Infectious Diseases Emergencies

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Disclosures

- I have a grant from 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 c/o severe headache for 3 days, associated with fever, nausea, and vomiting
- Self-diagnosed “sinus infection” but did not take any antibiotics
- Her family called EMS when she became disoriented

Meningoencephalitis

A Continuum of Syndromes

- Meningitis
  - Acute: Fever, headache, +/- altered mental status
  - Chronic: More gradual, less severe

- Encephalitis
  - Mental status change may occur early and may progress to obtundation or coma
  - Behavioral and speech disturbances

Analyzing the CSF

The CSF formula

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

Normal Values

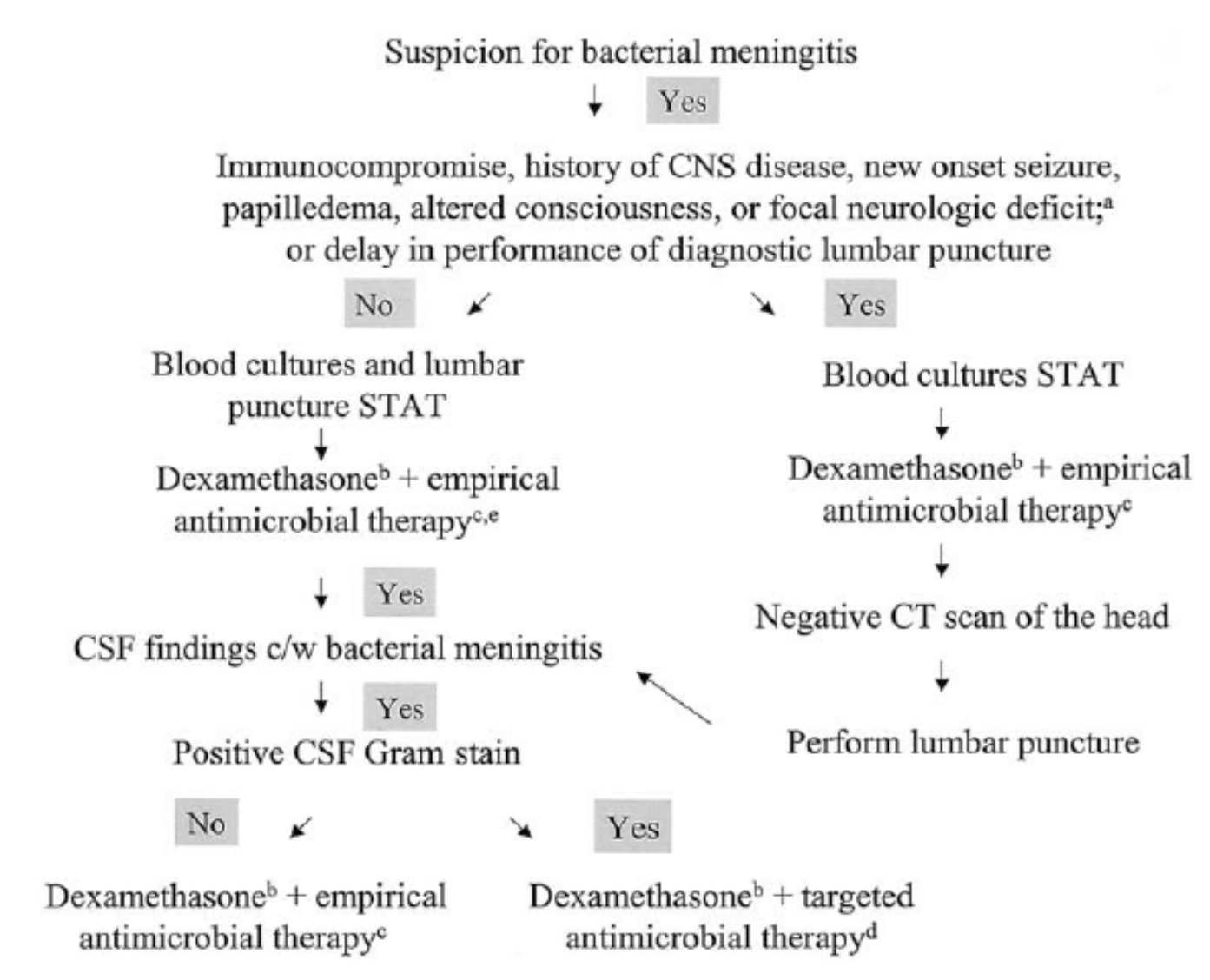
- Pressure 9 – 18 cm H_2O
- WBC/mm^3 0 – 5
- Protein mg/dL 15 – 40
- Glucose mg/dL 50 – 75
- Appearance - Clear

Do not "waste" CSF on unnecessary tests;
it is difficult to get more!

Differential Diagnosis

50-100 WBC 90% mononuclear Normal glucose Mildly elevated protein	Viral or “Aseptic” Neurosyphilis	Enteroviral PCR West Nile IgM HSV PCR VDRL
1000+ WBC 90% neutrophils Glucose < 10 Elevated protein	Bacterial	Await Gram stain and culture Blood cultures
20-200 WBC 90% mononuclear Glucose < 40 Very elevated protein	Fungal TB	Fungal culture Cryptococcal Ag Coccidioides Ab AFB culture

Management


Suspicion for bacterial meningitis
Yes
Immunocompromise, history of CNS disease, new onset seizure, papilledema, altered consciousness, or focal neurologic deficit;[a] or delay in performance of diagnostic lumbar puncture
No
Yes
Blood cultures and lumbar puncture STAT
Dexamethasone[b] + empirical antimicrobial therapy[c,e]
Yes
CSF findings c/w bacterial meningitis
Yes
Positive CSF Gram stain
No
Yes
Dexamethasone[b] + empirical antimicrobial therapy[c]
Dexamethasone[b] + targeted antimicrobial therapy[d]
Blood cultures STAT
Dexamethasone[b] + empirical antimicrobial therapy[c]
Negative CT scan of the head
Perform lumbar puncture

Treatment of *S. pneumoniae*

- Penicillin resistance is increasing
- Antibiotic levels in CSF reach only 2-10% of serum levels
- PCN CSF breakpoints:
  - <0.1 ug/ml
  - 0.1 – 1.0 ug/ml
  - ≥ 2.0 ug/ml

Treatment

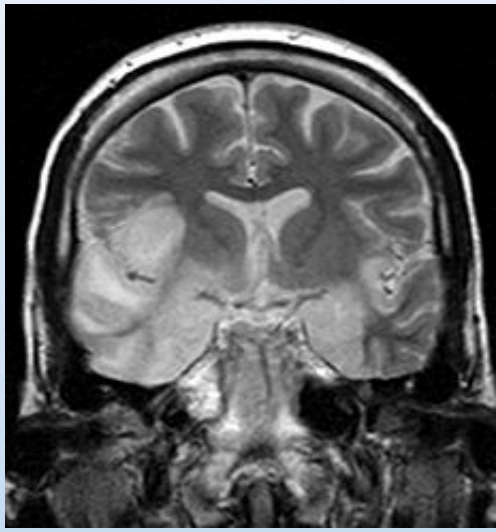
Microorganism	Recommended therapy	Alternative therapies
Streptococcus pneumoniae	Vancomycin plus a third-generation cephalosporin[a,b]	Meropenem (C-III), fluoroquinolone[c] (B-II)
Neisseria meningitidis	Third-generation cephalosporin[a]	Penicillin G, ampicillin, chloramphenicol, fluoroquinolone, aztreonam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

“My father is just not himself”

- An 82 year old man presented to the clinic with fever, fatigue, urinary incontinence, confusion, and was reported to have been walking naked in the house
- Urinalysis showed significant bacteriuria and pyuria and was diagnosed with a UTI and was prescribed Levofloxacin
- The following day he continued to have fever and worsening confusion
- He was transferred to the ED that evening with reports of having developed aphasia, ataxia, and an episode of seizure

Herpes Simplex Virus (HSV) Encephalitis

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



Herpes Simplex Virus (HSV) Encephalitis

Meningitis	Encephalitis
HSV 2 >> 1	HSV 1 >> 2
Associated with primary infection	Usually not primary in adults
Normal mental status	Abnormal mental status
Can be recurrent (Mollaret)	Usually no oral lesions
Benign	Acyclovir decreases mortality

Whitley et al JAMA 1982:247:317

“My Foot is Swollen”

- A 50-y/o woman presented to the ED 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
- The skin appeared cyanotic and cool. The foot was mottled with a black eschar; the swelling extended up the thigh

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

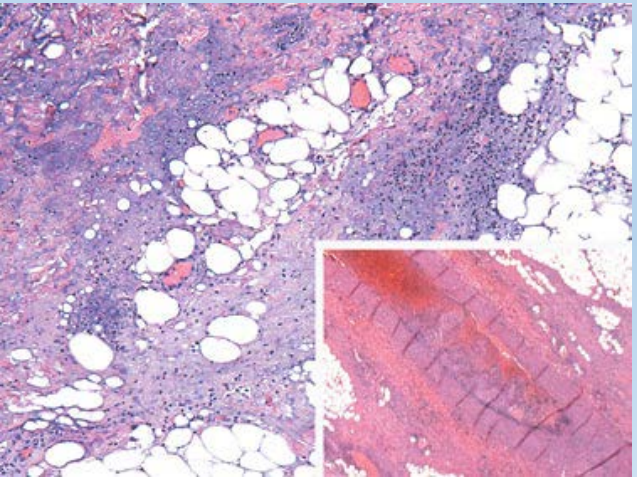
Clinical Presentation

Clinical features suggestive of necrotizing fasciitis:

- 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



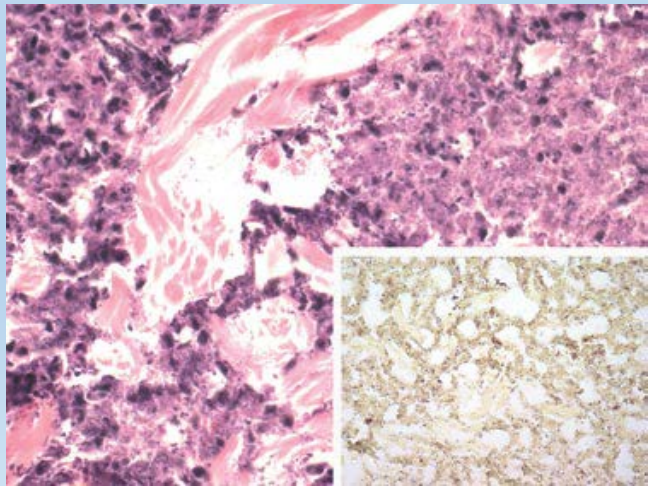


Table 1. Factors Conferring a Predisposition to Specific Necrotizing Soft-Tissue Infections.*

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

* Gas gangrene is also known as clostridial myonecrosis.

Stevens DL, Bryant AE. N Engl J Med ;377:2253-2265

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
Streptococcus	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

Staphylococcus aureus	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
Clostridium 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 00 units/kg/dose every 6 h IV
Aeromonas hydrophila	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
Vibrio vulnificus	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

IDSA Guidelines 2014

Clindamycin is highly recommended for the treatment of Necrotizing fasciitis caused by which bacteria?

A. *MRSA*
B. *MSSA*
C. *Vibrio Vulnificus*
D. *Streptococcal pyogenes*
E. *Anaerobic infection with Bacteroides species*
F. *Streptococcal agalactiae*

Group A streptococci

- Clindamycin has greater efficacy against Group A streptococci because of greater activity against large bacterial populations in stationary phase of growth

- Suppression of toxins and virulence factors by inhibiting bacterial protein synthesis

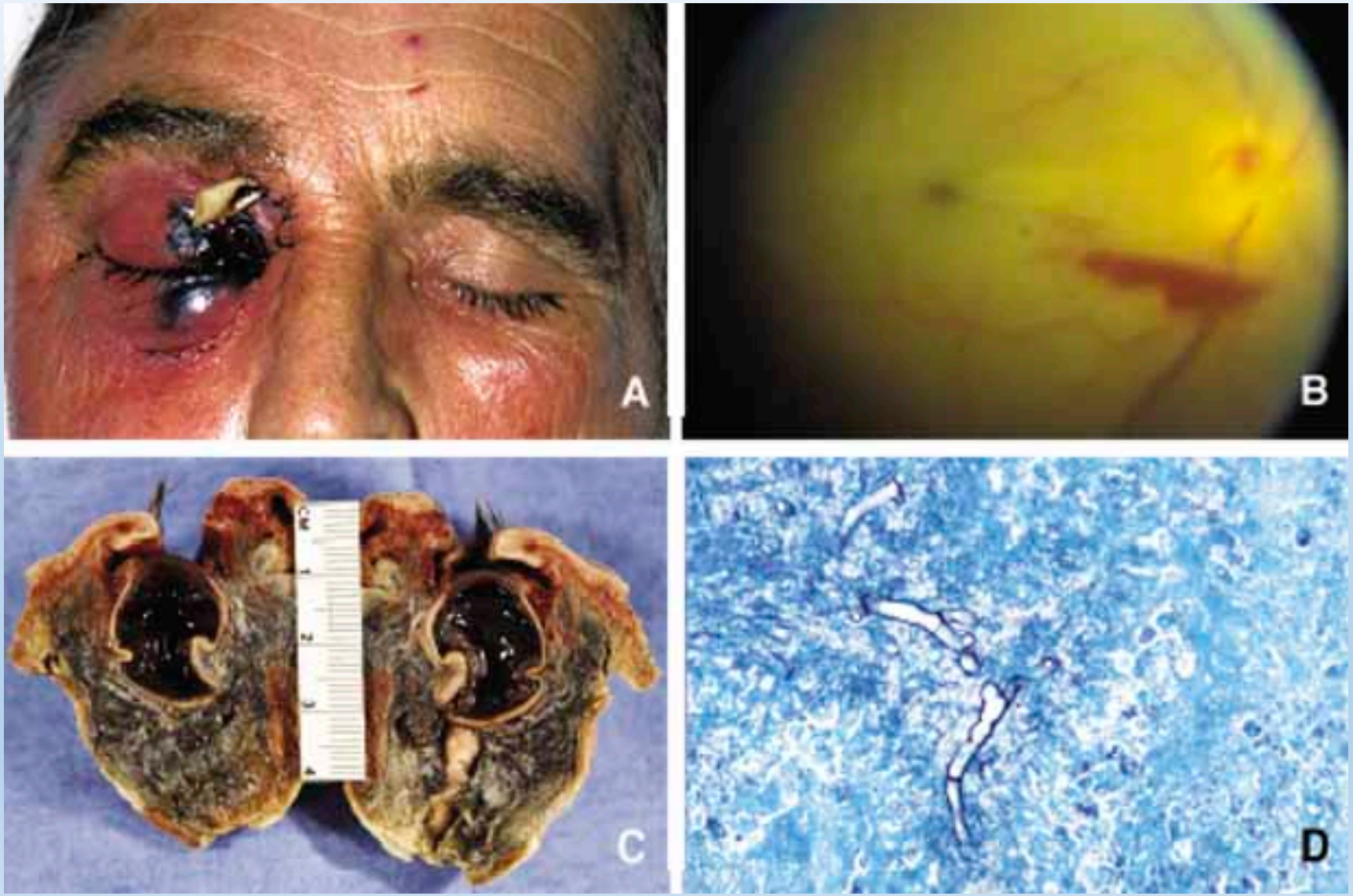
- For group A streptococcal and b-hemolytic streptococci, treatment may be narrowed to the combination of penicillin and clindamycin

“Please examine me!”

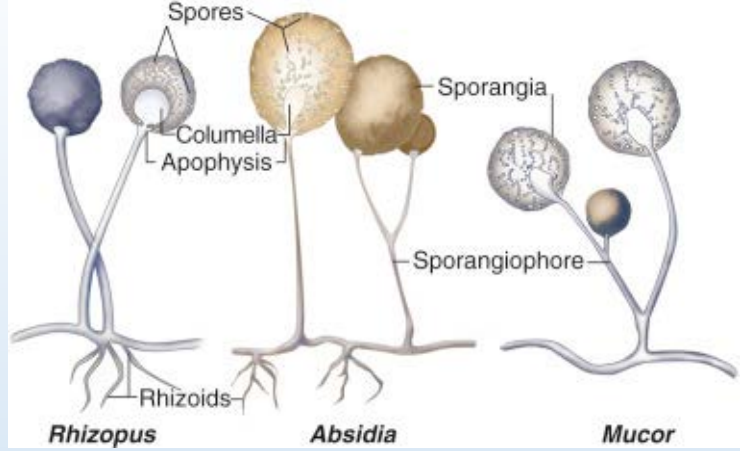
- 45 y/o woman with Diabetes is in the ICU with respiratory failure on broad spectrum antibiotics

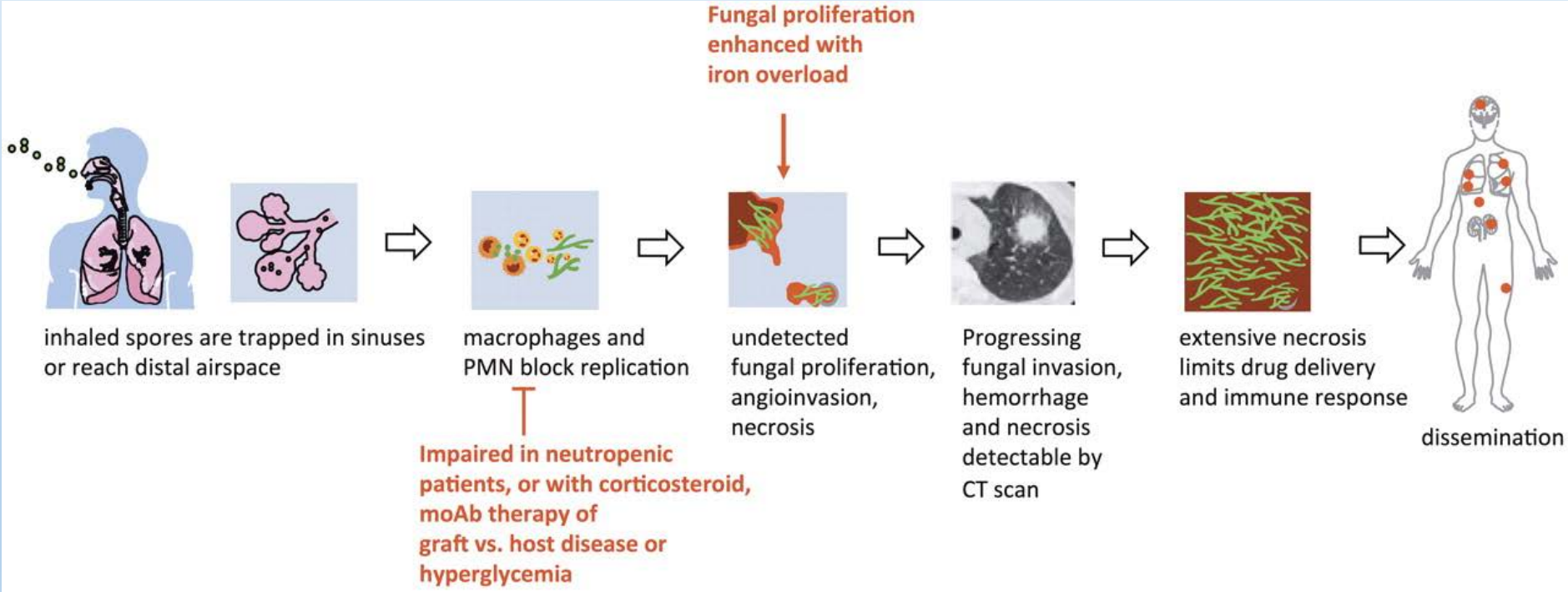
- On day 3 of ICU admission the nurse notifies you that the patient has developed periorbital and facial swelling, and has dark material present on the palate

Invasive Orbitorhinocerebral Mucormycosis



Pathogenesis





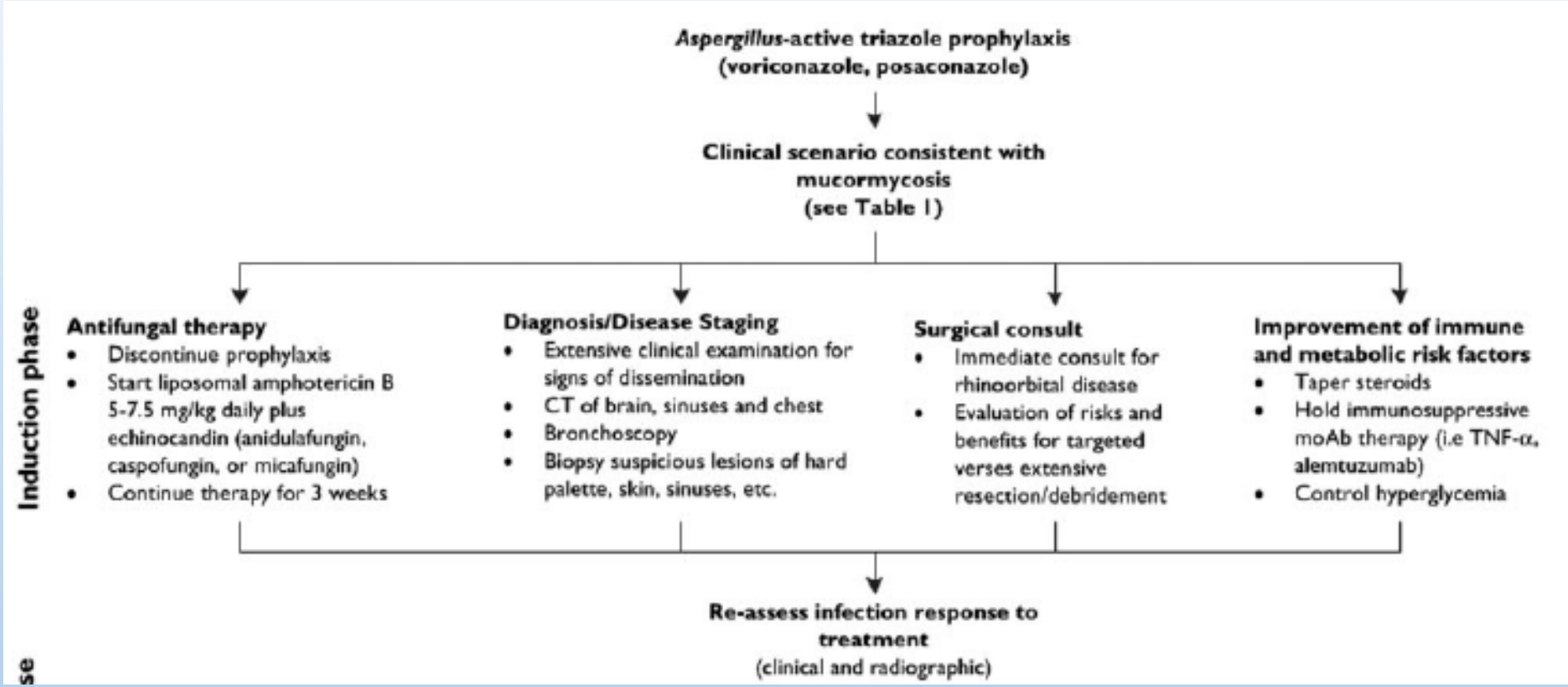
Role in Diabetic Ketoacidosis: Diminished capacity of transferrin to bind to and sequester free iron at a pH of <7.4

Risk Factors

Table 2 Factors predisposing patients to zygomycosis

Diabetes mellitus
Diabetic ketoacidosis
Poorly controlled diabetes mellitus
Chronic metabolic acidosis
Renal failure
Chronic salicylate poisoning
Deferoxamine therapy
Iron overload
Immunosuppression
Neutropenia (due to malignancies or chemotherapy)
Corticosteroid therapy
Organ or hematopoietic cell transplantation
HIV infection
Skin or soft tissue breakdown
Burn
Trauma
Surgical wound
Miscellaneous
Intravenous illicit drug use
Neonatal prematurity
Malnourishment
Prolonged use of broad-spectrum antimocrobial agents

Management

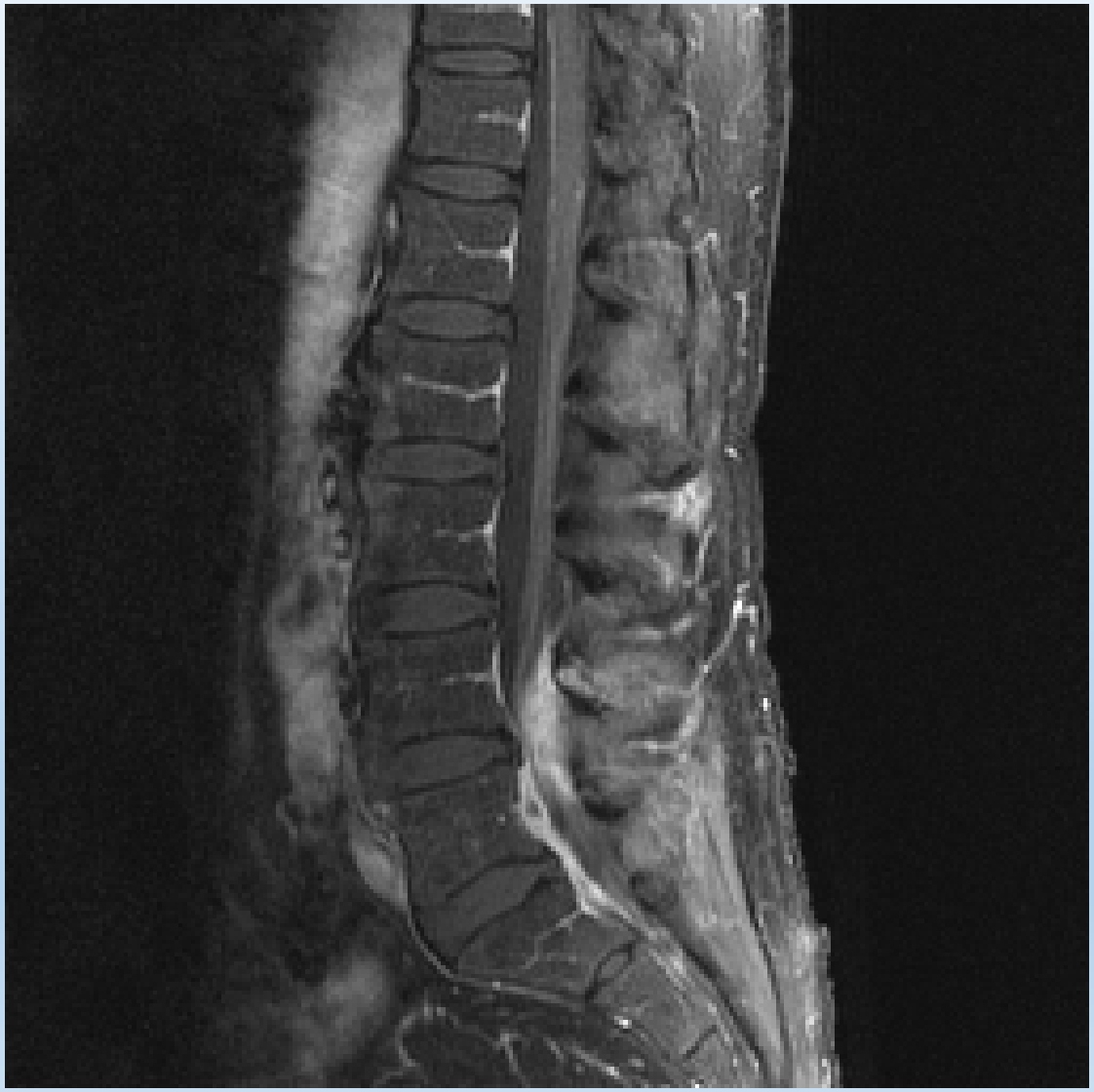


- Histopathology with culture is recommended for identification
- Broad, non-septate hyphae with right-angle branching using calcofluor white and methenamine silver stains

“My back is killing me”

- A 24 y/o Woman presents to the ED with c/o fever, severe back pain described as "shooting” and stabbing in nature, lower extremity weakness with decreased sensation, difficulty walking, and bladder dysfunction

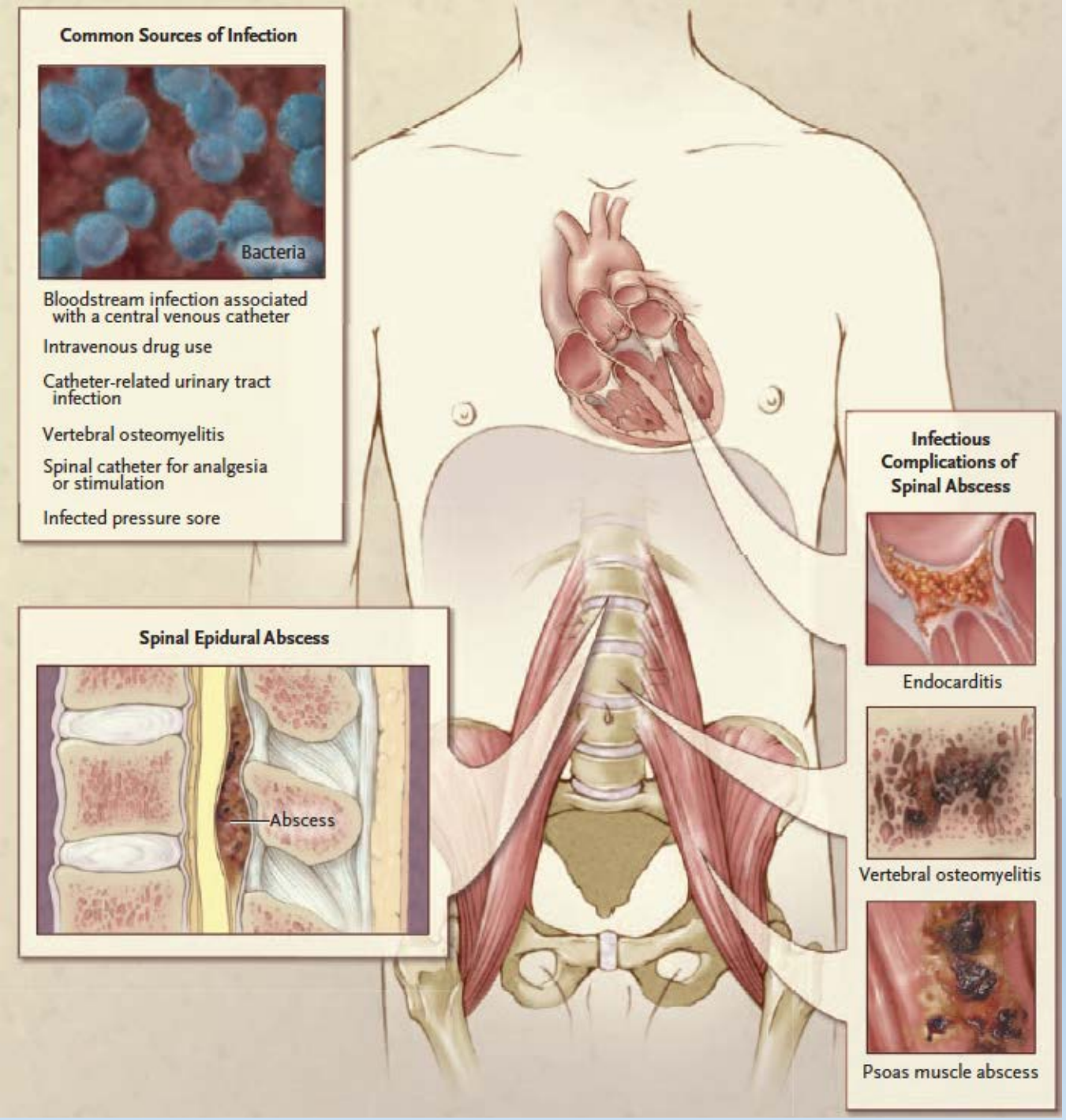
Imaging



- Epidural abscess extending from the L4-S1 levels causing severe thecal sac stenosis with cauda equina impingement

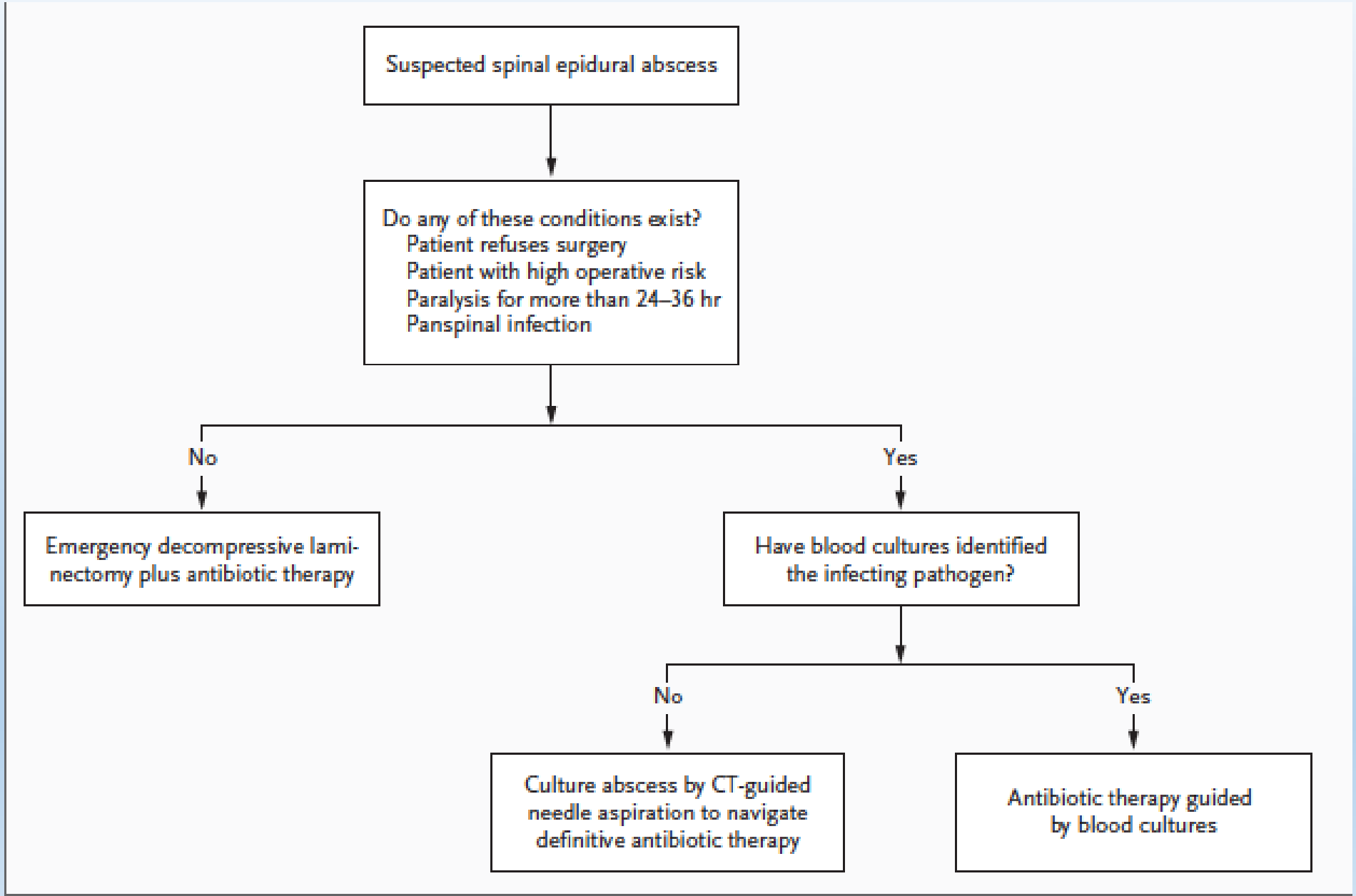
Microbiology

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



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

Management of Spinal Epidural Abscess

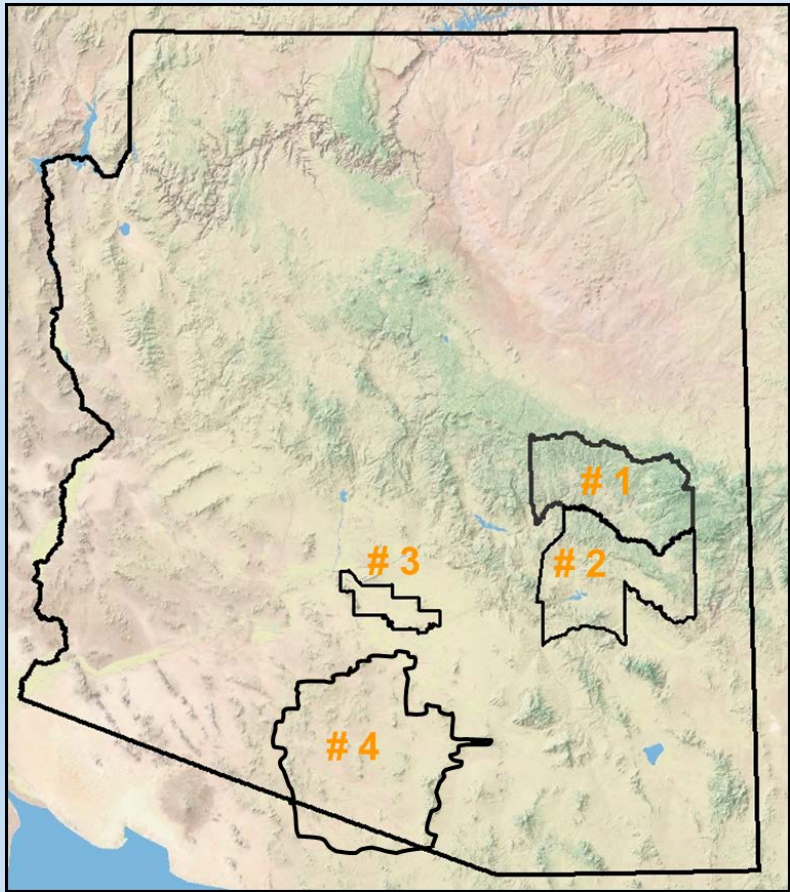


“I feel like I am going to die”

- A 23 year old man is admitted with c/o of fever, chills, headaches, malaise, myalgias, nausea and vomiting
- He reported visiting family in White River three days prior to his presentation
- Labs: Sodium 121, Hemoglobin 10, Platelets 94,000, AST 210, ALT 250

Rocky Mountain Spotted Fever in Arizona

- From 2002-present, over 266 cases of RMSF have been reported in Arizona
- There have been 21 deaths
  —Case fatality 7%, ~ 15 X higher than the U.S. rate
- 2013: Confirmed-9 Probable-54 death-1
- Cases occur in clusters due to common household exposures



The Primary Arizona Tick Vector of RMSF

Rhipicephalus sanguineus
Brown dog tick

Arizona Department of Health Services

RMSF: Clinical Manifestations

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

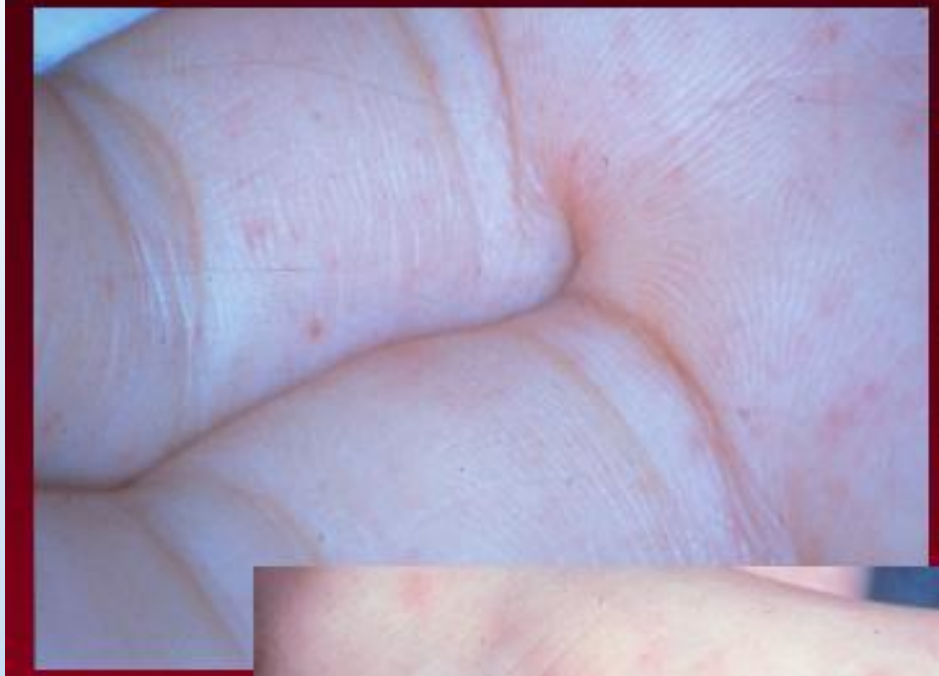
Arizona Department of Health Services

RMSF: The Rash

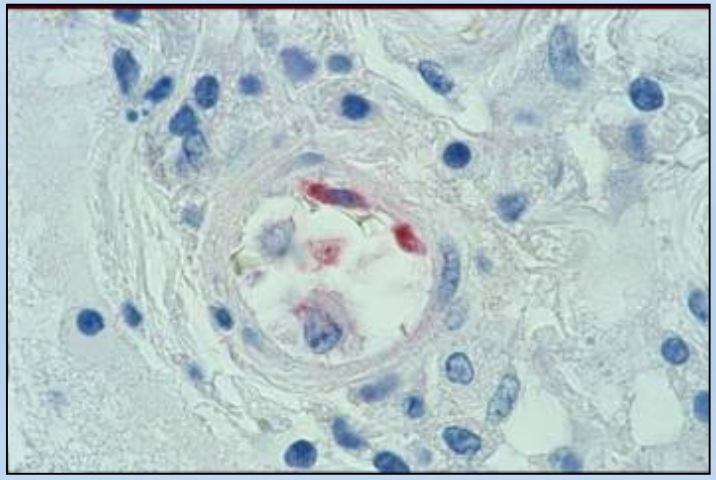
- Generally not apparent until day 2-5 of symptoms (only seen in 68% of AZ patients)
- Begins as 1 to 5 mm macules progressing to maculopapular
- May begin on ankles, wrists, and forearms, spreads to trunk
- Petechial rash is a late finding, occurs on or after day 6
- Rash may be asymmetric, localized,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

Arizona Department of Health Services

Rashes of RMSF



Severe Sequelae



Antimicrobial Therapy of RMSF

Pregnant adult or tetracycline allergic	Non-pregnant adult or child ≥45 kg	Child <45 kg
Chloramphenicol 500 mg qid, less likely to prevent death	Doxycycline 100 mg bid p.o. or i.v.	Doxycycline 4.4 mg/kg/day in 2 divided doses p.o. or i.v.

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***

Brain Abscess

PREDISPOSING CONDITION	USUAL MICROBIAL ISOLATES
Otitis media or mastoiditis	Streptococci (anaerobic or aerobic), *Bacteroides* and *Prevotella* spp., Enterobacteriaceae
Sinusitis (frontoethmoid or sphenoid)	Streptococci, *Bacteroides* spp., Enterobacteriaceae, *Staphylococcus aureus, Haemophilus* spp.
Dental infection	Mixed *Fusobacterium, Prevotella, Actinomyces,* and *Bacteroides* spp., streptococci
Penetrating trauma or postneurosurgical	*S. aureus,* streptococci, Enterobacteriaceae, *Clostridium* spp.
Lung abscess, empyema, bronchiectasis	*Fusobacterium, Actinomyces, Bacteroides,* and *Prevotella* spp., streptococci, *Nocardia* spp.
Bacterial endocarditis	*S. aureus*, streptococci
Congenital heart disease	Streptococci, *Haemophilus* spp.
Neutropenia	Aerobic gram-negative bacilli, *Aspergillus* spp., Mucorales, *Candida* spp., *Scedosporium* spp.
Transplantation	*Aspergillus* spp., *Candida* spp., Mucorales, *Scedosporium* spp., Enterobacteriaceae, *Nocardia* spp., *Toxoplasma gondii, Mycobacterium tuberculosis*
Human immunodeficiency virus infection	*T. gondii, Nocardia* spp., *Mycobacterium* spp., *Listeria monocytogenes, Cryptococcus neoformans*

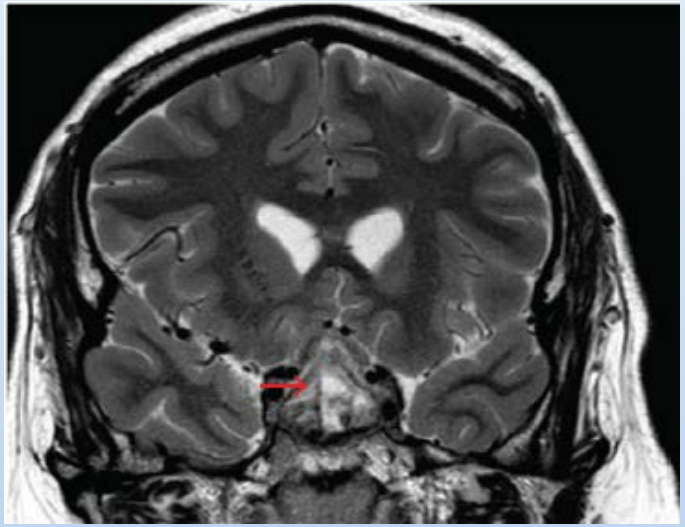
Brain Abscess: Clinical Presentation

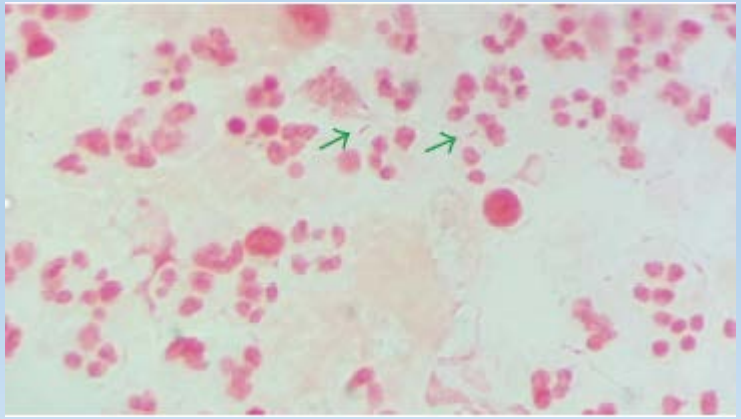
SYMPTOM OR SIGN	FREQUENCY (%)
Headache	49-97
Mental status changes	28-91
Focal neurologic deficits	20-66
Fever	32-79
Triad of headache, fever, and focal deficit	<50
Seizures	13-35
Nausea and vomiting	27-85
Nuchal rigidity	5-52
Papilledema	9-51

Polymicrobial Pituitary Abscess Predominately Involving *Escherichia coli* in the Setting of an Apoplectic Pituitary Prolactinoma

Norman Beatty, Luis Medina-Garcia, Mayar Al Mohajer, and Tirdad T. Zangeneh

Division of Infectious Diseases, Department of Medicine, University of Arizona College of Medicine, Banner-University Medical Center, 1501 N. Campbell Avenue, Tucson, AZ 85724, USA





Disseminated Infection Caused by *Eggerthella lenta* in a Previously Healthy Young Man: A Case Report

Ahmad Salameh,[1] Stephen A. Klotz,[2] and Tirdad T. Zangeneh[2]

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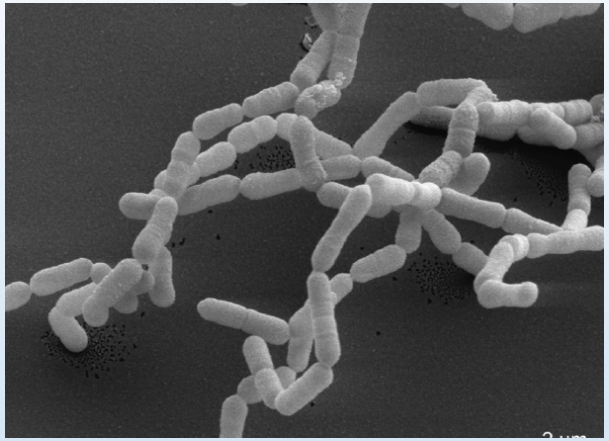
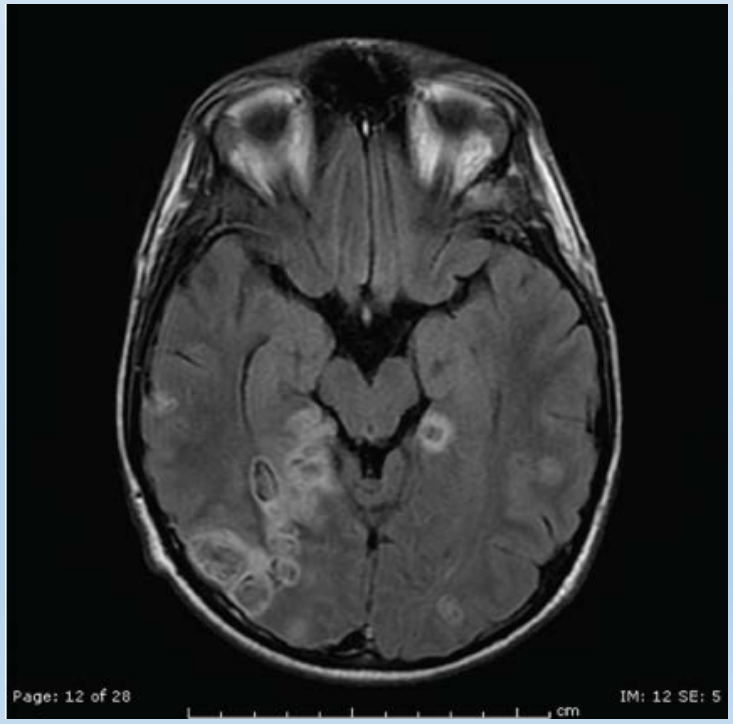
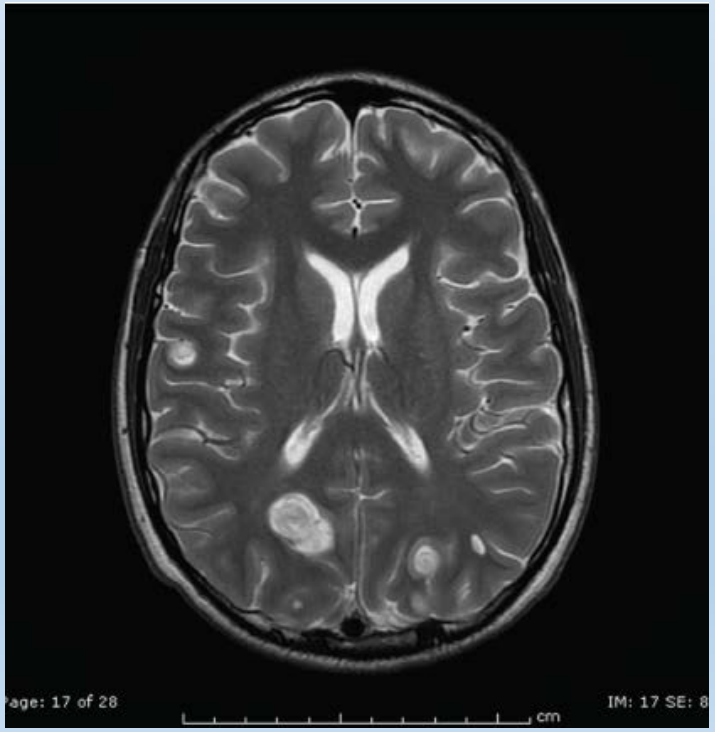
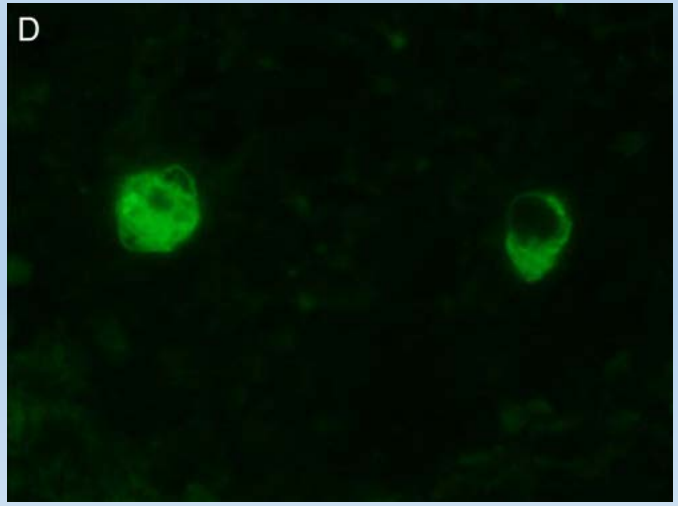
[2] *Division of Infectious Diseases, Department of Medicine, The University of Arizona Medical Center, University of Arizona, Tucson, AZ 85724, USA*

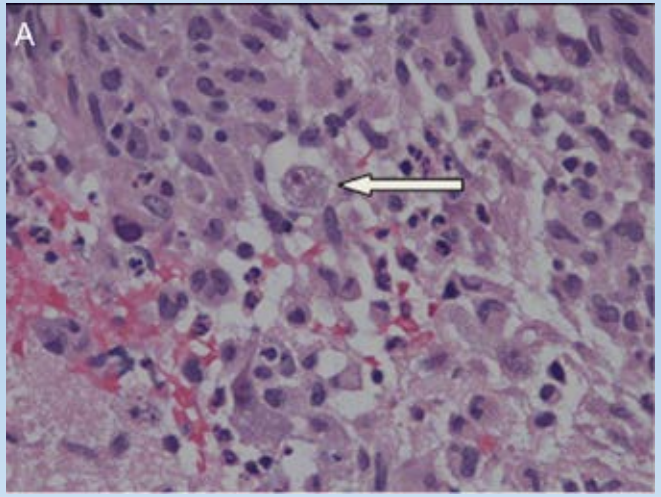


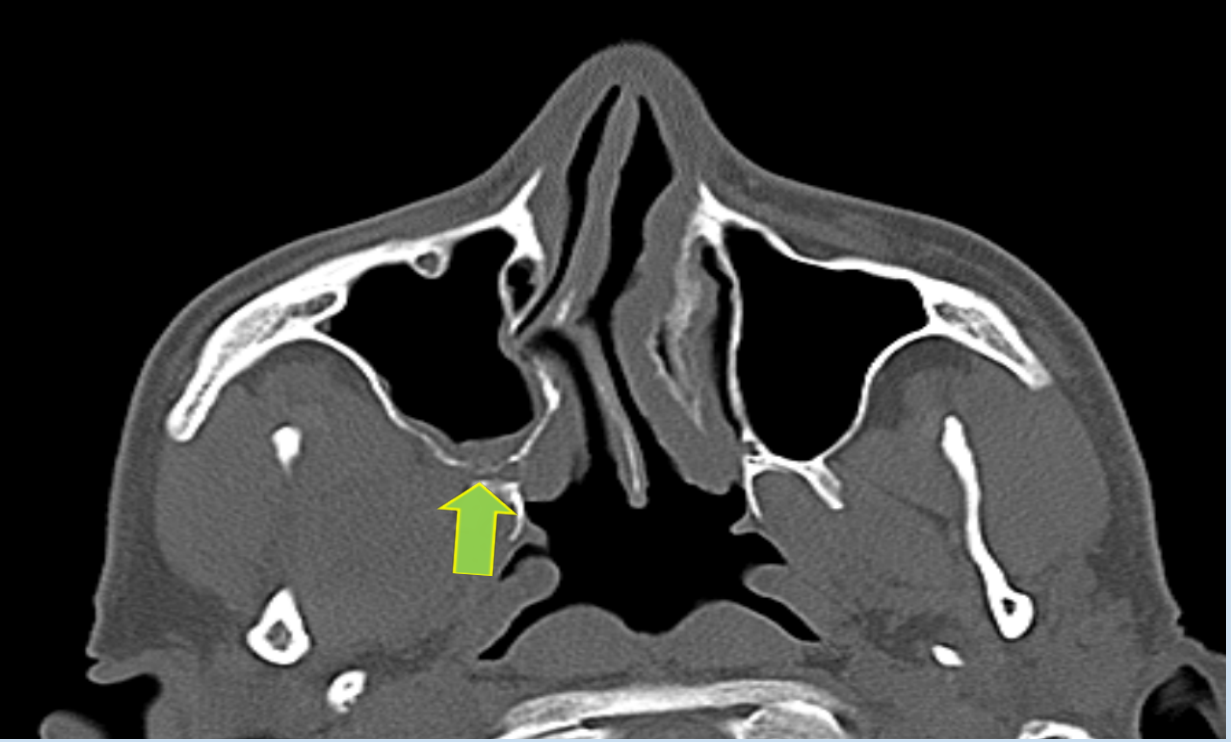




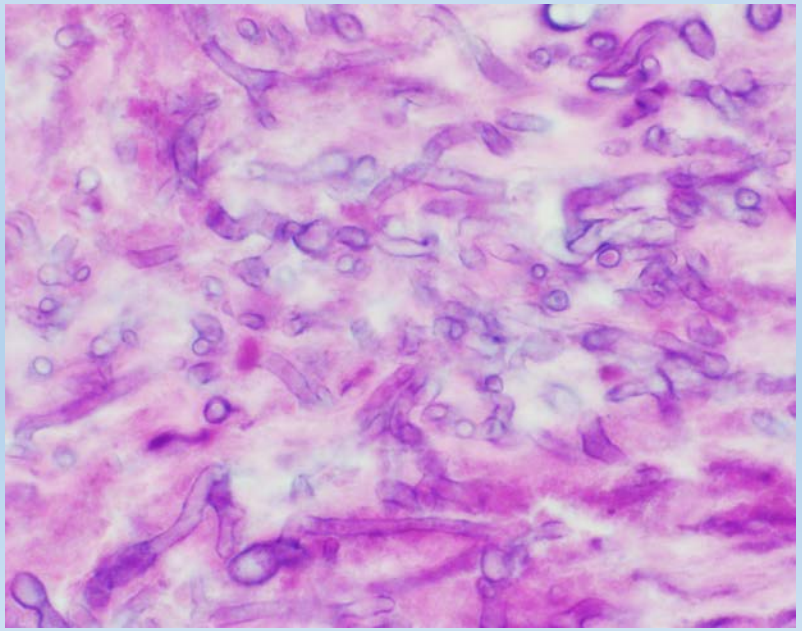
Fatal Granulomatous Amoebic Encephalitis Caused by *Acanthamoeba* in a Patient With Kidney Transplant: A Case Report

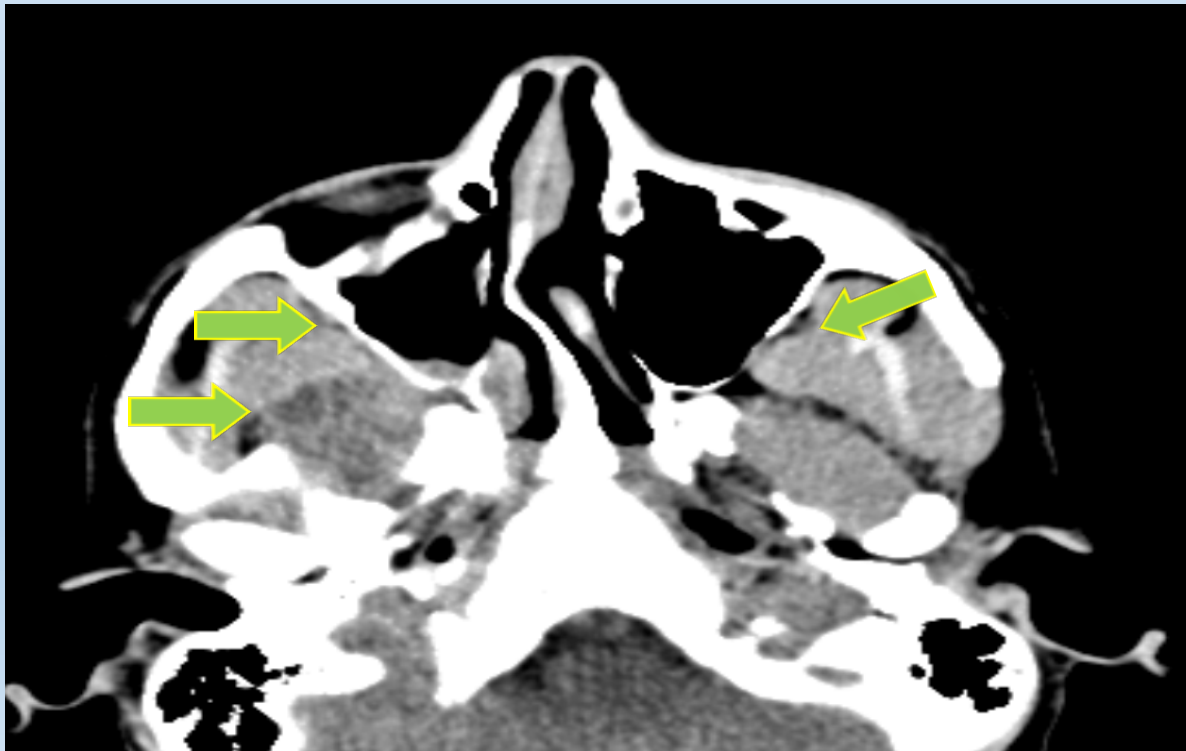






Fatal *Aspergillus fumisynneamatus* Sinusitis with CNS invasion in a healthy 36 year old man





Red Herring

- A 75 year old man was seen in the clinic for having had fever, fatigue, and weight loss. He was admitted for further workup

- Urinalysis indicated hematuria and pyuria and cultures grew >100,000 CFU/mL of *E. Coli*

- One out of 4 blood cultures grew Viridans streptococci which was regarded as a contaminant

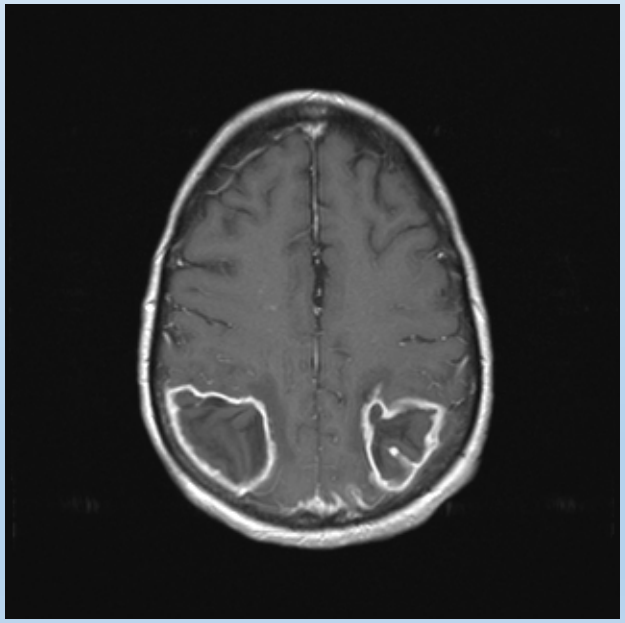
Red Herring

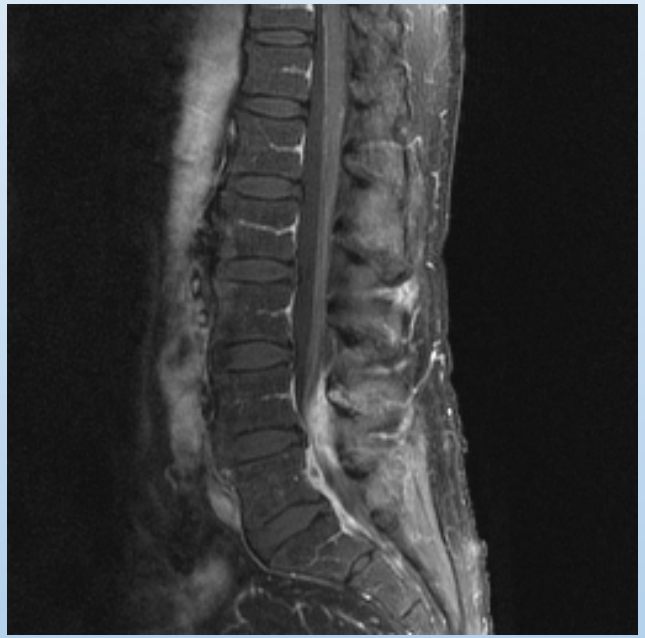
- He was discharged with a seven day course of Ciprofloxacin, but his symptoms persisted for another two months and he was prescribed several courses of antibiotics for reoccurring UTIs

- He presented to the ED three months after the initial hospitalization with altered mental status and heart failure

- He complained of back pain described as stabbing in nature, lower extremity weakness with decreased sensation, difficulty walking, and bladder dysfunction

Actual Diagnosis: Subacute Bacterial Endocarditis due to Viridans streptococci resulting in spinal epidural and brain abscesses



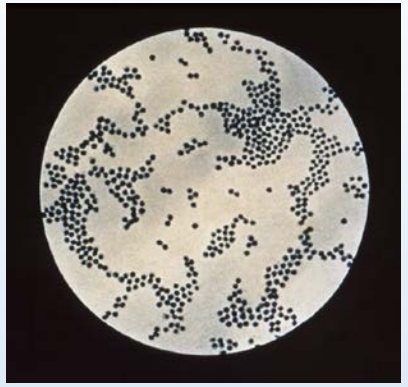


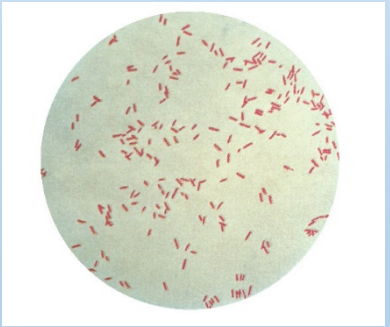
Infective Endocarditis (IE)

- 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 staph*ylococci — 11 percent
- *Streptococcus bovis* — 7 percent
- Non-HACEK gram-negative bacteria — 2 percent
- Fungi — 2 percent
- HACEK — 2 percent

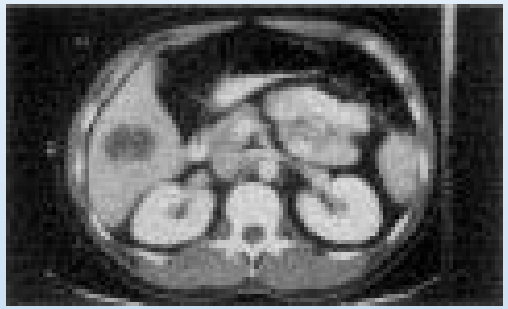




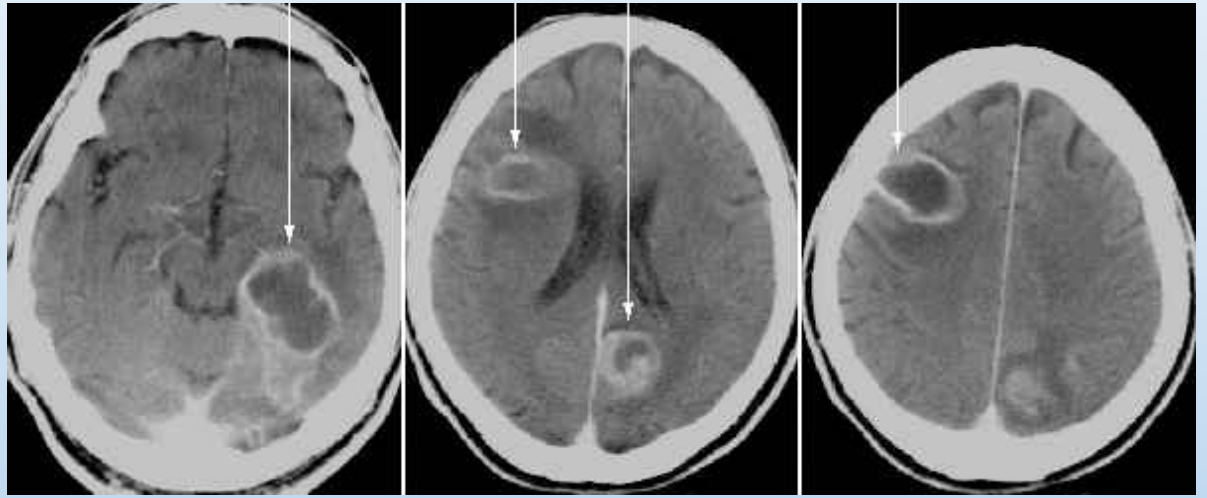
**Haemophilus spp*
Aggregatibacter [formerly *Actinobacillus* spp.]
Cardiobacterium hominis
Eikenella corrodens
Kingella kingae

Consequences of Septic Emboli

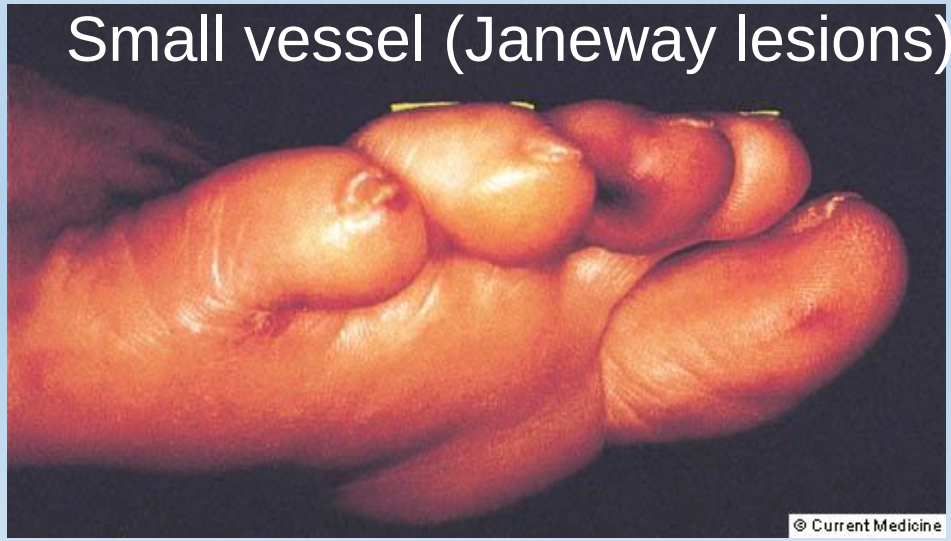
Mitral or aortic valve → Left ventricle → Aorta



Large vessel



Small vessel (Janeway lesions)



CNS Involvement

- Patients with left-sided IE were prospectively evaluated with cerebral MRI regardless of neurologic symptoms
- The total cerebrovascular complication rate was 65%, including 35% (symptomatic) and 30% (clinically silent)
- Middle cerebral artery and its branches are involved commonly
- Hemorrhagic transformation of septic emboli commonly results in fatal intracerebral hemorrhage

Martin et al. *Clin Infect Dis*. 2008; 47:23

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

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

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

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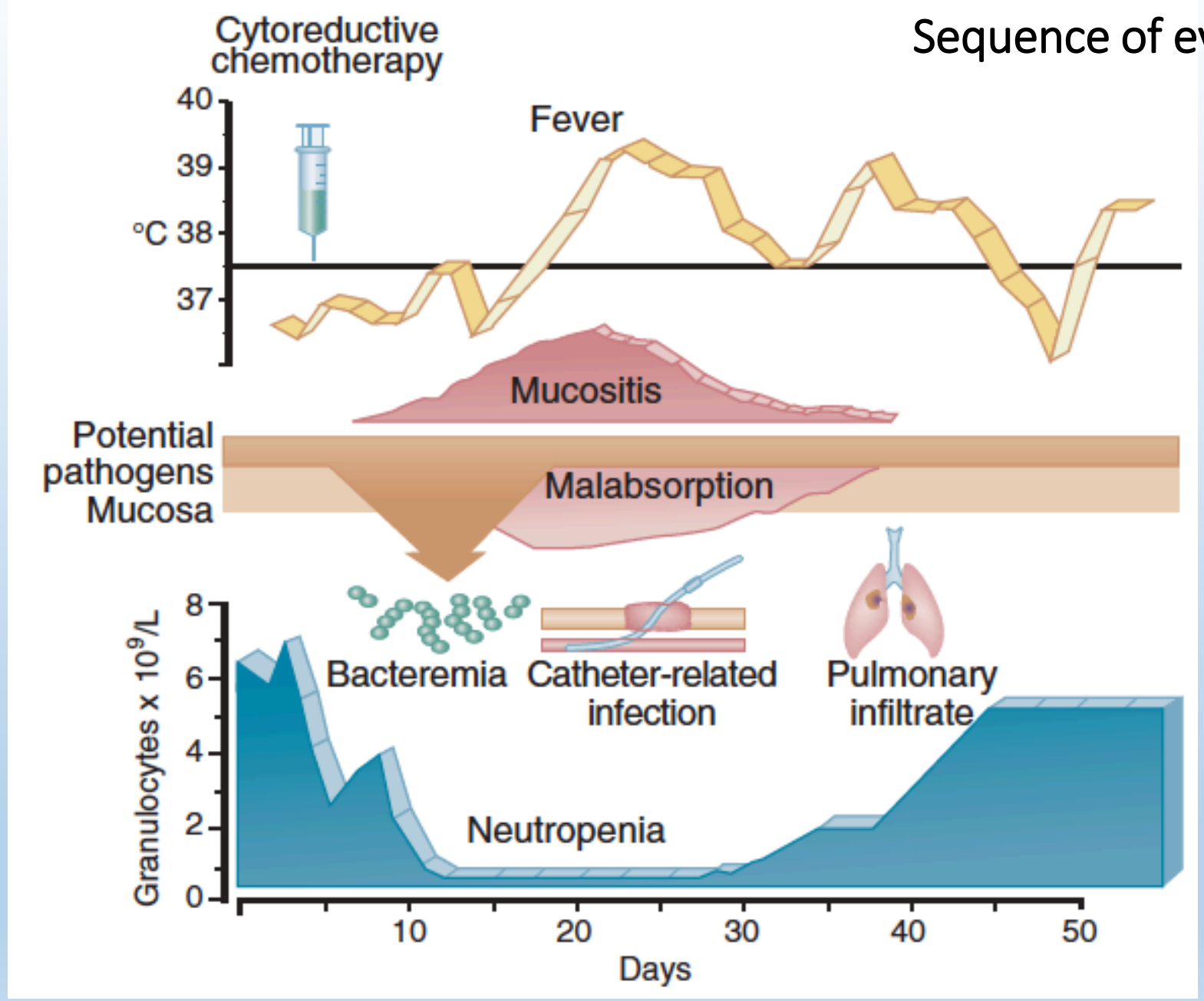
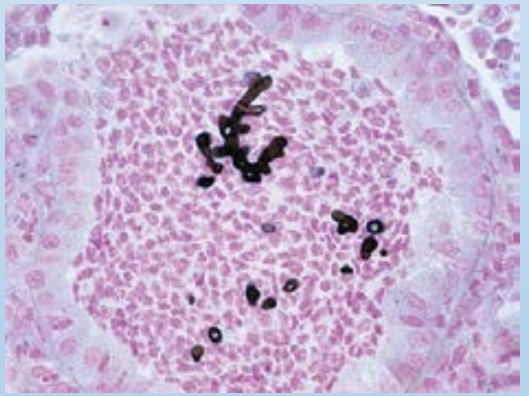
Neutropenic Fever

- Hospitalization for febrile neutropenia (FN) is associated with considerable morbidity, mortality, and cost
- By the early 1960s Gram-negative bacteremia in neutropenic patients carried a mortality rate of 90%
- 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

Kuderer NM, Cancer. 2006, Legrand M, Crit Care Med. 2012
Klastersky J, Journal of Antimicrobial Chemotherapy. 2009

Sequence of events during neutropenia





Mandell GL, Principals and Practice of Infectious Diseases, 8th edition, 2016

Definitions

- Fever: A single oral temperature of ≥38.3°C (101°F) or a temperature of ≥38.0°C (100.4°F) sustained over 1 hour
- Neutropenia: ANC <500 cells/mm^3 or ANC that is expected to decrease to <500 cells/mm^3 during the next 48 hours
- The term ‘‘profound’’ is used to describe neutropenia in which the ANC is <100 cells/mm^3 and prolonged >7 days
- Functional neutropenia refers to qualitative defects of circulating neutrophils

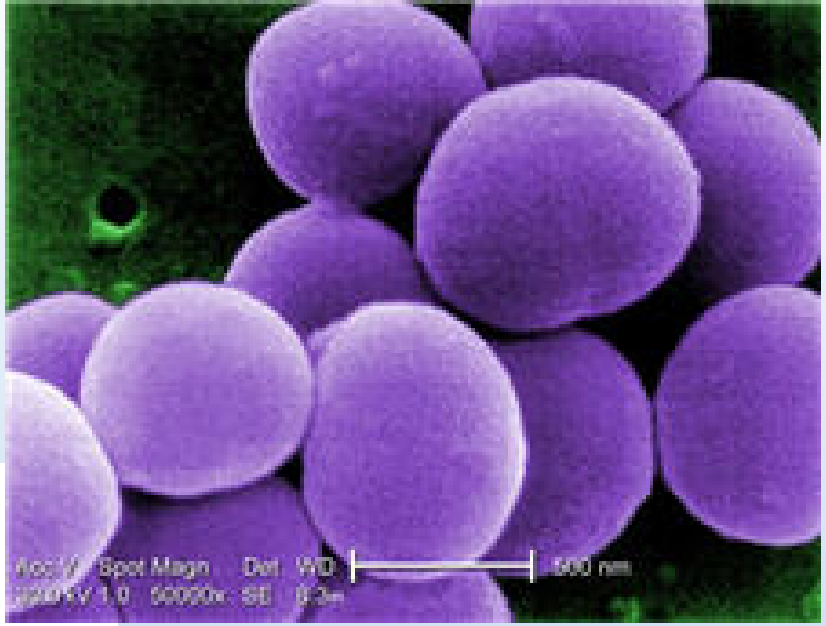
Freifeld AG, CID. 2011

Etiology

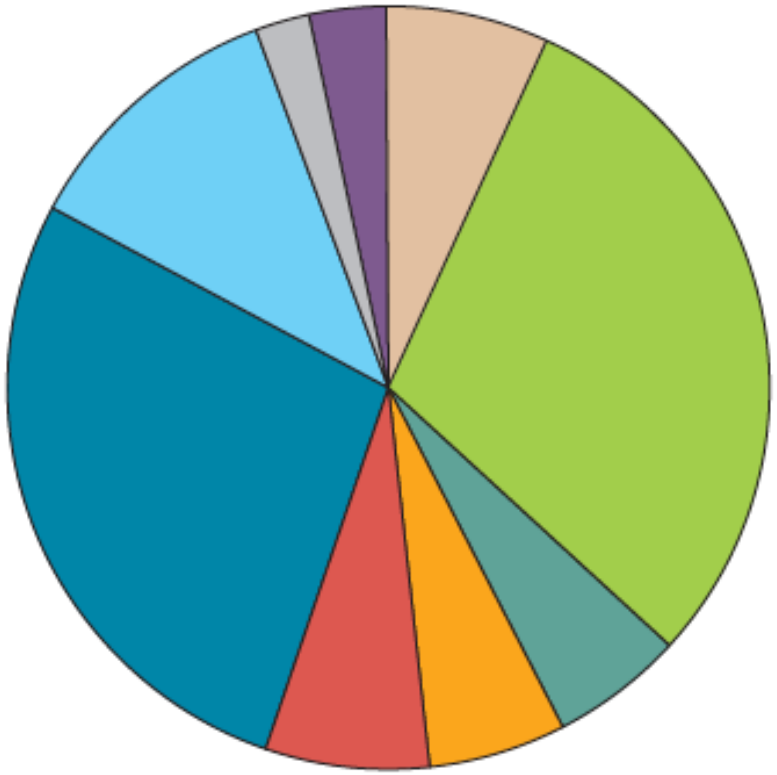
- Most patients will have no infectious etiology documented and clinically documented infections occur in 20%–30% of episodes
- Common sites of tissue-based infection include the intestinal tract, lungs, and skin
- Bacteremia occurs in 10%–25% of patients, with most occurring in the setting of prolonged or profound neutropenia (ANC <100 neutrophils/mm^3)

Klastersky J. CID 2004; 39:S32–7
Ramphal R. CID 2004; 39:S25–31

Etiology of Bacteremia



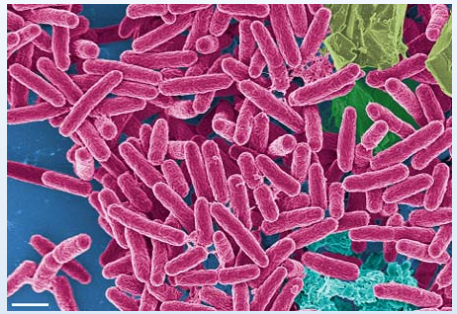
REVIEW OF LITERATURE FROM YEARS 2005-2011



- *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%)

Mandell GL, Principals and Practice of Infectious Diseases, 8th edition, 2016

IDSA GUIDELINES



Clinical Practice Guideline for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer: 2010 Update by the Infectious Diseases Society of America

Alison G. Freifeld,[1] Eric J. Bow,[9] Kent A. Sepkowitz,[2] Michael J. Boeckh,[4] James I. Ito,[5] Craig A. Mullen,[3] Issam I. Raad,[6] Kenneth V. Rolston,[6] Jo-Anne H. Young,[7] and John R. Wingard[8]

- Fever occurs frequently during chemotherapy-induced neutropenia: 10%–50% of patients with solid tumors
- Clinically documented infections occur in 20%–30% of febrile episodes
- Greater than 80% of those with hematologic malignancies will develop fever during ≥1 chemotherapy cycle associated with neutropenia

Freifeld AG, CID. 2011

Initial in-Hospital Treatment (A-II)

- Anticipated prolonged (>7 days duration) and profound neutropenia (ANC <100 cells/mm^3)
- Co-morbid conditions, hypotension, pneumonia, new-onset abdominal pain, or neurologic changes
- High-risk patients require intravenous empirical antibiotics with an antipseudomonal b-lactam agent (A-I)
- Low-risk patients with anticipated brief (<7 days duration) neutropenic period or few co-morbidities, are candidates for oral empirical therapy

Freifeld AG, CID. 2011

Initial Empiric Therapy

- In high-risk patients requiring hospitalization for empirical antibiotic therapy, monotherapy with an anti-pseudomonal b-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

Freifeld AG, CID. 2011

Indications for Use of Empiric Antibiotics Active Against Gram-Positive Organisms

- Hemodynamic instability, severe sepsis, or Pneumonia
- Positive blood culture for gram-positive bacteria, before final identification and susceptibility testing is available
- Clinically suspected serious catheter-related infection, skin or soft-tissue infection at any site
- Colonization with MRSA, vancomycin-resistant *enterococcus*, or penicillin-resistant *Streptococcus pneumoniae*
- Severe mucositis, with fluoroquinolone prophylaxis

Freifeld AG, CID. 2011

How Long Should Empirical Antibiotic Therapy be Given?

- In patients with unexplained fever, initial regimen is continued until there are clear signs of marrow recovery
  - Increasing ANC that exceeds 500 cells/mm3

- If appropriate treatment course has been completed and signs and symptoms of a documented infection have resolved, patients who remain neutropenic may resume oral fluoroquinolone prophylaxis until marrow recovery

Freifeld AG, CID. 2011

Empirical or Preemptive Antifungal Therapy

- Empirical antifungal therapy and investigation is considered for patients with persistent or recurrent fever after 4–7 days of antibiotics and duration of neutropenia of >7 days

- Invasive mold infections, occur almost exclusively in high-risk patients with profound neutropenia lasting longer than 10–15 days

- With preemptive treatment, antifungals are given when evidence is suggested, using a combination of clinical, serologic, and imaging findings

Freifeld AG, CID. 2011

Cutaneous Presentations

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