Definitions of Bacterial Skin Infections

A. **Macule** is a flat, red inflammatory response to microbe or toxin
B. **Papule** is raised, red with more marked inflammation
C. **Vesicle** is blister
D. **Boils** and **carbuncles** are due to infection of hair follicle
E. **Impetigo** is a bullous, crusted or pustular eruption
F. **Erysipelas** is well-defined spreading inflammation of dermal lymphatics
G. **Cellulitis** is acute inflammation due to infection of subcutaneous fat
H. **Necrotizing fascitis** is inflammatory response in soft tissue below site of infection
## SKIN MANIFESTATIONS OF SYSTEMIC INFECTIONS

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Syndrome</th>
<th>Skin manifestation</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Salmonella typhi</em></td>
<td>Typhoid fever</td>
<td>Contaminated petechia</td>
</tr>
<tr>
<td><em>Neisseria meningitidis</em></td>
<td>Septicemia, meningitis</td>
<td>Contaminated petechia</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>Septicemia</td>
<td>Contaminated lesion</td>
</tr>
<tr>
<td><em>Treponema pallidum</em></td>
<td>Secondary syphilis</td>
<td>Contaminated rash</td>
</tr>
<tr>
<td><em>Rickettsia prowazekii</em></td>
<td>Typhus</td>
<td>Hemorrhagic rash</td>
</tr>
<tr>
<td><em>Streptococcus pyogenes</em></td>
<td>Scarlet fever</td>
<td>Erythematous rash</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>Toxic shock syndrome</td>
<td>Rash &amp; Desquamation</td>
</tr>
<tr>
<td><em>Blastomyces dermatitidis</em></td>
<td>Blastomycosis</td>
<td>Granulomatous lesion</td>
</tr>
</tbody>
</table>

## SKIN INFECTION VIA DIRECT INOCULATION

<table>
<thead>
<tr>
<th>Infection site</th>
<th>Microbe</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keratinized epithelium</td>
<td>Dermatophytic fungi</td>
<td>Ringworm</td>
</tr>
<tr>
<td>Epidermis</td>
<td><em>Streptococcus pyogenes</em> and/or <em>Staphylococcus aureus</em></td>
<td>Impetigo</td>
</tr>
<tr>
<td>Dermis</td>
<td><em>S. pyogenes</em></td>
<td>Erysipelas</td>
</tr>
<tr>
<td>Hair follicles</td>
<td><em>S. aureus</em></td>
<td>Folliculitis, boils (furuncles), carbuncles</td>
</tr>
<tr>
<td>Subcutaneous fat</td>
<td><em>S. pyogenes</em></td>
<td>Cellulitis</td>
</tr>
<tr>
<td>Fascia</td>
<td>Anaerobes</td>
<td>Necrotizing fascitis</td>
</tr>
<tr>
<td>Muscle</td>
<td><em>Clostridium perfringens</em></td>
<td>Gas gangrene</td>
</tr>
</tbody>
</table>
BACTERIA CAUSING SKIN INFECTIONS

*Staphylococcus aureus*

I. Virulence factors relevant to Skin & Soft Tissue Infections

A. $\alpha$-toxin

1. Pore-forming cytolysin; kills erythrocytes, leukocytes
2. Complement-like mechanism of action

Ribbon diagram showing subunit structure of staphylococcal $\alpha$-toxin.
B. Toxic shock syndrome toxin (TSST-1)
1. Pyrogenic exotoxin related to those produced by Group A streptococci
2. Superantigen that cross-links T-cell receptor and MHC II causing cytokine release
3. Massive cytokine release causes diverse effects; enhances endotoxic shock

Pathogenesis of toxic shock syndrome. **Panel A**: Vaginal colonizers carrying TSST-1 gene. **Panel B**: Tampon use facilitates growth and toxin production. **Panel C**: Toxin is absorbed and enters the circulation. TSST-1 functions as a superantigen, binding directly to the V_ portion of the T cell receptor and to the class II MHC receptor.
C. Exfoliative toxins (Staphylococcal Scalded Skin Syndrome)
   1. Two types, chromosomal and plasmid-encoded
   2. Induce intercellular splitting between stratum spinosum and stratum granulosum
D. Exoproteins for spread
   1. Hyaluronidase that hydrolyzes connective tissue
   2. Staphylokinase that promotes fibrinolysis
E. Antiphagocytic components
   1. Protein A that binds the Fc portion of IgG
   2. Coagulase that promotes surface polymerization of fibrin to resist phagocytosis
   3. Catalase that neutralizes H$_2$O$_2$

II. Etiology / Pathogenesis
A. Transmission
   1. High skin and nasal carriage rates in humans; no acquired immunity
   2. Transmission by fomites (inanimate objects)
B. Furuncle
   1. Colonization of hair follicle (folliculitis)
   2. Coagulation of fibrin around lesion
C. Carbuncle
   1. Focal suppuration (abscess)
   2. May lead to entry of organism into bloodstream via lymphatics
D. Scalded skin syndrome (bullous exfoliation)
   1. Neonates and children
   2. Caused by exfoliative toxin
   3. Bullous impetigo is localized scalded skin syndrome

Fig. 23.7 Scalded skin syndrome results from infection of the skin with strains of *Staphylococcus aureus* producing a specific toxin, which destroys the intercellular connections in the skin resulting in large areas of desquamation. The appearance may be confused with a burn. (Courtesy of A du Vivier.)

E. Toxic shock syndrome
   1. Caused by TSST-1
   2. Vaginal colonizers or wound infection

F. Wound contamination
   1. Bacteremia: spread to bloodstream via lymphatics
   2. Endocarditis, osteomyelitis, meningitis, pulmonary infection results from bacteremia
III. Clinical identification of organism
   A. Specimen collection: surface swab, blood, pus cultured on blood agar
   B. Gram positive cocci in clusters

   C. Catalase test positive
      1. Production of O₂ bubbles when H₂O₂ added to culture
      2. Differential for staphylococci vs. streptococci
   D. Coagulase positive
      1. Coagulation of citrated plasma by culture
      2. Differential for virulent *S. aureus* vs. *S. epidermidis* and *S. saprophyticus*
   E. Antimicrobial susceptibility testing important for Staphylococci
**Streptococcus pyogenes**

I. Virulence factors relevant to Skin & Wound Infections

A. M protein

1. Anti-phagocytic; subject to antigenic variation ⇒ type specific immunity
2. Mediates binding to epidermis
3. Fibrillar structure with C-terminus anchored in peptidoglycan of cell wall
4. Amino terminus variable due to genetic recombination; >80 serotypes
5. Cross-reactive antibodies contribute to acute glomerulonephritis
B. Protein F and Protein G
   1. Protein F mediates fibronectin binding at wound sites
   2. Protein G (≡ protein A) binds the Fc portion of antibodies to facilitate immune evasion

C. Streptolysin O (SLO) & Streptolysin S (SLS)
   1. Cause β-hemolysis on blood agar plates
   2. SLO is oxygen-labile or “sulphydryl-activated”
   3. SLO is cytolysin, attacking cell membranes and forming large pores
   4. Antibodies to SLO mediate self-attack and augment cell lysis

D. Streptococcal Pyrogenic Exotoxins (Spe A-C)
   1. SpeA produced by lysogenized (bacteriophage-carrying) Group A Streptococcus
   2. Superantigens, sequence homology with staphylococcal pyrogenic exotoxins
   3. Induce cytokine release leading to fever, rash, T-cell stimulation, endotoxin sensitivity

E. Hydrolytic enzymes responsible for thin, runny pus in streptococcal infections
   1. Streptokinase dissolves fibrin to facilitate spread
   2. Therapeutic use for streptokinase, it dissolves blood clots

II. Etiology / Pathogenesis
A. Pyoderma a.k.a. Impetigo
   1. Infection through minor trauma, insect bite typically on face or and lower extremities
   2. Small vesicle that ruptures, serous exudate, superficial spread, honey-colored crust
   3. Epidemics occur with children (2-5 yr.); hot, humid climate, poor hygiene, crowding
   4. Transmission is person-person and by fomites (e.g. shared towels)
   5. S. aureus can cause bullous (blisters) impetigo or contaminate streptococcal lesions
   6. Causative M protein types differ from respiratory serotypes

B. Poststreptococcal Sequelae: Acute glomerulonephritis
   1. May follow impetigo; Rarely follows respiratory tract infection in children
   2. Edema, hypertension, hematuria, proteinuria 3 weeks following skin infection
   3. Caused by nephritogenic M serotypes
   4. Cross-reactivity with M protein, deposition of immune complexes in glomerulus

C. Erysipelas
   1. Rapidly spreading infection of deeper layers, may progress to necrosis & septicemia
   2. Symptoms associated with infection: edema, fever, lymphadenopathy
   3. Commonly on face and following streptococcal sore throat

D. Cellulitis
   1. Extension of skin infection or wound
   2. Caused by Group A S. pyogenes or S. aureus
E. Nosocomial infections
   1. Decreasing incidence of clean (surgical) wound and burn infections
   2. 19th cent. Puerperal (childbed) fever ⇒ physician transmission, need for hand washing

F. Toxic shock-like syndrome (TSLS)
   1. Emerged in 1980s, rapid death following wound infection with *S. pyogenes*
   2. Symptoms: shock, renal impairment, rash, respiratory failure, diarrhea ⇒ superantigen
   3. Caused by highly invasive ("flesh-eating") strains that produce SPE A
   4. Up to 30% mortality rate

III. Clinical identification of organism
A. Specimen collection: surface swab, blood, pus, cultured on BAP with 10% CO₂
B. Classification
   1. Gram positive cocci in chains
   2. β-hemolytic on blood agar plates (SLO and SLS); Pyogenic (pus-forming)
   3. Lancefield classification (carbohydrate antigen in cell wall): Group A
C. Biochemical tests
   1. Catalase test negative (differentiation from *Staphylococcus*)
   2. Serotyping for Lancefield Group A antigen extracted from cell wall
   3. Bacitracin sensitivity assay on agar plate
D. Serologic tests
   1. Rise in antibody titers to *S. pyogenes* antigens
   2. Titers of antibodies to SLO (ASO), M protein

<table>
<thead>
<tr>
<th>Organism</th>
<th>Hemolytic reaction</th>
<th>Lancefield group</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Streptococcus pyogenes</em></td>
<td>Beta</td>
<td>A</td>
<td>Impetigo, Scarlet fever, Rheumatic fever</td>
</tr>
<tr>
<td><em>Streptococcus agalactiae</em></td>
<td>Beta</td>
<td>B</td>
<td>Neonatal sepsis, meningitis</td>
</tr>
<tr>
<td><em>Streptococcus bovis</em></td>
<td>Alpha</td>
<td>D</td>
<td>Endocarditis</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>Alpha</td>
<td>None</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>Viridans Streptococci</td>
<td>Alpha</td>
<td>None</td>
<td>Endocarditis</td>
</tr>
<tr>
<td><em>Enterococcus spp.</em></td>
<td>Alpha</td>
<td>D</td>
<td>Urinary tract infections</td>
</tr>
</tbody>
</table>
Propionibacterium spp.

I. Virulence factors relevant to Skin & Wound Infections
   A. *Propionibacterium* spp. skin flora, break down sebum lipids \(\rightarrow\) fatty acids
   B. Organic (propionic) acid produced by organism contribute to inflammatory process
   C. Hormone production at puberty alters sebum secretion and enhances growth of *P. acnes*

II. Etiology / Pathogenesis
   A. *P. acnes* is predominant anaerobe of normal flora skin; it can contribute to acne
      1. Increased sebum production in response to hormone levels in puberty
      2. High cell numbers in hair follicles and associated sebaceous glands
      3. Acne vulgaris by *P. acnes*; inflammation of hair follicle and associated sebaceous glands
      4. Formation of keratin, sebum, and bacteria \(\Rightarrow\) “blackhead”
   B. *P. acnes* as normal flora can cause infections
      1. Infections in the severely immunocompromised
      2. Endocarditis, contamination of prosthetic heart valves, cerebrospinal shunts
      3. Contamination of blood cultures, must be differentiated from true pathogen

III. Clinical identification of organism
   A. Gram positive rods, pleomorphic (multiple shapes), resemble *Corynebacterium*
   B. Anaerobic or microaerophilic growth

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Classification</th>
<th>Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Pasteurella multocida</em></td>
<td>Gram neg. rod</td>
<td>Animal bites</td>
</tr>
<tr>
<td><em>Clostridium perfringens</em></td>
<td>Gram + rod, anaerobic, spores</td>
<td>Wound (\Rightarrow) Gas gangrene</td>
</tr>
<tr>
<td><em>Clostridium tetani</em></td>
<td>Gram + rod, anaerobic, spores</td>
<td>Wound (\Rightarrow) Tetanus</td>
</tr>
</tbody>
</table>
FUNGI CAUSING SKIN INFECTIONS

*Candida albicans*

I. Virulence factors relevant to Skin & Wound Infections

A. Adhesion

1. Adhesion through mannoprotein complexes that extend from cell wall
2. Receptor site in human host is fibronectin

B. Invasion

1. Invasive hyphae bind to fibronectin, collagen, and laminin
2. Invasion via hyphae extension across mucosal barriers
3. Proteases and elastases may have role in the invasion process

*Figure 47–2.* Pathogenesis of *Candida albicans* infections. Proposed mechanisms of *C. albicans* attachment and invasion are shown. Surface glucosamn mannan receptor(s) on the yeast may bind to fibronectin covering the epithelial cell or to elements of the extracellular matrix (ECM) when the epithelial surface is lost or the *Candida* have invaded beyond it. Invasion is associated with formation of hyphae and production of proteinases, which may digest tissue elements.
C. Immune system evasion
   1. Neutrophils are first line of defense
   2. Chronic candidiasis indicates T-cell deficiency

II. Etiology / Pathogenesis
   A. Folliculitis: Infection of hair follicle & Intertrigo: in folds of skin
   B. Skin infections occur in crural folds
      1. Wet, macerated surfaces chronically exposed
      2. Erythematous papules, tender cracked areas associated with chronic irritation
   C. Occupational hazards
      1. Dishwashers susceptible to infection on hands
      2. Diaper rash caused by *C. albicans*
   D. Chronic mucocutaneous candidiasis
      1. Localized to skin, hair, or mucocutaneous junctions
      2. Indicates T-cell deficiency
III. Clinical identification of organism
   A. Specimen collection: Exudate or epithelial scrapings
   B. KOH or Gram stain reveals budding round or oval yeast cells with hyphae
   C. Germ tube (hyphae) formations speciate *C. albicans*
I. Etiology / Pathogenesis

A. Sporotrichosis is a subcutaneous infection caused by *S. schenckii*
   1. *S. schenckii* is ubiquitous saprophyte in soil and on plants
   2. Infection usually on extremities, e.g. in gardeners, farmers
   3. Mold is infectious form, inoculation of conidia (spores) by trauma (thorn prick)

B. Local multiplication at site⇒ pyogenic and granulomatous inflammatory reactions
   1. Initial stage is painless papule weeks to months post-inoculation
   2. Papule can ulcerate and become chronic with draining lymph channels
   3. Spread to bone, eyes, lungs, CNS in <1% of cases

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**Fig. 23.35** Sporotrichosis spreading up the draining lymphatics of the hand following a primary infection in the nailbed of the third finger. (Courtesy of TF Sellers, Jr.)
II. Clinical identification of organism
   A. Definitive diagnosis requires culturing of infected pus or tissue
   B. Dimorphic growth phases
      1. Cigar-shaped yeast in tissue and culture at 37°C
      2. Mold with thin, septate hyphae and terminal conidia at 25°C
Dermatophytes: \textit{Epidermophyton}, \textit{Trichophyton}, \textit{Microsporum}

I. Virulence factors relevant to Skin & Wound Infections
   A. Adaptation to nonliving keratinized tissue of nails, hair, stratum corneum of skin
   B. Invasion of hair shaft by arthroconidia

II. Etiology / Pathogenesis
   A. Three genera
      1. \textit{Trichophyton}
      2. \textit{Epidermophyton} that never infects hair
      3. \textit{Microsporum} that rarely infect nails
      4. \textit{Malassezia furfur} also included in this grouping
         a. Commensal that can cause superficial mycosis
         b. Infection referred to as pityriasis or tinea versicolor, a patchy discoloration
   B. Superficial infections of skin, usually of extremities
      1. Lateral spread giving appearance of tunneling worms hence “tinea” or “ringworm”
      2. Common names
         a. Ringworm (tinea corporis - body or tinea capitis-scalp)
         b. Athlete’s foot (tinea pedis)
         c. Jock itch (tinea cruris)
      3. Skin lesions often in moist skin folds, maceration promotes infection
      4. Arthroconidia invade outside or within hair shaft, plug root \Rightarrow ring-shaped hair loss
      5. Invasion of nail bed causes malformed growth

<table>
<thead>
<tr>
<th>Skin Disease</th>
<th>Location</th>
<th>Clinical Appearance</th>
<th>Responsible Fungi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tinea corporis</td>
<td>Nonhairy, smooth skin</td>
<td>Circular patch, advancing red border, pruritic</td>
<td>\textit{Microsporum canis} \textit{Trichophyton mentagrophytes}</td>
</tr>
<tr>
<td>(ringworm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tinea pedis</td>
<td>Interdigital spaces of feet</td>
<td>Red vesicles, scaling, pruritic</td>
<td>\textit{Trichophyton rubrum} \textit{T. mentagrophytes} \textit{Epidermophyton floccosum}</td>
</tr>
<tr>
<td>(athlete’s foot)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tinea cruris</td>
<td>Groin</td>
<td>Erythematous scaling lesion, pruritic</td>
<td>\textit{T. rubrum} \textit{T. mentagrophytes} \textit{E. floccosum}</td>
</tr>
<tr>
<td>(jock itch)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tinea capitis</td>
<td>Scalp, fungus inside or on surface of hair shaft</td>
<td>Circular bald patches</td>
<td>\textit{M. canis} \textit{T. tonsurans}</td>
</tr>
<tr>
<td>Tinea barbae</td>
<td>Beard</td>
<td>Edematous, erythematous lesion</td>
<td>\textit{T. rubrum} \textit{T. mentagrophytes}</td>
</tr>
<tr>
<td>Tinea unguim</td>
<td>Nail</td>
<td>Thickened, discolored nails esp. of foot</td>
<td>\textit{T. rubrum} \textit{T. mentagrophytes} \textit{E. floccosum}</td>
</tr>
</tbody>
</table>
C. Source of infection: domestic and wild animals or soil
   1. Dermatophytes have low infectivity and virulence
   2. Person-person transmission requires close contact or contact with infected skin or hair
D. Infection induces advanced skin growth that limits spread
   1. Immunosuppressive agents decrease shedding of keratinized layers, prolongs infection
   2. Cell-mediated immune response important, immunity can be acquired
   3. Infection induces delayed hypersensitivity (DTH) reaction
   4. Chronic infections associated with impaired T-cell function and lack of DTH reaction
III. Clinical identification of organism

A. Sampling: Scrapings from edge of lesion or infected hairs, stained with KOH or calcifor
   1. Scrapings may also be cultured; growth in culture takes up to 4 weeks
   2. Culture and microscopy used for identification

B. *Microsporum spp.* fluoresce under UV light (Wood’s lamp) - aids specimen collection

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**Fig. 23.27** Arthrospores of *Trichophyton tonsurans* in an infected hair shaft. These thick-walled spores are the form in which infection is spread. They can survive in the environment for weeks or months before infecting a new host. (Courtesy of AE Prevost.)
CASE STUDY FOR
SKIN AND SOFT TISSUE INFECTIONS

A 4-year-old boy is brought to his pediatrician’s office in July with a low-grade fever, swelling around the face and blood in his urine. Physical exam revealed numerous insect bites on the boy’s legs. Several of the bites were infected. The infected sites were warm to the touch and yellow-colored pus could be extruded with slight pressure. Organisms were cultured from the infected insect bites using blood agar.

Questions:
1. Identify the etiologic agent; include its Gram reaction and relevant biochemical tests.
2. What virulence factor contributes to the pathology of this case?
3. Identify other potential complications of this boy’s skin infection.