FOURNIER'S GANGRENE

(Evidence based review)

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Introduction

Fournier's gangrene is a necrotising fascitis involving the genital, perianal or perineal regions. The infective process leads to thrombosis of subcutaneous blood vessels, resulting in gangrene of the overlying skin. Early recognition of this condition with prompt surgical treatment and early antibiotics form the cornerstone in it is management.

This article is an evidence-based review looking at various aspects in the development and management of Fournier's gangrene.

Historical background

1883: Prof Jean-Alfred Fournier

Jean Alfred Fournier, a Parisian dermatologist and venereologist in 1883 was the first to be associated with this condition in a specific region of the body, namely scrotum. His initial description was based on 5 young men with scrotal gangrene. The cardinal points of that description included (1) sudden onset in a healthy young man, (2) rapid progression to gangrene and (3) absence of a definite cause.

1764: Bauriene
1924: Meleney (streptococcal gangrene)
1952: Wilson (necrotising fascitis)
1990s: "Flesh-eating" bacteria

Although Jean Alfred Fournier gave the condition its eponymous name in 1883, Baurienne first described Fournier's gangrene over 100 years previously in 1764.

Meleny in 1924, while in China, described a more generalised form of the disease and termed it "streptococcal gangrene". In the 1990s sensational medical journalists dramatized the whole process of necrotising fascitis by associating it with flesh-eating bacteria.

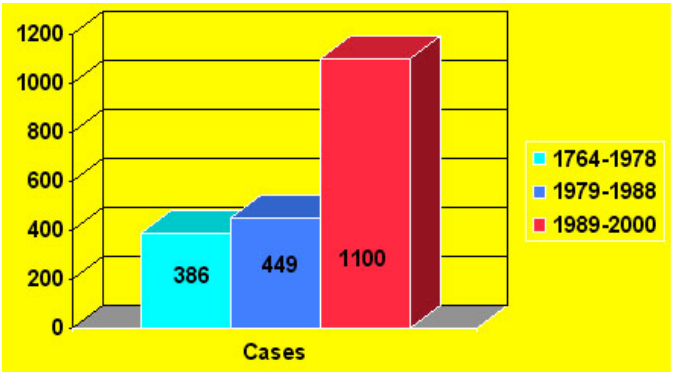
Epidemiology

· Age group

· Sex- Male: Female = 10:1

The epidemiology has changed from the original description in that the disease is no longer restricted to young men but may affect a wide age range from neonates to the very elderly. Fifty-five cases have been reported in the paediatric literature, two-thirds of who were younger than 3 months. The mean age of patients appears to have increased from 40 years in cases reported before 1945 to 50 years in more recent series.

Though this disease process is more common in males, there are also several reports of genital gangrene occurring in women.



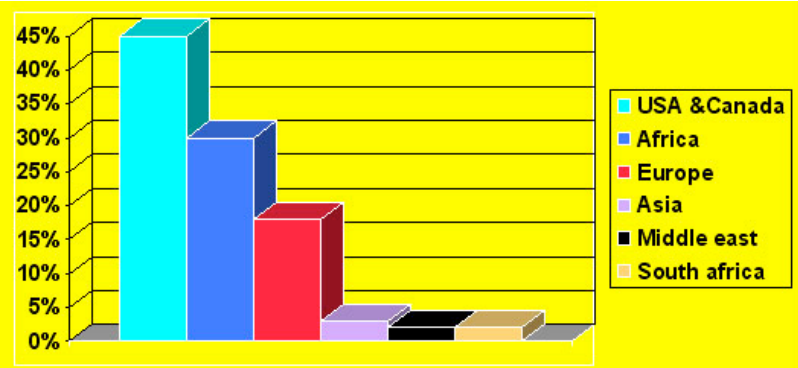
The chart above shows the there has been an increase in the number of cases reported in the literature over the last decade.This probably is because of better recognition of this condition and an increase in the reporting of this condition in the medical literature.

Epidemiology

Eke, BJS 2000

Socio-economic status: ??
Poor

There has been some suggestion that poor socioeconomic conditions contribute to the development of Fournier's gangrene. Though a report from Europe stated that the disease is not so frequent in the civilized world, Fournier's gangrene does occur in affluent as well as poor communities, as evidenced by many reports from affluent regions of the USA and Europe. Among the English-speaking regions, the highest incidence of the disease occurs in the USA and Canada



There also have been claims that the condition is especially prevalent in Africa and Asia, and the pattern of this disease in Africa and India differs from that in Europe and America. Skin as the source of sepsis is more common in the developing world and the mortality rate is much lower. It has been speculated, without proof, that there may be a strong resistance to infection in the Negro race or that the organisms involved in Africa lack sufficient virulence for more severe sepsis.

Associated disorders
Smith Br J Urol 1998

· Diabetes: 40 - 60%Chronic alcoholism: 25 - 50%

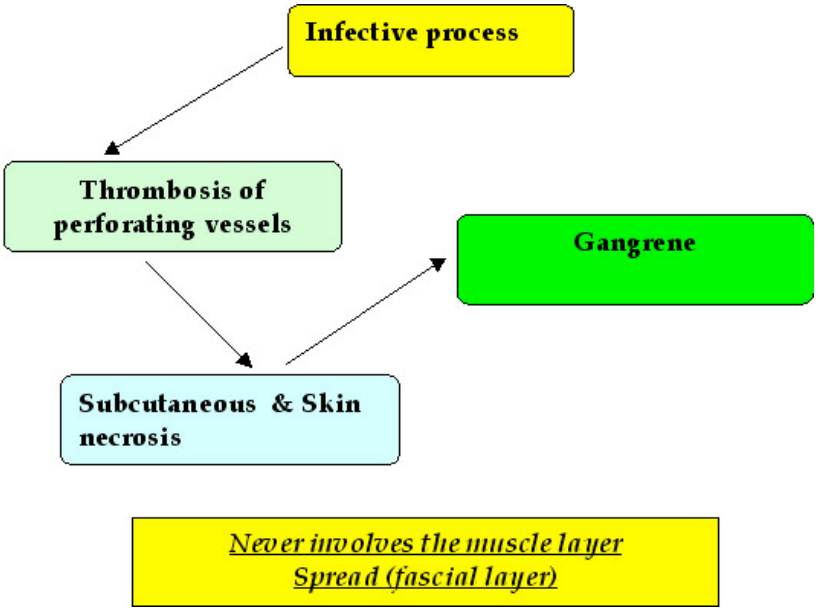
· Immunosuppression

The most striking change in presentation over the recent years is that victims of the disease are now almost always recognized to have an underlying systemic disorder. The most common associations are diabetes and chronic alcoholism.

Immunosuppression, either after organ transplantation or caused by chemotherapy for malignant disease, has also been associated with an increased risk.

With the emergence of HIV, a new group of patients at risk has been recognized in both in Africa and the developed world, and Fournier's gangrene has been reported as a presenting sign of undiagnosed HIV infection.

Pathology



The infective process leads to thrombosis of subcutaneous and cutaneous blood vessels including the perforating vessels. This results in gangrene of overlying skin.

Histologically, Fournier's gangrene is characterized by obliterative endarteritis and thrombosis of the subcutaneous vessels, fascial necrosis, and leukocyte infiltration

The spread of Fournier's gangrene is noted to be along the fascial layer and is determined by the attachments of Colles' fascia of the perineum and abdominal wall. The dartos is a continuation of this layer over the scrotum and penis. Whilst, posteriorly the fascia is attached to the perineal body and urogenital diaphragm, laterally, it is attached to the pubic rami. These posterior and lateral attachments tend to limit the spread of the infection in these directions. However, antero-superiorly, Colles' fascia merges with Scarpa's fascia of the anterior abdominal wall and there is therefore no barrier to spread in this direction, resulting in a widespread gangrene.

Testicular involvement is rare as the blood supply to the scrotum comes from the pudendal arterial branches of the femoral artery, while the testicular artery is a direct branch from the aorta. However, testicular involvement has been reported and if this does occur it usually indicates a retroperitoneal or an intra-abdominal source of infection.

Microbiology	
Polymicrobial (Aerobic + anaerobic) Type 1 infections Type 2 infections	Common organisms: E. Coli*, P. Mirabilis, K. Pneumoniae, Bacteroides* Streptococci*, Staphylococci*, Peptostreptococci, Clostridia, & Pseudomonas * Frequently isolated organisms

Necrotising fascitis is caused by either polymicrobial (Type 1) or monomicrobial (Type 2) infections. Fournier's gangrene is always due to mixed aerobic and anaerobic bacteria and this type of infection is also

associated with diabetes mellitus and cervical necrotizing fasciitis.

Both aerobes and anaerobes are almost invariably present, but anaerobes are less frequently isolated. A mean of four different organisms is usually cultured from each patient. Overall, the most commonly isolated species are enterobacteria, particularly Escherichia coli, followed by Bacteroides and streptococcal species. Staphylococci, Peptostreptococci and Clostridia are also frequently identified

Type 2 infections, due to group A streptococcus, is associated with history of blunt trauma, varicella, intravenous drug use, penetrating injury and possibly with non-steroidal anti-inflammatory drugs.

Portal of entry Clayton, Surg Gynaecol Obstet 1990		
Urogenital (45%)	Anorectal causes (33%)	Cutaneous (21%)
Periurethral infections Urethral strictures Bladder carcinoma Indwelling catheter Traumatic catheterisation Epididymo-orchitis Prostatic biopsy	Perianal abscess Complications of: *Colorectal cancers* *Haemorrhoidectomy* *Anal dilatation* *Rectal biopsy* *Appendicitis* *Diverticulitis* *Rectal perforation* *Crohn's disease*	Occult trauma Complications: *Vasectomy,* *Orchidectomy,* *Hydrocelectomy* *Herniorraphy* *Superficial skin abscess*

Although Fournier was unable to identify a cause in his initial series, most present-day clinicians would agree that the condition is rarely idiopathic, although specific investigations may be required to determine the portal of entry for the infection. This reflects both increased understanding of the condition and a more rigorous approach to investigation of established cases. When the cause is not found, it is likely that the portal of entry has been overlooked.

The source of infection may be either urogenital (45%), anorectal (33%) or cutaneous (21%) and the causes are detailed above.

However, in women genital gangrene typically arises from vulval or Bartholin's abscess and spreads to involve the vulva or perineum. It may also complicate episiotomy, hysterectomy, septic abortion, and cervical or pudendal nerve blocks.

Clinical features

· TRIAD: severe pain + swelling + fever

· Bullae; Crepitus (50 to 62%)

· Gangrene

· "Dirty dishwater fluid"

Cutaneous signs >> Tip of an iceberg

Insidious onset (2 to 7.4 days) It is important to recognize that patients in the early stages may present with minimal cutaneous manifestations of the underlying infection, making prompt diagnosis difficult.

Pain out of proportion to the physical findings is the most consistent feature noted at the time of presentation. The classical triad of pain, swelling and systemic sepsis is very commonly noticed. Presence of bullae filled with serous fluid is an important diagnostic clue and should raise the suspicion of this condition. Induration of the skin and surrounding structures is also commonly present.

Presence of cyanosis, blistering or bronzing of the skin usually indicates deep infection. Poignant descriptions of the clinical presentation include 'dirty dishwater fluid' to describe the pus discharging from

a Fournier's gangrene.

Once gangrene is established, pain often diminishes. In the early stages, patients often have systemic symptoms of sepsis, which appear disproportionate to the appearance of the scrotal skin.

Shock, intestinal ileus and delirium are common and progression to single or multi-organ failure may occur and is the usual cause of death in patients who succumb.

Diagnosis

CLINICAL DIAGNOSIS

"Finger test" / "Frozen section"
Plain X-ray: Air in soft tissues
US: Scrotal wall thickening
Subcutaneous Air / Peri-testicular fluid
CT: Delineates the extent of necrosis accurately
Defines the cause

The diagnosis of this condition is mainly based on clinical signs and symptoms. In doubtful cases, additional bedside techniques (finger test and rapid frozen section biopsy) or other investigations can be used.

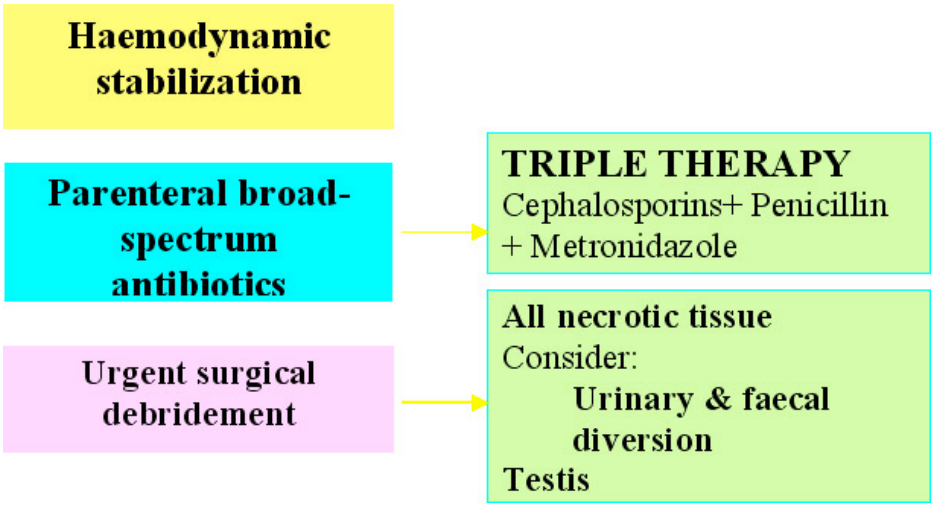
The finger test is performed in the following manner: the area of suspected involvement is infiltrated with local anesthesia. A 2-cm incision is made in the skin down to the deep fascia. A gentle, probing manoeuvre with the index finger is performed at the level of the deep fascia. If the tissues dissect with minimal resistance, the finger test is positive. In addition, lack of bleeding is considered as an ominous sign of a necrotizing process. On many occasions, a "murky dishwater fluid" can also be noted in the wound.

Plain radiographs can show the characteristic marked swelling of the scrotal tissues and air density within the involved tissues.

Ultrasound is a useful diagnostic tool as it has the capacity to distinguish Fournier's gangrene from intra-scrotal pathology that also commonly produces scrotal pain, erythema and swelling. In the former condition, it usually reveals diffuse swelling and thickening of the scrotal wall and possibly the phallus and may also detect gas within the scrotal wall, which may be useful in cases when crepitus is not clinically evident. Small amounts of peri-testicular fluid may be detectable on the scan but the testes and epididymes tend to be relatively normal.

CT can be of value in defining the cause and depicting the extent of necrosis accurately and a pre-operative scan though not essential may be helpful if the source of infection is a retroperitoneal or intra-abdominal process.

Treatment



The mainstay of treatment of patients with either established or suspected fournier's gangrene is three-fold.

Firstly, patients should be actively resuscitated, especially if they show signs of systemic toxicity or septic shock.

Secondly, after blood cultures are taken, they should be commenced on antibiotics (triple therapy).

Thirdly, they do require prompt debridement with patient in a lithotomy position. All visible necrotic skin and affected subcutaneous tissues should be excised aggressively. Debridement of deep fascia and muscle is not usually required as these areas are rarely involved.

It is important to recognize that the extent of the disease cannot be judged from the margins of cutaneous necrosis. Separation of the skin and subcutaneous tissue with a haemostat can be used to define the limits of excision, with debridement stopping where these tissues do not separate easily.

Some authors have recommended managing areas of questionable viability with through-and-through drains. However, these techniques should not be applied in the hope of salvaging areas of established necrosis, as drainage of frankly necrotic tissue without debridement is associated with an extremely high mortality.

Debridement often results in exposure of the testes and if desired, the testes can be temporarily implanted into a lower abdominal subcutaneous pouch or a medial thigh pouch until healing or reconstruction is complete. As mentioned earlier the testes are rarely involved and orchidectomy is not common. However the reported incidence of orchidectomy ranges from 10 to 30% in occasional studies.

In cases, where the primary source is either urological or anorectal, appropriate diversion methods should be considered.

Following the initial debridement it is important to reassess the wound again in the first 24-48 hours to check if further debridement is required. Multiple procedures are often required, with a mean of 2-4 procedures per patient.

Treatment- Wound

Secondary healing

Skin grafts (Paty 1992; Hejase et al, 1996)
Myocutaneous flaps (Laucks, 1994; Yu P, et al 2002)

Following the debridement and clearance of the infection, the focus should change to the management of the wound. Majority of the wounds do heal by secondary intention and this is the most common form of

managing the wound.

However, some authors recommend skin grafts or myocutaneous flaps once the wound shows healthy granulation. Scrotal reconstruction after Fournier's gangrene remains a major challenge and is important for functional, cosmetic, and psychological reasons. Protection of the exposed testicles is necessary for both hormonal production by the Leydig cells and spermatogenesis.

Topical wound care

- Hydrogen peroxide (Hejase et al, 1996)
- Povidone - Iodine
- Sodium hypochloride solutions (Dakins solution)
- Natural unprocessed honey (Efem 1993; Dunford 2000)
  - Digest necrotic tissues
  - Contains antimicrobial agents
  - Enhances epithelialization
  - Physically dehydrates edema from wounds

With regards to the topical wound care post-operatively, any of the above agents can be used.

Hydrogen peroxide generates nascent oxygen, which helps to destroy the anaerobic organisms. However, application of this agent can be very painful in the early dressings and good analgesia is recommended.

Recently, there has been an interest in the use of topical unprocessed honey, which has an impressive acceleration of the healing process. Honey has a low pH (3.6) and contains enzymes that digest dead and necrotic tissue. It also stimulates growth and multiplication of epithelial cells at the wound edges. It is interesting that these changes occur within a week of application to the wound.

Most honey available on the UK market is not intended for application to wounds. Honey available for consumption is not sterilised and cannot be recommended for use on wounds. Commercial honeys intended for use on wounds are available; they have standardised antibacterial activity and are sterilised by gamma irradiation. In the UK, honey is not currently licensed under pharmaceuticals or medical devices and hence it strongly advised that practitioners exercise caution before using any unregulated, unlicensed treatment.

Hyperbaric oxygen therapy

1. ↑ Tissue oxygenation
2. Optimize neutrophil function (Aid phagocytosis)
3. Inhibit anaerobic growth
4. ↑ Generation of free radicals
5. Transport of antibiotic agents across the bacterial cell wall
6. Improves collagen formation, fibroblast growth & angiogenesis
7. ↓ Systemic toxicity
8. ↑ Demarcation

Hyperbaric oxygenation increases tissue oxygen tension to a level that inhibits and kills anaerobic bacteria, while also reducing systemic toxicity, limiting necrosis and enhancing the demarcation of gangrene.

Technically, the delivery of hyperbaric oxygen occurs when the patient rests the whole body and breathes 100% oxygen in a treatment chamber that is pressurized to higher than sea level. Pressurization is usually between 1.4 and 3.0 atmosphere.

When available hyperbaric oxygen is most commonly initiated as soon as patients are stabilized following

initial debridement. Treatment is often continued until wounds are healed.

There have been no reported randomized studies of the efficacy of adjuvant hyperbaric oxygen. A clear demonstration that this treatment is beneficial and cost-effective is yet to be established, leaving room for controversy.

This form of treatment is probably best reserved for patients who remain toxic despite maximal debridement and those with clinical or microbiological evidence of anaerobic infection, particularly in view of the limited availability of hyperbaric chambers.

Use of hyperbaric oxygen
Capelli et al, J of Urol 1998

References	Total No. Pts (No. hyperbaric oxygen group)	No. Treatment/Pt	Duration (minutes)	%Hyperbaric Oxygen Treated Mortality	No. Hyperbaric Oxygen Group Surgeries/Patient
Riegels-Nielsen et al 54	5 (4)	2-7	70	20	*
Gozal et al 75	16	5	90	12/5	1-3
Riseman et al 64	29 (17)	7.4 (mean	90	23	1.2
Elliott et al 67	158 (196)	31.7 (mean)	90	25	†
Shupak et al 65	37 (25)	2/Day ‡	90	36	3.3
Pizzerno et al 61	11 (11)	5-24	90	0	9/Group
Hollabaugh et al 57	26 (14)	14	90	7	3.0

*Extensive debridement before first hyperbaric oxygen treatment followed by surgical revision when necessary
†A mean of 3.8 debridements and a mean of 1.6 total reconstructions were done for all patients.
‡Patients received hyperbaric oxygen twice daily during acute wound management and once daily after toxic signs resolved

Hollabaugh et al reported a significant lower mortality with the use of hyperbaric oxygen (7%; 1/14 patients) compared to those treated without hyperbaric oxygen (42%; 5/12 patients) ($p = 0.05$).

Riseman et al, similarly from a retrospective review of 29 patients with necrotizing fasciitis were able to demonstrate a significantly lower mortality in the group treated with hyperbaric oxygen (23%, 4/17) compared to the untreated group (67%, 8/12) ($p < 0.025$). In addition, the number of debridements required per patient was significantly lower in the treated group (1.2 Vs 3.3) ($p < 0.03$).

Complications

Major systemic:
· Acute renal failure
· ARDS / Pneumonia
· Gastrointestinal bleeding
· Heart failure
Hypocalcemia

The major complications mentioned-above are related to the degree of sepsis at presentation and require appropriate supportive management.

In addition, hypocalcemia can occur and is considered by some authors as an important diagnostic clue in early Fournier's. It's believed to be caused by bacterial lipases, which release free fatty acids that chelate

calcium in its ionized form

Outcome

- Mortality rates: 3 -40%
- Poor prognostic factors
  - Age
  - Female gender
  - Anorectal causes*
  - Number of organ failure @ admission*
  - Delay in presentation & treatment*
  - ? Diabetes* / HIV

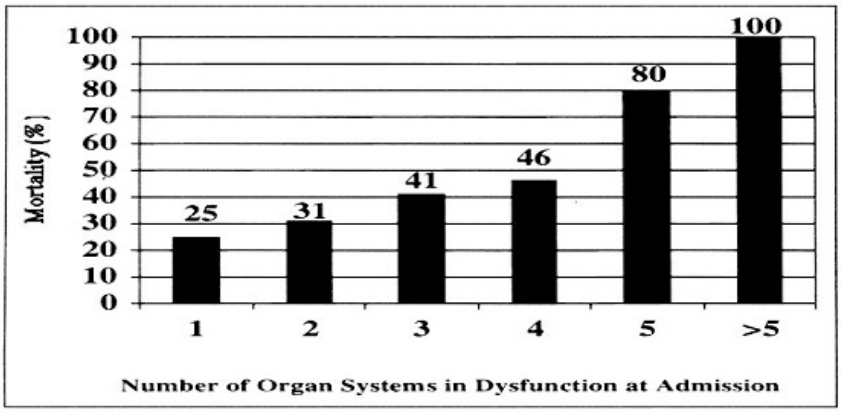
*** Most important prognostic factors.**

Despite modern supportive measures, the reported mortality rate still is high and this is due in part to the aggressive nature of the infection and in part to the underlying co-morbid diseases.

Although not universally agreed on, it seems that the extent of local disease (in the absence of altered homeostasis) is not a predictor of the outcome.

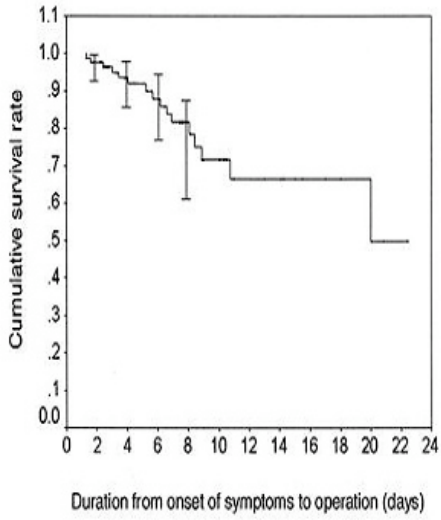
Outcome

Elliot, Am J Surg 2000



Outcome

Wong et al, JBJS 2003



The Kaplan-Meier curve on the left shows a decrease in the cumulative survival rate as the time between admission and the operation increases. The point estimates and their respective 95% confidence intervals at twenty-four, forty-eight, seventy-two, and ninety-six hours are indicated on the graph. The cumulative survival rate at twenty-four hours was 93.2% (95% confidence interval, 99.8 to 86.6). This rate declined to 75.2% (95% confidence interval, 88.4 to 62.0) at forty-eight hours.

Likewise, the Kaplan-Meier curve on the right demonstrates a decrease in cumulative survival rate as the time between the onset of symptoms and the operation increases. The point estimates and their respective 95% confidence intervals at two, four, six, and eight days after the onset of symptoms are indicated.

Outcome

Church et al, DCR 2000

Table 4.
Outcome of Fournier's Gangrene in Different Studies

	Country	N	Mortality Rate (%)	Mean duration of Hospitalization (days)	Percentage of Survivors not in Need of Skin Grafting or Reconstructive Surgery
Present study (1999)	Jordan	10	20	24.5	87.5
Kouadio *et al.*[10] (1998)	Ivory Coast	30	27	45	100
Brissiaud *et al.*[14] (1998)	Senegal	44	34	42	48
Pizzorno *et al.* (1997)[15]	Italy	11	0	—	73
el Khader *et al.*[75] (1997)	Morocco	32	28	26.5	—
Benchekroun *et al.*[16] (1997)	Morocco	55	9	—	90
Picramenos *et al.*[18] (1995)	Greece	10	30	38	60
Palmer *et al.*[65] (1995)	New York	30	43	41	—
Attah[21] (1992)	Nigeria	13	0	10	100
Clayton *et al.*[11] (1990)	Chicago	57	18	48	—
Wolach *et al.*[36] (1989)	California	10	20	41	50
Fahal and Hassan[12] (1988)	Sudan	9	25	69	100

Summary

· Prompt clinical recognition
· Polymicrobial treatment
· Early surgical debridement

All necrotizing fasciitis of the perineum, including the genitalia in both sexes and at all ages, regardless of

the aetiology, with or without proven infection, should be brought under the umbrella of Fournier's gangrene. The understanding of the aetiology and pathogenesis of Fournier's gangrene has increased greatly since the condition was first described.

The diagnosis of Fournier's gangrene is mainly on clinical grounds and there should be a high index of suspicion. The basic treatment of Fournier's gangrene involves prompt excision of all non-viable tissue (after aggressive resuscitation and early antibiotics), limitation and abolition of any infective process present, and occasional anatomical reconstruction.

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