

Necrotizing soft tissue infection & specific surgical infection

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Definition

- NSTI comprise of a spectrum of diseases characterized by extensive rapidly progressive soft tissue necrosis which usually involves deep subcutaneous tissue, superficial or deep fascia or muscle or combination of the three.
 - Necrotizing fasciitis (types I-III)
 - Necrotizing myositis (type II)
 - Necrotizing cellulitis (clostridial and non-clostridial)

Historical background:

- NSTI was first described by Hippocrates in the 5th century BC. He described it as a complication of acute streptococcal infection, writing “[m]any were attacked by the erysipelas all over the body when the exciting cause was a trivial accident...flesh, sinews, and bones fell away in large quantities...there were many deaths.”
- The first English-language descriptions of NSTIs were by the British surgeon Leonard Gillespie and British physicians Gilbert Blaine and Thomas Trotter in the late 18th century. The disease was known as phagedaenic ulcer, phagedena gangrenous, gangrenous ulcer, malignant ulcer, putrid ulcer, or hospital gangrene.

Historical background:

- The term hospital gangrene became the dominant term and is how the disease was first described in the United States by Confederate Army surgeon Joseph Jones in 1871, when he reported on 2642 cases with a mortality rate of 46%
- In 1883, Dr Jean-Alfred Fournier described a necrotizing infection of the perineum and scrotum, and the term Fournier gangrene is still in common usage.

Historical background:

- **Necrotizing fasciitis**, the most commonly used term to describe NSTI, was first coined by Wilson. Recently, the term NSTI is used to encompass infections not only of the fascia, as in necrotizing fasciitis, but also of the other soft tissues affected.
- The taxonomy is further complicated by the use of other terms, such as
 - “complicated skin and skin structure infections” and
 - “acute bacterial skin and skin structure infections.”

NSTI types

1. Necrotizing fasciitis type 1 (Polymicrobial)
2. Necrotizing fasciitis type 2 (Monomicrobial)
3. Necrotizing fasciitis type 3 (Marine vibrios)
4. Necrotizing fasciitis type 4 (Fungal)
5. Specific syndromes:
 - Clostridial myonecrosis (gas gangrene)
 - Fourniers gangrene
 - Necrotizing infection of the head and neck

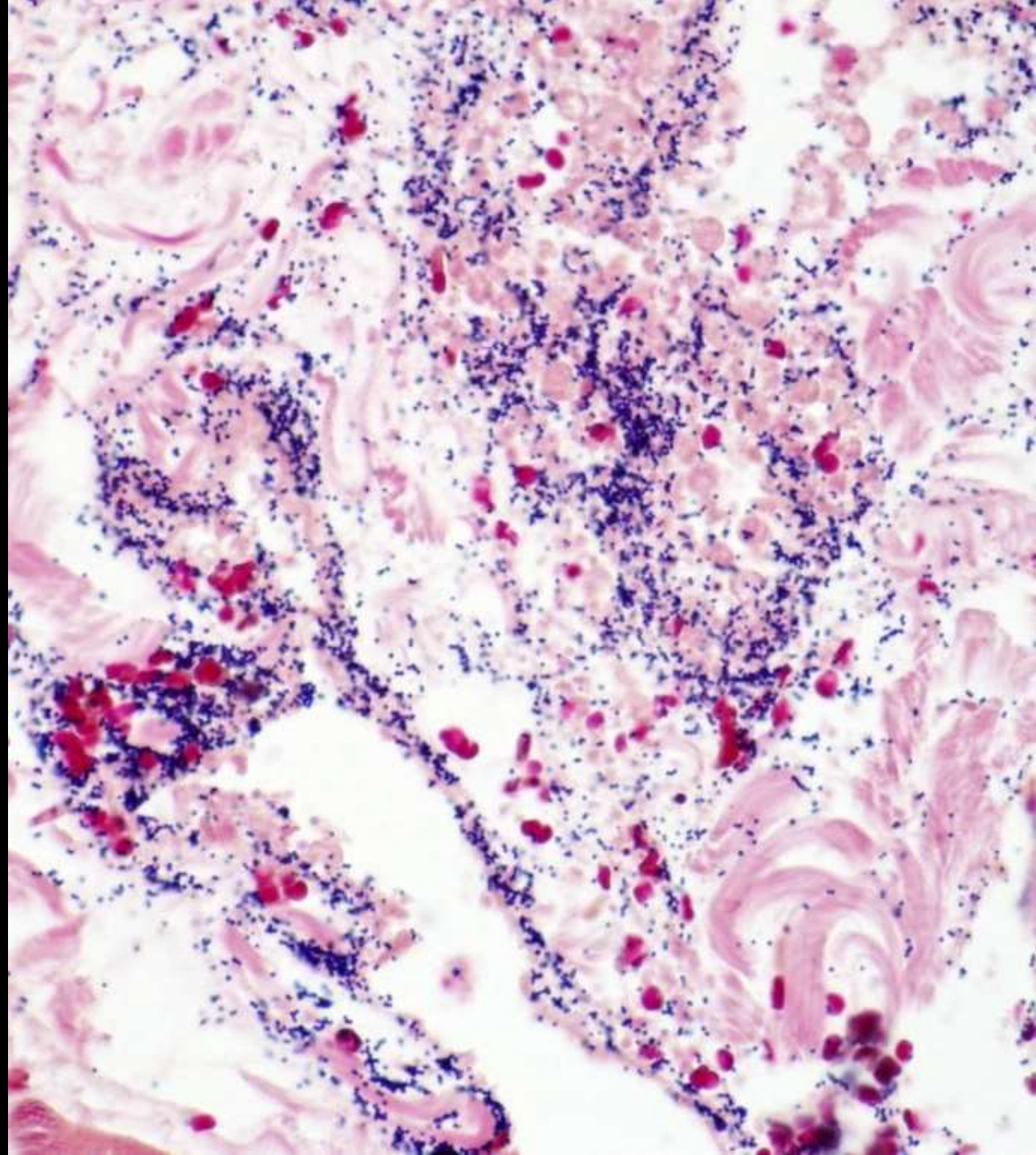
NSTI types

Type	Species	Localization
Type 1	Polimicrobial: at least one anaerobic $\pm$ facultative anaerobes (<i>Enterobacteriaceae</i> , nongroup A streptococci)	Trunk, abdomen, and perineum
Type 2	Monomicrobial: group A β -hemolytic streptococci and/or other streptococci $\pm$ staphylococci	Extremities
Type 3	Marine <i>Vibrios</i>	Extremities

Modified from Low and McGeer.⁵

NSTI type 1 (polymicrobial)

- At least 1 anaerobic +/- facultative anaerobes
- The average case had 4-6 isolates
 - Staphylococcus aureus
 - Streptococci
 - Enterococci
 - Escherichia coli
 - Peptostreptococcus
 - Prevotella
 - Porphyromonas
 - Bacteroides fragilis
 - Clostridium



NSTI type 1 (polymicrobial)

Pathogens	No. of patients (%) (N = 143)	Died	Survived	Mortality rate of pathogen (%)
Gram-positive aerobic pathogens	58 (40.6)	9	49	15.5
Beta-hemolytic Streptococcus	18 (12.6)	3	15	16.7
MRSA	18 (12.6)	5	13	27.8
MSSA	14 (9.8)	0	14	0
Viridans Streptococcus	1 (0.7)	0	1	0
CoNS	7 (4.9)	1	6	14.3
Gram-negative aerobic pathogens	60 (42.0)	12	48	20
<i>Vibrio vulnificus</i>	36 (25.2)	4	32	11.1
<i>Vibrio cholerae</i> non-O1	2 (1.4)	1	1	50
<i>Klebsiella pneumoniae</i>	5 (3.5)	3	2	60
<i>Aeromonas hydrophila</i>	4 (2.8)	2	2	50
<i>Aeromonas sobria</i>	3 (2.1)	1	2	33.3
<i>Pseudomonas aeruginosa</i>	3 (2.1)	1	2	33.3
<i>Proteus mirabilis</i>	1 (0.7)	0	1	0
<i>Escherichia coli</i>	3 (2.1)	0	3	0
<i>Morganella morganii</i>	2 (1.4)	0	2	0
<i>Chryseobacterium meningosepticum</i>	1 (0.7)	0	1	0
Fungus				
<i>Penicillium</i> sp	1 (0.7)	1	0	100
No growth	24 (16.8)	0	24	0

MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; CoNS, coagulase-negative *Staphylococcus*.

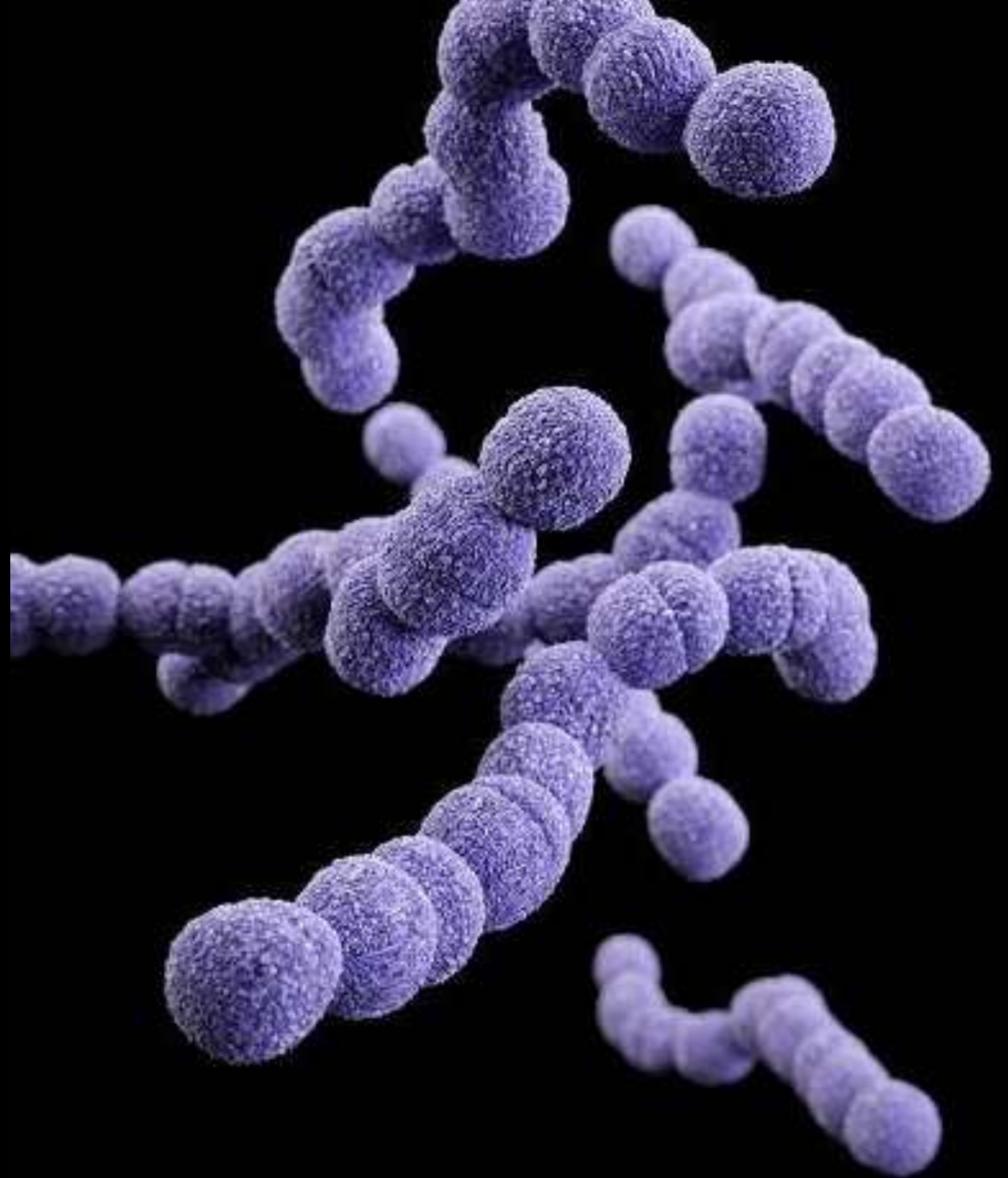
^ap < 0.05; significant difference.

NSTI type 1 (polymicrobial)

- Usually occurs after trauma or surgery
- Subcutaneous fat and fascia overlying muscle are prominently involved
- Course of disease is usually somewhat slower than that seen with type II (streptococcal) necrotizing fasciitis and clostridial myonecrosis
- Location on the trunk, abdomen and perineum
 - Fourniers gangrene

NSTI type 2 (Monomicrobial)

- Caused by virulent subtypes of streptococcus pyogenes group A.
- The bacteria is often referred to as a flesh-eating bacteria.
- The incidence of this infection increased in the last two decades
- Result of an organism virulence
 - The presence of the M1 and M3 proteins is associated with virulent infection.
 - Most of the general features of NSTI the presence of gas in tissues is unusual.
- The typical location - extremities



NSTI type 3 (Marine vibrios)

- Caused by the Marine vibrios, gram negative rods from salt water
 - *Vibrio vulnificus*,
 - *Vibrio parahaemolyticus*,
 - *Vibrio damsela*,
 - *Vibrio alginolyticus*
- Open wound (puncture wound from fish, cut or insect bite) is exposed to warm seawater with high concentrations of *Vibrio*
- Consuming raw or undercooked seafood, particularly raw oysters - primary septicemia
- Case-fatality rates are greater than 50 percent for primary septicemia and about 15 percent for wound infections



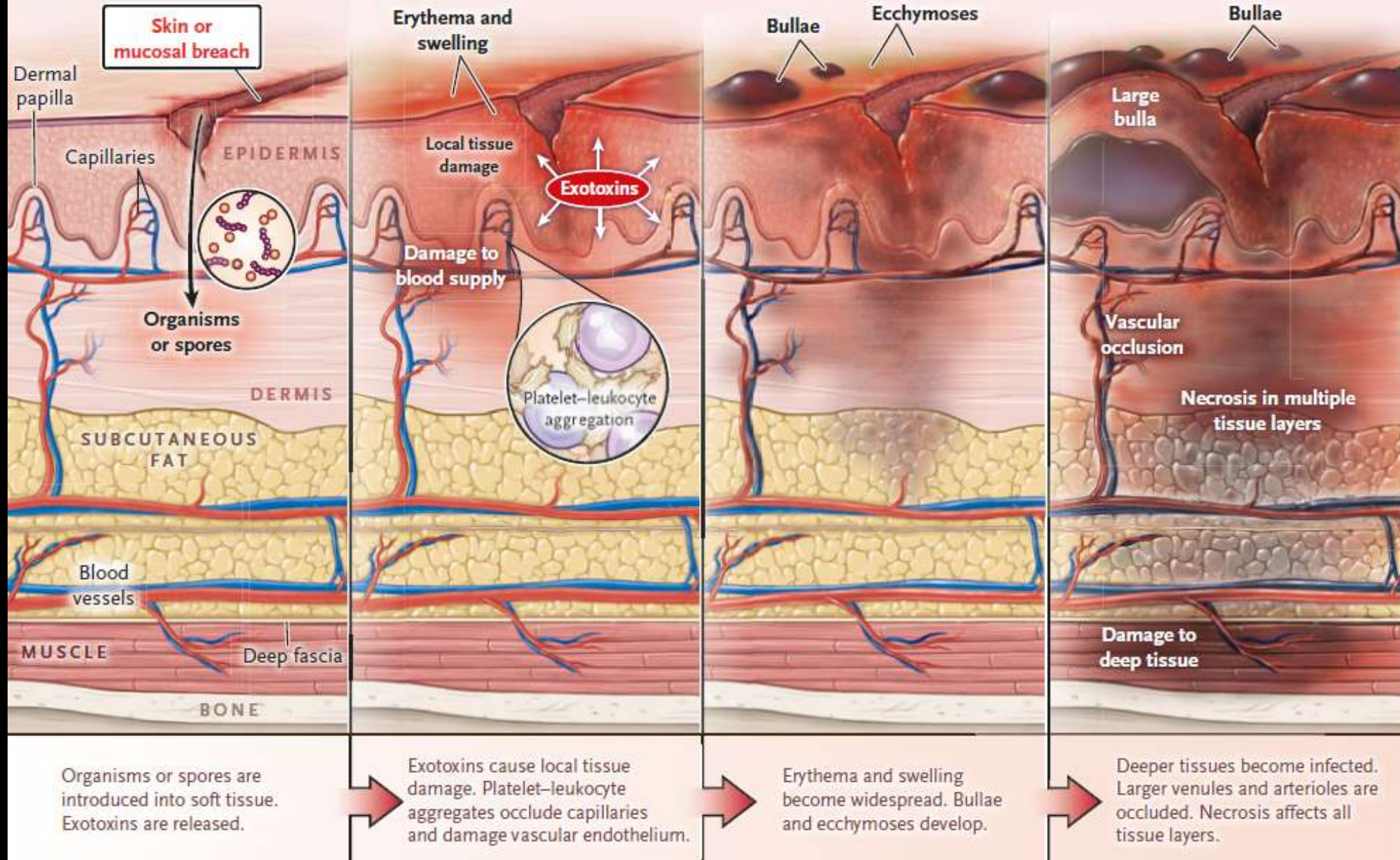
Pathogenesis

- Necrotizing fasciitis is characterized by a microbial invasion causing local thrombosis and necrosis.
- The histology findings are varied, but all are related to the thrombosis.
- In the initial horizontal phase the edema and the inflammation infiltrate the fascia, the subcutaneous fat, and the reticular dermis, progressing to superficial fascial necrosis, fascia infiltration by polymorphonuclear leukocytes (though their presence varies and may even be minimal depending on the causative agent), thrombosis of the veins and arteries passing through the fascia, with a large-scale proliferation of the microorganism.
- At this time the patient presents intense local pain, swelling, redness, poorly defined margins, local heat, fever and increasing general malaise

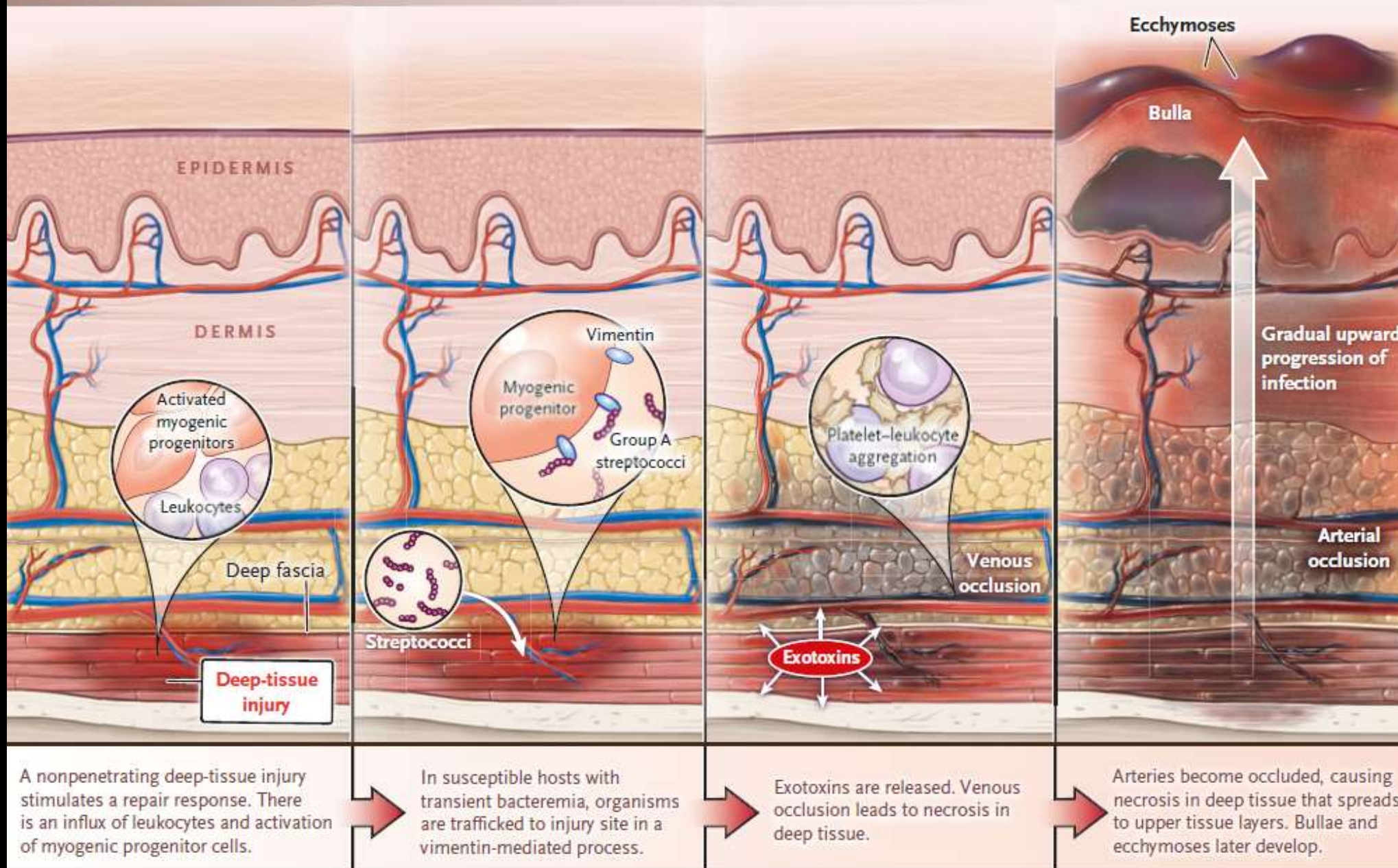
Pathogenesis

- The horizontal phase is followed by the vertical phase, characterized by ischemic necrosis of the skin and gangrene of the subcutaneous fat and dermis. There may also be areas of muscle necrosis.
- At this time, the formation of small blisters, initially containing serum, raises the suspicion of severe necrotizing fasciitis.
- These blisters (though not always present) increase in size as the condition progresses, converge with each other, and with time contain serum and blood .
- Fluctuation, crepitus and focal necrosis of the skin may also be observed resembling deep burns, with superficial serous-purulent exudate, and finally, after the necrosis of the subcutaneous nerves, hypoesthesia or local numbness .
- With the release of toxins into the bloodstream the patient's general state may worsen, with signs and symptoms of septic shock.
- Distant septic emboli and formation of metastatic abscesses in the liver, kidneys, spleen, lungs, and heart have been described.
- Depending on the patient and the virulence of the organism, evolution may be very fast, and may even result in a fatal outcome in 24-48 hours.
- Mortality is almost 100% if the patient is not treated promptly.

A Defined Portal of Entry



B No Defined Portal of Entry



Risk Factors for NSTI

- Major penetrating trauma
- Minor laceration or blunt trauma (muscle strain, sprain, or contusion)
- Skin breach (varicella lesion, insect bite, injection drug use)
- Recent surgery (including colonic, urologic, and gynecologic procedures as well as neonatal circumcision)
- Mucosal breach (hemorrhoids, rectal fissures, episiotomy)
- Immunosuppression (diabetes, cirrhosis, neutropenia, HIV infection)
- Malignancy
- Obesity
- Alcoholism
- In women: pregnancy, childbirth, pregnancy loss, gynecologic procedures

Risk Factors for NSTI

Classification of Necrotizing Fasciitis

Type	Microorganism	Associations
I	Polymicrobial	Diabetes, Immunocompromise, Peripheral Vascular Disease
II	Monomicrobial ● Group A Streptococcus ◆ MRSA	● Otherwise healthy, history of trauma (may be minor) or surgery ◆ IVDU, athlete, institutionalized
III	<i>Vibrio vulnificus</i>	Marine exposure
IV	Fungal	Immunocompromise

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

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

Clinical signs of NSTI

- Stage I (early):
 - tenderness to palpation (beyond area of cellulitis)
 - erythema/warmth
 - edema
- Stage II (intermediate):
 - bullae formation
 - skin fluctuation or induration
- Stage III (late):
 - hemorrhagic bullae
 - skin necrosis
 - crepitus



Clinical signs of NSTI

- Erythema (without sharp margins; 72%)
 - Edema that extends beyond the visible erythema (75%)
 - Severe pain (out of proportion to exam findings in some cases; 72%)
 - Fever (60%)
 - Crepitus (50%)
 - Skin bullae, necrosis, or ecchymosis (38%)
- The process progresses rapidly over several days, with changes in skin color from red-purple to patches of blue-gray. Within three to five days after onset, skin breakdown with bullae (containing thick pink or purple fluid) and frank cutaneous gangrene can be seen.

















Additional tests

- Blood samples
- Testing for elevated or lowered creatinine, glucose, CPK, bicarbonate, albumin, and calcium levels.
- X-ray
- CT, and MRI scanning in advanced cases
- Antibiotic culture and sensitivity tests

Value	LRINEC score, points
C-reactive protein, mg/L	
<150	0
>150	4
WBC count, cells/mm ³	
<15	0
15–25	1
>25	2
Hemoglobin level, g/dL	
>13.5	0
11–13.5	1
<11	2
Sodium level, mmol/L	
≥135	0
<135	2
Creatinine level, mg/dL	
≤1.6	0
>1.6	2
Glucose level, mg/dL	
≤180	0
>180	1

Risk category	LRINEC score, points	Probability of NSTI, %
Low	≤5	<50
Intermediate	6–7	50–75
High	≥8	>75

Imaging

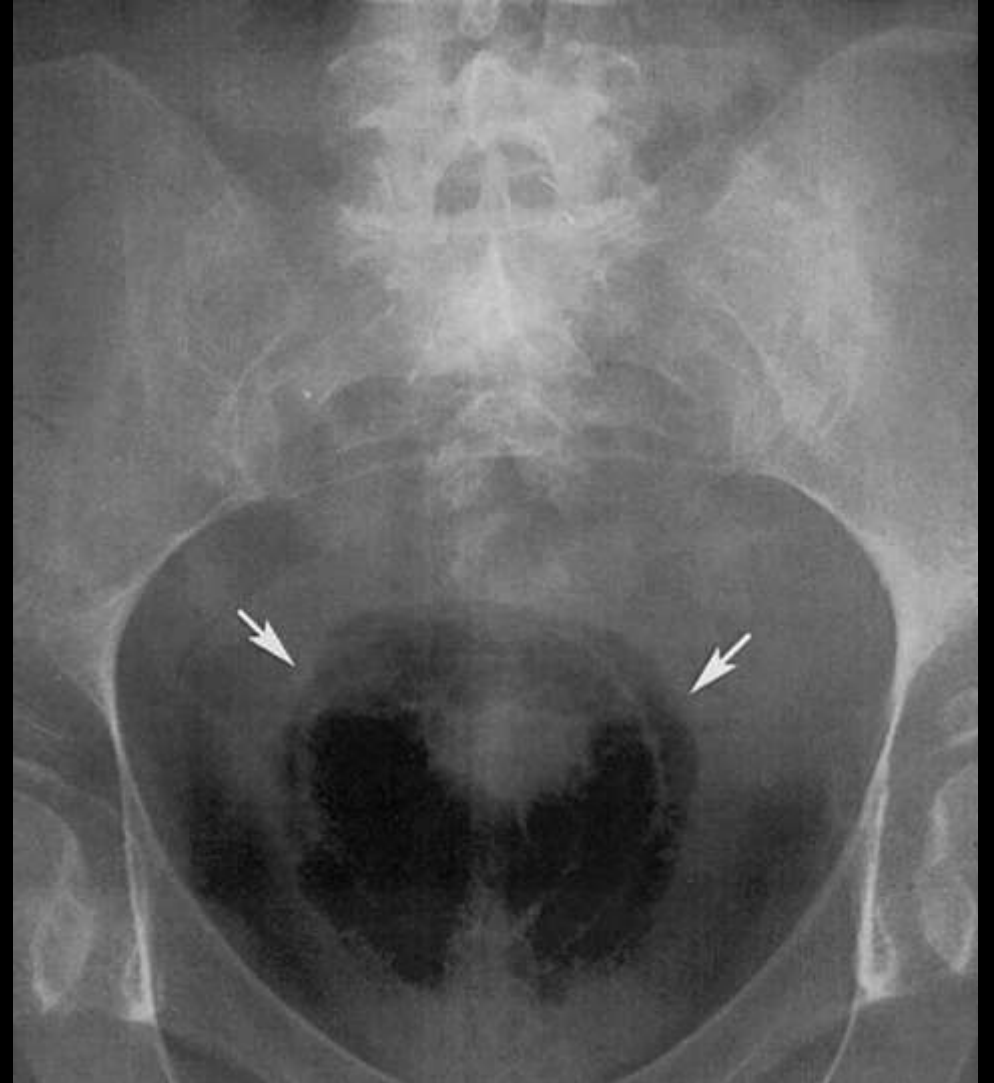
- X-ray: presence of subcutaneous gas is a typical X-ray finding but is not a sensitive finding .
- CT-scan: the computed tomography scan findings suggestive of NSTI include the extent of abnormal soft tissue gas dissecting along the fascial planes, fascial stranding, and asymmetric thickening of fascial planes .
- MRI with contrast (gadolinium) is useful in stable, conscious, cooperative, and not seriously septic patients . The findings significantly suggestive of necrotizing infection include thick (≥ 3 mm) abnormal signal intensity on fat-suppressed T2-weighted images, low signal intensity in the deep fascia on fat-suppressed T1-weighted images, a focal or diffuse nonenhancing portion in the area of abnormal signal intensity in the deep fascia, extensive involvement of the deep fascia, and involvement of three or more compartments in one extremity.

X-ray

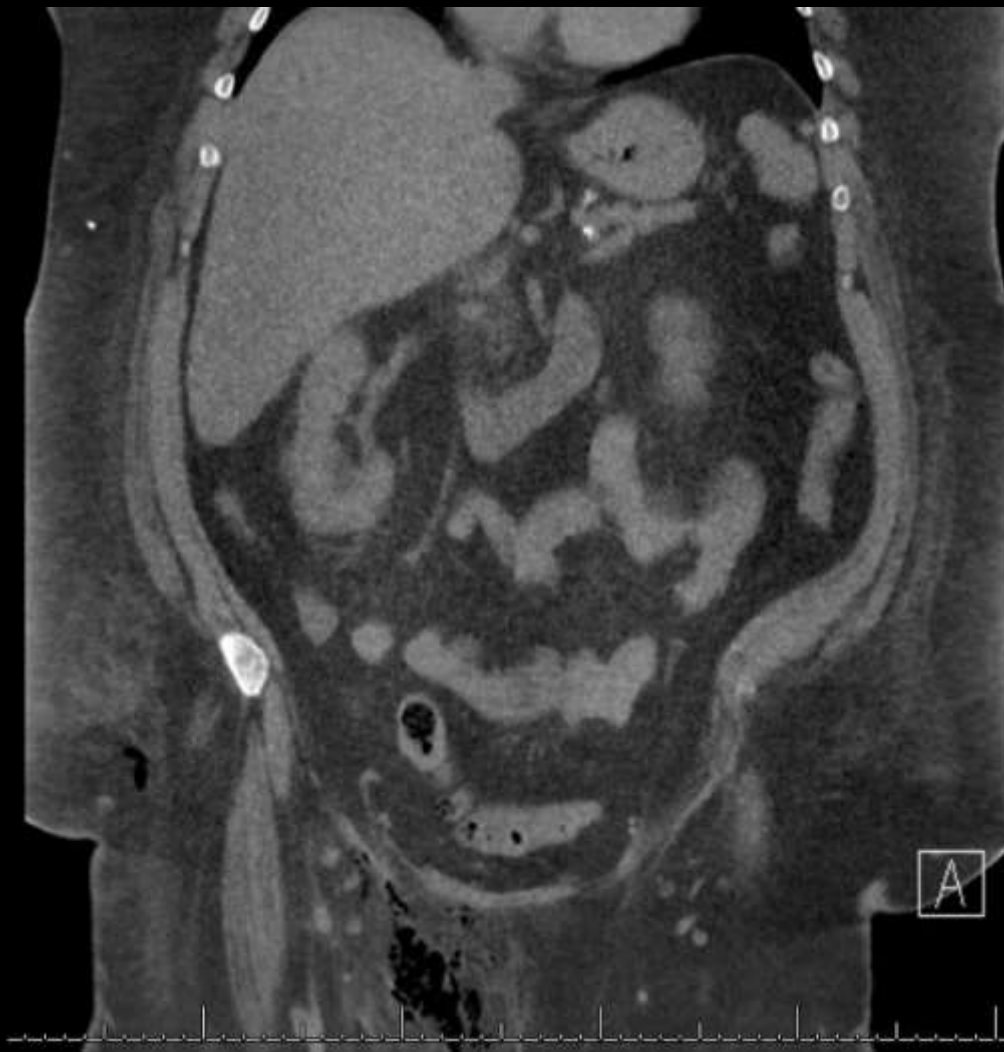


X-rays gas formation

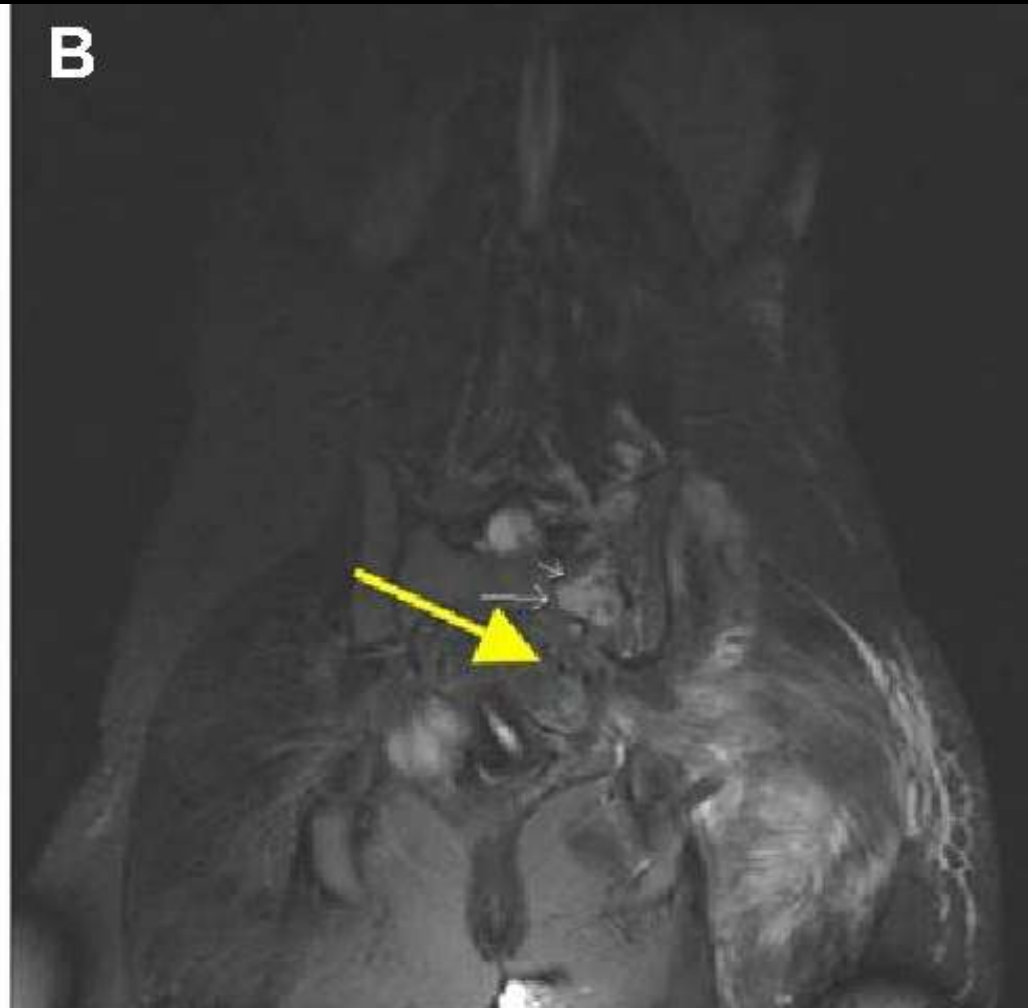
X-ray and CT



CT



MRI



Clinical Symptoms

Swelling, erythema, pain

Systemic Signs

Tachycardia, >120 beats/min; hypotension;
elevated CK level; CRP, >15 mg/dl;
LRINEC score, >6

No systemic signs

Radiographic Evidence

Gas in the tissue

No gas in the tissue

Immediate Surgery

Inspection and débridement
Specimen collection

Inspection and débridement
Specimen collection

Gram's Staining and Culture

Gram-positive
rods

Mixed aerobes
and anaerobes

Gram-positive
cocci

Gram-negative
rods

Differential Diagnosis

Clostridial myonecrosis (aggressive)
Spontaneous — *Clostridium septicum*
Traumatic — *C. perfringens*
Gynecologic — *C. sordellii*
Clostridial anaerobic cellulitis (indolent)

NF Type I
Nonclostridial crepitant cellulitis
Synergistic necrotizing cellulitis
Progressive bacterial synergistic gangrene

NF Type II
Streptococcus pyogenes
Staphylococcus aureus
or group A streptococcal myonecrosis

NF Type II
Aeromonas
Freshwater
Vibrio
Saltwater

Cellulitis
Erysipelas
Cutaneous abscess

Table 2. Pitfalls in the Diagnosis of Necrotizing Soft-Tissue Infection.*

Pitfall	Explanation
Absence of fever	Fever is often absent in patients with necrotizing soft-tissue infections because of NSAIDs that are self-administered or prescribed in the emergency department or in postsurgical settings. Fever is also absent in patients with necrotizing infection due to <i>C. sordellii</i> .
Absence of cutaneous manifestations	Patients with spontaneous or cryptogenic necrotizing infections (i.e., infections without an obvious bacterial portal of entry) that begin in the deep soft tissues often do not have cutaneous signs of infection until late in the course of the disease.
Attributing severe pain to injury or procedure	Severe pain is a key finding in patients with necrotizing infections. However, when such infections develop after surgery or parturition, pain may be erroneously attributed to the procedure itself. Similarly, perineal pain may be attributed to hemorrhoids, epididymitis, or vaginal or rectal trauma. Severe pain associated with spontaneous or cryptogenic infections is often wrongly attributed to muscle strain or venous thrombosis. If pain is out of proportion to the suspected cause or requires opioids or ketorolac for management, a developing necrotizing infection should be considered. Pain may be absent because of the use of narcotics or NSAIDs or because of neuropathy in patients with diabetes.
Nonspecific imaging tests	In patients with necrotizing infections, radiographs may show only edema, with no evidence of gas in the deep tissue. Since this finding is consistent with noninfectious causes (e.g., soft-tissue injury and postsurgical and postpartum conditions), it may confound the diagnosis.
Attributing systemic manifestations to other causes	Nausea, vomiting, and diarrhea may be early manifestations of toxemia from group A streptococcal infection, though they are often wrongly attributed to food poisoning or viral illness.

Treatment

- Clinical suspicion
- Early surgical exploration
- Aggressive and repetitive debridement
- Antibiotics
- Intensive treatment unit care
- Nutritional support
- Hyperbaric oxygen

Surgery in NSTI

- Early and aggressive surgical exploration and debridement
- This should be done in the first 24 hours of symptoms
 - Surgical mortality 6% (<24hrs), 24% (>24hrs)
- Surgical incisions often extend beyond the areas of induration (the hardened tissue) to remove the damaged blood vessels that are responsible for the induration.
- After the wound debridement, adequate dressings should be applied to prevent exposure of bones, tendons, and cartilage so that such structures do not dry out and to promote wound healing/
- Repeat debridement should be repeated daily until all necrotic tissue has been removed (typically 2-4 times)
- For severe necrotizing infection involving the extremities, amputation may be needed to control the infection
- Skin grafting



Wound care

- Reexploration of the wound is done every 6–48 hours and redebridement may be required until all the necrotic tissue has been removed.
- The use of a vacuum- assisted closure system can accelerate wound contraction and time to closure, but this should not be initiated until the necrosis and infection are controlled and granulation tissue has appeared.
- The exposed area should not be covered with skin grafts before the acute infection has resolved.
- Once the infection has resolved and a healthy granulation tissue appears, wound closure may be accomplished by skin grafts, flap cover, by direct approximation, or with the help of skin regenerative matrices.

Antibacterial therapy

Table 2. Recommended IV Empiric Therapy for Adults		
Type of NSTI	Combination Therapy	Monotherapy
Type I	Piperacillin-tazobactam 3.375 g q6h + clindamycin 600-900 mg q6h + ciprofloxacin 400 mg q12h	Imipenem-cilastin 500-1,000 mg q6h <i>OR</i> meropenem 1 g q8h
Type II	Clindamycin 600-900 mg q6h + penicillin 2-4 million units q4-6h	N/A
Type III	Clindamycin 600-900 mg q6-8h + penicillin 2-4 million units q4-6h <i>OR</i> linezolid 600 mg q12h <i>OR</i> vancomycin 30 mg/kg/day in 2 divided doses	Doxycycline 1 g q12h
<i>N/A: not applicable; NSTI: necrotizing soft-tissue infection. Source: References 1, 3.</i>		

Hyperbaric oxygenation (HBO)

- Can be used as an adjunct to surgical intervention and antibiotics in the treatment of NSTI.
- It ameliorates tissue hypoxia that is induced by microcirculatory thrombosis.
- HBO therapy has been shown to improve wound healing and therefore reduce the number of debridements and amputations required

Intravenous immune globulin (IVIG)

- This is a concentrated pooled product that primarily contains IgG isotypes derived from multiple human donors.
- IVIG has an anti-inflammatory effect and contains broad-spectrum antibodies that enhance bacterial opsonization, neutralize virulence factors and toxins, and inhibit super-antigen-elicited T-cell activation
- Reduced 30-d mortality in streptococcal toxic-septic shock treated with clindamycin: 33.7 to 15.7%.
- In NSTI due to Gr. A Streptococcus reduced 90-day mortality.
- The combination of clindamycin and IVIG is likely efficacious by reducing circulating toxins produced by Gr. A Streptococcus.

Organ support

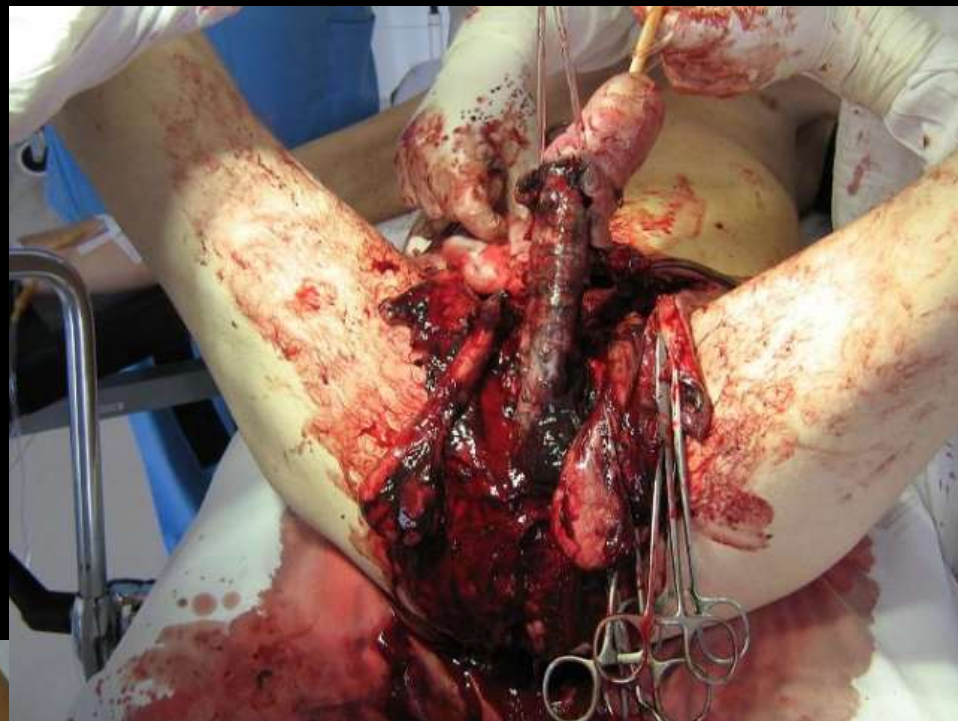
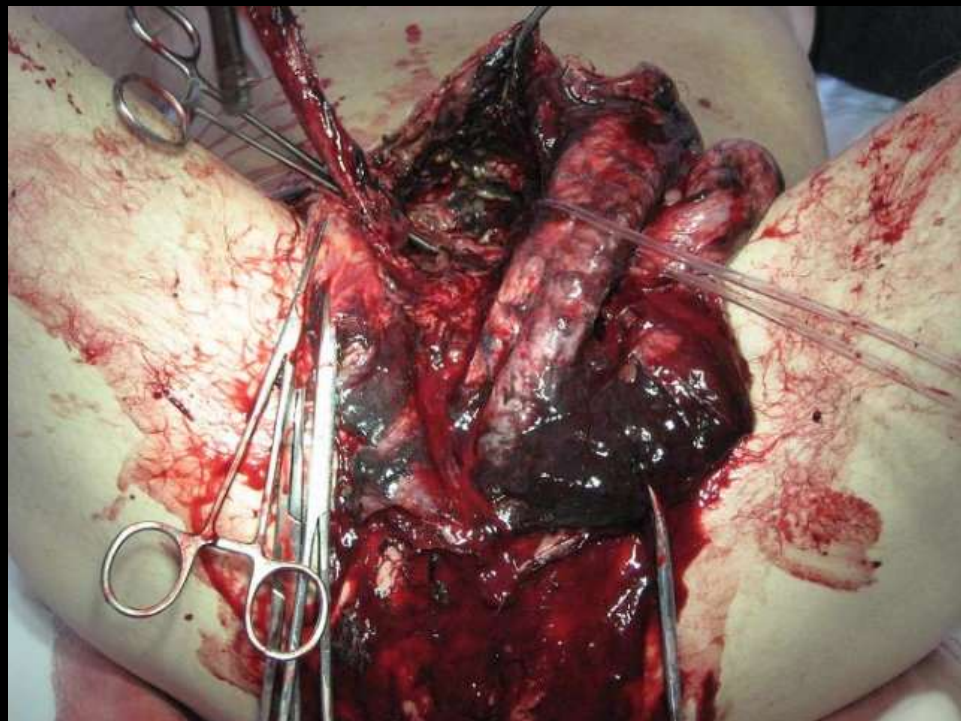
- Patients who are hypotensive after appropriate fluid resuscitation should receive vasopressors and should be monitored in an intensive care unit .
- Extracorporeal membrane oxygenation is required in patients with cardiopulmonary failure .
- Often, the best way to support organ systems is by rapidly controlling the infectious process, which then allows the physiologic environment to return to normal.

Fournier's gangrene

- First described by French venereologist JEAN ALFRED FOURNIER who witnessed a rapidly progressing gangrene of the penis and scrotum of 5 previously healthy young men. - A polymicrobial necrotizing fasciitis (NF) of the perinium, perianal area, or genitals.
- It may involve either men or women.
- Mostly age 30-60, although all ages have been reported

Fournier Gangrene







A photograph of a surgical site showing a large, open wound. The wound is characterized by dark, necrotic tissue and visible ribs, indicating a severe infection such as gas gangrene. The text "GAS GANGRENE" is overlaid in white capital letters.

GAS GANGRENE

Gas gangrene

- It is a rapidly progressive, potentially fatal condition characterized by widespread necrosis of the muscles and subsequent soft-tissue destruction.
- This is a dreaded consequence of inadequately treated missile wounds, crushing injuries and high-voltage electrical injuries.

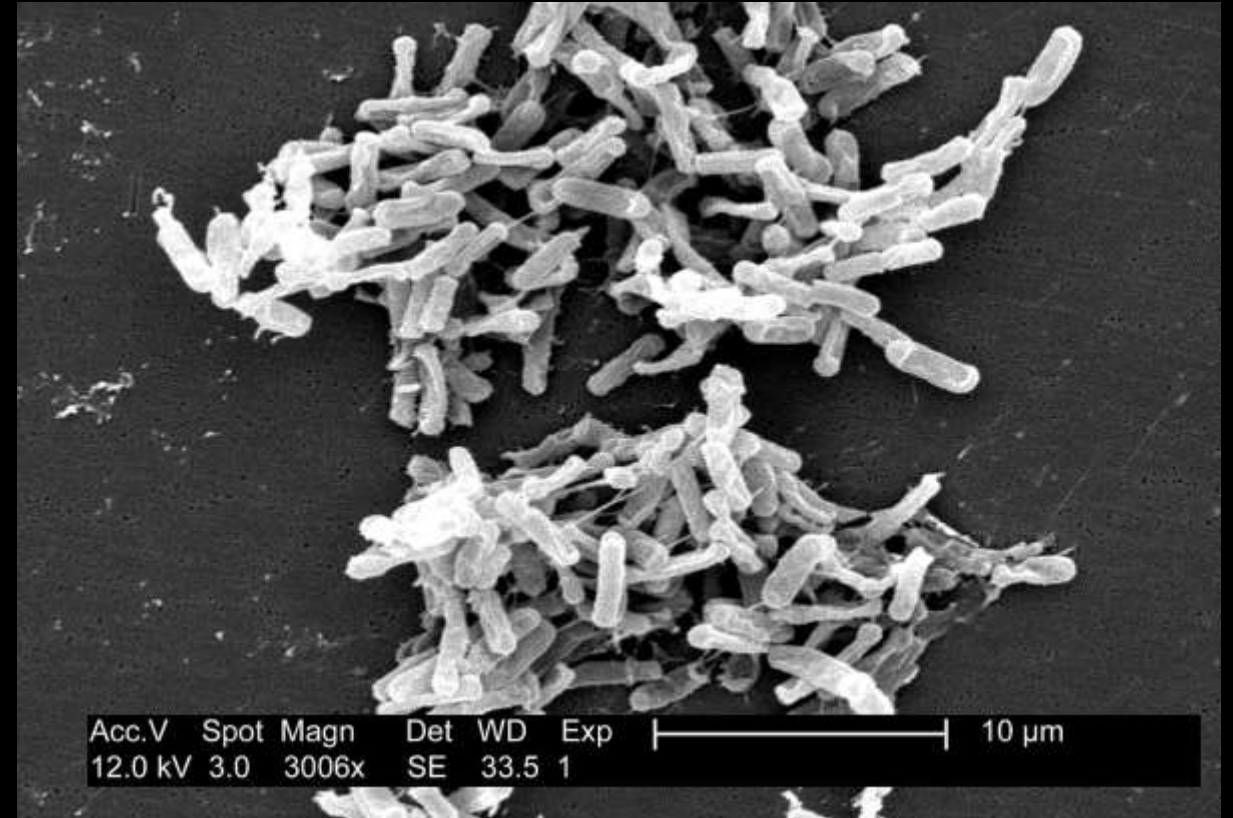
Causative agent

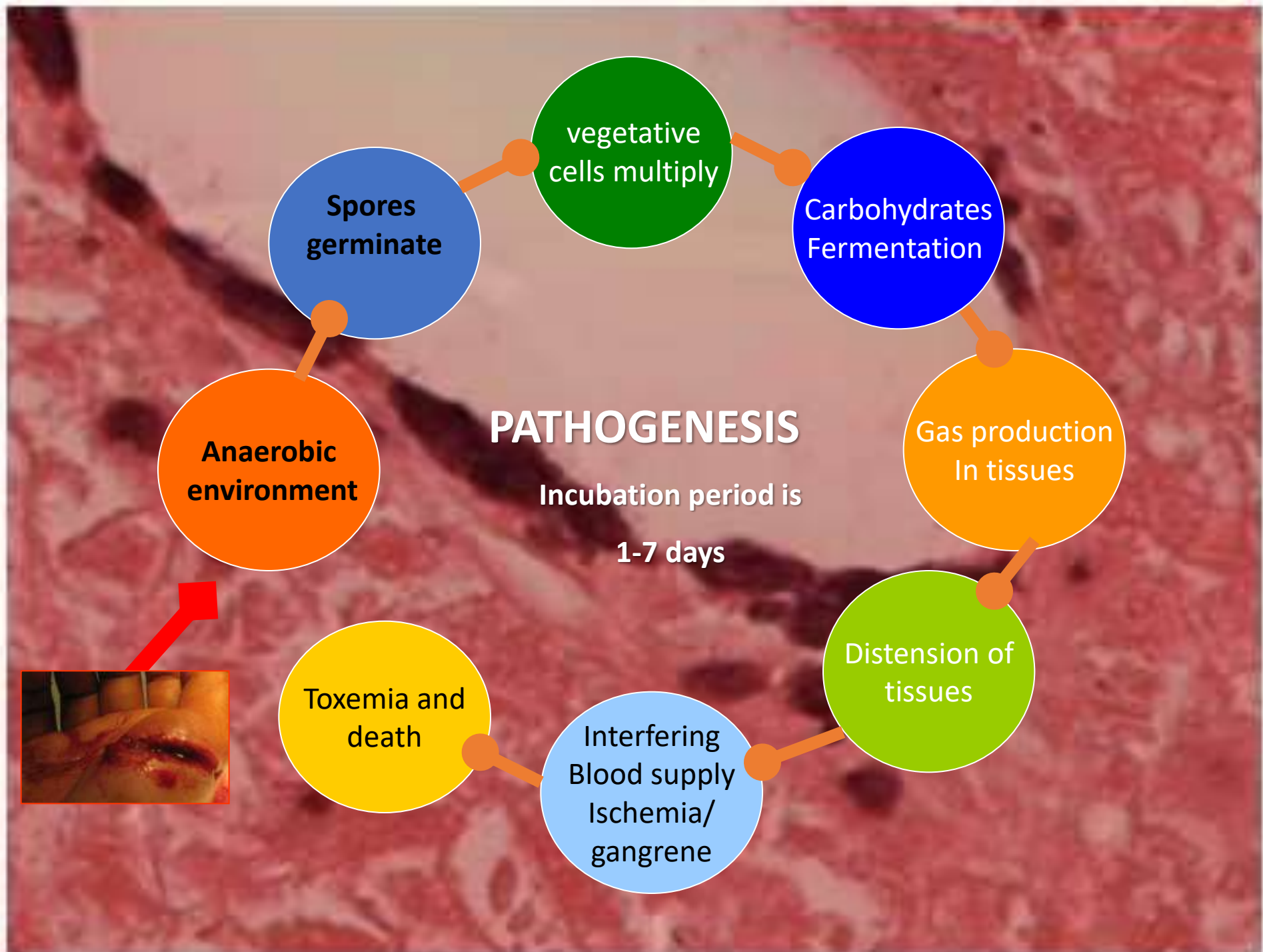
- *Clostridium perfringens* 44-50%
- *Clostridium oedematiens* 15-50%
- *Clostridium septicum* 10-30%
- *Clostridium histolyticum* 2-6%



Clostridium

- They are present in the soil and have also been isolated from the human gastrointestinal tract and female genital tract.
- Non-clostridial gas-producing organisms such as coliforms have also been isolated in 60–85% of cases of gas gangrene.

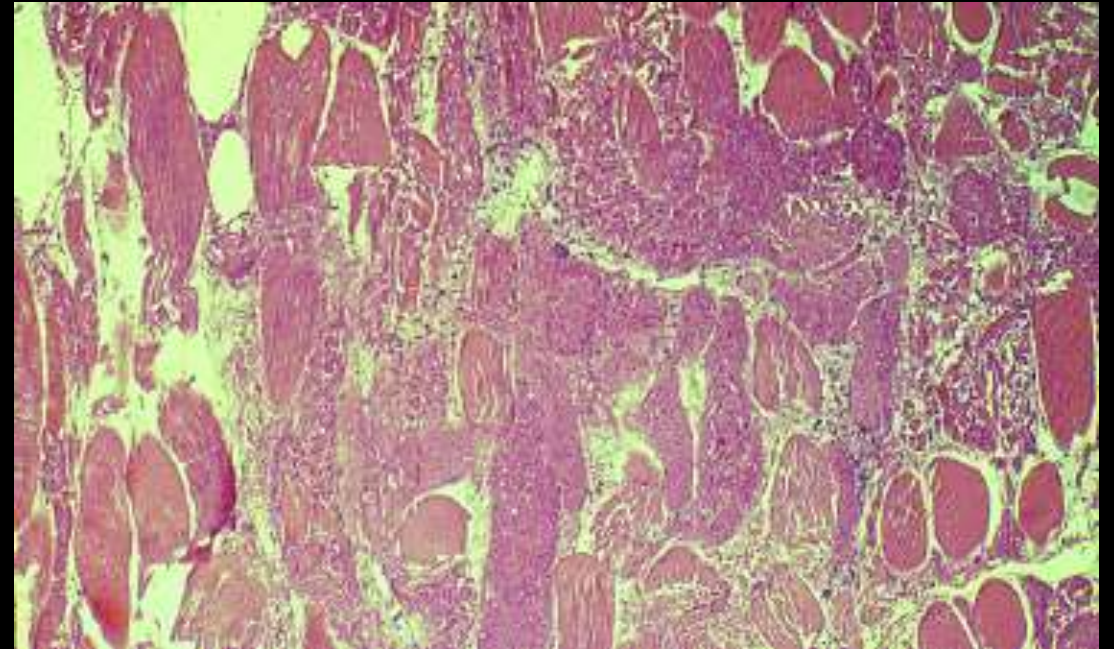




Serosae inflammation



Clostridial cellulitis



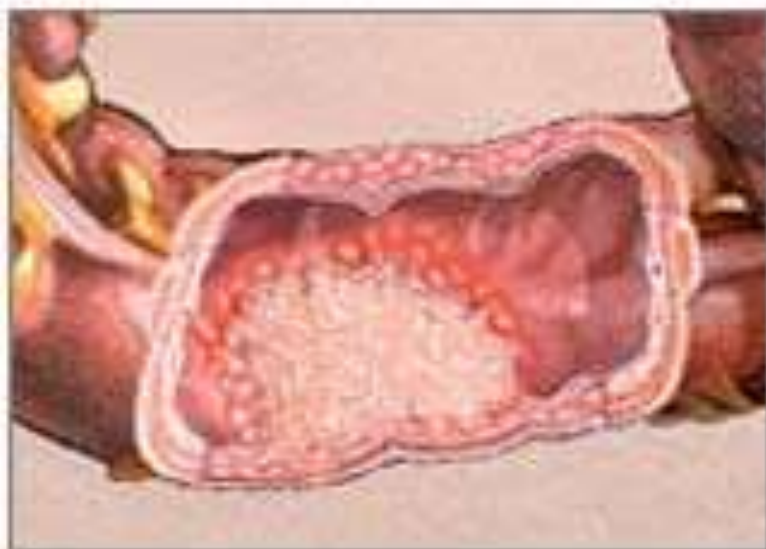
Clostridial myositis

Risk factors

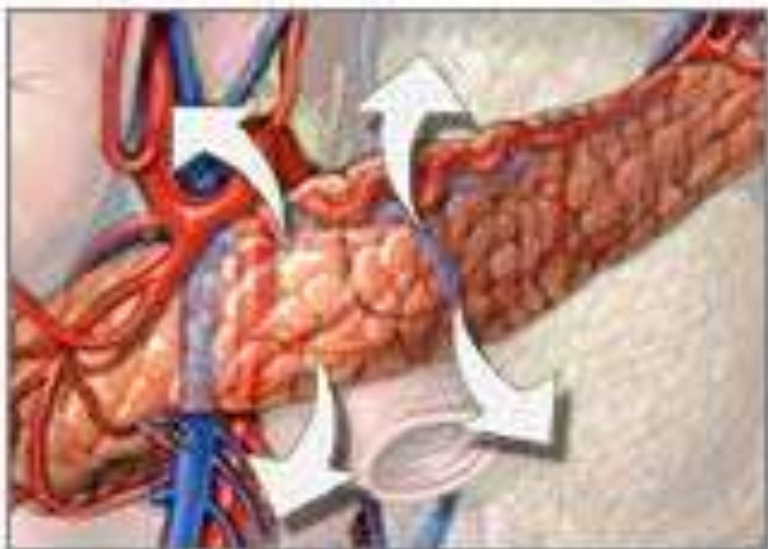
- Big amount of necrotic tissues
- Extensive injuries of muscles and bones
- Deep wound canal
- Wound cavity without connection with environment
- Tissue ischemia (injury of large vessels, arterial tourniquet)



Atherosclerosis



Colon cancer



Diabetes

Patients with these
diseases are more
prone to developing
gas gangrene

Clinical signs

- Pronounced edema without tissue hyperemia
- Local hypothermia
- Intense spreading pain
- Signs of gas production (crepitation, cork champagne symptom, spatula, razor blade symptoms)
- Skin Changes:
 - Tension of the skin with the formation of blisters (white face)
 - Spots of cyanotic and bronze color (blue and bronze erysipelas)
- Muddy non-purulent exudate with an unpleasant odor, hemorrhagic impurities
- Necrosis of tissues - muscles of the form of boiled meat with the imbibition of the products of decay and exudate



Crepitation in tissues,
sickly sweet odor discharge,
rapidly progressing necrosis,
fever, hemolysis, toxemia,
shock, renal failure, and death

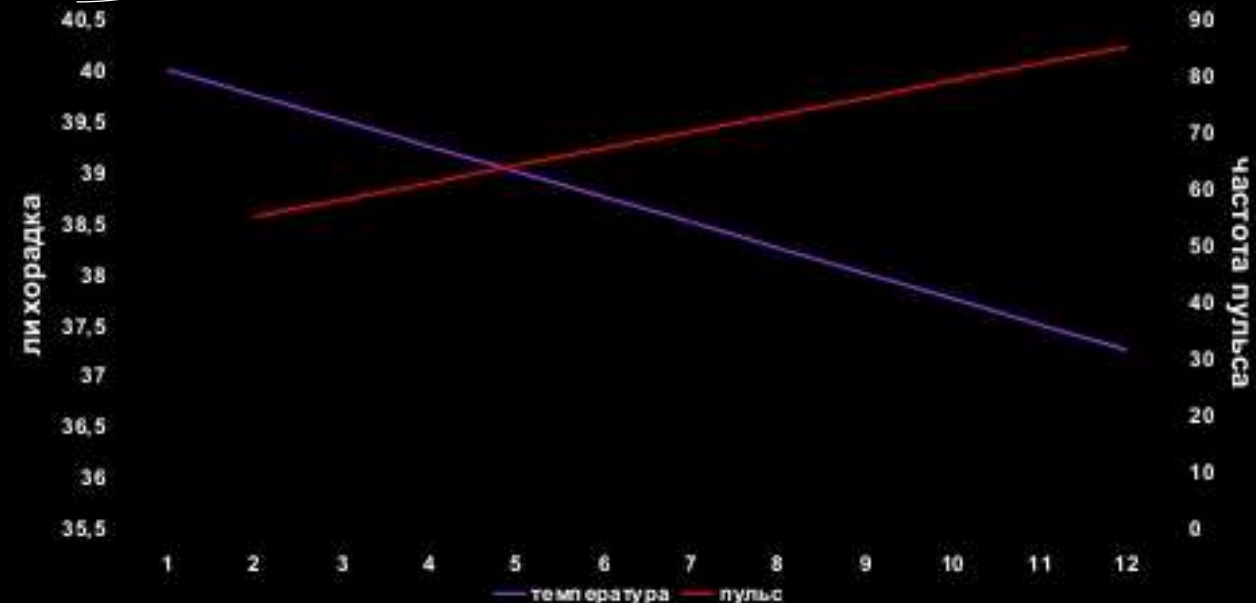


Clinical signs

- Euphoria, turning into apathy
- Tachycardia (more than 100 per min)
- Subfebrile condition (rarely hyperthermia more than 40 ° C)
- Hypotension
- Tachypnoea (more than 20 per minute)
- Multiple organ dysfunction

Toxic scissors

симптом ножниц - "Чертов крест"



Diagnosis

- Local hypothermia (in contrast to purulent inflammation)
- Signs of gas formation (R-graphy, ultrasound)
- Laboratory: leukocytosis more than 15,000 with a shift to the left, an increase in ESR, signs of myonecrosis (increase in CPK, creatinine, urea, potassium)
- Wounds-prints of the wound surface, stained by Gram
- Gas-liquid chromatography (volatile fatty acids)



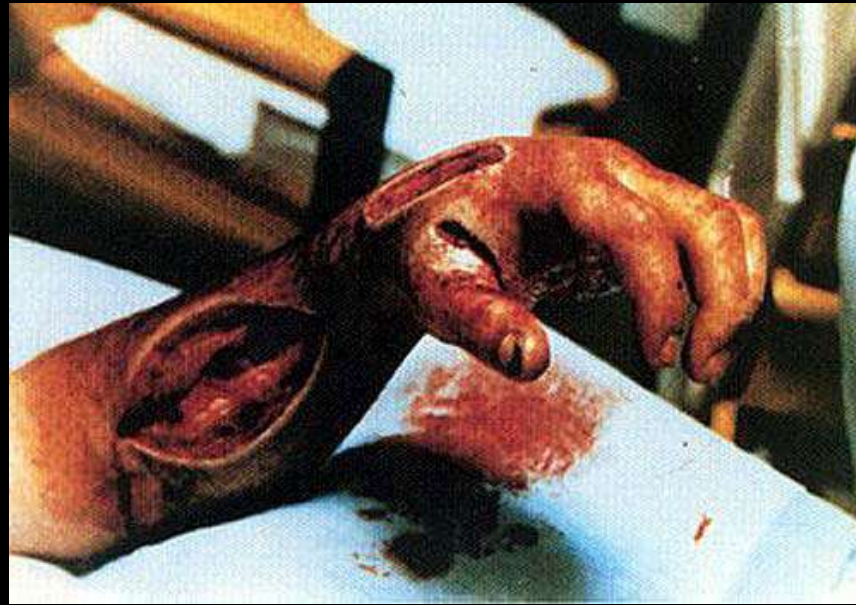
Lab. Investigations

Culture and sensitivity
Storming fermentation
Lecithinase test

Treatment

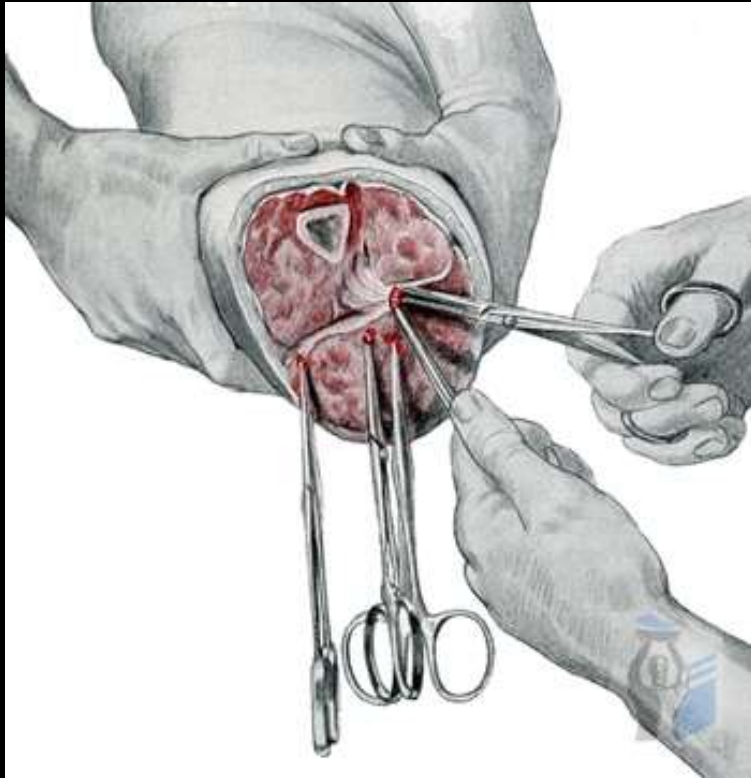
- Lamp-cuts (trouser stripe incision)
- Necrectomy
- Amputation:
 - Threat of transition to the trunk
 - Total defeat of limb
 - Injury of the main vessels
 - Severe limb injury
- Anti-gangrenouse serum 150,000 IU
- Metronidazole, clindamycin, metronidazole, tinidazole
- Infusion and symptomatic therapy
- HBO

Lamp-cuts (trouser stripe incision)



Amputation

- Guillotine method without shelter stump, if necessary, supplemented with lamp-cut



Treatment

- Patients should be admitted to ICU and treated aggressively with careful monitoring.
- The role of HBO is not as clear as in necrotising fasciitis but it is recommended in severe cases if the facilities are available.
 - Increases the normal oxygen saturation in the infected wounds by 1000-fold leading to
 - Bacteriocidal effect,
 - Improves neutrophil function,
 - Enhanced wound healing

Prophylaxis

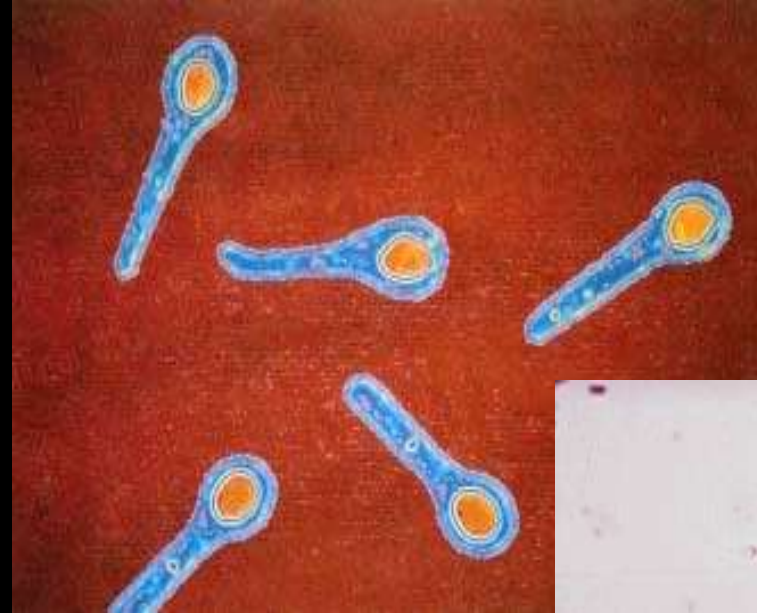
- Precise surgical debridement of the wound
- Avoidance of primary sutures at the risk of anaerobic infection
- Specific prevention (military, land surveyors):
 - Sixantoxin - botulinum toxoid A, B, E, tetanus toxoid, Cl.perfringens, Cl.novyi toxoid



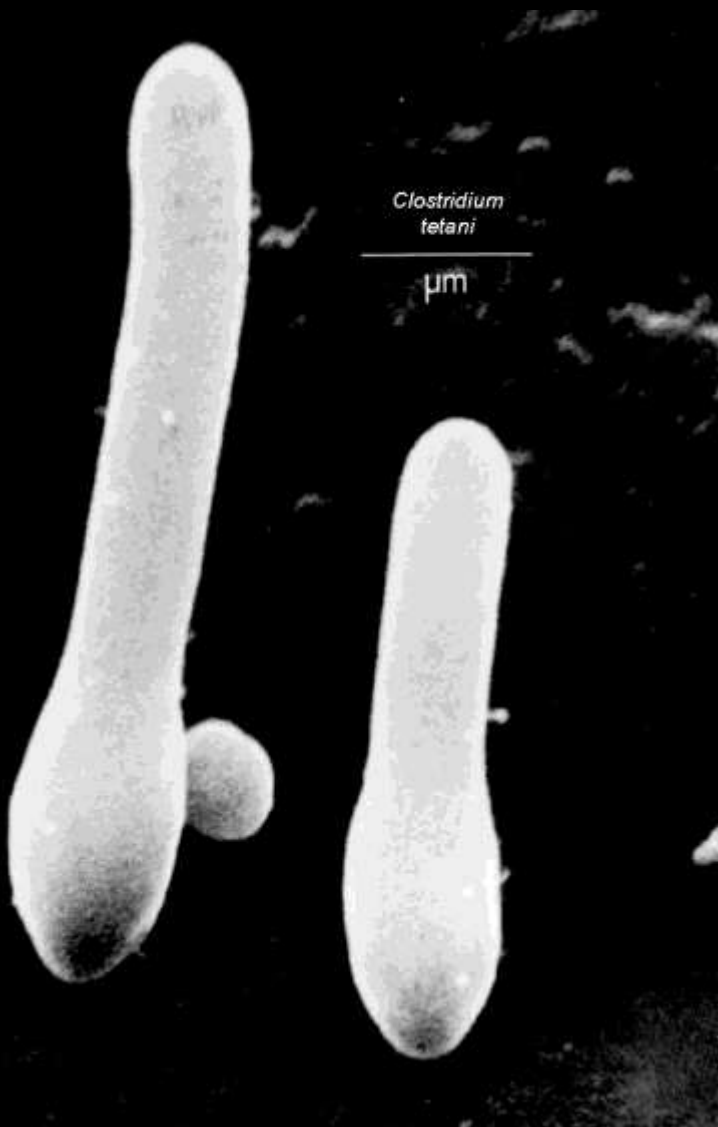
Tetanus

Tetanus

- An infectious disease caused by contamination of wounds from the bacteria *Clostridium tetani*, or the spores they produce that live in the soil, and animal feces
- Greek words - “tetanos and teinein”, meaning rigid and stretched, which describe the condition of the muscles affected by the toxin, tetanospasmin, produced by *Clostridium tetani*



Sporulated



Vegetative



Causes

- Tetanus spores are found throughout the environment, usually in soil, dust, and animal waste.
- Tetanus is acquired through contact with the environment; it is not transmitted from person to person.



Cause

- The usual locations for the bacteria to enter the body:
 - Puncture wounds (such as those caused by rusty nails, splinters, or insect bites.)
 - Burns, any break in the skin, and IV drug access sites are also potential entryways for the bacteria.



Route of Entry

- Apparently trivial injuries
- Animal bites/human bites
- Open fractures
- Burns
- Gangrene
- In neonates usually via infected umbilical stumps
- Abscess
- Parenteral drug abuse

Epidemiology

- Tetanus is an international health problem, as spores are ubiquitous.
- The disease occurs almost exclusively in persons who are unvaccinated or inadequately immunized.
- Tetanus occurs worldwide but is more common in hot, damp climates with soil rich in organic matter.
- More common in developing and under developing countries.
- More prevalent in industrial establishment, where agricultures workers are employed.
- Tetanus neonatorum is common due to lack of MCH care.

Incubation Period

- Varies from 1 day to several months.
- It is defined as the time from injury to the first symptom.

Period of onset

- It is the time from first symptoms to the reflex spasm.
- An incubation period of <4 days,
or
- A period of onset <48 hours is associated with the development of severe tetanus.

1. *C. tetani* enters body from through wound.

2. Stays in sporulated form until anaerobic conditions are presented.

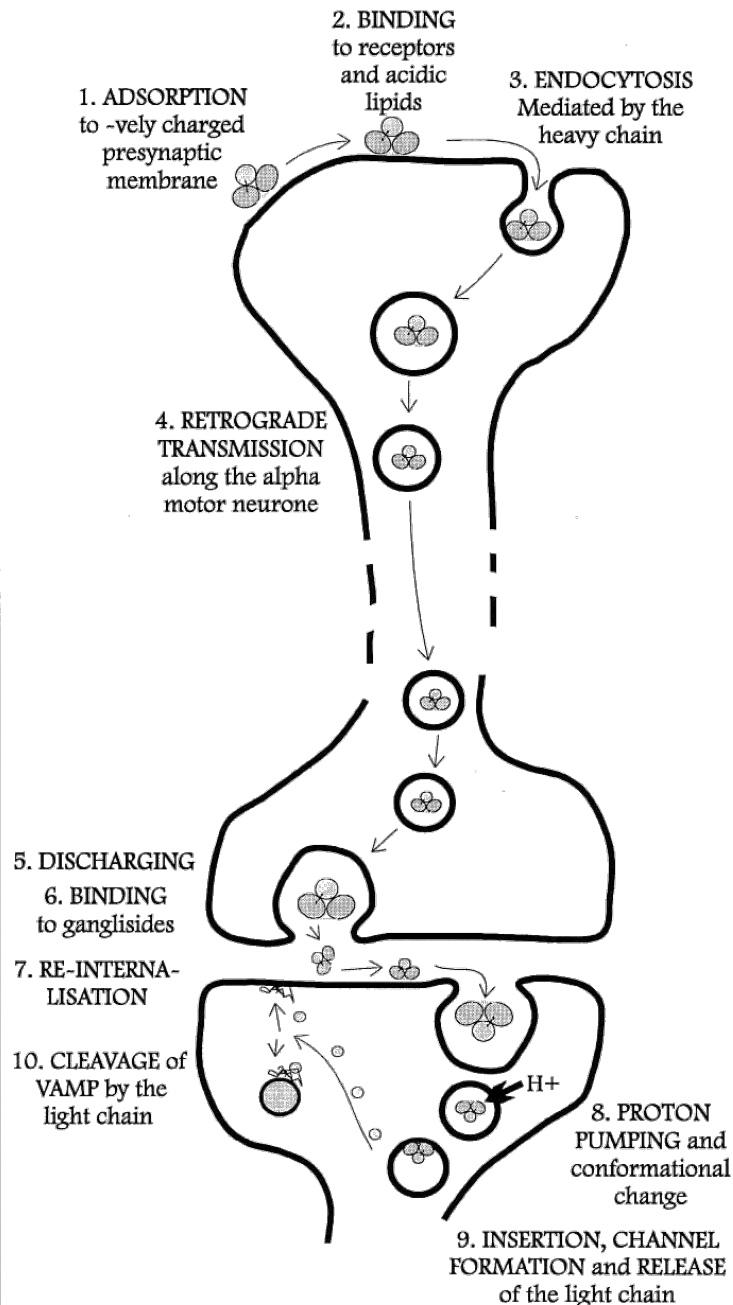
3. Germinates under anaerobic conditions and begins to multiply and produce tetanospasmin.

4. Tetanospasmin spreads using blood and lymphatic system, and binds to motor neurons.

5. Travels along the axons to the spinal cord.

6. Binds to sites responsible for inhibiting skeletal muscle contraction.

MECHANISM OF ACTION



Pathogenesis

- Initially binds to peripheral nerve terminals
- Transported within the axon and across synaptic junctions until it reaches the central nervous system.
- Becomes rapidly fixed to gangliosides at the presynaptic inhibitory motor nerve endings, then taken up into the axon by endocytosis.
- Fix and cleave synaptobrevin, the protein responsible for the exocytosis of vesicles containing glycine and GABA
- Irreversibly damages nerve endings, and nerve function can be restored only through the formation of new terminals and synapses

How the toxin acts?

- Blocks the release of inhibitory neurotransmitters (glycine and gamma-amino butyric acid) across the synaptic cleft, which is required to check the nervous impulse.
- If nervous impulses cannot be checked by normal inhibitory mechanisms, it leads to unopposed muscular contraction and spasms that are characteristic of tetanus.

Tetanus prone wound

- A wound sustained more than 6 hr before surgical treatment.
- A wound sustained at any interval after injury which is puncture type or shows much devitalised tissue or is septic or is contaminated with soil or manure.

Clinical features

- Risus sardonicus: Contraction of the muscles at the angle of mouth and frontalis
- Trismus (Lock Jaw): Spasm of Masseter muscles.
- Opisthotonus: Spasm of extensor of the neck, back and legs to form a backward curvature.
- Muscle spasticity
- Prolonged muscular action causes sudden, powerful, and painful contractions of muscle groups. This is called tetany. These episodes can cause fractures and muscle tears.
- If respiratory muscle is involved – apnoea.



Signs and Symptoms

Other symptoms include:

- Drooling
- Excessive sweating
- Fever
- Hand or foot spasms
- Irritability
- Swallowing difficulty
- Uncontrolled urination or defecation

Diagnosis

- There are currently no blood tests that can be used to diagnose tetanus.
- Diagnosis is done clinically.

Differential Diagnosis

- Masseter muscle spasm due to dental abscess
- Dystonic reaction to phenothiazine
- Rabies
- Hysteria

Principle of Treatment

1. Neutralization of unbound toxin with Human tetanus immunoglobulin

2. Prevention of further toxin production by

- Wound debridement
- Antibiotics (Metronidazole)

3. Control of spasm

- Nursing in quiet environment
- Avoid unnecessary stimuli
- Protecting the airway

4. Supportive care

- Adequate hydration
- Nutrition
- Treatment of secondary infection
- Prevention of bed sores.

Prevention

- Tetanus is completely preventable by active tetanus immunization.
- Immunization is thought to provide protection for 10 years.
- Begins in infancy with the DTP series of shots. The DTP vaccine is a "3-in-1" vaccine that protects against diphtheria, pertussis, and tetanus.



Prevention

- Can be achieved by active immunization by tetanus toxoid (5 doses).
- Older teenagers and adults who have sustained injuries, especially puncture-type wounds, should receive booster immunization for tetanus if more than 5 years have passed since the last booster.
- Clinical tetanus does not produce immunity to further attacks. Therefore, even after recovery patients must receive a full course of tetanus toxoid.
- Active and passive immunization:
 - Tetanus toxoid to renew the immune response
 - Tetanus serum to protect from possible complications