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Review

Microbiology and management of soft tissue and muscle infections

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ABSTRACT

This review summarizes the microbiological aspects and management of soft tissue and muscle infections. The infections presented are: impetigo, folliculitis, furunculosis and carbuncles, cellulitis, erysipelas, infectious gangrene (includes necrotizing fasciitis or streptococcal gangrene, gas gangrene or clostridium myonecrosis, anaerobic cellulites, progressive bacterial synergistic gangrene, synergistic necrotizing cellulitis or perineal phlegmon, gangrenous balanitis, and gangrenous cellulitis in the immunocompromised patient), secondary bacterial infections complication skin lesions, diabetic and other chronic superficial skin ulcers and subcutaneous abscesses and myositis. These infections often occur in body sites or in those that have been compromised or injured by foreign body, trauma, ischemia, malignancy or surgery. In addition to Group A streptococci and *Staphylococcus aureus*, the indigenous aerobic and anaerobic cutaneous and mucous membranes local microflora usually is responsible for polymicrobial infections. These infections may occasionally lead to serious potentially life-threatening local and systemic complications. The infections can progress rapidly and early recognition and proper medical and surgical management is the cornerstone of therapy.

1. Introduction

Skin, soft-tissue and muscular infections are among the most common infections, and may sometimes lead to serious local and systemic complications. These infections can be potentially life-threatening infections that may have rapid progress. Their early recognition and proper medical and surgical management is therefore of primary importance.

Anaerobic infections of the skin and soft tissue frequently occur in areas of the body that have been compromised or injured by foreign body, trauma, ischemia, malignancy or surgery. Because the indigenous local microflora usually is responsible for these infections, anatomic sites that are subject to fecal or oral contamination are particularly at risk. These include wounds associated with surgery of the intestine or pelvic tract, human bites, decubitus ulcers in the perineal area, pilonidal cysts, omphalitis, and cellulitis around the fecal monitoring site (see Fig. 1).

Some of the clues to the anaerobic origin of such infections are putrid discharge, gas production, and extensive tissue necrosis with a tendency to burrow through subcutaneous and fascial planes.

Many wound and skin infections that complicate surgical operations or trauma are caused by mixed bacterial flora. Aerobic and anaerobic, Gram-negative and Gram-positive organisms, whose origins are most often lesions or perforations of

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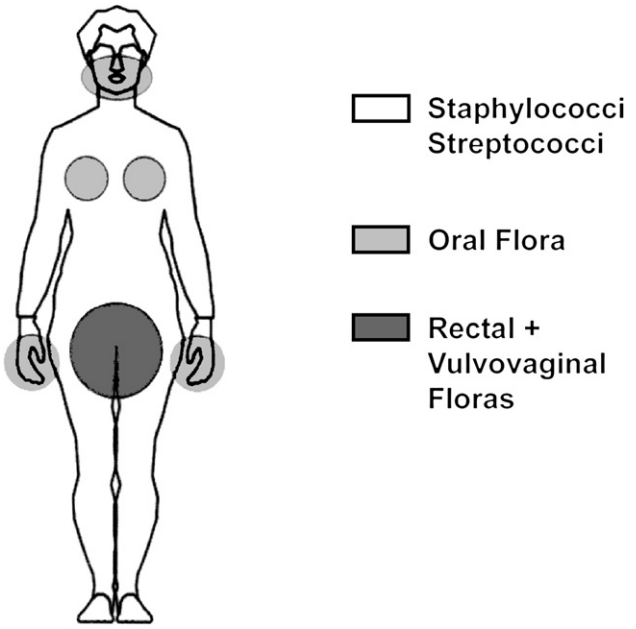

Fig. 1 – Distribution of organisms in abscesses, wounds, burns and decubitus ulcers.

the gastrointestinal, respiratory, or genitourinary tracts, may be present in such infections, and they may exist synergistically. All clinical manifestations can be seen: cellulitis, abscess formation, thrombosis, necrosis, gangrene, and crepitus.[1]

The majority of skin infections are associated with a mixed aerobic and anaerobic flora. There are, however, certain classic syndromes caused by specific anaerobes that have distinctive clinical presentations.

2. Classification and diagnosis

2.1. *Impetigo*

Impetigo is a superficial vesiculopustular skin infection occurring mostly on exposed areas of the face and extremities. Affected patients usually have multiple lesions but little or no systemic toxicity. Infection typically arises at the site of minor skin trauma such as insect bites or abrasions. Streptococcal impetigo manifests itself as appearance of small vesicles, that rapidly pustulate and rupture. After the purulent discharge dries, a golden-yellow crust forms. The lesions remain superficial and do not ulcerate or infiltrate the dermis. Pain and scarring do not occur.

There are two rare forms of impetigo: An ulcerative form (called ecthyma) which is due to Group A beta hemolytic streptococcus (GABHS) and bullous impetigo, most often seen in newborns and younger children, which is due to *Staphylococcus aureus* (phage group II, usually type 71).[2]

The initial vesicles turn into fluid bullae that quickly rupture, leaving a moist red surface, that then generates ''varnish like'' light brown crusts. Nikolsky sign and scarring do not occur.

The most severe form of *S. aureus* infection is Staphylococcal scalded skin syndrome (SSSS), which is caused by a strain that produces exfoliative exotoxin, producing widespread bullae and exfoliation, with a positive Nikolsky sign.[1] It starts abruptly, with fever, skin tenderness and scarlatiniform rash. Bullae appear over 2–3 days, are large and rupture promptly, leaving bright red skin surface.

2.2. *Folliculitis*

Folliculitis is a pyoderma localized to hair follicles. Factors predisposing to *S. aureus* infection is nasal carriage, and exposure to whirlpools, swimming pools, and hot tubs with inadequate chlorination predispose to *Pseudomonas aeruginosa* infection.

The lesions are often multiple, clustering, pruritic and usually measure 5 mm or less in diameter, are erythematous and may have a central pustule. There is no systemic toxicity. Lesions may spontaneous drain or resolve without scarring.

2.3. *Furunculosis and carbuncles*

Furunculosis is a painful inflammatory, draining nodule that involves the hair follicle, that generally follows an episode of folliculitis. A carbuncle is a series of interconnected furuncles in the subcutaneous tissue that drain via hair follicles. *S. aureus* is the most common cause of both lesions. Systemic symptoms such as fever are more common in those with carbuncles.

Close contact with individuals with furunculosis is a risk factor for the development of the infection.[3]

2.4. *Cellulitis*

Cellulitis generally appears following trauma, with appearance of local tenderness, pain and erythema. The area involved is red, hot and swollen, with non-elevated borders, and is sharply demarcated Streptococcal cellulitis following surgery can develop within 6–48 h, be associated with hypotension, and a thin serous discharge. Regional lymphadenitis and bacteremia are common and can cause thrombophlebitis. The infection can spread rapidly in patients with dependent edema. Recurrent episodes of cellulitis of the lower extremities due to streptococci non-Group A can occur in patients whose saphenous veins have been removed for coronary bypass.[4] The patients often have systemic manifestation of fever, toxicity and chills, and edema, erythema and tenderness along the saphenous venectomy site.

2.5. *Erysipelas*

Erysipelas is a characteristic form of cellulitis that affects the superficial epidermis, producing marked swelling. The erysipelas skin lesion has a raised border, which is sharply demarcated from normal skin. The affected skin is painful, edematous, intensely erythematous, and indurated. Onset is abrupt and is in accompanied with fever, systemic toxicity, and prolonged rigors.

Predisposing conditions include skin ulcers or eczematous lesions, chronic fungal infections, local trauma, and venous or lymphatic compromise.

2.6. *Infectious gangrene (gangrenous cellulitis)*

This is a rapidly progressive infection that involves extensive necrosis of the subcutaneous tissues and overlying skin. It includes several entities (Table 1):

1) Necrotizing fasciitis (streptococcal gangrene).
2) Gas gangrene (clostridium myonecrosis) and anaerobic cellulitis.
3) Progressive bacterial synergistic gangrene.
4) Synergistic necrotizing cellulitis (perineal phlegmon) and gangrenous balanitis.
5) Localized skin necrosis complicating cellulitis.
6) Gangrenous cellulitis in the immunocompromised patient.

2.6.1. *Necrotizing fasciitis*

Streptococcal gangrene is an infection due to either group A, C or G streptococci, that is initiated as an area of painful erythema and edema, that is followed in 24–72 h by dusky skin, and yellowish to red-black fluid filled bullae.[5] The area is demarcated and is covered by necrotic eschar, surrounded by erythema resembling a 3rd-degree burn. Unless treated a rapid progression occurs with frank cutaneous gangrene, accompanied sometimes by myonecrosis. Penetration along fascial planes can occur, followed by thrombophlebitis in the lower extremities, bacteremia at metastatic abscesses and rapid death. Differentiation between cellulitis and necrotizing fasciitis (NF) is important. Cellulitis can be treated with alone antimicrobials while NF requires also surgical debridment of necrotic tissues.

GABHS infection can be associated with streptococcal toxic shock like syndrome (TSLS),[6] which is manifested by fever, tachycardia, hypotension, multi-organ failure, and in 80% evidence of soft tissue infection.

NF of the newborn can occur as a complication of omphalitis, mastitis, or postoperative wound infections. The infection may involve the anterior abdominal wall and can extend to the flanks and the chest wall. It can also occur on the scalp and at the external genitalia after circumcision.

NF due to mixed anaerobic-aerobic flora is usually associated with endogenous source of the organism, and presents in slightly different fashion. The involved area is first erythematous, swollen, hot, tender, painful and has no sharp margin.[7] Progression occurs within 3–5 days, with skin breakdown with bullae, and cutaneous gangrene. The involved area becomes anesthetic because of small vessels thrombosis that supply the superficial nerves. The development of anesthesia can antedate the appearance of skin necrosis, and signifies the presence of NF and not simple cellulitis. Easy passage through an incision in the lesion along a plane with a probing hemostat, is also diagnostic. Subcutaneous gas and foul smell are often present in polymicrobial infection, especially in those with diabetes. Systemic toxicity and elevated temperature are common. NF of the face, eyelids, neck and lips[8–10] are rare but can be life-threatening. Crepitus, severe pain and necrosis of the epidermis and superficial fascia are evident. The infection can spread rapidly to other areas in the neck.

2.6.2. *Gas gangrene, anaerobic cellulitis*

In clostridial anaerobic cellulitis, the onset is gradual after a few days of incubation, and is in a form of minimal local pain and swelling and no systemic toxicity. This distinguishes the process from true gas gangrene. A thin, dark, sometimes foul smelling discharge and extensive tissue gas formation manifesting crepitus is seen. The clinical presentation of non-clostridial anaerobic cellulitis is similar to clostridial cellulitis.

2.6.3. *Progressive bacterial synergistic gangrene*

The infection generally starts as a local area of tenderness, swelling and erythema that subsequently ulcerates. The painful ulcer enlarges and is surrounded by violaceous zone that fades into pink edematous border. Left untreated, the ulcer enlarges and may burrow through tissue emerging in distant sites (Meleney's ulcer).[11]

2.6.4. *Synergistic necrotizing cellulitis*

This infection in the form of Fournier's gangrene, starts as cellulitis, adjacent to the entry point, and involves the deep

Table 1 – Clinical presentations of soft tissue infections

	Necrotizing fasciitis (streptococcal gangrene)	Gas gangrene (clostridial myonecrosis)	Progressive bacterial synergistic gangrene	Synergistic necrotizing Cellulitis	Pseudomonas gangrenous cellulitis
Fever	High	Moderate to high	Minimal or absent	Moderate	High
Systemic toxicity	Significant	Very significant	Minimal	Significant	Significant
Pain	Minimal	Significant	Significant	Significant	Mild
Crepitus	Absent	Present	Absent	Often present	Absent
Anaesthesia of lesions	Sometimes present	Absent	Absent	Absent	Sometimes present
Appearance of infection	Subcutaneous tissue and fascial necrosis. Overlying skin necrotic and dark	Significant oedema. Yellow-brown discolouration of skin. Brown bullae. Necrotic area composed of green-black patches. Serosanguinous discharge	Necrotic central ulcer, dusky margin and erythematous periphery	Crepitus cellulitis with foul-smelling, thick discharge from necrotic skin	Black/gray eschar. Dark discharge with surrounding erythema

fascia. Pain, fever and systemic toxicity occur. Swelling and crepitus of the scrotum increases, and gangrene develops. Abdominal wall involvement can be especially rapid in diabetics.

2.6.5. *Gangrenous cellulitis in the immunocompromised host*
Cellulitis in the immunocompromised can be caused by expected pathogens as well as opportunistic ones. *Pseudomonas aeruginosa* is the major pathogen causing a sharply demarcated necrotic area with black eschar and surrounding erythema that may evolve from initial hemorrhagic bulla. *Rhizopus* spp. can be indolent, with slowly enlarging black ulcer, or may be rapidly progressive. The lesion has a central anesthetic black necrotic area with surrounding violaceious cellulitis and edema.[12] Ulcerative or nodular lesions due to opportunistic organisms can develop in immunocompromised patients after trauma.

2.7. *Diabetic and other chronic superficial skin ulcers and subcutaneous abscesses and secondary bacterial infections complication skin lesions*

Diabetic foot infections are divided into non-limb-threatening infection and limb-threatening infection. Non-limb-threatening infections are superficial, lack systemic toxicity, have minimal cellulitis that extends <2 cm from port of entry, if ulceration is present it does not extend through the skin, and does not show signs of ischemia. Limb-threatening infections are associated with ischemia, have more extensive cellulitis, lymphangitis is present, and the ulcers penetrate through the skin into the subcutaneous tissue. Epidermal cysts in the chest, trunk, extremities and vulvovaginal and scrotal areas can also become severely infected.[13] Other skin lesions that can be secondarily infected with bacteria are: scabies,[14] eczema herpeticum,[15] psoriasis,[16] poison ivy,[17] diaper dermatitis,[18] Kerion,[19] and atopic dermatitis.[20]

2.8. *Myositis*

Infectious myositis is an acute, subacute, or chronic infection of skeletal muscle. Once considered a tropical disease, it is now seen in temperate climates as well, especially with the emergence of human immune deficiency virus (HIV) infection. In addition to HIV, other viruses, bacteria (including mycobacteria), fungi, and parasites can cause myositis. Risk factors for bacterial infection include strenuous activity, muscle trauma, skin infections, infected insect bites, illicit drug injections, and diabetes. Symptoms include fever, malaise and muscle pain.

3. Microbiology (Table 2)

Table 2 – Bacterial aetiology

Impetigo and cellulitis, diabetic and chronic skin ulcers
Streptococcus group A
Staphylococcus aureus
Anaerobic oral flora (*Prevotella*, *Fusobacterium* and *Peptostreptococcus* spp.) around oral area and head and neck
Colonic flora: *Enterobacteriaceae* and anaerobes (i.e. *Escherichia coli* and *Bacteroides fragilis* group) around rectum and lower extremity
Necrotizing fasciitis
Streptococcus group A (rarely also groups C or E)
Staphylococcus aureus
Enterobacteriaceae
Enteric or oral anaerobes
Gas gangrene and crepitus cellulitis
Clostridium perfringens and other *Clostridium* species
Progressive bacterial gangrene
Peptostreptococcus spp.
Microaerophilic streptococci
Proteus spp.
Myositis
Staphylococcus aureus
Streptococcus groups A, B, C and G
Enterobacteriaceae
Yersinia entercolitica
Pseudomonas spp.
Aeromonas spp.
Clostridium spp. (especially *perfringens*)
Peptostreptococcus spp.
Bacteroides spp.

3.1. *Impetigo*

Most cases of impetigo and cellulitis are attributed to *S. aureus* and GABHS alone or in combination.[21] A recent retrospective study investigated both the aerobic and anaerobic microbiology of non-bullous impetigo in 40 children.[22] Aerobic or facultative anaerobic bacteria only were present in 24 patients (60%), strict anaerobic bacteria only in 5 patients (12.5%), and mixed anaerobic-aerobic flora was present in 11 patients (27.5%). Sixty-four isolates were recovered: 43 aerobic or facultative, and 21 anaerobic. The predominant aerobic and facultative bacteria were *S. aureus* (29 isolates), and GABHS.[13] The predominant anaerobes were *Peptostreptococcus* spp.,[12] pigmented *Prevotella* spp.,[5] and *Fusobacterium* spp.[2] Single bacterial isolates were recovered in 17 patients (42.5%), 13 of which were *S. aureus*. *S. aureus* alone or mixed with GAS or *Peptostreptococcus* spp. were isolated from all body sites. Mixed flora of *Peptostreptococcus* spp. with *Prevotella* spp. or *Fusobacterium* spp. was mostly found in infections of the head and neck, while *E. coli* mixed with *Bacteroides fragilis* and *Peptostreptococcus* spp. were isolated from one infection of the buttocks area.

3.2. *Folliculitis*

The most common pathogens include *S. aureus*, *P. aeruginosa*, and *Candida* spp. Less common etiologic organisms include *Klebsiella oxytoca*[23] *Acinetobacter baumannii*,[24] and non-tuberculous mycobacterial infections.[25]

3.3. *Furunculosis and carbuncles*

There is an increasing incidence of community-acquired infections due to methicillin-resistant *S. aureus* (CA-MRSA), which cause these infections as well as other skin and soft tissue infections.[26] Risk factors to MRSA infection is close contact with other individuals with CA-MRSA infections. Outbreaks of

mycobacterium furunculosis affected customers using whirlpool footbaths at nail salons.[27]

3.4. Cellulitis

GABHS is the major cause and *S. aureus* is a minor cause of the classic erysipelas. Streptococci other than Group A were isolated in lower extremity cellulitis involved in post saphenous venectomy (Groups C, G, B)[4] and were in neonatal cellulitis. Cellulitis due to *Streptococcus pneumoniae* through bacteremic route were also described.[28] *Enterobacteriaceae* and fungi *Cryptococcus neoformans*, were recovered from cellulitis in the immunocompromised host. *E. coli* was recovered from children with nephrotic syndrome who developed cellulitis.[29] *Aeromonus hydrophila* is recognized as a cause of cellulitis after laceration that occurred when swimming in fresh water and *Vibrio* spp. can infect wounds sustained in salt water.[30] Bacteremia and cellulitis due to *Vibrio vulnificus* may follow ingestion of raw oysters, especially in patients with alcoholic cirrhosis.[31] *Pseudomonas aeruginosa* is the major pathogen in bacteremia associated cellulitis in the immunocompromised host.

The microbiology of cellulitis and its correlation to the site of infection was investigated in 278 swab and 64 needle aspirate specimens.[32] Aerobic or facultative bacteria only were present in 138 (53%) of swab samples, anaerobic bacteria only in 69 (27%), and mixed aerobic/anaerobic flora in 52 (20%). In total, there were 582 isolates, 247 aerobic or facultative and 335 anaerobic bacteria (2.2 isolates/specimen). The predominance of certain isolates in different anatomical sites correlated with their distribution in the normal flora adjacent to the infected site. The highest recovery rates of anaerobic bacteria were from the neck, trunk, groin, external genitalia and leg areas. Aerobes outnumbered anaerobes in the arm and hand. The predominant aerobes were *S. aureus*, GAS, and *E. coli*. The predominant anaerobes were *Peptostreptococcus* spp., *B. fragilis* group, *Prevotella* spp., *Porphyromonas* spp. and *Clostridium* spp. Certain clinical findings correlated with the following organisms: swelling and tenderness with *Clostridium* spp., *Prevotella* spp., *S. aureus* and GABHS; regional adenopathy with *B. fragilis* group; bullous lesions with *Enterobacteriaceae*; gangrene and necrosis with *Peptostreptococcus* spp., *B. fragilis* group, *Clostridium* spp. and *Enterobacteriaceae*; foul odor with *Bacteroides* spp.; and gas in tissues with *Peptostreptococcus* spp., *B. fragilis* group and *Clostridium* spp. Certain predisposing conditions correlated with the following organisms: trauma with *Clostridium* spp.; diabetes with *Bacteroides* spp., *Enterobacteriaceae* and *S. aureus*; and burn with *P. aeruginosa*.

3.5. Erysipelas

Most cases are caused by GABHS. Rare causes especially in patients with underlying venous or lymphatic compromise are other beta-hemolytic streptococci, such as group G or C. Rare causes are *S. aureus, Streptococcus pneumoniae*, enterococci, and aerobic gram-negative bacilli.

3.6. Necrotizing fasciitis

There are two main bacterial causes of NF: GABHS and synergistic infection due to facultative and anaerobic bacteria. Streptococcal gangrene is due to either groups A, C or G streptococci. However, GAS can be recovered mixed also with other organisms. The predominant organisms present in synergistic infection, including those of the male genital area, *Enterobacteriaceae*, *S. aureus*, *Peptostreptococcus* spp., *Clostridium* spp., *Fusobacterium* spp., and *Bacteroides fragilis* group.

The most common GABHS recovered in recent outbreaks have been M1/T1 or M12/T12 types, that contained pyrogenic exotoxin A or C genes.[33]

Brook and Frazier[10] studied the microbiological and clinical characteristics of 83 patients with NF. Bacterial growth was noted in 81 out of 83 (98%) specimens from patients with NF. Aerobic or facultative bacteria only were recovered in eight (10%) specimens, anaerobic bacteria only in 18 (22%) specimens, and mixed aerobic/anaerobic flora in 55 (68%) specimens. In total, there were 375 isolates, 105 aerobic or facultative bacteria and 270 anaerobic bacteria (4.6 isolates/specimen). The recovery of certain bacteria from different anatomical locations correlated with their distribution in the normal flora adjacent to the infected site. Anaerobic bacteria outnumbered aerobic bacteria at all body sites, but the highest recovery rate of anaerobes was in the buttocks, trunk, neck, external genitalia, and inguinal areas. The predominant aerobes were *S. aureus*, *E. coli* and group A streptococcus. The predominant anaerobes were *Peptostreptococcus* spp., *Prevotella* spp., *Porphyromonas* spp., *B. fragilis* group and *Clostridium* spp. Certain clinical findings correlated with some bacteria: edema with *B. fragilis* group, *Clostridium* spp., *S. aureus*, *Prevotella* spp. and GAS; gas and crepitation in tissues with *Enterobacteriaceae* and *Clostridium* spp.; and foul odor with *Bacteroides* spp. Certain predisposing conditions correlated with some organisms: trauma with *Clostridium* spp.; diabetes with *Bacteroides* spp., *Enterobacteriaceae* and *S. aureus*; and immunosuppression and malignancy with *Pseudomonas* spp. and *Enterobacteriaceae*.

A smaller study evaluated specimens obtained from eight children with necrotizing fasciitis (NF).[34] A total of 21 isolates were recovered, 13 anaerobic and 8 aerobic or facultatives. The facultative organism *Streptococcus pyogenes* was present alone in two (25%) instances, and mixed aerobic and anaerobic bacteria were isolated in six (75%). The predominant isolates were *Peptostreptococcus* spp. (6 isolates, including 3 *Peptostreptococcus magnus*), GABHS,[4] *Bacteroides fragilis* group,[3] *Clostridium perfringens*,[2] *Escherichia coli*,[2] and *Prevotella* spp.[2] Organisms similar to the ones isolated from the NF aspirates were recovered in the blood of all patients except one. These included GABHS (3 isolates). *B. fragilis* group,[2] *E. coli*,[1] and *P. magnus*[1] and *Clostridium perfringens*.[1] All patients underwent surgical fasciotomy, and four required skin grafting. Antimicrobials were administered to all children. Despite extensive resection and intense supportive therapy, three patients died from sepsis accompanied by shock acidosis and disseminated intravascular coagulation. These findings illustrate the polymicrobial aerobic-anaerobic flora of NF in children.

3.7. Gas gangrene, and crepitant cellulitis

Clostridium perfringens is the most common *Clostridium* spp. causing the infection. *C. septicum* and other species

(*Clostridium novyi*, *bifermentans*, *histolyticum* and *fallax*) have also been recovered. Occasionally the clostridium is recovered mixed with other aerobic and anaerobic bacteria.

3.8. *Progressive bacterial synergistic gangrene*

Anaerobic or microaerophilic streptococci can be recovered from the advanced margin of the lesion, while *S. aureus* and sometimes gram negative aerobic bacilli (especially *Proteus* spp.) can be isolated from the ulcerated area.

3.9. *Diabetic and other chronic superficial skin ulcers and subcutaneous abscesses and secondary bacterial infections complication skin lesions*

Decubitus ulcers can be colonized and infected by a variety of aerobic and anaerobic bacteria. The distribution of organisms depends on the location of the ulcer. While GABHS and *S. aureus* can be isolated in all body sites, organisms of oral flora origin (*Fusobacterium* spp., pigmented *Prevotella* and *Porphyromonas* and *Peptostreptococcus* spp.) can be isolated in ulcers and wounds proximal to that site, while organisms of colonic or vaginal flora origin (*B. fragilis* group, *Clostridium* spp., *Peptostreptococcus* spp., and *Enterobacteriaceae*) can be recovered from lesions proximal to the perianal area.[35] This principle applies to recovery of organisms in other skin and soft tissue wounds and abscesses,[35,36] secondarily infected wounds and skin lesions caused by scabies,[14] superficial thrombophlebitis,[37] decubitus ulcers,[38] diaper dermatitis,[18] atopic dermatitis.[20] Kerion lesions,[19] and secondarily infected eczema herpeticum,[15] psoriasis lesions[16] and poison ivy.[17] Foot infections in diabetic patients are infected with *S. aureus*, group B *Streptococci*, *Enterococcus* spp., *Enterobacteriaceae* and other gram-negative aerobic bacteria, as well as *Peptostreptococci* and *B. fragilis* group.[39,40]

3.10. *Myositis*

S. aureus is the predominant cause of tropical and non-tropical infection.[41] GABHS as well as other groups (B, C and G), as well as *S. pneumoniae* and *Streptococcus anginosus* can be recovered. Gram-negative aerobic and facultatives have also been rarely recovered. These include *Enterobacteriaceae*, *Yersinia enterocolitica*, *Pseudomonas* spp., *Haemophilus influenzae*, *Neisseria gonorrhoeae*, and *Aeromonas* spp.

Anaerobic bacteria such as *Bacteroides*, *Fusobacterium*, *Clostridium* and *Peptostreptococcus* spp. have also been recovered in studies where proper methods for their isolation were employed in adults[42] and children.[43] Pyogenic myositis can be classified into several major groups according to the organisms recovered: GABHS necrotizing myositis, clostridial myonecrosis (gas gangrene), and non-clostridial (crepitant) myositis. *C. perfringens* accounts for 80–95% of cases, *C. novyi* for 10–40%, and *C. septicum* for 5–15%. Rarely other clostridial species can be isolated: *C. bifementans*, *C. fallax* and *C. histolyticum*. Other organisms such as *E. coli*, *Enterococci* and *Enterobacter* spp. can also be recovered mixed with *Clostridium* spp. Non-clostridial myositis can be divided into subgroups: Anaerobic streptococcal myonecrosis – which is a mixed infection of GABHS or *S. aureus* with *Peptostreptococcus* spp.; synergistic non-clostridial anaerobic myonecrosis – due to polymicrobial flora; infected vascular gangrene – due to Bacteroides and other anaerobes plus *Proteus* spp., and *Aeromonas hydrophila* – myonecrosis. Psoas abscess – is generally due to *S. aureus* or polymicrobial aerobic-anaerobic flora.

4. Pathogenesis

Soft tissue and muscular infections frequently occur in areas of the body that have been compromised or injured by foreign body, trauma, ischemia, malignancy or surgery. Because the indigenous local microflora usually is often responsible for these infections, anatomic sites that are subject to fecal or oral contamination are particularly at risk. These include wounds associated with surgery of the intestine or pelvic tract, human bites, decubitus ulcers in the perineal area, pilonidal cysts, omphalitis, and cellulitis around the fetal monitoring site.

4.1. *Skin and subcutaneous infection*

Predisposing conditions to progressive bacterial synergistic gangrene include (Table 3) surgery and draining sinus; to synergistic necrotizing cellulitis – diabetes, to streptococcal gangrene – diabetes, myxedema and prior abdominal surgery; to clostridial myonecrosis (gas gangrene) – trauma, to necrotizing cutaneous mucormycosis – diabetes and corticosteroids therapy; to bacterial *Pseudomonas* gangrenous cellulitis – burns, and immunosuppression; and to pyoderma gangrenosum – ulcerative colitis and rheumatoid arthritis.

The acquisition of a potential pathogen as part of the skin flora such as GABHS, generally antedates the emergence of impetigo by about 10 days.[44] This organism can also colonize

Table 3 – Risk factors for soft tissue and muscular infections

Skin and subcutaneous infection
Progressive bacterial synergistic gangrene
– Surgery, draining sinus trauma
Synergistic necrotizing cellulitis
– Diabetes, trauma
Streptococcal gangrene
– Trauma, diabetes, myxoedema, abdominal surgery, steroid and non-steroidal anti-inflammatory, varicella
Clostridial myonecrosis (gas gangrene)
– Diabetes, corticosteroid therapy, trauma
Necrotizing cutaneous mucormycosis
– Diabetes, corticosteroid therapy
Bacterial pseudomonal gangrenous cellulitis
– Burns, immunosuppression
Pyoderma gangrenosum
– Ulcerative colitis, rheumatic fever

the naso-pharynx in about a third of the patients with skin infection. Infection caused by GABHS may follow minor trauma such as abrasion or insect bite, especially during the hot and humid summer period. In contrast, facial impetigo occurring in cooler climates are generally a result of a contiguous spread from the nasopharynx.

Impetigo due to *S. aureus*, however, generally follows nasal colonization that is later followed by skin colonization.[45] Trauma, or an underlying skin lesion (ulcer, furuncle), predisposes to the development of cellulitis. Rarely blood borne spread can cause the infection. Cellulitis due to non-GABHS streptococci can develop in patients whose saphenous veins were used for coronary artery bypass.[4] Cellulitis due to group B and D streptococci can occur in patients with lower extremity lymphedema secondary to radical pelvic surgery, radiation therapy or neoplasm of the pelvic lymph nodes.[46] This infection is often associated with recent coitus.[47] Cellulitis due to water-borne organisms can be caused after laceration sustained in fresh water (*Aeromonas hydrophila*)[48] salt water (*Vibrio* spp.).[31]

Gangrenous cellulitis generally follows introduction of the infecting organism to the infected site. It can also develop from extension of the infection from deeper sites to the subcutaneous and skin tissues. This can follow intestinal surgery where clostridial myonecrosis develop, or when perirectal abscess dissects the perineal area to cause phlegmona.

Progressive bacterial synergistic gangrene following abdominal surgery is more common when wire sutures are used, in cases of ileostomy or colostomy, at the exit of a fistulous treat adjacent to chronic ulceration in an extremity.[11,49]

Gangrenous cellulitis can also start at a site of a metastatic infection due to bacteremia. An example is clostridial myonecosis due to *Clostridium septicum*, that originated from a colonic malignancy, or in Aspergillus or pseudomonas gangrenous cellulitis.

A compromised patient is more susceptible to many skin and subcutaneous infections caused by a variety of organisms, many of which do not cause infection in the normal host. Mucormycotic gangrene can develop in diabetic patients, those who receive immunosuppressive therapy or have an extensive burn wound. This infection occurs more frequently in conjunction with local factors such as fistulous tracts, ileostomy stomas and open fracture sites. Infection with *Rhizopus* spp. can follow the use of Elastoplast contaminated with the spores.[12] Patients with chronic renal failure (with secondary hyperparathyroidism), those who are in chronic dialysis, or have extensive calcification of small arteries, can develop skin and subcutaneous fat necrosis.[50] Skin lesions (such as eczematous dermatitis, traumatic lesions, etc.) can become secondarily infected, causing minimal to extensive infections.[14–20]

Diabetic foot and other superficial skin ulcers can also become infected. The nature of the ulcer which includes tissue necrosis and extensive undermining, and its location near mucous membrane orifices (anal, vaginal, or oral), that is colonized with aerobic and anaerobic flora, enables the adjacent flora to invade the ulcers. Infection in diabetic patients generally follows minor trauma in individuals with neuropathy and arterial vascular insufficiency. It then may progress to cellulitis, soft tissue necrosis, osteomyelitis with a draining sinus.

Clostridial anaerobic cellulitis is most often caused by *Clostridium perfringens* that is usually introduced into subcutaneous tissues through a contaminated or inadequately debrided wound. The source of the infection can also be a pre-existing infection especially of the perineum, abdominal wall, buttocks and lower extremities that can become contaminated with fecal flora. The presence of necrotic tissue or foreign material in the wound enhances infection with *Clostridium* spp. The source of *C. septicum* cellulitis in patients with leukemia and granulocytopenia,[51] is bacteremia that originate from intestinal erosions.

NF due to GABHS, can occur after trauma, burn, childbirth, insect bite, muscle strain, penetrating wounds and splinters, surgery (especially in patients with diabetes, peripheral vascular disease, varicella infection, cirrhosis and non-steroidal anti-inflammatory and corticosteroid therapy.[52] Predisposition to Fournier's gangrene, which is a form of NF in the male genitals, include local trauma, diabetes, paraphimosis, periurethral extravasation of urine, and perirectal or perianal infection and surgery in the area (i.e., herniorrhaphy, circumcision).[53] The infection can extend to the abdominal wall, especially in patients with diabetics, obesity, advanced age and cardiorenal disease.

Trauma often predisposes to NF of the periorbital or facial areas and oral, pharyngeal or dental infection predisposes to cervical infection. NF in the newborn is often a complication of omphalitis. NF in older individuals can affect any body part. The portal of entry is usually a site of trauma, laparotomy in the presence of peritoneal soiling, or other surgical procedure, IM injections and IV infusions, local hypoxia, perirectal abscess, decubitus ulcers in intestinal perforation.[54] Predisposing conditions include diabetes mellitus, alcoholism and parenteral drug abuse.[10]

Some subcutaneous infections, mostly subcutaneous abscesses, are a manifestation of osteomyelitis. This is as a result of a rupture of a subperiostal abscess into the subcutaneous tissue. A draining sinus can be caused by chronic osteomyelitis. Bacteremia or endocarditis can predispose to metastatic pyogenic infection, in the subcutaneous tissues in the form of an abscess.

4.2. *Myositis*

Infectious myositis caused by bacteria can invade from contiguous sites such as skin and subcutaneous abscesses, ulcers, penetrating wounds and osteomyelitis; or through hematogenous spread. Trauma is a common cause in children.[43,48] Vascular insufficiency in an extremity can also facilitate the process. However, primary muscle abscess can also occur in the absence of a predisposing site of infection.[55] No conclusive evidence exists that relate tropical pyomyositis causality to predisposing conditions unique to the tropics (i.e., filariasis, malaria, arbovirus). However, about 2/3 of tropical myositis cases have predisposing condition that include diabetes, alcoholism, corticosteroid therapy, immunosuppressive therapy, and hematological illnesses, and HIV infection.[41]

The increased susceptibility of HIV patients to pyomyositis is believed to be due to the combination of the underlying cell-mediated immunodeficiency, defective neutrophils activity,

and the potential of muscle injury (HIV myopathy, anti-retroviral-associated mitochondrial myopathy, and concomitant bacterial infection). Clostridial myonecrosis usually follows muscle injury and contamination by dirt or during surgery. Contamination of the muscle can occur as a result of compound fracture penetrating war wounds,[56] surgical wounds, especially following bowel or biliary tract surgery, arterial insufficiency of an extremity,[57] and rarely after parenteral injection of medication, especially epinephrine in oil.

Spontaneous, non-traumatic gas gangrene is mostly due to *C. septicum*, that spreads by bacteremic route. Intestinal abnormalities that include necrotizing enterocolitis, volvulus, colon cancer, diverticulitis and bowel infarction, and leukemia, neutropenia and diabetes mellitus are the major predisposing conditions.

Psoas abscess generally develops as a result of spread from an adjacent structure, either as an extension of intra-abdominal infection (appendicitis, diverticulitis, chrons' disease), perinephric abscess, or infected retroperitoneal hematoma. It can also originate from vertebral tuberculosis or *S. aureus* osteomyelitis. Osteomyelitis of the illium or septic arthritis of the sacro-iliac joint can produce iliacis or psoas abscess.

5. Diagnostic tools

The recovery of fastidious organisms depends on employment of proper methods for collection, and transportation of specimen, and cultivation of organisms. Since many potential pathogens are part of the normal skin or mucous membrane flora, specimens should be obtained using methods of collection that will bypass the normal skin and mucous membrane flora. Therefore, disinfecting the skin, obtaining deep tissue or surgically obtained aspirates will yield reliable specimens.[58] A recent study compared the skin swab and needle aspirate methodology to establish the aerobic and anaerobic microbiology of perianal cellulitis in 10 children.[59] This study demonstrated the superiority of needle aspirates in establishing the microbiology of the infection. Complete or partial concordance in microbiology between skin swabs and needle aspirates was present in six instances. In four instances, isolates recovered from needle aspirates were not isolated from the skin surface.

Radiological studies of soft tissue can reveal the presence of free gas in the tissue. This can assist in the differentiation between NF due to either streptococcal or mixed polymicrobial aerobic-anaerobic infection, and also signify the presence of gas forming bacteria in other types of necrotic infections. A feathery linearly pattern of gas can be observed in infected muscles in clostridial myonecrosis.

The presence of osteomyelitis as a cause of subcutaneous abscess, or sinus tract can be discovered by radiological and radionuclide scanning studies. Plain radiograph can show osteopenia or osteolytic lesions, periosteal elevation and periosteal new bone formation. Sclerotic lesions can be seen when the infection has been present for longer than a month.

Radionuclide scanning is useful in early diagnosis of osteomyelitis. Technetium-labeled methylenediphosphonate isotope is used most frequently since its uptake by infected bone is enhanced with increased osteoblastic activity. In some cases, decreased uptake can be observed, reflecting compromised vascular supply to the bone. The technique of SPECT/CT imaging is the most advanced method capable of co-localizing inflammatory signals with musculo-skeletal/internal structures.[60]

Radionuclide (^{67}Ga) scanning can be used in the diagnosis of pyomyositis. It shows diffuse uptake in the involved area, but does not differentiate intramuscular abscess from necrotizing myositis or NF.

Computed tomography CT can show low-density areas with muscle loss, and a surrounding rim of contrast enhancement typical of pymositis. Magnetic resonance imaging (MRI) can detect alteration in soft tissue and is particularly useful in differentiating cellulitis from pus and abscess formation. MRI can show enlargement of involved muscles and areas of signal attenuation suggestive of fluid collection. Sonography or CT can be used to guide diagnostic aspiration.

CT scanning is the most rapid and sensitive method to diagnose psoas and iliacus muscle infection. It can show diffuse enlargement of the involved muscle, and may demonstrate the presence of gas within the muscle suggesting the presence of an abscess.[61] MRI is more sensitive in showing early inflammatory changes prior to development of frank abscess cavity and can show enlarged muscles. However, some infections can develop very rapidly, to life-threatening systemic illness, and definitive diagnosis of the nature and extent of NF or myositis is made only on surgical exploration.

6. Management

Systemic antibiotics do not appear to be helpful in treating local impetigo and folliculitis. Topical therapies such as warm saline compresses and topical antibacterial or antifungal agents are generally adequate.

Certain clinical conditions requiring prompt and urgent action. This is required in SSSS, when a widespread rapid progressing bullae and exfoliation occurs that starts abruptly, that is accompanied with fever, skin tenderness and scarlatiniform rash. Fluid replacement and antimicrobials should be given without delay. STLS manifested by fever, tachycardia, hypotension, multiorgan failure, also requires urgent care.

Rapid surgical and medical responses are indicated in cellulitis that progresses into thrombophlebitis and bacteremia. Similarly urgent intervention is needed in any of the Infectious gangrenes (gangrenous cellulitis) which are rapidly progressive infection that involves extensive necrosis of the subcutaneous tissues and overlying skin. Special attention to progression should be given to necrotizing fasciitis where penetration along fascial planes can occur, followed by thrombophlebitis in the lower extremities, bacteremia and metastatic abscesses, systemic toxicity and rapid death. The development of local anesthesia can antedate the appearance of skin necrosis, and signifies the presence of NF and not simple cellulitis. Abdominal wall involvement can progress especially rapid in diabetics with synergistic necrotizing cellulitis. Special attention should be given to the immunocompromised host with gangrenous cellulitis.

NF of the face, eyelids, neck and lips can be life-threatening. Crepitus, severe pain and necrosis of the epidermis and

superficial fascia are evident heralds a rapid spread to other areas in the neck.

6.1. Surgical treatment

Treatment of infectious gangrene and gangrenous cellulitis consists of immediate surgical drainage with longitudinal incisions extending throughout the deep fascia and beyond the gangrenous and undermined areas.[5] Areas of cutaneous necrosis should be excised and non-viable fascus should be debrided. Wide excision of the tissues should extend well into the normal tissue.

Surgical management of diabetic foot and decubitus ulcers includes unroofing of encrusted areas and wound probing to determine the extent of tissue destruction and potential bone involvement. Open ulcers should be carefully packed with sterile gauze moistened one strength betadine or with normal saline, 3 times a day. Surgical debridement and drainage should be performed in those with deep tissue necrosis or suppuration.[62] Infected cysts and subcutaneous abscesses should be promptly surgically drained. In cases where myositis is suspected, surgical exploration is important in order to determine the presence of muscle involvement.

In cases of NF, immediate surgical debridement is mandatory. Extensive incisions throughout the skin and subcutaneous tissue should be made, proceeding beyond the area of involvement until normal flora is reached. Necrotic fascia and fat should be excised, and the wound should be left open. An additional second procedure is often needed within 24 h, to ensure the adequacy of the initial debridement.

In patients with pyomyositis, an emergency surgical exploration is warranted. This is done in order to define the nature of the infective process (crepitant cellulitis vs. gas gangrene), which is done by direct examination of the involved muscles. Furthermore, the surgical intervention is needed to perform appropriate debridement. Immediate performance of extensive surgery is necessary to treat gas gangrene. The muscles involved should be removed, and fasciotomies to decompress and drain the swollen fascial compartment are performed. Complete amputation may sometimes be necessary.

6.2. Antimicrobial therapy

Intensive surgical and medical therapy that includes the administration of intravenous fluids and management of septic shock are the hallmarks of treatment. Antimicrobial therapy is an essential element in management of skin, soft tissue and muscle infection. Establishing the bacterial etiology and the bacterial susceptibility initially by Gram stain, and later by culture can allow for selection of proper antimicrobial therapy. Often, however, the initial therapy is empiric, based on epidemiological, historical and clinical features.

In cases where streptococcal etiology is suspected, parenteral penicillin is used. If staphylococcal infection is suspected, or when no initial clue for etiology is available, a penicillinase-resistant penicillin (e.g., oxacillin, methicillin) is given. Macrolides or vancomycin can be used in penicillin allergic individuals, and an aminoglycoside, or quinolone, or a fourth generation cephalosporin (i.e., ceftazidime cefipime) can be given when a gram-negative aerobe bacilli is suspected. Recently, there have been an increase in the isolation MRSA. Patients with serious staphylococcal infections should therefore be initially started on agents active against MRSA until susceptibility results are available. Vancomycin, daptomycin, linezolid, quinupristin/dalfopristin and tigecycline can be administered to treat these infections.

In infections that involve *Clostridium* spp. the combination of penicillin and clindamycin is recommended. Since many of the infections are polymicrobial aerobic-anaerobic in nature, coverage against these organisms is often necessary.

The gram-negative anaerobic bacilli, *Prevotella* spp., and *Fusobacterium* spp. previously susceptible to penicillins have been shown in the last decade to have increased rates of resistance to these and other antimicrobial agents. The production of the enzyme beta-lactamase is one of the main mechanisms of resistance to penicillins by many gram-negative anaerobic bacilli, including members of the *B. fragilis* group. Complete identification and testing for antimicrobial susceptibility and beta-lactamase production are therefore essential for the management of infections caused by these bacteria.

Antimicrobial therapy for mixed aerobic and anaerobic bacterial infections is required when polymicrobial infection is suspected.[57] Antimicrobial agents that generally provide coverage for methicillin susceptible *S. aureus* as well as anaerobic bacteria include cefoxitin, clindamycin, a carbapenem (e.g., imipenem, meropenem, ertapenem), and the combinations of a beta-lactamase inhibitor (i.e., clavulanic acid) and a penicillin (i.e., ticarcillin) and the combination of metronidazole plus a beta-lactamase-resistant penicillin. Cefoxitin, the carbapenems, and a penicillin plus a β-lactamase inhibitor also provide coverage against members of the family *Enterobacteriaceae*. However, agents effective against these organisms (i.e., aminoglycosides, fourth generation cephlosporins, and quinolones) should be added to the other agents when treating infections that include these bacteria. Tigecycline is effective against all these organisms as well as MRSA.

Hyperbaric oxygen (HBO) therapy for clostridial myonecrosis is controversial.[63] HBO increases the normal oxygen saturation in the infected wounds by a thousand fold, leading to a bacteriocidal effect, improved polymorphonuclear cells function, and enhanced wound healing. No controlled studies were done, and the published reports do not provide evidence of beneficial effect. The potential toxicity of hyperbaric oxygen is also of concern. The most important limitation of utilizing hyperbaric oxygen therapy is the lack of availability of appropriate hyperbaric chambers in most hospitals. Transportation of a seriously ill patient to a facility possessing a hyperbaric unit is hazardous, and the separation from immediate care for the unstable patient is risky. Transportation should not be done prior to extensive surgical debridement. However, the use of hyperbaric oxygen should be considered when the involved tissue cannot be completely excised surgically, as may be the case in paraspinal or abdominal wall sites.

An addition mode of treatment is the negative pressure wound therapy, or vacuum assisted closure. This is a very effective method of reducing bacterial load by removal of infected tissue debris and wound fluid.[64]

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