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#### **Review Article**

# Gangrene: Early Detection, Emerging Therapies, and The Role of Artificial Intelligence

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### **ABSTRACT**

Gangrene is a serious and life threatening condition in which body tissues die due to poor blood flow, severe infection, or both. It is seen more often in people with diabetes, vascular diseases, or injuries that do not heal properly. This review highlights recent progress in the diagnosis and treatment of gangrene, with a special focus on regenerative therapies and digital health technologies. The article explains common warning signs, risk factors, and how gangrene typically develops. Newer diagnostic tools, such as artificial intelligence-based wound analysis, infrared thermal imaging, and smart wearable sensors, are helping doctors detect changes earlier and monitor wounds more accurately. Although standard treatment including antibiotics, wound care, surgical removal of dead tissue, and hyperbaric oxygen therapy continues to play a major role, modern research is opening exciting new possibilities. Regenerative approaches like stem cell therapy, platelet rich plasma (PRP), growth factor dressings, and nanotechnology-based materials show encouraging results in improving blood flow, speeding up healing, and reducing the chances of amputation. Herbal and plant-based compounds are also being explored for their anti-inflammatory and wound healing effects. Combined with digital tools, AI prediction models, and personalised treatment planning, these innovations may transform how gangrene is managed in the future. Overall, the review suggests that integrating traditional medical care with advanced technologies and regenerative medicine can greatly improve recovery, quality of life, and long-term outcomes for patients with gangrene.

### **INTRODUCTION**

Cell death in the body happens mainly in two ways: apoptosis and necrosis. Apoptosis is a

natural and controlled process that removes damaged or old cells without harming nearby tissues. Necrosis, however, is uncontrolled and happens when cells die due to poor blood flow,

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serious infections, or injuries. This causes tissue damage and inflammation. Gangrene is the visible result of necrosis, occurring when a large area of tissue dies because of reduced blood supply and infection.<sup>1,2</sup>

Gangrene, also called tissue death or mortification, happens when blood cannot reach certain body parts. Without oxygen and nutrients, tissues start to die. It can develop after injuries, infections, or in people with long term conditions like diabetes. If not treated promptly, gangrene can spread, leading to serious infections or even death.<sup>1</sup>

One common cause is peripheral vascular disease (PVD), where blood flow to limbs, especially legs and feet, is reduced due to atherosclerosis (fatty deposits in arteries). Weak tissues are easily infected. Early treatment with antibiotics, wound care, and removal of dead tissue can often save the affected area. Delayed care may require amputation. Gangrene can be dry, wet, or gas gangrene. Dry develops slowly due to poor circulation, wet occurs with infection, and gas spreads rapidly with gas formation in tissues.<sup>3</sup>

Recent advances in AI technology are helping doctors detect gangrene earlier. AI can analyze images of wounds and predict tissue damage faster than traditional methods. New devices using infrared scanning, thermal imaging, and smart sensors can detect poor blood flow before gangrene becomes severe.<sup>3</sup> Additionally, herbal treatments like turmeric, neem, and aloe vera show promise in supporting wound healing and reducing infection. These natural remedies, alongside modern medicine, may improve recovery and prevent complications.

In India, gangrene affects around 5% of the population, mainly between 20 and 40 years, highlighting a major health concern. Combining early detection, AI technology, modern treatment, and supportive herbal care can help doctors manage gangrene more effectively and improve patient outcomes.<sup>2</sup>

#### **MATERIALS AND METHODS:**

A structured literature review was performed in PubMed, Scopus, and Google Scholar databases between 2010 and 2025 using the keywords Gangrene, Ischemia, Necrosis, Regenerative Medicine, Artificial Intelligence, and Wound Healing. Articles were limited to English language human studies, reviews, and clinical trials. Case reports, non-peer reviewed materials, and purely experimental animal studies were excluded. Data were qualitatively synthesised under thematic categories including epidemiology, diagnosis, therapeutic strategies, and technological innovations.

#### EPIDEMIOLOGY AND RISK FACTORS

Gangrene is a dangerous problem that occurs when body tissues die because of a lack of blood flow or an infection.<sup>2</sup> It affects millions of people all over the world and can cause serious illness or even death if not treated in time. The global distribution and risk factors related to gangrene are illustrated in Figure 1. Globally, more than 200 million people have peripheral artery disease (PAD), and about 10% of them develop a severe form called critical limb ischemia, which can lead to gangrene. People with mild PAD or leg pain while walking (known as intermittent claudication) also have a 5–10% chance of developing serious blood flow problems within five years.<sup>4</sup>,<sup>5</sup>

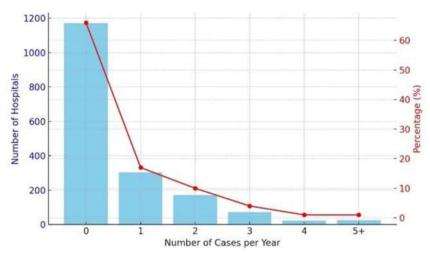


Figure 1: Epidemiology of gangrene across different regions.

The figure presents reconstructed data illustrating the prevalence of gangrene based on global reports. Data and concept adapted from [4].

Clostridial gas gangrene, although rare, is one of the most dangerous types because it spreads fast and has a very high death rate. It often happens after trauma. surgery with contaminated instruments, or sometimes without any clear cause.<sup>2</sup> People with weak immune systems, those who use intravenous drugs, take blood thinners, or have cancer are more likely to develop it. Older adults usually have infections caused by many bacteria together, while younger patients often get it from a single germ like Staphylococcus or Streptococcus.<sup>5</sup>

Environmental exposure also plays a role since *Clostridium* spores are found widely in soil, making injuries in such areas risky. Natural disasters and road accidents can increase cases of gangrene. In Europe, outbreaks among drug users have shown very high death rates.<sup>4</sup> Some medicines, such as SGLT2 inhibitors used for diabetes, have also been linked to rare cases of gangrene.<sup>2</sup>,<sup>4</sup>

In the United States, critical limb ischemia affects about 1% of people over 50 years old. In India, growing cases of diabetes, obesity, and vascular

disease increase the risk, especially in rural areas where early medical care is limited. Poor wound care and late diagnosis make the problem worse.<sup>2</sup>,<sup>5</sup>

# ETIOPATHOGENESIS AND CLINICAL TYPES

# **Aetiology**

Gangrene happens when parts of the body die because they don't get enough blood, get infected, or are injured. Usually, more than one factor is involved. The main cause is poor blood flow, which is common in people with blocked arteries, diabetes, or other blood vessel problems. Infections make it worse because dead tissue lets bacteria and fungi grow easily.6 Certain bacteria, like Clostridium perfringens and C. septicum, can cause fast spreading gas gangrene. Fournier gangrene is a serious infection in the genital and perineal area, often coming from skin or urinary infections. Injuries, burns, cuts, pressure sores, surgeries, or small wounds in diabetics can also lead to gangrene. Rarely, injuries to the penis in children or adults may cause it.2

### Pathophysiology of Gangrene

Gangrene is a fast spreading infection that destroys muscles and soft tissues. Most cases are caused by



bacteria called Clostridium, especially C. perfringens, which is responsible for about 80 to 90% of cases.¹ Other species like C. septicum and C. histolyticum can also cause it. These bacteria are found in soil, dust, and in the gut or genital areas of humans. Not every wound gets infected; it depends on factors like immunity, diabetes, nutrition, and how deep or damaged the wound is.6 The detailed mechanism of infection, toxin release, and tissue damage is illustrated in Figure 2.

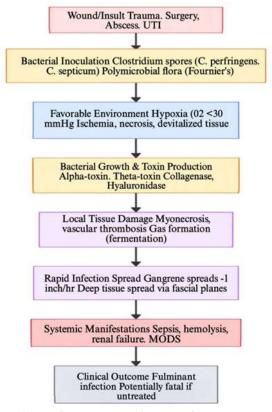


Figure 2: Pathophysiology of gangrene.

This schematic illustrates how reduced blood flow, infection, and tissue necrosis interact to cause gangrene.

In areas with low oxygen, the bacteria grow quickly. C. perfringens releases toxins, such as alpha toxin, that destroy cells, blood vessels, and tissue, while other enzymes help it spread rapidly. Gas is produced during bacterial growth, leading to the characteristic crackling under the skin.

Fournier gangrene affects the genital area and involves multiple bacteria working together, often after a urinary infection, abscess, or minor injury.<sup>2</sup> Non-Clostridial bacteria like E. coli and Klebsiella also contribute to the condition. The toxins can enter the blood, causing sepsis and organ failure.<sup>1</sup>

# **Types of Gangrene**

Gangrene is mainly divided into dry, wet, and gas gangrene, each with different causes and seriousness.

Dry Gangrene happens when blood flow is very poor, usually in fingers or toes. Lack of oxygen makes tissue die and dry out. It often occurs in people with diabetes, blocked arteries, high cholesterol, or long term smoking. The affected area turns dark, shrivelled, and clearly separated from healthy tissue. If it lasts long, the dead part may fall off naturally. Early on, infection is usually low, but it can turn into wet gangrene if bacteria invade.<sup>7</sup> The typical appearance of dry gangrene is shown in Figure 3.



Figure 3: Clinical presentation of gangrene.

(a) Foot A: Dark, dry, and shriveled tissue consistent with dry gangrene. This type of gangrene is often caused by lack of blood supply without bacterial infection, develops slowly, and is common in people with diabetes or peripheral artery disease.

(b) Foot B: Swollen, reddish purple, and black discoloration with blistering and wet appearance, consistent with wet gangrene. This form involves both reduced blood flow and bacterial infection, spreads rapidly, and can be life threatening. Reproduced from Tsutsumi Y.<sup>7</sup> Licensed under Creative Commons Attribution (CC BY 3.0).

Wet Gangrene occurs when dead tissue gets infected by bacteria. It spreads fast, causing swollen, smelly, and discoloured tissue, sometimes with blisters. It is dangerous because bacteria and toxins can enter the blood, leading to sepsis. Diabetes, severe artery disease, and kidney problems increase the risk.<sup>6</sup>,<sup>7</sup> An example of wet gangrene is illustrated in Figure 4.



Figure 4: Clinical presentation of wet gangrene.

- a. Large, irregularly shaped ulcer on the dorsum of the foot with a red base and yellow slough. The surrounding skin appears discoloured and inflamed, consistent with a chronic ulcer such as a venous stasis ulcer.
- b. Ulcer on the toe with a necrotic, dark appearance, characteristic of diabetic gangrene or other severe vascular ulcers. The surrounding skin is discoloured.
- c. Photomicrograph of a tissue sample, used to differentiate between types of skin ulcers; microscopic features help distinguish venous ulcers from conditions such as pyoderma gangrenous or vasculitis. Reproduced from

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Gas Gangrene is a severe type of wet gangrene, mostly caused by Clostridium perfringens. It can follow a wound (traumatic) or come from inside the body in sick or diabetic patients (non-traumatic). Gas forms in tissue, causing crackling under the skin, and it spreads very fast, often needing urgent treatment.<sup>7</sup> The characteristic findings of gas gangrene are depicted in Figure 5.



Figure 5: Clinical features of gas gangrene.

The image highlights tissue necrosis, edema, and crepitus caused by gas producing bacteria. Reproduced from Tsutsumi Y.<sup>7</sup> Licensed under Creative Commons Attribution (CC BY 3.0).

# CLINICAL PRESENTATION AND DIAGNOSIS

Gangrene, including Fournier gangrene, presents with clinical signs that reflect tissue ischemia and infection. The earliest symptom is severe pain, often throbbing or burning, which may worsen with movement, particularly in patients with peripheral vascular disease (PVD). Pallor of the affected area, especially when elevated, indicates reduced blood flow, and the tissue may feel cool to the touch due to impaired perfusion.<sup>4</sup>,<sup>8</sup>

Loss of sensation is common, particularly in patients with diabetic neuropathy, which can mask

pain and delay recognition. As gangrene progresses, ulceration develops, usually over bony prominences, and a gangrenous odour may arise from necrotic tissue colonised by bacteria, signalling advanced infection. Early recognition of

these features is crucial, as prompt surgical intervention can prevent rapid progression and systemic complications.<sup>8</sup> The key clinical and diagnostic findings of gangrene are summarised in Table 1.

Table 1: Conventional and emerging diagnostic methods for gangrene – findings and clinical utility

Sr.	Diagnostic	v		References
No	method			
1	AI-assisted	Detects early tissue changes	Enables earlier and more accurate	3
	Imaging &	in images (photos, infrared,	diagnosis, helps clinicians prioritize	
	Predictive Models	MRI, CT) and predicts	treatment, monitors wound healing	
		progression of gangrene	trends, and reduces reliance on	
			subjective assessment	
2	Laboratory Test	Leukocytosis, elevated	Confirms infection/sepsis: guides	9
		CRP/procalcitonin	management	
3	Ultrasound	Subcutaneous gas. Edema.	Rapid bedside detection of early	9
		Fascial thickening.	necrosis	
		Cobblestoning		
4	X-ray	Subcutaneous gas	Quick detection: absence does not	9
		-	rule out disease	
5	CT scan	Fascial thickening. Fat	Most sensitive and specific:	2
		stranding, gas, abscesses,	assesses extent/source	
		fluid collections		
6	MRI	Soft tissue edema, gas on	High resolution soft tissue imaging:	9
		gradient-echo. T2 high signal	limited by cost/time	
7	Doppler/Ankle	Reduced blood flow. Arterial	Evaluates vascular status, important	9
	brachial index	occlusion	in PVD	

# TREATMENT AND MANAGEMENT OF GANGRENE

Gangrene management requires an integrated approach involving pharmacological, non-pharmacological, and emerging interventions. The primary goals are infection control, restoration of perfusion, tissue preservation, and prevention of systemic complications.

### **Pharmacological Management**

The main goal of drug treatment in gangrene is to stop infection, control pain, improve blood flow, and prevent the disease from spreading to other parts of the body. Starting the right medicines early can help reduce complications and increase the chance of saving the affected tissue.<sup>11</sup>

# 1. Antibiotic Therapy

In cases of wet or gas gangrene, strong antibiotics are started right away to fight both oxygen loving (aerobic) and oxygen free (anaerobic) bacteria. Doctors often begin with broad medicines like piperacillin tazobactam or carbapenems (such as imipenem or meropenem) that work against many types of germs. If the infection is caused by Clostridium perfringens, high doses of penicillin G or clindamycin are used since they can block toxin effects. Once lab tests show the exact bacteria, the antibiotics are changed to match. Using a mix of antibiotics usually gives better results, especially in diabetic or poor blood flow cases where several germs are present.<sup>10</sup>,<sup>11</sup>

#### 2. Pain and Inflammation Control

Gangrene often causes strong pain and swelling because of tissue death and infection. Painkillers like NSAIDs or opioids are used to relieve the pain. But NSAIDs should be used carefully if the person has kidney or blood vessel problems. Sometimes, doctors may give a short course of steroids to reduce inflammation, but these are avoided if the infection is still active.<sup>11</sup>

### 3. Blood Thinners and Blood Flow Medicines

Medicines that help improve blood flow can be helpful, especially in dry gangrene caused by poor circulation. Drugs like heparin or low molecular weight heparin stop blood clots and improve flow in small blood vessels. Vasodilators such as pentoxifylline or alprostadil can also help bring more oxygen to the tissues and reduce pain from poor blood supply, though their success varies among patients.<sup>12</sup>

# 4. Supportive Medicines

Some additional medicines can help recovery. Antioxidants like vitamin E and alpha lipoic acid may support healing, and creams with silver sulfadiazine or iodine help prevent wound infection. Drugs that improve oxygen delivery to tissues can also be used along with hyperbaric oxygen therapy for better healing.<sup>13</sup>

### Non-Pharmacological Management

Non drug treatment plays an important role in managing gangrene and works together with medicines to help recovery. These methods mainly focus on improving blood flow, removing dead tissue, stopping infection, and helping wounds heal properly. A combined effort from surgeons, infection doctors, and wound care teams gives better results for the patient.

### 1. Surgical Treatment

Surgery is important in treating gangrene. The main procedure is called debridement. This involves carefully removing dead or infected tissue to stop the infection from spreading and to allow healthy tissue to grow. In severe cases, amputation might be necessary to save the patient's life and prevent the infection from entering the bloodstream. If gangrene occurs due to poor blood flow, procedures like angioplasty, bypass grafting, or stent insertion can help restore circulation and promote healing. Getting surgical care early greatly lowers the chance of losing a limb.<sup>2</sup>

## 2. Wound Care and Dressings

Proper wound care is very important for healing and preventing new infections. Dressings that keep the wound slightly moist such as hydrogel, hydrocolloid, or honey based dressings can help new skin grow faster. A special method called negative pressure wound therapy (vacuum assisted closure) helps remove extra fluid, reduce swelling, and increase blood flow around the wound. Cleaning the wound regularly and changing dressings under clean conditions are necessary steps for good recovery.<sup>11</sup>

# 3. Hyperbaric Oxygen Therapy (HBOT)

In HBOT, the patient breathes pure oxygen inside a chamber with increased air pressure. This process helps more oxygen reach the affected tissues, slows the growth of infection causing bacteria, and promotes the repair of damaged areas. When used together with surgery and antibiotic treatment, HBOT has been found to improve healing and lower the risk of losing a limb.<sup>2</sup>

# 4. Lifestyle and Supportive Care



Healthy habits play a strong role in both preventing and treating gangrene. People with diabetes should control their blood sugar levels carefully. Quitting smoking, eating a balanced diet, and doing light exercise or physiotherapy can help improve blood flow and speed up healing. Patients should also learn proper foot and skin care and report any small cuts or sores early to avoid serious infection or tissue damage.<sup>14</sup>

### **Novel and Adjunctive Therapies**

Even with progress in standard treatments, gangrene still causes high illness and death rates. New and supportive therapies are being explored to improve healing, stop infection, and repair damaged tissue. These modern approaches integrate ideas from biotechnology, artificial intelligence, and traditional medicine to develop more comprehensive and effective treatment plans.

### 1. Herbal and Natural Remedies

Natural and herbal medicines are getting more attention for their helpful effects in gangrene care. Many plants have antibacterial, antioxidant, and blood flow-improving properties. For example, curcumin (from turmeric) helps reduce swelling and supports wound healing by controlling inflammation and fighting harmful oxygen molecules. Aloe vera helps the skin repair itself by increasing new cell and collagen growth. Neem and turmeric have strong germ killing effects against bacteria that cause gangrene. Plant chemicals like flavonoids and polyphenols also help improve blood flow and oxygen to tissues. While human studies are still limited, early research suggests these natural remedies may help wounds heal faster when used with regular treatment.14

### 2. Regenerative and Cellular Therapies



New treatments in regenerative medicine aim to repair damaged tissues and improve blood supply. Stem cell therapy, especially using mesenchymal stem cells (MSCs), helps grow new blood vessels and supports tissue healing by releasing helpful growth factors like VEGF and TGF-β. Platelet rich plasma (PRP) therapy uses a patient's own platelets, which contain substances that promote healing and help close wounds. These treatments look very promising for diabetic and poor circulation–related gangrene, but more studies and standard treatment methods are still needed before they become common.<sup>15</sup>

# 3. Artificial Intelligence and Digital Health

Artificial intelligence (AI) is playing a growing role in finding and managing gangrene early. Machine learning tools can study wound pictures and tell the difference between healthy and dead tissue with good accuracy. AI can also help doctors choose the right antibiotics, predict how bad an infection might get, and follow the healing process through digital wound tracking. Deep learning systems and mobile health apps can even help diagnose wounds remotely, which is especially useful in areas with fewer medical facilities. Using AI in treatment helps doctors make faster and more accurate decisions.3 An overview of AI and machine learning approaches for gangrene detection and management is illustrated in Figure 6.

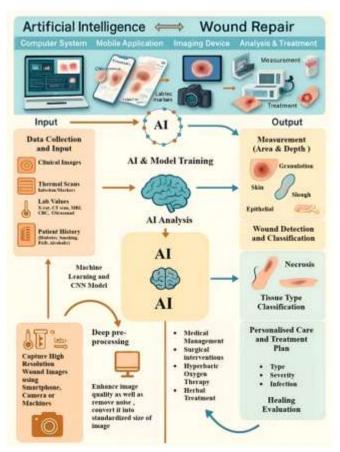


Figure 6: Artificial intelligence—assisted detection of gangrene wounds.

The image illustrates a machine learning model analyzing wound images to detect early tissue necrosis and predict disease progression.

# 4. Nanotechnology and Advanced Biomaterials

Nanotechnology offers new ways to treat gangrene more effectively. Nanoparticle based dressings that include silver, zinc oxide, or herbal extracts can fight bacteria and help new tissue grow at the same time. Hydrogel materials mixed with nanoparticles or growth factors create a healthy environment for wound healing and controlled medicine release. These new materials could make long term wound care safer and more effective by speeding up healing and reducing side effects from medicines.16 A summary of pharmacological, nonpharmacological, and emerging treatment strategies for gangrene is presented in Table 2.

Table1: Conventional and Emerging Treatment Modalities for Gangrene: Mechanisms and Clinical Utility

		Othity							
Pharmacological Management of Gangrene – Mechanisms and Clinical role									
Drug class	Examples	Mechanisms	Clinical role	References					
Antibiotics	Piperacillin	Inhibit Bacterial	First line infection	10,11					
	Tazobactam,	growth and toxin	control						
	Clindamycin	production							
Analgesic/	Ibuprofen,	Pain and inflammation	Symptomatic relief	11					
NSAID's	Morphine	reduction							
Anticoagulant/	Heparin,	Prevent	Adjunct for	12					
Vasodilators	Alprostadil	microcirculation,	ischemic limbs						
	_	prevent clot forming							
Antioxidant/	Vitamin E, Silver	Enhance wound	Supportive therapy	13					
Topical agent	Sulfadiazine	healing, control local							
		infection							
Non-pharmacological management of Gangrene – interventions and clinical utility									
Interventions	Mechanisms		Clinical utility	Reference					
Debridement/	Removal of necrotic tissue and infection		Prevents spread	2					
Amputation	source		and promotes						
			healing						
Revascularization/	Restores arterial blood flow		Enhances tissue	11					
(Bypass, Angioplasty)			oxygenation						

Wound dressing/NPWT	Maintains moisture, removes exudate	Accelerates wound healing	11			
Hyperbaric Oxygen Therapy	Increases oxygen delivery to ischemic tissues	Reduces infection, improves recovery	2			
Lifestyle modification	Glycemic control, smoking cessation, nutrition	Prevents recurrence, enhances outcomes	14			
Emerging and Adjunctive Therapies for Gangrene – Mechanism and Clinical Potential						
Therapy	Mechanism	Clinical benefits	References			
Herbal Compounds	Anti-inflammatory. Antimicrobial, wound	Enhances tissue	14			
(Curcumin. Neem, Aloe vera)	healing	repair				
Stem Cell Therapy / PRP	Promotes angiogenesis and regeneration	Restores perfusion and healing	15			
Artificial Intelligence	Image based diagnosis, wound monitoring	Early detection, precision management	3			
Nanotechnology Based Dressings	Targeted antimicrobial delivery	Reduces infection. Accelerates healing	16			

# IMPACT OF COMORBIDITIES IN PROGNOSIS

The outcome of gangrene largely depends on other health problems a person may have. Diabetes is one of the biggest factors that make recovery harder. It slows down wound healing, reduces blood flow in small vessels, and weakens the immune system. People with diabetes are more likely to get repeated infections and often need

larger or multiple amputations compared to those without diabetes.<sup>16</sup> Peripheral artery disease (PAD) and atherosclerosis also make things worse by reducing blood supply to tissues, causing them to die. In these cases, procedures like angioplasty or bypass surgery play a crucial role in whether the limb can be saved and the patient survives.<sup>16</sup>, <sup>17</sup> An overview of the impact of common comorbidities on gangrene prognosis is illustrated in Figure 7.



Figure 7: Impact of comorbid conditions on gangrene outcomes.



The diagram demonstrates how conditions such as diabetes, peripheral vascular disease, and immune deficiencies can worsen disease prognosis.

Chronic kidney disease (CKD) can also worsen outcomes. Poor blood vessel health, toxin buildup, and weak immunity increase tissue damage and complications. Rare cases like penile gangrene in dialysis patients show how severe CKD related problems can be. Obesity can indirectly make recovery harder by reducing local blood flow, raising infection risk, and making surgery more difficult. For gangrene caused by infections, such as gas gangrene, quick recognition and prompt surgical removal of dead tissue are vital. Delays increase the risk of serious infections and death. Antibiotics and proper wound care are also crucial.<sup>17</sup>

In general, recovery depends on how much tissue is affected, how fast treatment starts, and how well infections are controlled. Saving the limb is always the goal, but sometimes major amputation is necessary. Advances in surgery, prosthetics, and coordinated care have improved quality of life, but early detection and managing other health problems remain key to better outcomes.<sup>16</sup>

# PREVENTION AND EARLY DETECTION OF GANGRENE

- Avoid tobacco and protect hands and feet from injuries, burns, or extreme cold.
- Keep blood sugar under control if you have diabetes.
- Perform daily foot checks, especially if you have diabetic neuropathy.
- Treat even small cuts, wounds, or infections promptly to prevent complications.
- Watch for early warning signs like unusual coldness, redness, darkening, or swelling in fingers, toes, or other areas, and see a doctor immediately.

- Regular medical check ups can help detect blocked blood vessels or poor circulation before serious damage occurs.
- Take care of skin infections, ulcers, or deep tissue injuries quickly.
- Improve blood flow to affected areas through proper care and exercises.
- Use proper footwear or offloading techniques to prevent pressure injuries.
- Maintain healthy blood pressure, cholesterol, and glucose levels.
- Avoid falls or injuries that could worsen tissue damage. 18, 19

#### **GUIDELINES AND RECOMMENDATIONS**

# **National Treatment Protocols and Preventive Screening (India)**

In India, management of gangrene is guided by recommendations from the Indian Council of Medical Research (ICMR) and the National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS). Clinical evaluation supported by Doppler studies is essential for early detection. In cases where tissue is unsalvageable, surgical debridement or amputation is indicated. Broad spectrum empiric antibiotics such as piperacillin tazobactam or meropenem are recommended initially, with modification based microbiological culture. Glycaemic control in diabetic patients is strongly emphasised, while hyperbaric oxygen therapy is used selectively. Preventive strategies under NPCDCS include routine foot examinations, monofilament testing, and ankle brachial index measurements in high risk populations, particularly diabetics.<sup>20</sup>,<sup>21</sup>

# International Treatment Protocols and Preventive Screening



Globally, the Infectious Diseases Society of America (IDSA) and the Centres for Disease Control and Prevention (CDC) recommend urgent surgical consultation in suspected necrotising infections, combined with empiric antibiotic therapy using carbapenems or beta-lactam/beta-lactamase inhibitor combinations with clindamycin and vancomycin. Hemodynamic support in intensive care is crucial in septic patients, and hyperbaric oxygen therapy can be used as an adjunct.

According to the European Society of Cardiology (ESC) and the National Institute for Health and Care Excellence (NICE), procedures such as angioplasty or bypass are recommended for patients with ischemic dry gangrene, aiming primarily to preserve the limb rather than resort to amputation. International guidelines also highlight the importance of preventive care, including annual thorough foot examinations, educating patients on daily self-inspection of their feet (ADA), establishing multidisciplinary diabetic foot clinics, and implementing population wide screening programmes for peripheral arterial disease, diabetes, and hypertension (WHO, ADA, ESC).<sup>22</sup>

# SOCIOECONOMIC AND PUBLIC HEALTH IMPACT

Diabetic foot ulcers (DFUs) are more common among Black and Hispanic people compared to White individuals. This happens because many people from these groups face challenges like low income, less education, and not having good health insurance.<sup>23</sup> These problems make it harder to get regular check ups or see specialists on time. As a result, many people visit doctors only when the ulcers are already serious, which often leads to hospital stays or even amputations. Social issues such as living in poorer areas, fewer job opportunities, and unfair healthcare systems also

make the situation worse, showing how deeply inequality affects health.<sup>24</sup>

Where a person lives also makes a big difference. Amputation rates vary from place to place, often because some areas don't have enough medical facilities or trained doctors. People in rural or low income regions usually have to travel far to get help, so they may wait longer before getting treated, leading to more severe outcomes.<sup>23</sup>

These ulcers also put a big strain on both families and the healthcare system. Treating foot complications costs a lot more than regular diabetes care and often requires hospital visits, emergency care, and home treatments. Severe cases can cost tens of thousands of dollars, and people may also lose income or be unable to work. To fix this problem, everyone needs fair access to early treatment, proper foot care, and complete medical support from a team of healthcare professionals.<sup>25</sup>

#### **FUTURE PERSPECTIVE**

In the future, the management of gangrene will likely improve with better awareness, early diagnosis, and new treatment options. One major focus will be on finding gangrene at an early stage before tissue death becomes severe. This can happen with the help of simple screening tools and mobile health technology that allow quick detection, especially for people with diabetes or poor blood flow. Education and community programs will also play a big role in teaching people how to notice early warning signs and care for wounds properly.<sup>26</sup>,<sup>27</sup>

Medical treatment for gangrene will continue to grow with the use of advanced wound care, natural medicines, and better infection control.<sup>27</sup> Scientists are also studying how stem cells and tissue engineering can help repair damaged tissues and

improve blood flow to affected areas. These new methods may reduce the need for amputation in the future.<sup>23</sup>

In addition, better public health policies and access to healthcare will help prevent gangrene, especially in low income and rural areas where people often reach hospitals too late. Affordable healthcare, better diabetes control, and good hygiene practices will make a big difference.<sup>24</sup>,<sup>28</sup>

Overall, the future looks positive if technology, education, and healthcare systems work together. By combining prevention, early detection, and modern treatment, many lives and limbs can be saved from gangrene. The main goal for the coming years will be to reduce the number of cases and make sure every person gets the right care at the right time, no matter where they live.<sup>23</sup>,<sup>26</sup>,<sup>27</sup>

#### **CONCLUSION**

Gangrene is a serious issue that can lead to major health problems, such as infections, loss of a limb, or even death. However, if detected early and correctly, the outcomes improve treated significantly. People with diabetes, poor blood circulation, or weak immune systems are at higher risk for gangrene, so they should have regular check-ups. Doctors can identify it early through physical exams, lab tests, scans, and new AI tools that can spot damaged tissue more quickly. Treatment typically involves antibiotics, cleaning or removing dead tissue, caring for wounds, and sometimes using oxygen therapy at high pressure. New methods like stem cells, platelet rich plasma, herbal medicines, and special dressings made with nanomaterials are promising for helping wounds heal and preventing amputations. Managing other health issues, maintaining healthy habits, and recognising warning signs early are also crucial. Improved awareness, education, and better access to medical care, especially in rural or low income

areas, can help to avoid serious cases. Combining early detection, proper treatment, and knowledge can save lives and limbs.

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#### REFERENCES

- Leslie SW, Sajjad H, Taylor RS: Penile zipper and ring injuries. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025.
- 2. Buttolph A, Marietta M, Sapra A: Gangrene. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025.
- 3. Fahmy AM: Assessing the efficacy of AI models in medical imaging analysis for the early identification of diabetic foot ulcers and gangrene: a review. Premier Science; 2025.
- 4. Sorensen MD, Krieger JN, Rivara FP, et al: Fournier's gangrene: population-based epidemiology and outcomes. J Urol. 2009;181:2120–2126. DOI:10.1016/j.juro.2009.01.034.
- 5. Çalışkan S, Özsoy E, Sungur M, et al: Fournier's gangrene: review of 36 cases. Ulus Travma Acil Cerrahi Derg. 2019;25:479–483.
- 6. Buboltz JB, Murphy-Lavoie HM: Gas gangrene. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025.
- 7. Tsutsumi Y: Pathology of gangrene. In: Pathogenic Bacteria [Internet]. IntechOpen; 2020.



- 8. Kuzaka B, Wróblewska MM, Borkowski T, et al: Fournier's gangrene: clinical presentation of 13 cases. Med Sci Monit. 2018;24:548–555. DOI:10.12659/MSM.905836.
- 9. Lewis GD, Majeed M, Olang CA, et al: Fournier's gangrene diagnosis and treatment: a systematic review. Cureus. 2021;13:e18948. DOI:10.7759/cureus.18948.
- 10. Urbina T, Razazi K, Ourghanlian C, et al: Antibiotics in necrotizing soft tissue infections. Antibiotics (Basel). 2021;10:1104. DOI:10.3390/antibiotics10091104.
- 11. Yang Z, Hu J, Qu Y, et al: Interventions for treating gas gangrene. Cochrane Database Syst Rev. 2015;12:CD010577. DOI:10.1002/14651858.CD010577.pub2.
- 12. Grim Hostetler S, Sopkovich J, Dean S, et al: Warfarin-induced venous limb gangrene. J Clin Aesthet Dermatol. 2012;5:38–42.
- 13. Koakutsu T, Nomura R, Yamanouchi S, et al: Oxygen free radical and antioxidant status in necrotizing soft-tissue infection of the lower extremity. Ups J Med Sci. 2013;118:46–50. DOI:10.3109/03009734.2012.733738.
- 14. Bharati PL, Agrawal P, Prakash O: A case study on management of dry gangrene by Kaishore Guggulu, Sanjivani Vati and Dashanga Lepa. Ayu. 2019;40:48–52. DOI:10.4103/ayu.AYU 244 18.
- 15. Quiroz HJ, Parikh PP, Lassance-Soares RM, et al: Gangrene, revascularization, and limb function improved with E-selectin/AAV gene therapy. JVS Vasc Sci. 2020;2:20–32. DOI:10.1016/j.jvssci.2020.10.001.
- 16. Agrahari KA, Barewar SS, Bakal RL, et al: Advances in gangrene management: a comprehensive review. GSC Biol Pharm Sci. 2025;31:73–84. DOI:10.30574/gscbps.2025.31.3.0209.
- 17. Hong KS, Yi HJ, Lee RA, et al: Prognostic factors and treatment outcomes for patients

- with Fournier's gangrene. Int Wound J. 2017;14:1352–1358.
- 18. Anyaehie UE, Ede O, Eyichukwu GO, et al: Profile of geriatric extremity amputation in a LMIC. East Afr Orthop J. 2023;17:41–49.
- 19. McClean D, Rogers HJ, Williams BW: Early diagnosis of wound infection with special reference to gas gangrene. Lancet. 1943;1:355–360.
- 20. Indian Council of Medical Research: Standard treatment guidelines: management of diabetic foot ulcer. Ministry of Health and Family Welfare; 2016.
- 21. National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke: Operational guidelines. Directorate General of Health Services; 2013.
- 22. Isei TI, Abe M, Nakanishi T, et al: The wound/burn guidelines-3: diagnosis and treatment for diabetic ulcer/gangrene. J Dermatol. 2016;43:1153–1172. DOI:10.1111/1346-8138.13285.
- 23. Sockkalingam VS, Subburayan E, Velu E, et al: Fournier's gangrene: prospective study of 34 patients in a South Indian population. Pan Afr Med J. 2018;31:110. DOI:10.11604/pamj.2018.31.110.15495.
- 24. Bhargava A, Mahakalkar C, Kshirsagar S, et al: Prevalence of gangrene among patients with PVD in Central India. Cureus. 2024;16:e57038. DOI:10.7759/cureus.57038.
- 25. Tosun Y, Akıncı O, Küçük HF, et al: Risk factors for mortality in Fournier's gangrene of anorectal origin. Ulus Travma Acil Cerrahi Derg. 2022;28:1128–1133. DOI:10.14744/tjtes.2021.97866.
- 26. Alzahrani KA: Paediatric Fournier gangrene: diagnosis, management, and outcomes. Transl Pediatr. 2025;14.
- 27. Miceli G, Basso MG, Pennacchio AR, et al: SGLT2-I in diabetic foot prevention: state of the art & future perspectives. Medicina



- (Kaunas). 2024;60:1796. DOI:10.3390/medicina60111796.
- 28. Kaur A, Singh MP: Environmental contaminant—induced programmed cell death in fruit fly. Res J Pharm Technol. 2019;12:6174–6180.

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