Objectives

- To learn the normal functions of the integument
- To identify the importance of various layers of the skin
- To recognize common superficial skin infections on clinical evaluation
- To appreciate severe skin and soft tissue infections as life-threatening
- To use epidemiologic clues in the patient history to modify the microbiologic differential diagnosis

Outline

- Skin structure and function
- Pathogenesis of infection
- Microbiology
- Case-based review of clinical manifestations and management
  - Nonpurulent SSTIs
  - Pusulent SSTIs
  - Situations with less typical organisms
  - Severe SSTIs
Skin Structure

Skin Function

- Barrier
  - Infection
  - Environmental exposures:
    - Chemical
    - Mechanical
    - UV radiation
    - Desert climate
  - Temperature regulation
  - Melanin production
  - Sensory (pain, temperature, position)
  - Immunologic surveillance
  - Manifestation of systemic disease

Pathogenesis of Infection

- Uncommon for pathogens to directly enter intact skin, especially in healthy patients.
- Breach in integrity of the normal barrier
  - Scratch/cut/bite
  - Pre-existing skin disease (psoriasis, eczema)
  - Ulceration
  - Surgical incision
  - Trauma
  - Burn injury
- Allows access for both resident skin flora as well as foreign microbes
Microbiology

The most common pathogens:
- *Staphylococcus aureus*
- Beta-hemolytic streptococci
  - group A (*S. pyogenes*)
  - group B (*S. agalactiae*)
- MRSA
  - Methicillin-resistant Staphylococcus aureus
  - Methicillin: semisynthetic beta-lactamase-resistant penicillin
  - Resistance was demonstrated very quickly after its introduction
  - SCC mec: Mobile genetic element
    - Contains mecA—encodes PBP2a, an altered penicillin binding protein
      - with low affinity for binding beta-lactam antibiotics
      - Different SCC mec carried by healthcare-associated and community-acquired strains
  - Panton-Valentine Leukocidin (PVL): a cytotoxin associated with SCC mec IV and V
    - (community-acquired strains)
    - associated with skin infections and necrotizing pneumonias

Question #1

65yo female with a history of breast cancer, with mastectomy and lymph node dissection 10 years ago now in remission, hypertension, presents with onset of erythema and tenderness of her left hand and arm. She has chronic edema in that extremity which is worsened as well. Last night, the erythema was only on her hand and wrist but now it extends farther up her forearm. She notes, she had a similar episode last year. Her temperature is 98.8, heart rate and blood pressure are normal. Her right arm is more swollen compared to the left with erythema over the hand and proximal forearm. It is mildly tender to the touch without any crepitus.
Question #1


https://beta.nhs.uk/conditions/cellulitis/

Which antibiotic would be the most appropriate for treatment?

A. Ciprofloxacin
B. Trimethoprim-sulfamethoxazole
C. Doxycycline
D. Cephalexin
E. Azithromycin

Cellulitis

- Diffuse superficial skin infection—deeper dermis and subcutaneous fat
- Redness and warmth
- Fluctuance and fluctuant fluctum
- Tender
- Predisposing factors: diabetes mellitus, obesity, immunosuppression
- Microbiology: Streptococcus (A and other beta-hemolytic), less often Staphylococcus
- Erythema, paresthesia, swelling
- Treatment: oral antibiotics, incision and drainage, wound care

Almost always unilateral, lower extremity most common

Red (rubor), warm (calor), swollen (tumor), painful (dolor)

Variable systemic symptoms

Streptococci (group A and other beta-hemolytic strep) most prevalent, less often Staphylococcus

Microbiologic diagnosis difficult, usually empiric therapy for streptococci +/- staphylococci
Erysipelas

- Diffuse superficial skin infection—upper dermis and superficial lymphatics
- Classically on the face, extremities
- Raised, tender, intense color, very well circumscribed

Impetigo/Ecthyma

Impetigo
- Localized lesion, epidermis
- Transmissible, kids ages 2-5
- Honey-colored crust
- S. aureus > S. pyogenes
- Empiric therapy common
- Post-streptococcal GN

Ecthyma
- Deep epidermis and dermis
- Ulceration
- +/- bacteremia

Question #2

A 25 year old wrestler is seen because of a 3 day history of a swollen right leg. He thought he'd been bitten by a spider several days prior, although he never saw an insect. On physical exam, his temperature is 37.9 C, BP 126/84. His right leg has a nodular swelling that has a pustular point and surrounding erythema that he says has been worsening. An incision and drainage is performed.
Question #1

Which is the most likely causative pathogen?
A. Trichophyton rubrum (tinea pedis)
B. Staphylococcus aureus
C. Pseudomonas aeruginosa
D. Candida albicans
E. Streptococcus agalactiae (group B strep)

Purulent Skin and Soft Tissue Infections

- Cutaneous abscess - purulent collection in the dermal and subcutaneous tissue
- Furuncle (boil) - infection of the hair follicle that ruptures into the subcutaneous tissue to form an abscess
- Carbuncle - coalescence of multiple furuncles
- Pyomyositis - collection of pus in a muscle group, hematogenous seeding, localized pain +/- seeding
  - Predominantly S. aureus
  - Erythematous nodule +/- fluctuance
  - Discharge is the mainstay of therapy
  - Antibiotics if extensive, systemic signs of infection, poor response to therapy, immunocompromised, etc.
A 55yo male with cirrhosis due to chronic HCV infection is admitted through the emergency room with a suspected infection of his right lower leg. His home on the Florida coast was recently flooded during a hurricane and he has spent the last several days wading through the flood waters in his basement as part of his cleanup efforts. He noted yesterday that he had a cut on his left leg and today he has fluid-filled blisters over the area and increasing erythema. His temperature is 102.5, heart rate 125, and blood pressure 70/40.

In addition to common skin flora, empirical antimicrobial therapy should target which of the following organisms.

A. Mycobacterium marinum
B. Aspergillus fumigatus
C. Candida albicans
D. Erysipelothrix rhusiopathiae
E. Vibrio vulnificus
Water Exposure

Water exposure usually associated with trauma:
- *Aeromonas* species
- *Edwardsiella tarda*
- *Erysipelothrix rhusiopathiae*
- *Vibrio vulnificus*
- *Mycobacterium marinum*

Leeches used for medicinal therapy can also transmit *Aeromonas* infection, colonizes the foregut

Immunocompromised individuals (hepatic disease, malignancy) are at risk for disseminated life-threatening disease (fever, sepsis, multisystem organ failure) especially with *Aeromonas*, *Vibrio*, and *Edwardsiella*.

Bite Wounds

Animal and human bites

- Right wounds (i.e. punch to the mouth):
  - Human: *Eikenella corrodens*, * Fusobacterium*, * Peptostreptococcus*, * Porphyromonas*
  - Dog: *Capnocytophaga canimorsus*, * Pasturella multocida*
  - Cat: * Pasturella multocida*, * Bartonella henselae*

Diabetic Foot Ulcers

- Neuropathy and peripheral vascular disease predispose to ulceration
- When infected often polymicrobial
  - *S. aureus*, beta-hemolytic *β* (group B)
  - Gram negative rods: *P. aeruginosa*
    - bum injury patients
    - immunocompromised (i.e. neutropenia)
Necrotizing Fasciitis

- Full thickness involvement to superficial fascia
- May be monomicrobial (S. pyogenes, S. aureus, Aeromonas, Vibrio vulnificus, Clostridial species) or often polymicrobial (wounds, associated anerobes)
- Pain out of proportion
- Bullous lesions, necrotic tissue, “woody” edema, rapid spread
- Fever, shock, multiorgan failure, altered mentation

Myonecrosis/Gas gangrene

- Classically associated with Clostridial infections
  - Traumatic + vascular compromise (contiguous spread): C. perfringens
  - Spontaneous (neutropenia, GI cancer or hematogenous): C. septicum
- Streptococci can also cause

- Rapid progression
- Failure to respond to therapy for more superficial infection
- Systemic toxicity with multiorgan failure
- Emergent surgical debridement
- Broad-spectrum antibiotics
  - Clindamycin to suppress toxin production
Toxic Shock Syndromes (TSS)

Streptococcal TSS
- Invasive S. pyogenes infection
- Often associated with a focus of necrotizing fasciitis or myonecrosis
- Hypotension and organ failure
- Progressive pain at site of infection
- Pyrogenic streptococcal exotoxins A and B, M protein fragments
- Isolation of Strep from blood, deep tissue, muscle
- Surgical debridement
- Penicillin + clindamycin

Staphylococcal TSS
- S. aureus
- Menstruating women and highly absorbent tampons
- Nonmenstrual cases: post-surgical, post-partum wounds, burn injury, trauma
- Hypotension and organ failure
- Erythroderma, maculopapular rash, late desquamation
- Toxic shock syndrome toxin 1 (TSST-1) (menstrual), other exotoxins (nonmenstrual)
- Isolation of Staph from blood is uncommon (toxin-mediated disease), thrombocytopenia
- Removal of foreign bodies, surgical debridement
- Antistaphylococcal antibiotics + clindamycin

Skin and Soft Tissue Infection Summary
- Pathogens usually gain entry through a breach in the skin
- Majority S. aureus and Streptococci
- History can provide important epidemiologic clues to infections with atypical organisms
- Necrotizing SSTIs and TSSs are life-threatening emergencies that require emergent surgical debridement and antibiotic therapy including one aimed to reduce toxin production
Bone and Joint Infections

Learning Objectives

- Understand the pathogenesis of osteomyelitis
- Identify risk factors predisposing to osteomyelitis
- Compare and contrast the clinical presentation of acute vs chronic osteomyelitis
- Understand the indications for surgical and medical management of osteomyelitis
- Understand the pathophysiology of septic arthritis
- Compare and contrast the management of both native and prothetic septic joints

Osteomyelitis

- Epidemiology
- Pathogenesis
- Microbiology
- Clinical Presentation
- Diagnosis
- Treatment
Epidemiology—Risk Factors

- Risk factors for bacteremia
  - Remote site of infection
  - IV drug use (IVDU)
  - Hemodialysis
  - Central line or cardiac devices
  - Skin ulcers
  - Peripheral artery disease
  - Penetrating trauma
  - Recent surgery
  - Bites

Pathogenesis

- Routes of infection:
  - Hematogenous
    - Most common in children—long bones
    - Adults—vertebral bones
  - Contiguous spread
    - Diabetic or ischemic ulcers
    - Decubitus ulcers
    - Polymicrobial
  - Direct inoculation
    - Trauma / bites
    - Surgery
    - Polymicrobial

Pathogenesis—Acute
Pathogenesis—Chronic

- Staphylococcus aureus
  - Most common
- Coagulase-negative staphylococci
- Streptococci
  - Group B streptococci (neonates)
- Enterococcus
- Gram negative rods
  - Pseudomonas aeruginosa (puncture wound)
  - H. influenzae (neonates)
- Salmonella species (sickle cell disease)

Microbiology
Clinical Presentation

- Contiguous
  - Subacute to chronic
  - Sloughing/necrotic ulcer
  - Increased drainage, erythema
- Direct inoculation
  - Subacute to chronic
  - Nonunion
  - Poor incisional healing/surgical site infection
- Hematogenous
  - Fever and chills may be present with acute onset
  - Kids—often spread to skin, soft tissue, joints
  - Adults—often just pain with vertebral disease

60 yo male with DM complicated by neuropathy has a chronic ulcer over his right plantar foot with purulent drainage for several weeks. No fever or pain.

Exam: afebrile

R foot: draining sinus tract on plantar surface, placement of a steel probe through the shallowest gout to bone

Culture of purulent drainage:
- *E. coli*
- *Enterococcus faecalis*

Which of the following should be done next?

A. Obtain X-ray of foot
B. Obtain MRI of foot
C. Start Vancomycin and Zosyn
D. Start oral clindamycin and levofloxacin
E. Schedule bone biopsy

Diagnosis

- WBC, ESR, CRP variably elevated
  - May be normal especially in chronic disease
- Nonspecific
  - Blood cultures may be helpful, especially in hematogenous cases or acute presentations
  - Typical pathogen may obviate need for more invasive microbiologic testing
Diagnosis

- **X-ray:**
  - Delayed by 2 weeks from time of onset
  - Inaccurate
- **MRI:**
  - Modality of choice, good negative predictive value
  - Overcalls edema as osteo
  - Hardware presence may result in artifact
- **CT:**
  - Not as good as MRI alternative
  - Less sensitive and specific

- **Probe to bone test**
  - High positive predictive value
  - May obviate need for diagnostic imaging
- **Wound and sinus tract cultures**—poor correlation with bone biopsy culture result
  - Exception: presence of S. aureus
- **Bone biopsy—gold standard**

Treatment

- **Debridement**
  - Drainable fluid collection
  - Necrotic tissue
  - May need revascularization to heal
- **Antimicrobials**
  - Intravenous
  - Prolonged course (minimum 6 weeks)
Case #2

58yo male with DM, HTN admitted with 3 months of slowly worsening low back pain. Denies any trauma or strain. No fever or chills. He was born in Mexico and came to the United States as a child.

Exam: afebrile
Back: mild tenderness to palpation over the lumbar spine
An MRI (next slide) is obtained to evaluate his symptoms.
Blood cultures are negative.
A bone biopsy is obtained. The bacterial culture is negative. Pathology shows caseating granulomas.

What is the most likely pathogen?
A. S. aureus
B. Blastomycosis
C. M. tuberculosis
D. P. aeruginosa
E. Salmonella

Tuberculosis Osteomyelitis
- Bone infection
- 1/3rd of the time complicates pulmonary disease
- Usually hematogenously spread
- Long bones, vertebrae
- Usually solitary lesions
- Granulomatous inflammation
- Caseous necrosis, bone destruction
Osteomyelitis Summary

- Acute vs Chronic
- Type of spread includes hematogenous, contiguous, direct inoculation
- Leads to bone destruction (sequestrum) and new bone formation (involucrum)
- S. aureus is the most common pathogen
- Bone biopsy is the gold standard for diagnosis
- Prolonged intravenous antibiotic therapy indicated
- Surgical debridement may be needed as well

Septic Arthritis

- Epidemiology
- Pathogenesis
- Microbiology
- Clinical Presentation
- Diagnosis
- Treatment

Epidemiology: Risk Factors

- Elderly (age > 80)
- Prosthetic joint or other foreign material
- Recent joint surgery
- Intracutaneous steroid injection
- Intravenous drug use
- Alcoholism
- Endocarditis
- Immunosuppression / chronic diseases (DM)
- Joint Disease: RA, OA, Gout
- Skin infection / ulcer

*Not always present
Pathogenesis

- Synovial cells: no basement membrane
- Bacteria and inflammatory cells enter
  - Acute inflammatory response / infiltrate
  - Synovial membrane hyperplasia
  - Synovial effusion
- Inflammatory cells release cytokines and proteases
  - Cartilage damage
- Pressure necrosis from large synovial effusions
  - Cartilage / bone loss

65 yo female with RA presents with a 1 day history of pain and swelling of the 3rd right PIP joint.
Meds: Prednisone, Methotrexate.
PE: Temp 39.2
PIP joint is warm, erythematous, tender and has decreased ROM.
Which of the following is the most likely infectious cause of her symptoms?
A. Streptococcus pyogenes
B. Cryptococcus neoformans
C. Staphylococcus aureus
D. Pseudomonas aeruginosa
E. Parvovirus
Microbiology

- Bacterial (majority)
  - Acute pyogenic process; usually monoarticular
  - Rheumatologic emergency
- Viral
  - Acute, systemic; rarely polyarticular
- Fungal / Mycobacterial
  - Chronic in nature
  - Usually monoarticular
  - More often in immunocompromised host, but not always

Microbiology

- S. aureus
  - Native joints in adults, children
  - Early-onset and late prosthetic joint infection (PJI)
  - Bacteremia has high predilection for damaged joints (RA, OA)
- Coagulase-negative staphylococci
  - Delayed-onset PJI
- Streptococcus species
  - Gram negative
  - More common with IVDU, immunocompromised, elderly
  - Salmonella
  - H. influenzae
  - Late onset PJI
  - Polymicrobial
  - Penetrating trauma to joint, extension from bursal infection

Clinical Presentation

- Acute onset of joint symptoms
  - Pain, swelling, decreased function
  - Fever in >50%
  - Axial skeleton joints in IVDU
- Exam: effusion, erythema, decreased range of motion
- Fever is common
55 yo obese male with DM, CKD, OA, and HTN has a 1 day history of pain and swelling of the right knee.

Meds: HCTZ, insulin, ASA, losartan

PE: T 39.2
R knee: warm, erythematous, tender with decreased range of motion (ROM).

What is the next best step in management?
A. Prescribe prednisone for a gout flare
B. Intraarticular steroid injection for his OA flare
C. Perform diagnostic arthrocentesis
D. Prescribe ampicillin

Diagnosis
- Leukocytosis, elevated ESR and CRP (nonspecific)
- Blood cultures
- Imaging (XG, CT, MRI)
- Early soft tissue swelling and effusion
- Later loss of joint space, erosive and destructive changes
- Arthrocentesis
  - Positive culture is diagnostic (85-90% of typical bacterial causes)
  - WBC generally >50K, many >100K with neutrophilic predominance
Treatment

- Drainage
  - Daily aspirations
  - Surgical drainage
  - Prosthetic joint (debridement of prosthesis in 1 or 2 stages)

- Antibiotics
  - Empiric: based on clinical factors and gram stain
  - 3-4 weeks native joint
  - 6 weeks + for prosthetic joint

Case #5

25 yo female patient came to ED today with a 2 day history of right wrist pain. Her left knee was also painful initially but now it is her right knee that bothers her. She is sexually active (often unprotected) with multiple partners. Her LMP started 4 days ago. She was hiking in Wisconsin 1 week ago.

PE: T 38.9, HR 100, BP 100/70
R: Crisp, erythema and swelling and decreased ROM
L: Knee: unremarkable
R: Knee: mild effusion and tenderness
Skin: multiple macular dark erythematous lesions on legs and trunk
WBC: 18,000

Arthrocentesis of the R knee is performed but gram stain and culture are negative.

Her blood cultures turn positive with the gram stain below:

- The most likely etiology of the patient’s infection is:
  A. S. aureus
  B. Borrelia burgdorferi
  C. Neisseria gonorrhoeae
  D. Streptococcus pyogenes
Disseminated Gonococcal Infection (DGI)

- Most common in sexually active adolescents and young adults.
- Asymptomatic mucosal infection → Untreated → Disseminates.
- Many manifestations may be immune-mediated rather than direct invasion.
- Risk factors:
  - Pregnancy/post-partum
  - Menstruation
  - Terminal complement deficiencies

Gonococcal Clinical Manifestations

- Occult bacteremia
- DGI: classic triad
  - Dermatitis: numerous painless, non-pruritic macules, papules, pustular lesions.
  - Tenosynovitis: most common hands, wrists.
  - Migratory polyarthralgia or arthritis
  - Fever, malaise
- Septic joint: less common, but can occur with / without above occurring
  - Monoarticular—knees, wrists, ankles

Gonococcal Arthritis—Diagnosis

- Arthrocentesis
  - Similar cell counts to non-GC septic arthritis
  - Gram stains ~25% positive (gram neg diplococci)
  - Culture: only 50% positive (special media)
- NAAT testing of synovial fluid and mucosal sites (cervix, urethra). Has much higher yield.
Septic Arthritis - Summary

- Anyone can get, but there are risk factors
- S. aureus is the most common cause
- Clinical signs are not sufficient for diagnosis
- Arthrocentesis is necessary if any clinical suspicion
- Cell counts generally >50,000 but can be lower
- Culture: good for staph, not for gonococcal disease
- Treatment requires both antibiotics and drainage