

Musculoskeletal system

Skin and soft tissue infections 4

Harrison's infectious disease 2nd Ed

Oxford handbook of ID and MM

Necrotizing Fasciitis

Necrotizing fasciitis

Streptococcal gangrene

S. pyogenes

Fournier's gangrene

Mixed aerobic and anaerobic bacteria

Staphylococcal necrotizing fasciitis

Methicillin-resistant *S. aureus*

Necrotizing fasciitis

- **RAPIDLY** progressing infection in the area between the fascia and deep subcutaneous tissue.
- Many risk factors increase the risk (see table next slide)
- Fibrous bands in this area prevents spread of infection
 - *These bands are present in the head but not in the extremities (thus extremities are more susceptible)*
 - **>50% in extremities**
 - 20% in perineum or buttocks (esp in DM and alcoholics)
 - 18% in trunk
 - 9% head and neck

- *Necrotizing fasciitis (GAS) and gas gangrene (anaerobic clostridia infection) also induce bulla formation.*
- In the USA, the estimated incidence of invasive GAS infection is 3.5 cases per 100,000 persons—necrotizing infections account for 6% of these.

Risk factors associated with necrotizing fasciitis

<i>Malnutrition</i>	<i>Patient conditions</i>	<i>Immune compromised</i>	<i>Poor blood supply</i>	<i>Skin trauma in last 3 months</i>	<i>Breaks in mucosa of GI or GU tracts (anaerobes)</i>
<ul style="list-style-type: none"> -<u>Hypo-albuminemia</u> -<u>Alcoholism</u> -<u>Cirrhosis</u> 	<ul style="list-style-type: none"> - <u>>50 Year olds</u> -<u>Obesity</u> 	<ul style="list-style-type: none"> -<u>Cancer</u> -<u>Steroid therapy</u> 	<ul style="list-style-type: none"> -<u>Heart disease</u> -<u>PVD</u> -<u>DM</u> 	<ul style="list-style-type: none"> -<u>Burns penetrating trauma</u> -<u>IV drugs</u> -<u>surgery</u> 	<ul style="list-style-type: none"> -<u>colon cancer</u> -<u>diverticulae</u> -<u>hemorrhoids or fissures</u> -<u>urethral tears</u>

Signs and Symptoms – occur in order

- **Pain/tenderness**
- **Unexplained fever** (Early diagnosis may be difficult when pain or unexplained fever is the only presenting manifestation, remember infection is deep, might not present with pain yet)
- Later on: Swelling (infection at this point is severe)
- **Dark red induration** (indicates hemorrhage and early necrosis)
- **BULLAE**, filled with blueish or purple fluid
- Thrombosis of dermal blood vessels (*The affected area becomes anesthetic as a result of small vessel thrombosis and destruction of superficial nerves*)
- Extension **to deep fascia with rapid spread**
- **Most progressed symptoms : toxicity , shock and multi organ failures** (has progressed beyond local infection site)

Pain / redness



Dark red induration /swelling



Progressing to bullae /thrombosis





Microbiology causes:

- **A) Polymicrobial** (• Type I necrotizing fasciitis involves at least one anaerobic species (**Bacteroides or Peptostreptococcus spp.**), as well as one or more facultative anaerobic species (e.g. **non-GAS, E. coli, Enterobacter, Klebsiella, Proteus spp.**). What connects all these bugs? All have representatives in the enteric tract!
- Usually a **mix of aerobes and anaerobic bacteria** (*clostridium perfringens*)
- 1 -**Break in Gastrointestinal or Genitourinary mucosa**, typically on *trunk and extremities*
- 2- **Fournier's Gangrene** (*in genitalia/perineal area*)
- 3- **Mixed infection usually have comorbid states** (*DM, PVD, immunocompromised*)
- *21% mortality rate with optimal treatment*

Microbiology causes...cont

- B) **Type II necrotizing fasciitis** is usually caused by **GAS alone** or in **combination with other species (e.g. *S. aureus*)**. Group A , Beta hemolytic strep (GAS), *S. pyogenes* +- *S. aureus* (connection here is these are skin representatives)
- **Strains of MRSA that produce the Panton Valentine leukocidin (PVL)** toxin have been reported to cause necrotizing fasciitis. (also necrotizing pneumonia)
 - 1) Usually following trauma in otherwise healthy individual or IV drug abusers (skin popping) not like the previous picture of co morbid patient with gastric, genitourinary tract disruption.
 - 2) Fasciitis progresses to skin contusions due to seeding by transient bacteremia
 - 3) **Gas production if mixed infections occurs!!! (you need anaerobes)**
 - 4) **Severe toxicity and renal impairments → shock**
 - 5) Myositis (destruction of muscle tissue markedly increases CPK)
 - 6) Mortality is high (upto 50%! Even with optimal treatment)

Skin popping/drug abuse = basically
SubQ injections in same area over
and over



- *Necrotizing fasciitis caused by mixed aerobic-anaerobic bacteria begins with a breach in the integrity of a mucous membrane barrier, such as the mucosa of the gastrointestinal or genitourinary tract.*
- The portal can be a malignancy, a diverticulum, a hemorrhoid, an anal fissure, or a urethral tear.
- Other predisposing factors include *peripheral vascular disease, diabetes mellitus, surgery, and penetrating injury to the abdomen (see above table).*
- Leakage into the perineal area results in a syndrome called **Fournier's gangrene**, characterized by massive swelling of the *scrotum and penis with extension into the perineum or the abdominal wall and legs.*

Other forms

- In the newborn, necrotizing fasciitis may complicate omphalitis and spread to involve the abdominal wall, flanks, and chest wall.
- Fournier's gangrene is a form of necrotizing fasciitis that affects the male genitals and is usually polymicrobial (Part of GIT).
- Craniofacial necrotizing fasciitis is usually associated with trauma and caused by GAS (skin).
- Cervical necrotizing fasciitis is usually associated with dental or pharyngeal infections and is polymicrobial (part of GI tract).



Dx of necrotizing fasciitis

Clinical findings are suggestive + surgical exploration/sample:

- a) Altered mental status (systemic involvement)
- b) Soft tissue infection signs (redness/swelling/pain) 70-80% of cases

Bullae Pain is typically exaggerated out of exam

Tenderness is outside the red erythematous borders (indicates further progress)

are only seen in ¼ of cases

- a) **Fever in less than 50% of the cases!**
- b) Low BP in 21%
- c) Crepitation (feeling of air pockets under skin upon examination) in 20%

Rx - empiric

- 3 drug combo/ 2 drug combo/ 1 drug (each +MRSA coverage)

3 drug combo :

- 1- anaerobic coverage (and inhibits ribosomal production of toxins)= Clindamycin
- 2- G +ve coverage (Ampicillin-sulbactam) or (Piperacillin-tazobactam → antipseudomonal)
- 3- G-ve coverage (Ciprofloxacin)

- 2 drug combo (Cefotaxime covers G+ and G-bacteria) + (anaerobic coverage by metronidazole or clindamycin)
- 1 drug combo (Carbapenem / Imipenem, meropenem, ertapenem)
- The MRSA coverage to be added to any chosen empiric regimen includes = Vancomycin or Linezolid
- Hemorrhagic bullae may indicate presence of vibrio vulnificus, in which case doxycycline is used

Rx.

- **Surgical debridement**, and *treatment in hospital*
Emergency surgical exploration and debridement
1-confirm the diagnosis and are the 2- *mainstay*
of therapy.
- 3- Reducing compartment pressure in extremities
- **Prophylaxis for exposed house hold members**
(penicillin, rifampin, clindamycin or
azirthromycin)

Gas gangrene (Clostridium infection)

Gas production due to anaerobic bacteria

- Typically due to **contaminated DEEP wounds** -no oxygen- (surgery, car crash..etc) to introduce spores of G+ve clostridia into the wound (from environment)
- Also progresses similarly to other types: **fasciitis → toxemia → organ failure**
- Gangrene usually occurs *following muscle injury and contamination of the wound by soil or foreign material containing clostridial spores. (typical scenario)*
- **C. perfringens** is the predominant cause (80–95%), and its pathological effects are mediated by α and λ toxins

Alpha toxin

- Alpha toxin zinc-dependent, phospholipase C (PLC) with sphingomyelinase and lectinase activity and approximately 42.528 kDa
- Alpha toxin is responsible for intravascular hemolysis, platelet aggregation, and capillary damage → loss of blood supply = loss of oxygen.
- These factors stop leukocytes and oxygen from getting to the site of infection → favorable for the proliferation of *C. perfringens*.
- Alpha toxin, helps immune evasion by interfering in neutrophil migration to the infected tissue, minimizing the number of mature cells in the bone marrow, and causing the accumulation of neutrophils in adjacent vessels

Cont.. etiology and pathogenesis

- *Spontaneous or non-traumatic gas gangrene may occur in the absence of an obvious wound.*
- This form is usually caused by ***C. septicum*** and associated with intestinal abnormalities, e.g. colonic cancer, diverticulitis, bowel infarction, necrotizing enterocolitis. •

Clinical features

- The incubation period is usually 2–3 days but may be shorter.
- Patients present with acute onset of excruciating pain and signs of shock (*fever, tachycardia, hypotension, jaundice, renal failure*).
- Local edema and tenderness may be the only early signs, or there may be an open wound, herniation of muscle, a serosanguinous and foul smelling discharge, crepitus, skin discoloration, and necrosis.
- Progression is rapid, and death may occur within hours



02/gangrene-pictures-3.jpg



Diagnosis •

- The diagnosis is **usually clinical** but may be confirmed *by Gram stain of the wound or aspirate.*
- *Liquid anaerobic cultures may be positive within 6h.*
- *Plain radiographs may show gas in the affected tissues*

Management •

- Emergency **surgical exploration and debridement** of the affected area should be performed.
- • Empirical antibiotic therapy **with piperacillin–tazobactam plus vancomycin (if risk of MRSA)** is appropriate, pending cultures.
- • Definitive treatment for clostridial myonecrosis is with **penicillin and clindamycin.**
- Hyperbaric oxygen therapy is not recommended, as it has unproven benefits, may also delay resuscitation/surgery treatment

Cellulitis

Cellulitis

Staphylococcus spp., *Streptococcus* spp., various other bacteria

- Cellulitis is **an acute inflammatory condition** of the skin that is characterized by:
 - localized pain erythema, swelling, and heat (inflammation signs).

Usually caused by indigenous flora colonizing the skin (*S. aureus* and *S. pyogenes*) or by a variety of non colonizing exogenous bacteria.

To detect the source of the exogenous bacteria involved in cellulitis a thorough history (+ epidemiologic data) is needed, as these bacteria occupy small niches in nature.

Cellulitis

- Supporting data which gives clues to other exogenous causes include:
- *Physical activities - trauma - water contact - animal, insect, or human bites - immunosuppression.*
- Examples of exogenous bacteria :
Enterobacteriaceae, L. pneumophila, A. hydrophila, V. vulnificus, and C. neoformans.

Clinical features

- → **spreading**, **erythematous**, **hot**, tender lesion
- → usually accompanied by systemic symptoms.
- • The Dx is usually clinical, as cultures are **rarely positive** (only 20%)- this suggests bacterial numbers **are low and local to tissue** but the inflammatory effect is exaggerated due to toxins.
- Can do culture if there is drainage or a site of entry is seen
- • Treatment—empiric treatment:
- **IV flucloxacillin or clindamycin.**
- **Vancomycin, teicoplanin, linezolid, or daptomycin** are for MRSA cellulitis.
- **Gram-negative and anaerobic cover may be required for cellulitis in the context of diabetic ulcers (ulcer+cellulitis is the common case).**
- The affected limb should be immobilized and elevated.



<https://www.youtube.com/watch?v=4i8FxmMlgQA>

Remember; acute and spreading



Pathogenesis

- Cellulitis caused by *S. aureus* spreads from a central localized infection (*abscess, folliculitis, or an infected foreign body such as a splinter, a prosthetic device, or an IV catheter*).
- MRSA is rapidly replacing methicillin-sensitive *S. aureus* (MSSA) as a cause of cellulitis in **both** inpatient and outpatient settings.
- Recurrence is seen in patients with eosinophilia

- Cellulitis due to *S. pyogenes* is **more rapidly spreading**, diffuse process that is frequently associated with **lymphangitis and fever**.
- Recurrent streptococcal cellulitis of the lower extremities may be caused by organisms of group A, C, or G in association with chronic venous stasis or with saphenous venectomy for coronary artery bypass surgery.
- Also recurrent streptococcal cellulitis is **seen among patients with chronic lymphedema** resulting from elephantiasis, lymph node dissection, or Milroy's disease, **In both cases is due to poor drainage of limb**
- This is all due to the fact that **streptococci use the lymphatic system in their spread**.

- Cellulitis caused by group B *Streptococcus* occurs **mostly in elderly patients** (usually patients with diabetes mellitus or peripheral vascular disease).
- *H. influenzae* typically causes periorbital cellulitis in children in association with **sinusitis, otitis media, or epiglottitis**.
- It is unclear if this form of cellulitis will become less common as a result of the efficacy of the *H. influenzae* type b vaccine.

- Cats bites, dog bites → *Pasteurella multocida* and *Staphylococcus intermedius* and *Capnocytophaga canimorsus* (more in dog bites).
- Cellulitis and abscesses associated with dog bites and human bites also contain a variety of anaerobic organisms, including *Fusobacterium*, *Bacteroides*, aerobic and anaerobic streptococci, and *Eikenella corrodens*.
- *Pasteurella* is known to be resistant to dicloxacillin and nafcillin however, it is sensitive to all other β -lactams as well as to quinolones, tetracycline, and erythromycin.
- Thus for animal or human bites the treatment is usually → Ampicillin/clavulanate, ampicillin/sulbactam, and cefoxitin

- *Aeromonas hydrophila* → aggressive cellulitis in injuries sustained in freshwater (lakes, rivers, and streams).
- Treatment according to known sensitivity of this organism →, fluoroquinolones, chloramphenicol, trimethoprim-sulfamethoxazole, and third-generation cephalosporins (ampicillin doesn't work)

P. aeruginosa

- Causes 3 types of infections in MSS
- 1→ Ecthyma gangrenosum in neutropenic patients
- 2→ Hot-tub folliculitis
- 3→ Cellulitis following penetrating injury (usually stepping on a nail)
- Commonly seen in hospital setting/immune compromised patients.
- Rx: surgical inspection and drainage/debridement (recall biofilm of pseudomonas)
- empirical treatment :
- -Aminoglycoside - a third-generation cephalosporin (ceftazidime, cefoperazone, or cefotaxime) -semisynthetic penicillin (ticarcillin, mezlocillin, or piperacillin), or a fluoroquinolone(not in pediatric patient) pseudomonas is notoriously hard to treat.

ANTIBACTERIAL AGENTS

Table 5.1 Principal types of antibacterial agent (other than agents used exclusively in mycobacterial infection)

Agent	Site of action	Usual activity ^a against:					
		Staphylococci	Streptococci	Enterobacteria	<i>Pseudomonas aeruginosa</i>	<i>Mycobacterium tuberculosis</i>	Anaerobes
Penicillins	Cell wall	+R	+	V	V	-	+ ^b
Cephalosporins	Cell wall	+	+	+	V	-	+ ^b
Other β-lactam agents	Cell wall	V	V	+	V	-	V
Glycopeptides	Cell wall	+	+	-	-	-	+ ^c
Tetracyclines	Ribosome	+R	+R	+R	-	-	+R
Chloramphenicol	Ribosome	+	+	+	-	-	-
Aminoglycosides	Ribosome	+	-	+	V	V	-
Macrolides	Ribosome	+	+	-	-	-	+
Lincosamides	Ribosome	+	+	-	-	-	+
Fusidic acid	Ribosome	+	+	-	-	+	+
Oxazolidinones	Ribosome	+	+	-	-	-	-
Streptogramins	Ribosome	+	+ ^d	-	-	-	-
Rifamycins	RNA synthesis	+	+	+	-	+	+
Sulphonamides	Folate metabolism	+R	+R	+R	-	-	-
Diaminopyrimidines	Folate metabolism	+	+	+R	-	-	-
Quinolones	DNA synthesis	V	V	+	V	V	-
Nitrofurans	DNA synthesis	-	-	+	-	-	+
Nitroimidazoles	DNA synthesis	-	-	-	-	-	+

^aUsual spectrum of intrinsic activity

^bPoor activity against anaerobes of the *Bacteroides fragilis* group.

^cPoor activity against most Gram-negative anaerobes.

^dPoor activity against *Enterococcus faecalis*.

+, active; -, inactive; V, variable activity among different agents of the group. +R indicates that acquired resistance is very common.

Folliculitis

Folliculitis

Furunculosis

S. aureus

Hot-tub folliculitis

Pseudomonas aeruginosa

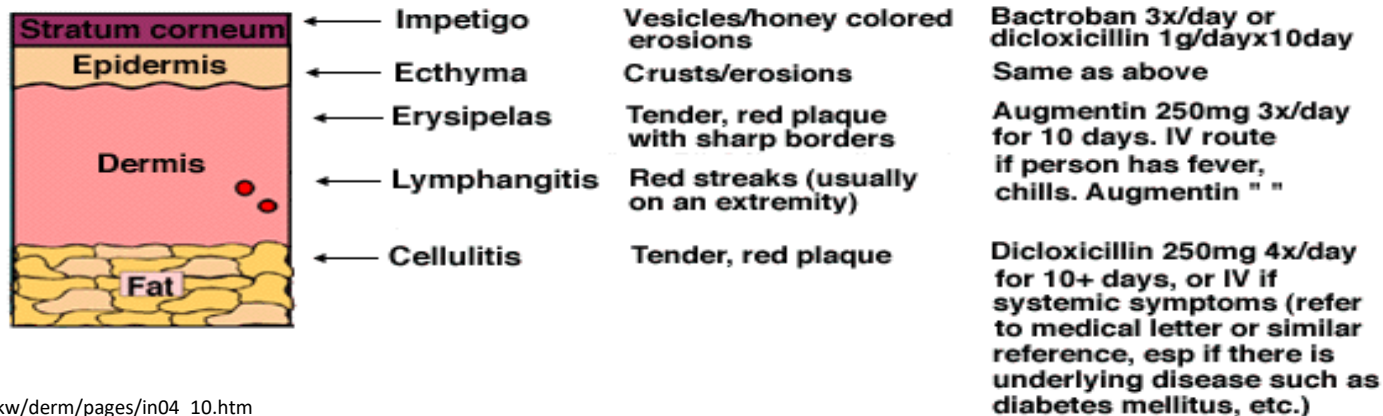
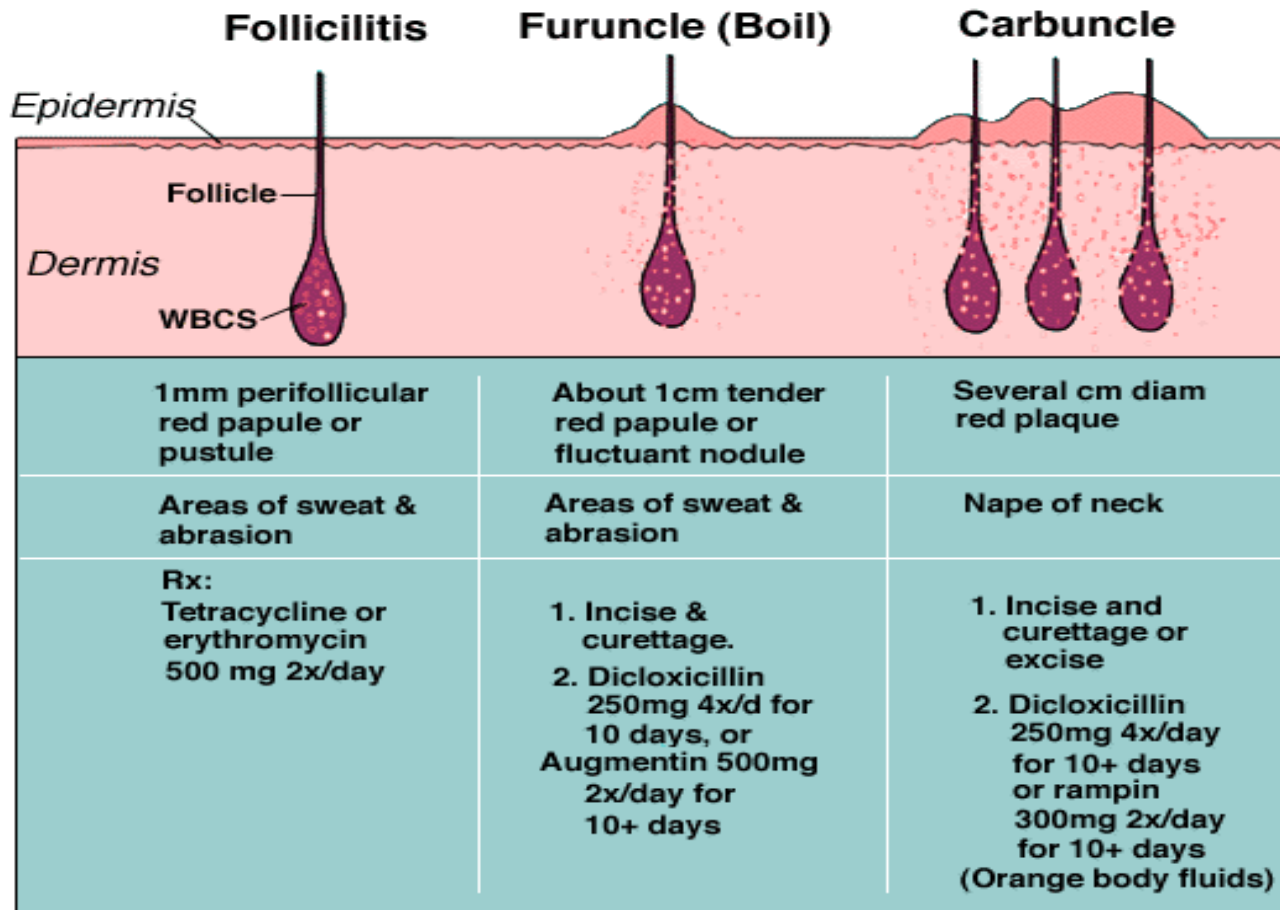
Swimmer's itch

Schistosoma spp.

Acne vulgaris

Propionibacterium acnes

Bacterial Infections



Folliculitis

- • A *superficial infection of the hair follicles* and apocrine structures.
- Causative organisms: *S. aureus* (commonest), *P. aeruginosa* ('hot tub' folliculitis), *Enterobacteriaceae* (complication of acne), *Candida spp.*, and *M. furfur* (in patients taking corticosteroids).
- Eosinophilic pustular folliculitis occurs in AIDS patients.
- Clinically: lesions consist of small, erythematous, pruritic papules, often with a central pustule.
- • Treatment—empiric treatment is with *oral flucloxacillin*.
- If the clinical response is slow → consider other pathogens.



Notice:
All follicles are affected

Patient is young

Hot tub folliculitis:

Usually self limited
In waters not sufficiently
Chlorinated and maintained
At 37 Celsius



Tinea veriscolor – *M. furfur*



Cutaneous abscesses

- • Collections of pus within the dermis and deeper skin structures.
- • Usually polymicrobial containing skin/mucous membrane flora; *S. aureus* is the sole pathogen in 25% of cases.
- • Clinical features—painful, tender, fluctuant nodules, usually with an overlying pustule and surrounded by a rim of erythematous swelling.
- • Treatment is I&D → Antibiotics are rarely necessary (except in extensive infection or systemic toxicity, or immunocompromised).

Notice:

raised lesion,
White head
Hair follicle might
Be port of entry



Furuncles and carbuncles

- • A furuncle (boil) is a deep inflammatory nodule that usually develops from preceding folliculitis.
- Occur in areas of the hairy skin, e.g. face, neck, axillae, and buttocks.
- • A carbuncle is a larger, deeper lesion made of multiple abscesses extending into the subcutaneous fat.
- Usually occur at the nape of the neck, on the back, or on the thighs.
- Patients may be systemically unwell.
- • Outbreaks of furunculosis caused by MSSA and MRSA have been described in groups of individuals with close contact, e.g. families, prisons, and sports teams.

Rx for furuncles

- application of moist heat promotes localization and spontaneous drainage.
- Large lesions require surgical drainage.
- Systemic antibiotics are indicated → *1- fever, 2-cellulitis 3-lesions are located near the nose or lip.*
- Outbreaks control with chlorhexidine soaps and stop sharing of clothing articles or towels, and decolonization of staph.

- Sebaceous glands that empty into the hair follicle maybe blocked and cause a swelling similar to an abscess (sebaceous cyst).
- Infection of sweat glands (*hidradenitis suppurativa*) can also mimic infection of hair follicles, particularly in the axillae.
- Chronic folliculitis is uncommon except in acne vulgaris, where constituents of the normal flora (e.g., *Propionibacterium acnes*) may play a role.



Hidradenitis Suppurativa

Usually in sweaty areas
Where skin folds (axilla,
Buttocks, breasts, inner thighs)



Swimmer's itch

- occurs when a skin surface is exposed to water infested with freshwater avian schistosomes.
- Warm water temperatures and alkaline pH are suitable for mollusks that serve as intermediate hosts between birds and humans.
- Freeswimming schistosomal cercariae readily penetrate human hair follicles or pores, but quickly die and elicit a brisk allergic reaction, causing intense itching and erythema.

LIFE CYCLE OF SWIMMER'S ITCH

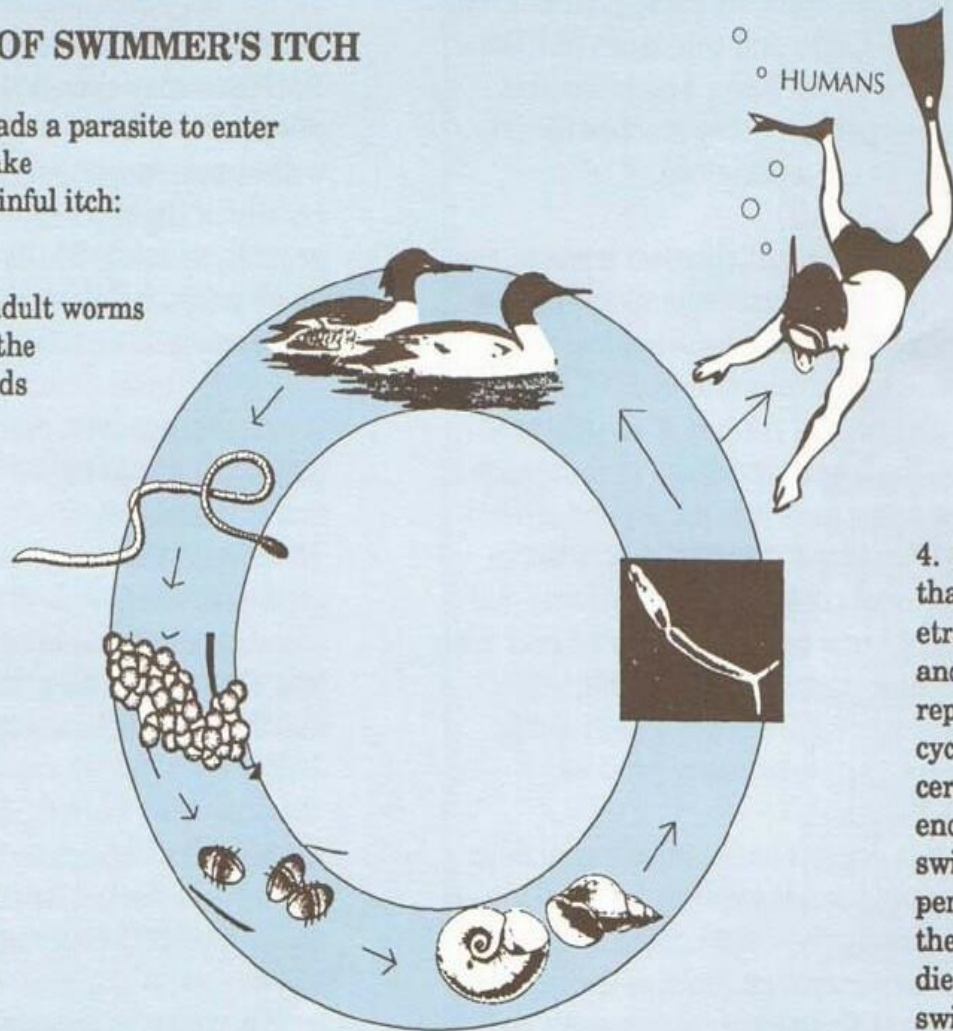
Here is the cycle that leads a parasite to enter the skin of vulnerable lake swimmers, causing a painful itch:

1. Flatworms become adult worms in veins that surround the intestines of certain birds and rodents. (Final Host Stage)

2. Female worms lay eggs that enter intestines and hatch when released into water through feces.

3. Eggs hatch into swimming larvae that enter snails. They elongate into germinating sacs that produce thousands of new parasites called cercariae. (Intermediate Host Stage)

4. Rather than penetrate birds and rodents, repeating the cycle, the cercaria may encounter swimmers, penetrate their skin and die, causing swimmer's itch.



Erysipelas

Erysipelas

S. pyogenes

- Erysipelas is due to *S. pyogenes* and is characterized by an abrupt onset of fiery-red swelling of the face or extremities.
- The distinctive features of erysipelas are **well-defined** indurated margins, particularly along the nasolabial fold; rapid progression; and intense pain.
- **Flaccid bullae** may develop during the second or third day of illness, but extension to deeper soft tissues is rare.
- Treatment : penicillin(flucloxacillin, clindamycin) or is effective
- swelling may progress despite appropriate treatment, although fever, pain, and the intense red color diminish.
- Desquamation of the involved skin occurs 5–10 days into the illness.
- Infants and elderly adults are most commonly afflicted, and the severity of systemic toxicity varies.