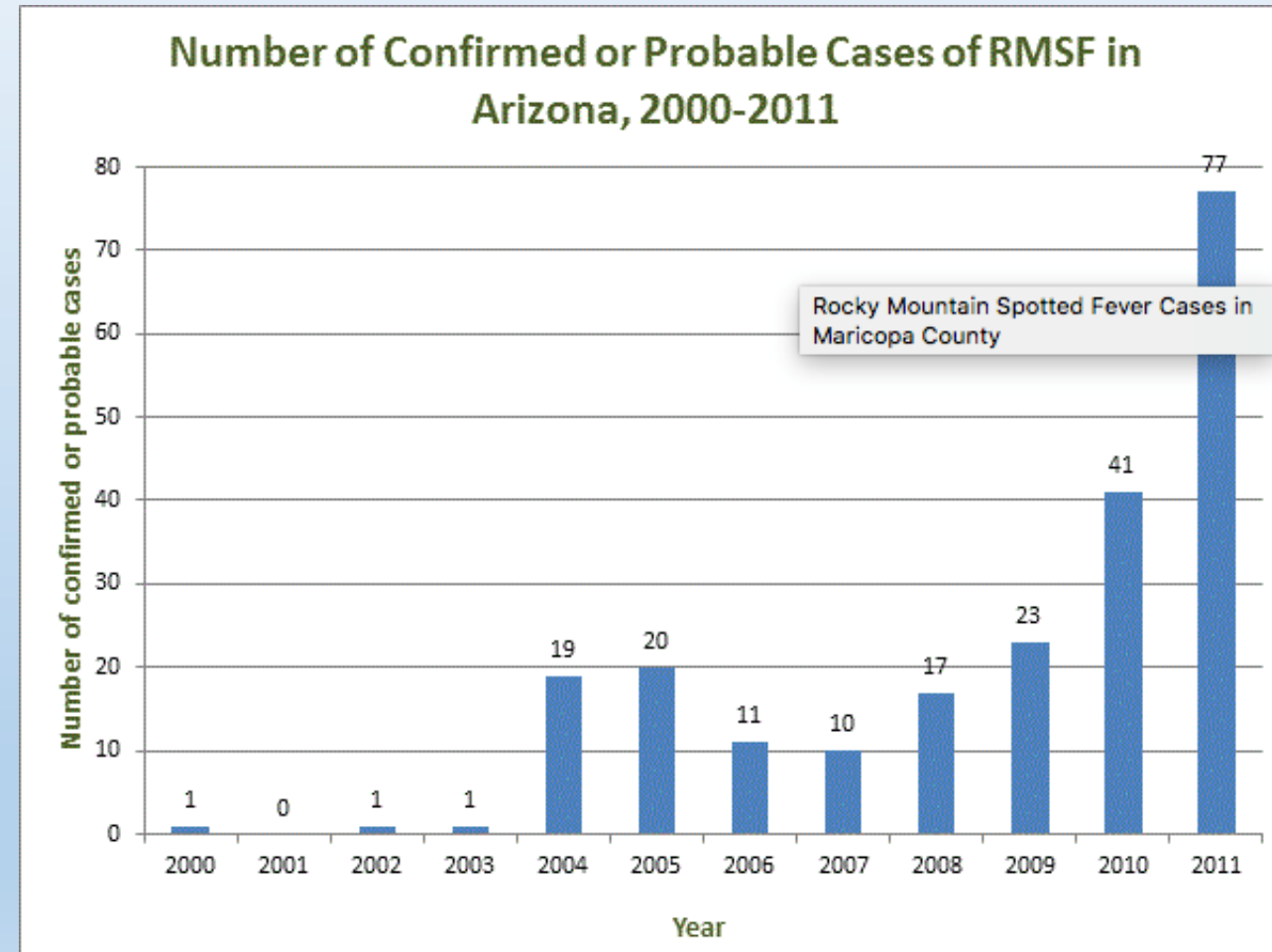
- A. Acute HIV infection
- B. Disseminated Coccidioidomycosis
- C. Influenza
- D. Rocky Mountain Spotted Fever
- E. Dengue Fever

Rocky Mountain spotted fever (RMSF)

- RMSF is a zoonotic disease that causes illness in both dogs and humans
- *Rickettsia rickettsii*, a small gram-negative obligate intracellular parasite from the family Rickettsiaceae
- RMSF was not recognized in dogs until the 1970's and *Rhipicephalus sanguineus* is the most common vector in Arizona
- The incubation period is 2-14 days followed by invasion of endothelial cells of the venules and capillaries resulting in vasculitis

RMSF in Arizona

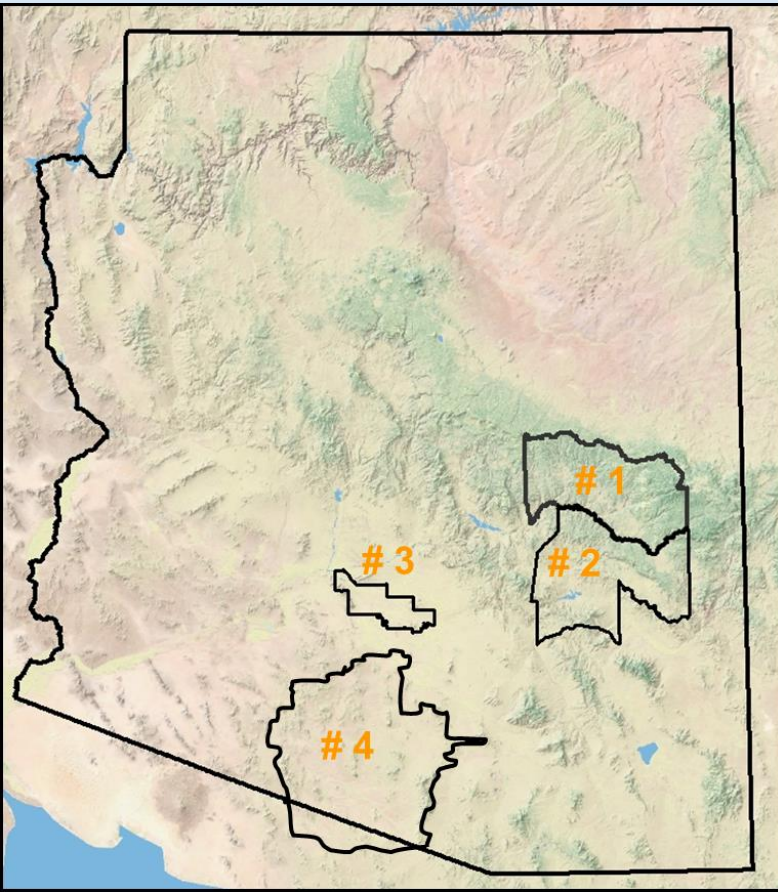
- Between 2003 and 2012, over 250 cases and 19 fatalities occurred
- Most cases occurred in areas with large amounts of free-roaming dogs and severe tick infestations, including six Tribal Lands
- During 2010-2011, RMSF in Arizona occurred at a rate of 200 times the national average



The Primary Arizona Tick Vector of RMSF



Rhipicephalus sanguineus (Brown dog tick)



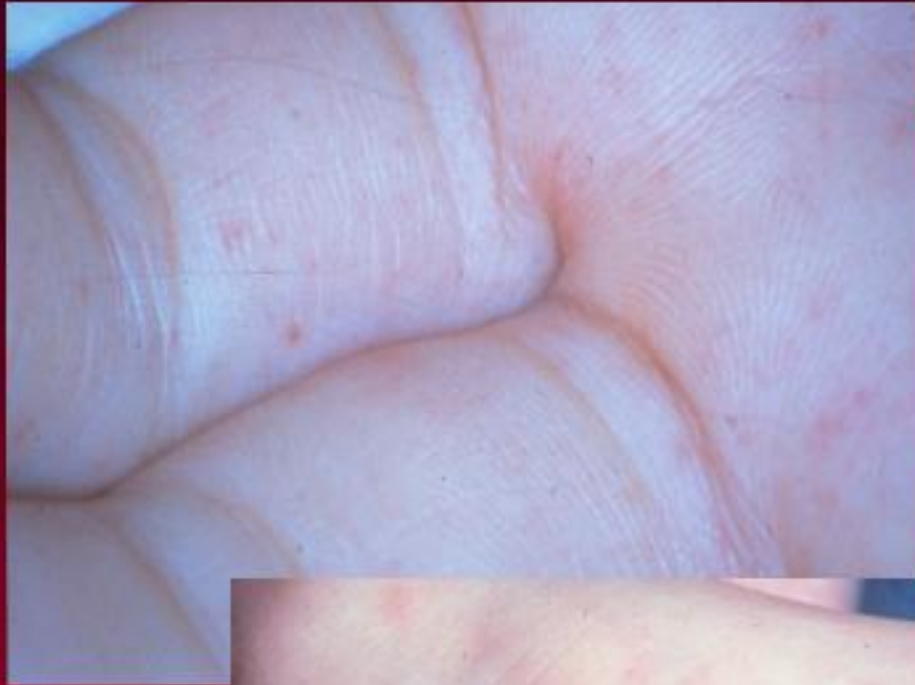
Clinical Manifestations

- Early (first 4 days): Fever, headache, myalgia, abdominal pain, nausea, vomiting, and light rash may be present
- Thrombocytopenia, hyponatremia, elevated liver enzymes may occur
- Late (day 5 or later): Definitive petechial rash, altered mental status, seizures, cough, dyspnea, arrhythmias, hypotension, and severe abdominal pain

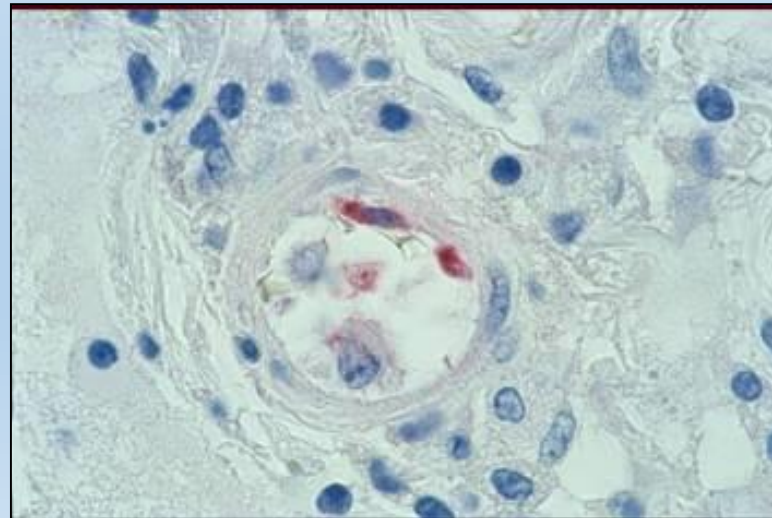
RMSF: The Rash

- Generally not apparent until day 2-5 of symptoms (only seen in 68% of AZ patients)
- Begins as 1 to 5 mm macules progressing to maculopapular
- May begin on ankles, wrists, and forearms, spreads to trunk
- Petechial rash is a late finding, occurs on or after day 6
- Rash may be asymmetric, localized, or absent

Rashes of RMSF



Severe Sequelae



Antimicrobial Therapy of RMSF

Pregnant adult or
tetracycline allergic

Chloramphenicol
500 mg qid, less
likely to prevent death

Non-pregnant adult
or child ≥ 45 kg

Doxycycline
100 mg bid

Child <45 kg

Doxycycline
4.4 mg/kg/day
in 2 divided
doses

Therapy should be continued at least 72 h after defervescence
AND until evidence of clinical improvement

Confirmation of *R. rickettsii*

- **Serology (RMSF titer)**
 - Indirect immunofluorescence assay (IFA)
 - Requires paired sera (acute and convalescent)
 - Look for a change (4-fold) in antibody titers for confirmed infections
 - Positive single titers or titers that do not rise are considered probable cases
- **PCR**
 - Available at CDC. Can give a rapid result (48 hours)
 - Skin biopsy (2-4mm)
 - Whole blood of severely ill/fatal cases
 - NOTE: Negative PCR does not rule-out RMSF

The Red Herring

- A 75 year old man was seen in the clinic for having had fever, fatigue, night sweats, and weight loss
- Urinalysis indicated pyuria and cultures grew $>100,000$ CFU/mL of *E. Coli*
- One out of 4 blood cultures grew Viridans streptococci, regarded as a contaminant

The Red Herring

- He was prescribed with a course of Ciprofloxacin, but his symptoms persisted for another two months
- He was prescribed several courses of antibiotics for reoccurring UTIs
- He presented three months after the initial visit with worsening mental status, shortness of breath, lower extremity edema, and painful lesions involving his fingers and feet
- He complained of back pain, lower extremity weakness with decreased sensation, difficulty walking, and bladder dysfunction

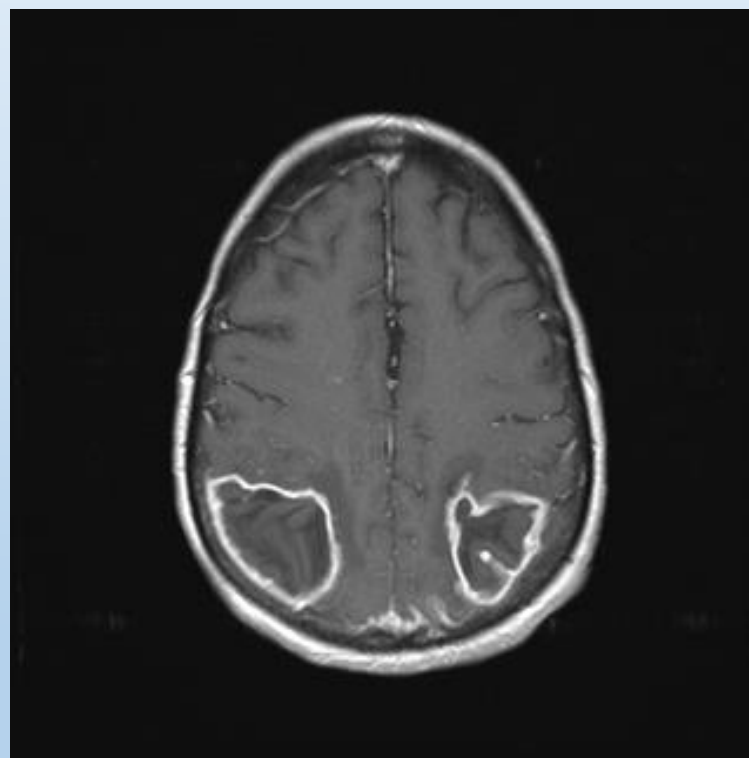
Why is the most likely diagnosis?

- A. Pyelonephritis
- B. Subacute Bacterial Endocarditis
- C. Meningitis
- D. Coccidioidomycosis
- E. Tuberculosis

Endocarditis due to Viridans streptococci



Bias

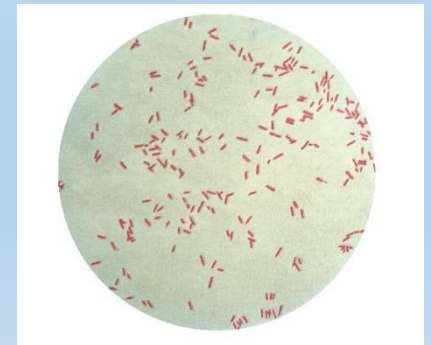
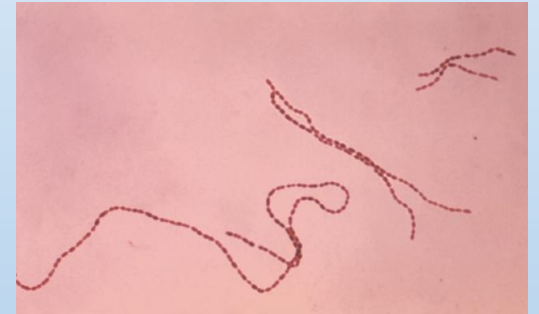
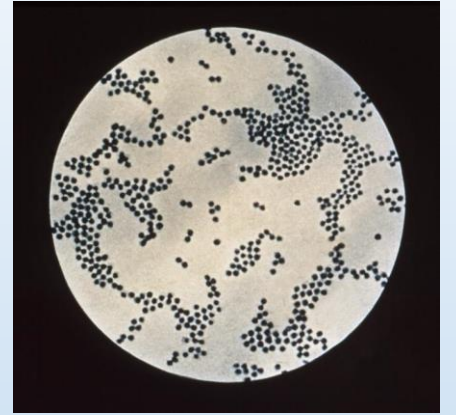


Infective Endocarditis (IE)

- Infection of the endocardium that involves the cardiac valves and adjacent structures
- Bacterial (most common), fungal, rickettsia
- Acute and subacute course

Microbiology

- *S. aureus* — 31 percent
- *Viridans* group streptococci — 17 percent
- *Enterococci* — 11 percent
- *Coagulase-negative staphylococci* — 11 percent
- *Streptococcus bovis* — 7 percent
- Non-HACEK gram-negative bacteria — 2 percent
- Fungi — 2 percent
- HACEK — 2 percent



**Haemophilus spp*

Aggregatibacter [formerly *Actinobacillus* spp.]

Cardiobacterium hominis

Eikenella corrodens

Kingella kingae

Consequences of Septic Emboli

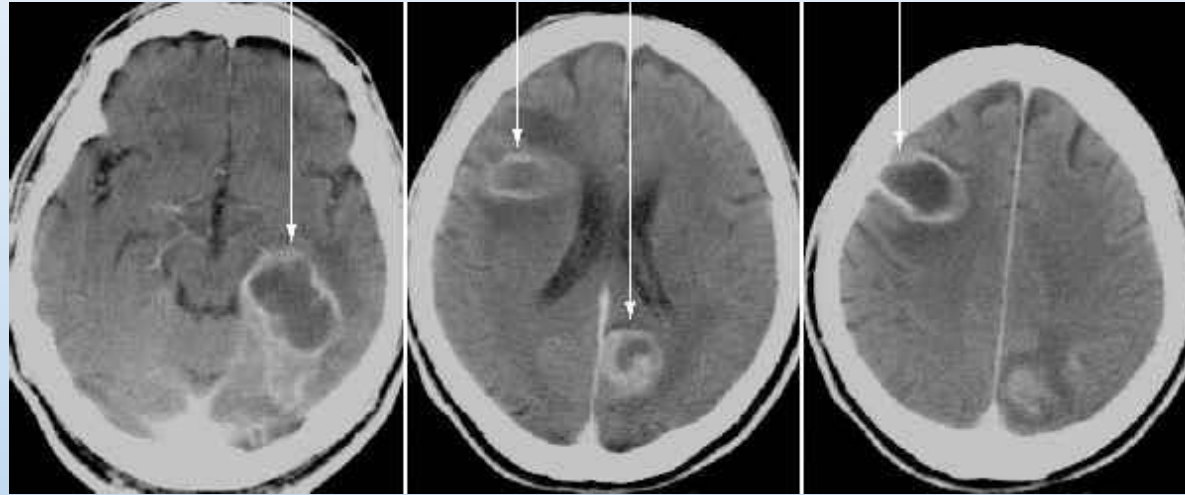
Mitral or aortic valve



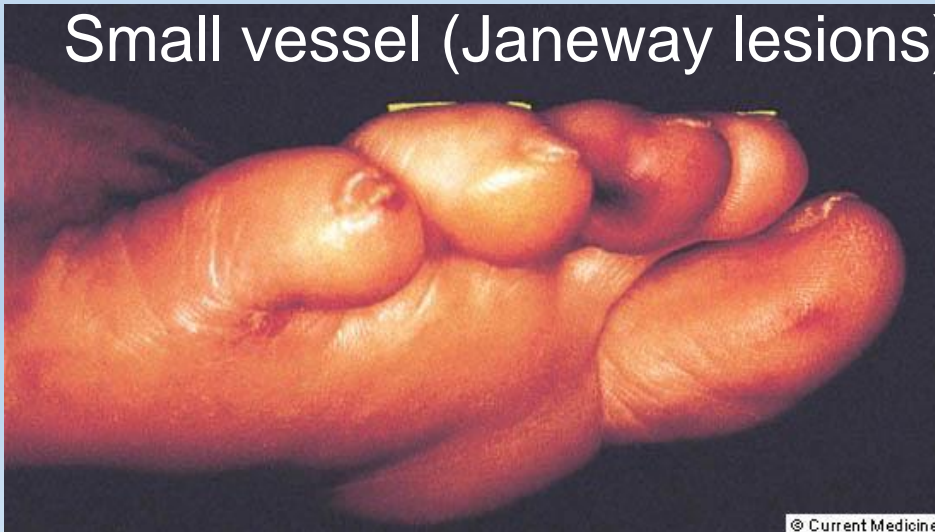
Large vessel

→ Left ventricle

→ Aorta



Small vessel (Janeway lesions)



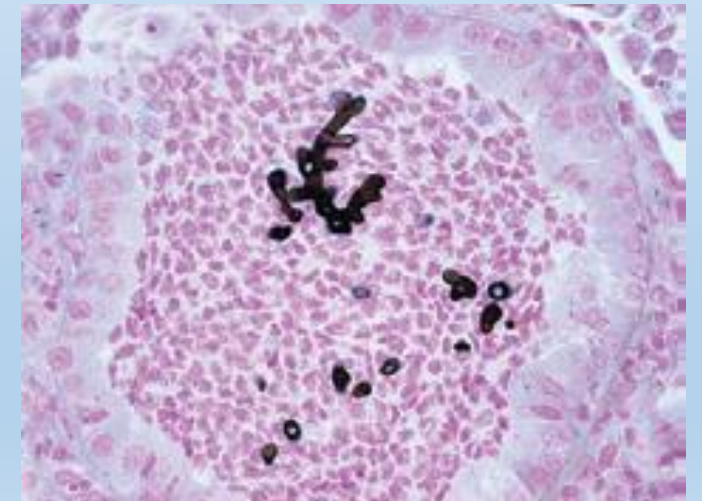
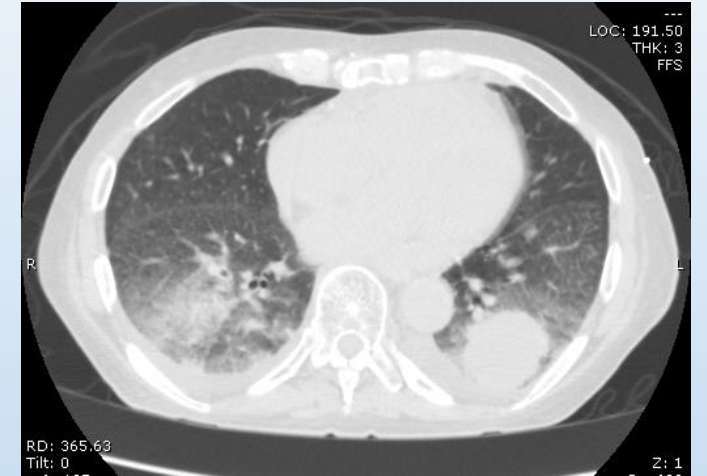
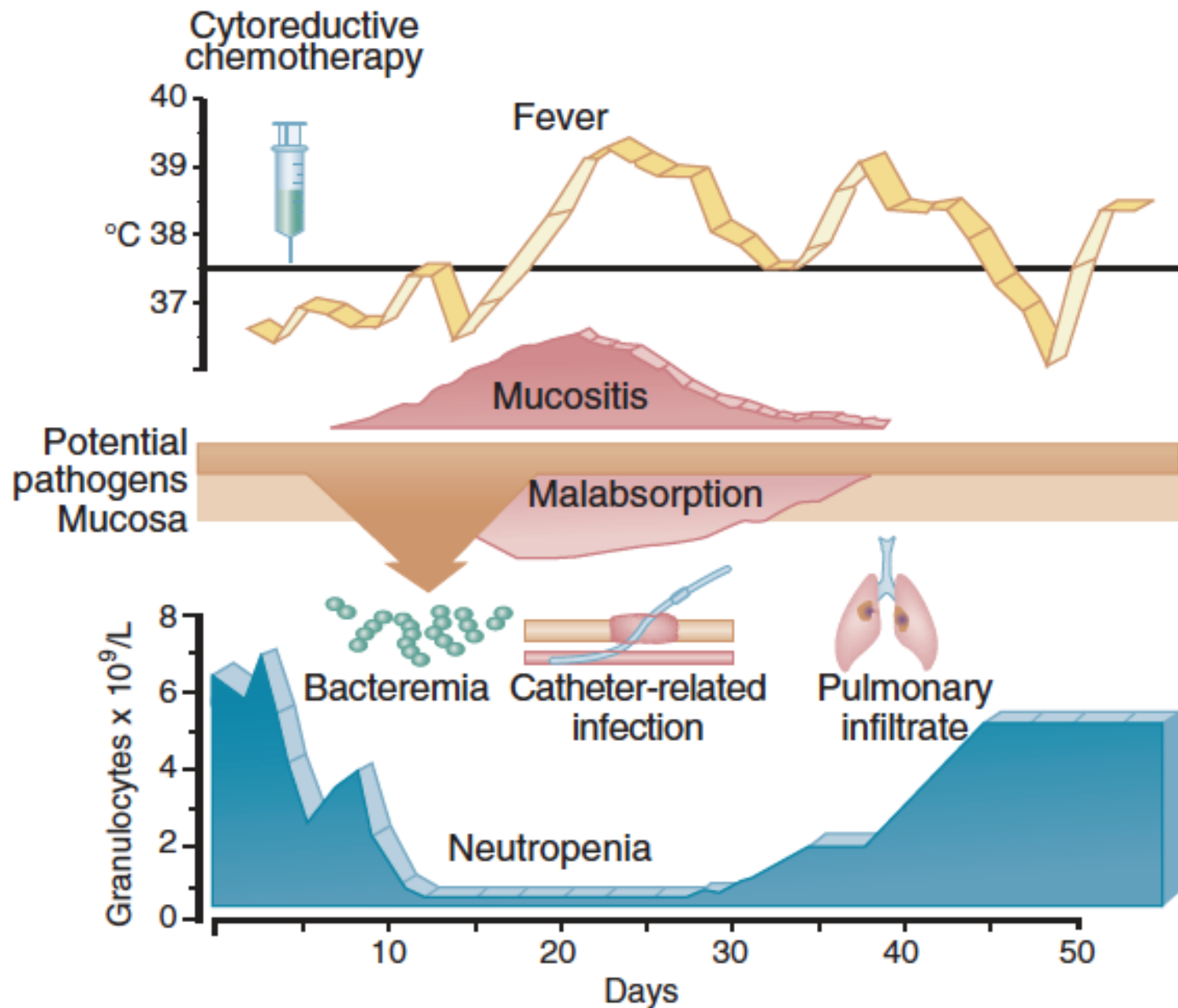
Which of the following would be the mostly likely pathogen in this rapidly expanding skin lesion in a febrile neutropenic patient?



- A) *Fusarium solani*
- B) *Streptococcus pyogenes*
- C) *Borrelia burgdoferi*
- D) *Pseudomonas aeruginosa*

Neutropenic Fever

- Hospitalization for febrile neutropenia (FN) is associated with considerable morbidity, mortality, and cost
- In-hospital mortality associated with FN was 9.5% between 1995 and 2000 across 115 US medical centers (total of 41,779 patients)
- Hospital mortality of 50% has been reported in neutropenic patients with severe sepsis
- Bacteremia occurs in 10%–25% of patients, with most occurring in the setting of prolonged or profound neutropenia (ANC <100 neutrophils/mm³)

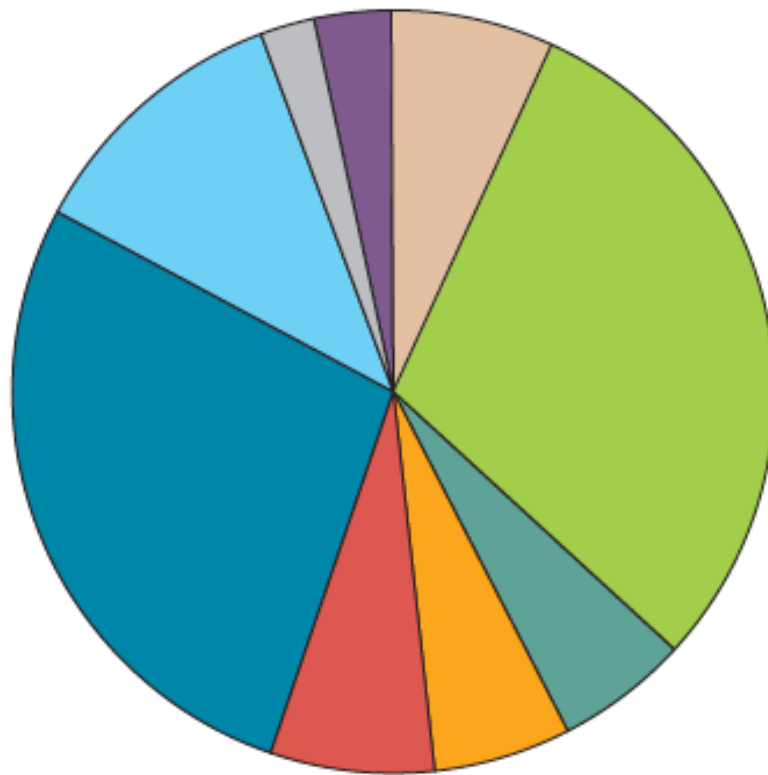


Definitions

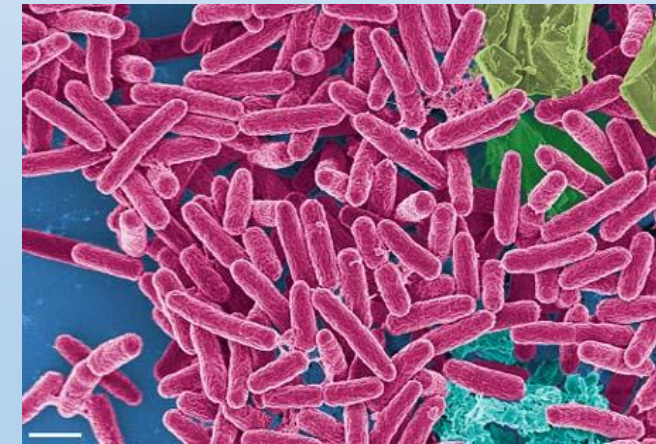
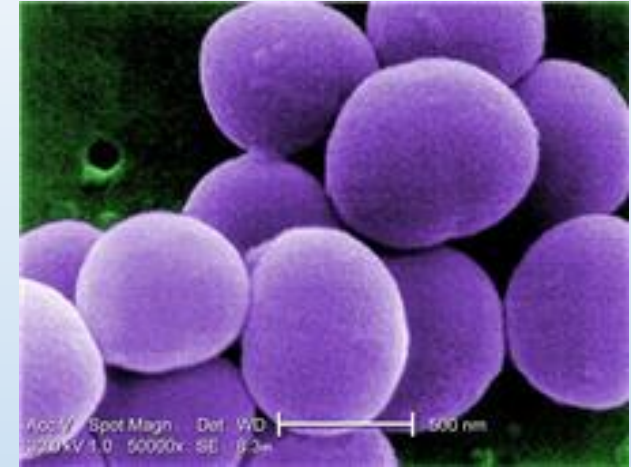
- Fever: A single oral temperature of $\geq 38.3^{\circ}\text{C}$ (101°F) or a temperature of $\geq 38.0^{\circ}\text{C}$ (100.4°F) sustained over 1 hour
- Neutropenia: ANC < 500 cells/mm³ or ANC that is expected to decrease to < 500 cells/mm³ during the next 48 hours
- The term “profound” is used to describe neutropenia in which the ANC is < 100 cells/mm³ and prolonged > 7 days
- Functional neutropenia refers to qualitative defects of circulating neutrophils

Etiology of Bacteremia

REVIEW OF LITERATURE FROM YEARS 2005-2011



- *S. aureus*, 6% (0%-20%)
- Coagulase-negative staphylococci 25% (5%-60%)
- Viridans streptococci, 5% (0%-16%)
- Enterococci, 5% (0%-38%)
- Other gram positives, 6% (0%-21%)
- Enterobacteriaceae, 24% (6%-54%)
- *P. aeruginosa*, 10% (0%-30%)
- *Acinetobacter*, 2% (0%-12%)
- Other gram negatives, 3% (0%-11%)



Initial in-Hospital Treatment (A-II)

- Anticipated prolonged (>7 days duration) and profound neutropenia (ANC <100 cells/mm³)
- Co-morbid conditions, hypotension, pneumonia, new-onset abdominal pain, or neurologic changes
- High-risk patients require intravenous empirical antibiotics with an antipseudomonal β -lactam agent
- Low-risk patients with anticipated brief (<7 days duration) neutropenic period or few co-morbidities, are candidates for oral empirical therapy

Initial Empiric Therapy

- In high-risk patients requiring hospitalization for empirical antibiotic therapy, monotherapy with an anti-pseudomonal β -lactam agent is recommended
 - Cefepime
 - Carbapenem (meropenem or imipenem-cilastatin)
 - Piperacillin-tazobactam
- Other antimicrobials may be added to the initial regimen for management of complications or if antimicrobial resistance is suspected or proven
 - Aminoglycosides
 - Fluoroquinolones
 - Vancomycin

Cutaneous Presentations in Neutropenic Fever

Skin Lesions



- Candidiasis
 - Small, tender papules
- Herpes
 - vesicular
- *Aspergillus*
 - ulcerative, necrotic
- Other filamentous fungi (*Fusarium*, *P. boydii*)
 - Multiple, erythematous, different stages
- *P. aeruginosa*
 - Ecthyma gangrenosum

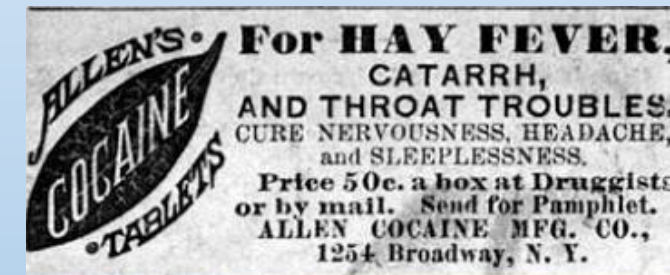
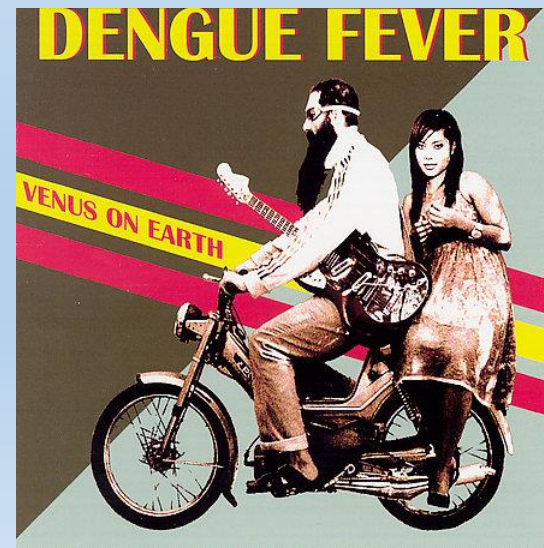


Working with your ID consultants

- Call your consultant early in the case of an ID emergency
- Obtain cultures before administering antibiotics when indicated
- Do not treat asymptomatic bacteruria (there are a few exceptions)
- Be familiar with local diseases and at risk hosts
- Dose adjust antimicrobials and monitor for drug interactions
- Talk to your consultant if you don't agree with the management plan
- Avoid using superficial swab cultures
- Narrow the antibiotic spectrum and duration when appropriate
- Test your patients for HIV at least once
- Avoid testing for a *Clostridium difficile* in the absence of diarrhea



Social History is Key in ID!!!



Other ID Emergencies

- Sepsis
- Severe Malaria
- Disseminated Coccidioidomycosis
- Brain Abscess
- Invasive Fungal Sinusitis
- Meningococemia
- Toxic Shock Syndrome
- Severe Clostridium difficile colitis
- Agents of Bioterrorism (Anthrax, Plague, Small Pox, Tularemia, Botulism)
- Viral Hemorrhagic Fevers

