Gangrene: A Review on Pathogenesis and Its Impact on Public Health

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***Abstract*—Gangrene is a severe and potentially fatal condition characterized by the death of body tissue resulting from infection, ischemia, or trauma. It poses a significant threat to global public health, particularly among populations with diabetes, peripheral arterial disease, and poor socioeconomic conditions. This review provides a comprehensive overview of the pathogenesis, types, clinical manifestations, epidemiology, and management of gangrene, including dry, wet, gas, Fournier's, and internal forms. The underlying mechanisms involve impaired blood circulation, bacterial infection—especially by Clostridium perfringens—and systemic inflammatory responses leading to tissue necrosis. Early diagnosis, surgical debridement, fluid resuscitation, and broad-spectrum antibiotic therapy remain the cornerstones of management. Emerging treatment modalities such as hyperbaric oxygen therapy, nanotechnology, and stem cell therapy show promise in enhancing wound healing and tissue regeneration. Preventive strategies, including blood sugar control, smoking cessation, and proper wound care, are critical for reducing disease burden. A multidisciplinary and proactive approach is essential to improve prognosis, minimize amputations, and lower mortality rates associated with gangrene.**

Index Terms*: *Gangrene; Pathogenesis; Tissue necrosis; Clostridium perfringens; Public health; Diabetes; Peripheral artery disease; Hyperbaric oxygen therapy; Surgical debridement; Wound management; Infection control; Prevention.

I.INTRODUCTION

Gangrene is a serious medical condition that occurs when body tissues die due to loss of blood supply or severe infection. It most commonly affects the extremities, such as fingers, toes, hands, and feet, but can also involve internal organs like the intestines or gallbladder. If not treated promptly, gangrene can spread rapidly and become life-threatening. The condition is generally classified into different types based on its cause and site of occurrence, including dry gangrene, wet gangrene, and gas gangrene, each with distinct features and treatment approaches [1-3]

- Dry gangrene: Dry gangrene occurs when blood supply to a body part is blocked, often due to diabetes, peripheral artery disease, or atherosclerosis. The tissue becomes dry, shriveled, and dark (black or brown) without infection, and it is more common in older people with poor circulation.
- Wet gangrene: Wet gangrene occurs when poor blood flow is combined with bacterial infection. The area becomes swollen, moist, red or purple, with blisters and foul odor. It spreads rapidly and can cause septic shock, making it a life-threatening condition.
- Gas gangrene: Gas gangrene is a severe infection caused by *Clostridium* bacteria that produce gas and toxins, leading to rapid muscle and tissue destruction. The area becomes swollen, painful, pale or grey, with gas bubbles causing a crackling sound. It spreads quickly and can lead to septic shock.
- Fournier's gangrene: Fournier's gangrene is a rare, severe infection of the genital and anal region. It causes swelling, severe pain, and dark (black or blue) tissue and can quickly lead to septic shock. Immediate medical treatment is required.

- Internal gangrene: Internal gangrene occurs when blood supply to an internal organ (such as the intestines, gallbladder, or appendix) is blocked, causing tissue death. It presents with severe abdominal pain, fever, nausea, vomiting, or blood in stool and requires urgent diagnosis and surgery.

II.SYMPTOMS

The affected area may show redness, swelling, and severe pain or numbness. If infection is present, symptoms may also include fever, foul-smelling discharge, blisters, and general weakness. [4-6].

- Skin color alterations (from red to brown and eventually to purple or blackish green)
- Crepitus when the skin is palpated
- Tachypnoea and tachycardia
- Hyperthermia and diaphoresis
- Anxiety
- Pyrexia
- Anorexia
- Intense pain
- Firm and tender skin
- Ulcers and blisters that discharge bloody or malodorous pus

III.AETIOLOGY OF GANGRENE

Blood is essential for maintaining health, as it delivers oxygen and nutrients to tissues. When blood flow is restricted, cells begin to die, infections can develop, and gangrene may occur. Conditions that impair circulation, such as diabetes, atherosclerosis, and peripheral artery disease, increase the risk of developing gangrene [7-10].

- ✓ ATHEROSCLEROSIS: Atherosclerosis is a condition where fatty deposits (plaques) build up in the walls of arteries, causing them to thicken and harden. This reduces blood flow and can lead to clot formation, increasing the risk of serious problems like heart attack or stroke.
- ✓ DIABETES: Diabetes mellitus is a disorder in which the body cannot produce or properly use insulin, leading to high blood sugar levels. It can damage blood vessels, eyes, kidneys, nerves, and heart, and may cause complications like heart disease, stroke, kidney failure, blindness, and limb amputation.
- ✓ PERIPHERAL ARTERIAL DISEASE: Peripheral artery disease (PAD) is a common complication of atherosclerosis, involving partial or complete blockage of arteries in the lower limbs. Inflammation plays a key role in its development, similar to coronary artery disease. Major risk factors, including smoking and diabetes, increase oxidative stress, which activates inflammatory pathways and contributes to the progression of PAD.
- ✓ PERIPHERAL ARTERIAL EMBOLISM: Blue thrombophlebitis, marked by severe pain and arteriosa's, can closely mimic the symptoms of an embolic blockage, making accurate diagnosis essential for proper treatment.
- ✓ TRAUMA: Coagulation is important in inflammation, but excessive activation can lead to systemic inflammatory response syndrome and sepsis. Burn injuries can cause different types of shock due to fluid loss. Frostbite occurs from extreme cold, damaging tissues through ice formation and cell injury; rewarming may worsen damage and can lead to tissue death or amputation.
- ✓ RAYNAUDS PHENOMENON: Raynaud's syndrome causes a triphasic color change in the fingers or toes—white (ischemia), blue (lack of oxygen), and red (reperfusion). Primary type is mild and harmless, while secondary type is severe, painful, and may lead to ulcers, tissue death, infection, or even amputation.
- ✓ BUERGERS DISEASE Buerger's disease is a condition causing inflammation and clotting in small and medium blood vessels of the hands and feet. It leads to reduced blood flow, causing pain, cold skin, and nail changes, and in severe cases may progress to gangrene and require amputation.
- ✓ HISTORY OF GANGRENE

  Gangrene is the death of body tissues caused by lack of blood flow or infection, with a history dating back to ancient Greek and Roman medicine. Over time, understanding and treatment evolved from medieval remedies like hot oil and vinegar to surgical techniques by Ambroise Paré and later classifications of dry, wet, and gas gangrene by physicians such as John Hunter and Pierre-François Blandin. In the modern era, antibiotics, vascular surgery, and hyperbaric oxygen therapy have improved management, yet gangrene remains a serious condition that can lead to amputation or death. It is triggered by factors like diabetes, peripheral artery disease, trauma, infection, and smoking and continues to be a significant focus in medical research and clinical care [11].

EPIDEMIOLOGY

- DRY GANGRENE: Dry gangrene occurs when blood supply to a body part (usually hands or feet) is cut off, leading to tissue death. The skin becomes dry, shriveled, and black without infection or foul odor. It is common in people with diabetes, smoking, or peripheral artery disease, and may lead to amputation if not treated early. [12].

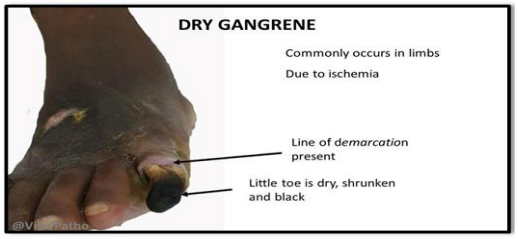

Figure 1: Structure of Dry Gangrene

- WET GANGRENE: Wet gangrene is a severe, fast-spreading tissue infection caused by bacteria, leading to rapid tissue death and gas formation. It usually affects the limbs and causes swelling, pain, redness, foul odor, and blackened skin. It is life-threatening and requires urgent treatment with antibiotics, surgery, and sometimes amputation. [13].

Figure 2: Structure of Wet Gangrene

- GAS GANGRENE: Gas gangrene is a severe, life-threatening infection caused by anaerobic bacteria (commonly *Clostridium perfringens*) that enter contaminated wounds. It causes rapid tissue death, gas formation, and systemic toxicity, and can lead to shock or death if not treated quickly. Urgent treatment with antibiotics, surgery, and proper wound care is essential. [14].

Figure 3: Structure of Gas Gangrene

- FOURNIER GANGRENE: Fournier gangrene is a rare but life-threatening infection of the genital and perineal area, usually seen in men with diabetes or weak immunity. It spreads rapidly, causing tissue death, gas formation, and sepsis. Immediate treatment with antibiotics and urgent surgical removal of dead tissue is essential. [15].

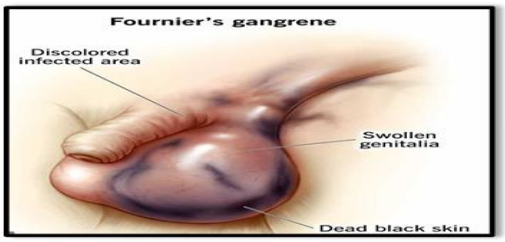

Figure 4: Structure of Fournier Gangrene

PATHOLOGY

- ✓ DRY GANGRENE: Dry gangrene occurs when blood flow to a body part (usually hands or feet) is blocked, causing tissue death. The skin becomes dry, shriveled, and black with clear edges and no infection or odor. It is common in people with diabetes, atherosclerosis, or smoking history and may lead to amputation if untreated.

Figure 5: Dry gangrene

Two cases show the typical appearance of dry gangrene. One shows a clearly defined dead area in a foot due to atherosclerosis. The other shows dry, blackened toes in a diabetic patient, with signs of progression to wet gangrene such as redness and blisters. [16-18].

- ✓ WET GANGRENE: Wet gangrene is an infected form of gangrene where dead tissue becomes infected and spreads quickly. The skin becomes swollen, soft, black, and may form blisters with a foul smell and gas under the skin. It is more severe than dry gangrene and often requires urgent treatment or amputation.

Figure 6: Wet gangrene

Two cases of wet gangrene show infected, irregular ulcers on the foot and toe. Microscopic

examination reveals gram-positive bacteria in the dead tissue, confirming the role of infection in wet gangrene. [19-21].

✓ GAS GANGRENE:

- TRAUMATIC GAS GANGRENE: Gas gangrene is a severe form of wet gangrene caused by *Clostridium perfringens* entering through wounds. It causes rapid tissue death, gas formation with crackling, foul odor, and severe muscle damage. It is a medical emergency with a poor prognosis and needs urgent treatment.

Figure 7: Traumatic gas gangrene

Gas gangrene of the thigh causes swelling due to gas in the tissues, producing a crackling sound on touch. It requires urgent surgical removal of the dead tissue (debridement) [22-24].

- NONTRAUMATIC GAS GANGRENE: *Clostridium perfringens*, normally found in the intestine, can cause non-traumatic gas gangrene in internal organs like the pancreas. In reported diabetic patients, it caused gas accumulation, severe necrotizing pancreatitis, and gas-filled spaces in organs, with Gram-positive rods seen in necrotic tissue.

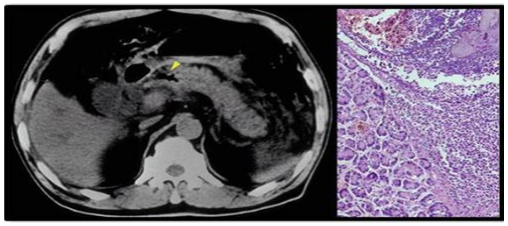

Figure 8: Acute hemorrhagic and necrotizing pancreatitis caused by clostridia (CT scan and H&E)

Clostridial infection can cause acute hemorrhagic and necrotizing pancreatitis, with gas seen in the pancreas on CT scan. Microscopy shows heavy neutrophil infiltration, indicating severe acute inflammation [25-27].

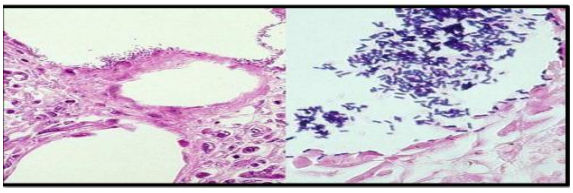

Figure 9: Acute necrotizing pancreatitis with c. perfringens infection (H&E and gram)

In acute necrotizing pancreatitis caused by *C. perfringens*, the dead pancreatic tissue contains gas bubbles with little inflammation. Gram staining shows irregular Gram-positive rods with partially visible spores in the necrotic areas.

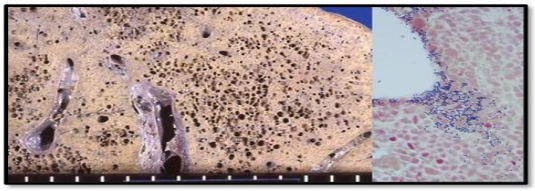

Figure 10: Gas gangrene of the liver (gross and gram)

Gas gangrene of the liver shows gas-filled spaces giving a spongy appearance, with ischemic liver cells and Gram-positive bacteria near the gas bubbles. Clostridial infection can also cause non-traumatic gas gangrene of the colorectum, especially in conditions like rectal cancer, leading to widespread tissue death, sepsis, and shock.

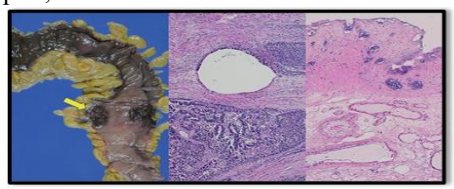

Figure 11: Nontraumatic gas gangrene related to rectal cancer

Rare cases show non-traumatic gas gangrene linked to cancer or mucosal injury. In one patient with rectal cancer, necrotic tumor tissue and colon showed gas formation and rod-shaped bacteria. In another diabetic patient, gastric gas gangrene occurred after tumor resection, with Gram-positive rods and gas-filled liver areas, confirming clostridial infection. [28-32].

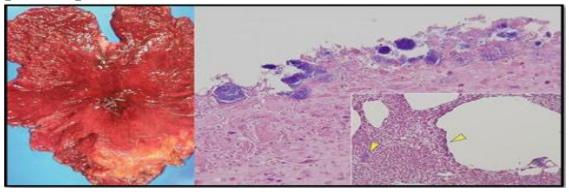

Figure 12: Gas gangrene of the stomach in 65-year-old diabetic male patient

Gas gangrene of the stomach can occur after procedures or mucosal injury, especially in diabetics. The stomach becomes swollen and infected, and gas may spread to the liver. Different *Clostridium* species can cause non-traumatic gas gangrene in various organs, showing gas-filled, foamy tissues and Gram-positive rods with spores on microscopy.
[33-35]

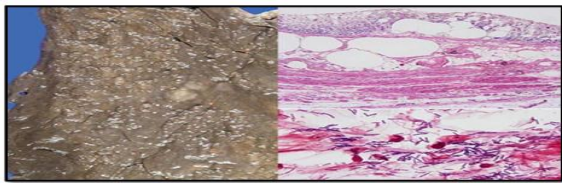

Figure 13: Gas gangrene of the stomach caused by clostridium butyricum

Gas gangrene of the stomach caused by *Clostridium butyricum* shows gas bubbles in the gastric wall. Microscopy reveals Gram-positive rods with clear, rugby-ball–shaped spores, consistent with this organism and associated with severe, often fatal infection [36].

- FOURNIER'S GANGRENE: Fournier's gangrene is a severe, rapidly spreading infection of the scrotum and perineum that causes tissue death, swelling, and red-black discoloration. It may produce gas and foul odor and can lead to sepsis. It mainly affects older men, especially those with diabetes or weak immunity, and requires urgent treatment.

Figure 14: Fournier's gangrene

Two cases of Fournier's gangrene show severe, rapidly spreading necrosis of the scrotum extending to nearby areas. The tissue appears black and swollen, and both cases were fatal. Microscopy shows extensive tissue death with mixed bacterial infection (including streptococci and anaerobes), and sometimes secondary fungal infection may occur [37 40].

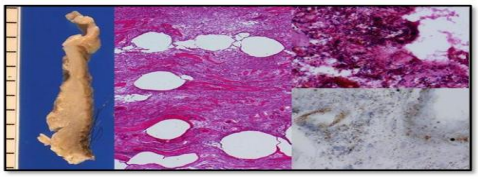

Figure 15: Fournier's gangrene, illustrated through gross examination

Fournier's gangrene shows severe scrotal tissue death with gas formation and mixed bacterial infection, often including streptococci (non-clostridial gas gangrene). It can occur in both males and females, especially in immunocompromised patients, and may be associated with conditions like rectal cancer [41-42].

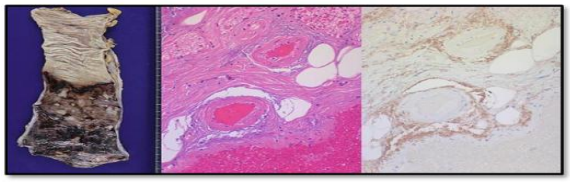

Figure 16: Fatal Fournier's gangrene of the rectum

Fatal Fournier's gangrene of the rectum shows widespread tissue death across the rectal wall. In this case, Gram-negative bacteria (*E. coli*) were identified, indicating severe mixed infection leading to gangrene and death.

III.TREATMENT AND MANAGEMENT

Gangrene can spread quickly (2–3 cm/hour), so early diagnosis and urgent treatment are critical. Management includes blood sugar control, antibiotics, antiplatelet drugs, regular wound care, and follow-up visits. Severe or infected cases (wet gangrene) often require surgical amputation [43-45].

- FLUID RESUSCITATION
  Fluid resuscitation with crystalloids or colloids is used to restore blood volume, improve cardiac output, and maintain organ perfusion. If not done effectively, it can lead to multi-organ failure and death.
- SURGICAL DEBRIDEMENT
  Surgical debridement is the main treatment for gas gangrene. All infected and dead tissue must be urgently removed, often repeatedly, because internal damage is usually more extensive than it appears. Prompt treatment is essential to prevent death.
- BROAD SPECTRUM ANTIBIOTICS
  Broad-spectrum antibiotics are essential early in severe infections (e.g., diabetic foot or gangrene). Common choices include carbapenems or β-lactam/β-lactamase inhibitor combinations, often with clindamycin or metronidazole. Therapy should be adjusted based on culture results, and deep infections usually need both antibiotics and surgical debridement.
- HEMODYNAMIC RESUSCITATION AND PATIENT OPTIMIZATION
  Early fluid resuscitation with balanced crystalloids (e.g., lactated Ringer's) is essential in septic patients. Treatment should be guided by vital signs, urine output, and lactate levels, with continuous monitoring to assess response and improve perfusion.

- AMPUTATION

Amputation is still used today as a life-saving procedure. In many low- and middle-income countries, preventable conditions still lead to amputation, especially in older patients with multiple comorbidities, making it a significant healthcare burden.

IV.PREVENTION

- To prevent gangrene,
- Avoid tobacco usage and external trauma (e.g., frostbite).
- Patients with diabetes should keep sugar levels under control and keep an eye on their feet for any signs of wounds, infection, or redness.
- Patients with diabetic neuropathy (numbness in the arms, legs, fingers, and toes) should do this every day.
- Any wound or burn should be treated right away, especially in diabetics. ϖ Anyone who notices coldness and redness in a specific place (e.g., toes, fingers) should see a doctor promptly.
- Dry gangrene can be avoided if a blood vessel obstruction is detected early. These strategies include timely skin therapy and deep tissue infections/foot ulcers, regional blood supply optimization, fall and stump injury prevention, routine self-foot care, appropriate foot unloading, and blood pressure, cholesterol, and glucose optimization, as well as smoking cessation [46,47].

V.CONCLUSION

Gangrene is a severe condition that requires prompt medical attention to prevent complications. Understanding its causes, types, and treatment options is crucial for effective management. Recent advances in nanotechnology, hyperbaric oxygen therapy, and stem cell therapy offer promising avenues for improving wound healing and tissue regeneration. Early diagnosis, surgical debridement, broad-spectrum antibiotics, and hemodynamic resuscitation are essential components of gangrene management. Preventive measures, such as controlling blood sugar levels and avoiding tobacco use, can help mitigate the risk of gangrene. A multidisciplinary approach is vital for optimizing patient outcomes.

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