Summary
The authors’ experience of fourteen patients with necrotizing fasciitis is reviewed. The pathognomonic feature of this condition is an extensive necrosis of subcutaneous tissue caused by a vicious cycle of infection, local ischaemia and reduced host defence mechanisms. The diagnosis can only be confirmed by immediate exploratory incision.

The reported mortality of 30–40% reflects the inadequacy of conservative surgery in the treatment of this serious condition. Mortality can be reduced by early recognition followed by radical excision of the necrotic fascia and overlying skin. The preservation and subsequent use of the excised skin has the advantage of economy in the use of donor areas and reduction in morbidity. Hyperbaric oxygen therapy does not halt the spread of the necrotizing process and is not a substitute for radical surgery.

Definition and historical background
Necrotizing fasciitis is a relentlessly destructive bacterial infection characterized by extensive necrosis of the subcutaneous tissues of the abdominal wall and, less frequently, the extremities. The condition is fortunately uncommon but is potentially fatal and demands early recognition in order that treatment may be effective. Although the serious nature of this condition was recognized as long as 100 years ago (Jones, 1871), confusion in the literature was compounded by the multiplicity of descriptive terminology and inadequate bacteriological data. Thus the condition has been referred to as ‘hospital gangrene’ (Jones, 1871), ‘acute infective gangrene’ (Fedden, 1909), ‘necrotizing erysipelas’ (Pfanner, 1918), ‘haemolytic streptococcus gangrene’ (Meleney, 1924, 1929), and ‘suppurative fasciitis’ (McCafferty and Lyons, 1948).

The first large series published in the present century was that of Meleney who, in 1924, reported twenty patients from China. Meleney described the condition as a rapidly developing gangrene which occurred more frequently in males and the extremities were affected in the large majority of cases. He stated that ‘the infection essentially produces a gangrene of the subcutaneous tissues, subsequently it causes death of a part of the overlying skin’. In Meleney’s report, bacterial culture showed that the haemolytic streptococcus ‘was the only organism invariably present’. Other organisms which were identified were fewer in number and none of them appeared regularly enough to be considered as the ‘causative organism’—hence the term ‘haemolytic streptococcus gangrene’.

Wilson (1952) was the first to use the descriptive term ‘necrotizing fasciitis’ because of the characteristic necrotic fascia and subsequently observed non-specificity of the pathogenic organism involved. Others in later reports (Rea and Wyrick, 1970; Meade and Mueller, 1968; Ledingham and Tehrani, 1975) have confirmed the validity of this statement and have continued to use this term in preference to other descriptive names.

Bacteriology
Pathogenic organisms undoubtedly play a major role in initiating and spreading the necrotizing process. The type of bacteria now encountered, however, seem to differ from those in earlier reports. In Wilson’s series of twenty-two patients (Wilson, 1952), haemolytic organisms were found in pure culture in 58% of cases studied bacteriologically and were present along with non-haemolytic bacteria in an additional 26% of the patients. The majority of organisms (88%) were pathogenic staphylococci. Rea and Wyrick (1970) reported forty-four patients with necrotizing fasciitis seen during 15 years at Parkland Memorial Hospital in Dallas. In this group, haemolytic streptococci and pathogenic staphylococci together accounted for 89% of the wound infections with enteric Gram-negative organisms responsible for the remaining 11%. In a recent report, Wilson and Haltalin (1973) described eleven children with necrotizing fasciitis. Haemolytic streptococci were found in 50% of cases. The other organisms were staphylococci and Pseudomonas aeruginosa. In the report by Ledingham and Tehrani (1975) the predominant organisms in initial wound culture, obtained through fresh incisions in the affected areas, were coliforms in combination most
frequently with enterococci and streptococci; in only one case was the streptococcus of the \(\alpha\)-haemolytic variety. Other organisms included *Bacteroides, diphtheroids, Clostridium welchii, Proteus, Staphylococcus* and *Ps. aeruginosa*. Since colonizing bacteria rapidly invade the affected area, bacteriological cultures, both aerobic and anaerobic must be taken from several sites at an early stage in the course of the disease.

**Pathogenesis**

Irrespective of the species of organism involved, the initial bacterial growth takes place in the subcutaneous tissues, i.e. the subcutaneous fat, superficial fascia and the superficial layer of the deep fascia, most commonly of the abdominal wall and lower extremities. The initiating injury responsible for introduction of the infection may follow minor trauma (abrasions, cuts, bruises, insect bites, minor burns) or surgical incision. At times, no obvious cause is found.

In the series reported by Rea and Wyrick (1970), minor trauma was responsible for 80% of the cases and in eight patients, no history of specific injury could be obtained. In the present series of fourteen patients, necrotizing fasciitis developed following ischio-rectal sepsis in six, abdominal surgery in five, and fractured pelvis, diabetic peripheral vascular disease and repeated supra-pubic aspiration of urine each in one patient. Similarly in eleven children, reported by Wilson and Haltalin (1973), the condition occurred following surgery in five, and traumatic laceration, varicella, osteomyelitis, abscess of buttock and bone marrow aspiration, each in one patient. In the final patient of this series no predisposing condition was present.

After the initial bacterial insult, the infection spreads rapidly along the fascial plane causing massive necrosis. The presence of ischaemic tissue further facilitates spread of the necrotizing process. The skin remains intact initially but later develops patchy necrosis and becomes gangrenous as a result of thrombotic occlusion of both venules and arterioles supplying the skin. Damage to cutaneous nerves causes numbness and subsequent anaesthesia of the part. Untreated, the affected skin becomes extensively necrotic. At an early stage, histological examination of full thickness skin biopsies reveals no abnormality. The subcutaneous fat and superficial fascia show a continuing non-specific inflammatory reaction, with fibrinoid arteriolitis and thrombosis of the vessels. Organisms may or may not be demonstrated in specially stained preparations.

The factors responsible for this alarming spread are unknown. An anaphylactic reaction similar to the Schwartzmann or Arthus phenomenon was suggested by Melaney (1933). McCafferty and Lyons (1948) postulated activation by streptokinase or staphylokinase of a serum proteolytic enzyme, present in the inflammatory exudate, causing progressive collagen necrosis.

Haemolytic streptococci are capable of producing haemolysins, leucocidines, fibrinolysins, erythrogenin toxin and the enzyme hyaluronidase. The filtrate of pathogenic staphylococci has haemolytic, necrotic and coagulating properties (Kellaway, Burnet and Williams, 1930). Other organisms such as *Pseudomonas* are known to produce collagenase with a primary effect on subcutaneous tissues and fascia (Meade and Mueller, 1968).

Another important factor which should be considered in the pathogenesis of a major infection of this sort is reduction in the host defence mechanisms (HDM). Primarily, local reduction in tissue resistance is achieved by the action of bacterial toxins added to the effect of bacterial kinases. This action is further enhanced by the general reduction in HDM occurring in the postoperative period, or by pre-existing systemic diseases such as diabetes, arteriosclerosis, agamma- or hypogammaglobulinaemia, rheumatoid arthritis, malnutrition and gastrointestinal haemorrhage (Table 1).

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<tr>
<th>Table 1. Factors involved in the pathogenesis of necrotizing fasciitis. HDM = host defence mechanisms</th>
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<tbody>
<tr>
<td><strong>Infection</strong> (non-specific bacteria)</td>
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<tr>
<td>Collagenase</td>
</tr>
<tr>
<td>Bacterial toxins</td>
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<td>Proteolytic enzymes</td>
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<tr>
<td>Reduced HDM</td>
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<tr>
<td>Necrosis of the superficial fascia</td>
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<tr>
<td>Ischaemia</td>
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<tr>
<td>Rapid spread along avascular fascial plane</td>
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<td>+ gross undermining</td>
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<tr>
<td>Secondary gangrene of skin</td>
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<td><strong>Postoperative</strong></td>
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<tr>
<td><strong>Diabetic</strong></td>
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<td><strong>Arteriosclerosis</strong></td>
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<tr>
<td><strong>Agamma/Hypogammaglobulinaemia</strong></td>
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<td><strong>R.h. arthritis</strong></td>
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<tr>
<td><strong>Malnutrition</strong></td>
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<tr>
<td><strong>Gastrointestinal haemorrhage</strong></td>
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Abele et al. (1960) reported a case of progressive fatal cutaneous gangrene associated with hypogammaglobulinaemia. In Buchanan's patient (Buchanan and Haserick, 1970) there was elevation of serum complement level and a slight increase in IgA, but its significance was unknown. In six patients in the present series, hypoalbuminaemia and hypergammaglobulinaemia were found. Clearly more detailed studies are required to detect the possibility of specific immunological defects contributing to the spread of necrotizing process. Diabetes
Necrotizing fasciitis is an important predisposing condition which reduces the host-defence mechanisms. In Crosthwait's series (Crosthwait, Crosthwait and Jordan, 1964), 50% of the deaths occurred in diabetic patients and in Meade and Mueller's report (1968), neither of the two diabetic patients who developed necrotizing fasciitis, survived. Six cases recently described by Roberts and Hester (1972) as synergistic bacterial gangrene, had most of the features of necrotizing fasciitis and all had diabetes and ketoacidosis. Infection, local ischaemia and reduced host defence mechanisms combine to form a vicious cycle which is responsible for the initiation and spread of the lesion (Fig. 1).

![Diagram of factors involved in initiation and spread of necrotizing fasciitis.](image)

**Fig. 1.** Factors involved in initiation and spread of necrotizing fasciitis.

**Diagnosis**

At an early stage the external appearance of the skin, in spite of the active underlying necrotizing process, is normal (Fig. 2a and b). Later the skin becomes red, hot, and oedematous, with no clear line of demarcation. Subsequently, dusky discoloration with patchy necrosis of the skin occurs and the involved part, which is initially painful, becomes numb. There is usually gross undermining of the skin. Co-incident with these local features of progressive infection, the general condition of the patient deteriorates. Toxaemia, dehydration and mental apathy ensue. Anaemia is a frequent occurrence and is due to haemolysis, cutaneous hypoaemia, loss of blood in extensive subcutaneous spaces and bone marrow depression. Hypoproteinaemia, hyponatraemia and hypocalcaemia, consequent to extensive fat necrosis, also commonly occur. Other systemic manifestations of severe infection such as disseminated intravascular coagulation, respiratory failure and septic shock lead to major haemodynamic disturbances. The majority of the patients in the present series required continuous haemodynamic monitoring in the Intensive Therapy Unit of the hospital. Death occurs as a result of sepsis, respiratory or renal failure. Multi-organ failure, therefore, is the terminal event leading to death in inadequately treated patients.

The diagnosis should be established as rapidly as possible by making small incisions in the affected part. The finding of gross undermining of the skin associated with necrotic subcutaneous tissue is pathognomonic of the condition and calls for urgent appropriate therapeutic measures.

The differential diagnosis from gas gangrene and progressive bacterial gangrene should not prove to be too difficult. Gas gangrene frequently occurs in association with penetrating wounds following major trauma. Invasion of muscles by clostridial organisms, crepitus and a 'mousy'-smelling discharge are characteristic. Incision reveals a characteristic bluish appearance of muscle which does not bleed. Progressive bacterial gangrene is a more slowly progressive lesion affecting the total thickness of skin.
but not involving the deep fascia. The condition, essentially a postoperative surgical complication, occurs as a result of the synergistic action of a non-haemolytic microaerophilic streptococcus with some other organism (Meleney, 1933), although several other synergistic combinations have been known to produce the same lesion (Lyall and Stuart, 1948; Webb and Berg, 1966). The lesion typically occurs at the site of the drainage tube or around the laparotomy wound. The initial cellulitis spreads circumferentially and its centre becomes necrotic. The gangrenous ulcer may reach tremendous proportions. Surrounding the border of the gangrenous area there is a tender purplish zone which in turn is surrounded by an area of oedematous red and tender skin. There is no undermining of the skin and the subcutaneous tissues and deep fascia are primarily intact. Pus formation is variable. The importance of an underlying systemic disease predisposing to the development of this condition should be borne in mind.

Management

Once the diagnosis is established, the aims of treatment are two-fold. Firstly, general treatment and secondly, local measures to eradicate the source of infection.

(I) General treatment consists of the administration of intravenous fluid, large doses of appropriate systemic antibiotics and, when necessary, resuscitative measures preferably in an Intensive Therapy Unit. The majority of the patients, particularly those with extensive trunk or lower limb involvement and those in whom the diagnosis has been delayed, exhibit features of severe toxaemia and septic shock. The importance of adequate volume replacement, monitored by measurement of central venous pressure and hourly urine output and electrolyte balance cannot be overstressed. Frequent daily bacteriological swabs, taken from the involved areas, and blood cultures should be done to achieve maximum therapeutic benefit from antibiotic therapy. Particular attention should be paid to preventing the respiratory and renal complications so commonly encountered in patients with septic shock. Adequate oxygenation and, at times, assisted ventilation with frequent blood gas estimation are required. Digitalisation may be necessary to reduce the risk of cardiac complications of septic shock (Ledingham, 1975). Likewise, daily coagulation screening is desirable for early detection of a consumptive coagulopathy. As part of general treatment in particular when the lower extremities are involved, a defunctioning transverse colostomy is usually required to prevent contamination of the involved areas.

(II) Local treatment. The principle of surgical management as initially outlined by Meleney (1924), and subsequently emphasized by Wilson (1952), Crosthwait et al. (1964), Meade and Mueller (1968) and Rea and Wyrick (1970), consists of multiple linear incisions over the affected area as far as the subcutaneous necrosis extends, thus exposing the entire area of necrotizing fasciitis. The extent of undermining is determined by passing a probe or by finger dissection. Fasciotomy and debridement is carried out to the limit of the undermined skin and subcutaneous tissue until it no longer separates from the deep fascia. Meleney (1924) immersed the area in hot water and others used multiple drainage or frequent daily antibiotic irrigation (Meade and Mueller, 1968). The denuded area is grafted with split-thickness skin grafts at a later date.

Although in some earlier reports, this relatively conservative approach to management was attended by excellent results with low mortality (Wilson, 1952), more recent reports have shown a disturbingly high mortality ranging between 30 and 40% (Table 2). As emphasized by Rea and Wyrick (1970), even if conservative surgery is used at an early stage, many patients require further operations because of extension of the infection. The inadequacy of conservative surgery in eliminating the source of infection is clearly shown from the experience in the management of the fourteen patients in the present series with this condition referred from different parts of the U.K. and treated in the University Department of Surgery, Western Infirmary, Glasgow, between 1965 and 1975.

<table>
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<tr>
<th>Series</th>
<th>No. of cases</th>
<th>Mortality (%)</th>
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<tbody>
<tr>
<td>Meleney (1924)</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Wilson (1952)</td>
<td>23</td>
<td>8 - 7</td>
</tr>
<tr>
<td>Crosthwait et al. (1964)</td>
<td>19</td>
<td>31 - 5</td>
</tr>
<tr>
<td>Rea and Wyrick (1970)</td>
<td>44</td>
<td>30</td>
</tr>
<tr>
<td>Wilson and Haltalin (1973)</td>
<td>11</td>
<td>38 - 2</td>
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In eight of the earlier patients of this series local treatment consisted of multiple incisions and drainage in five patients, and multiple incisions and excision of necrotic fascia in three. All eight patients received hyperbaric oxygen therapy (OHP). The initial response to treatment was good in five patients, fair in two and poor in another. The local lesion was completely arrested in only two patients. Seven patients (88%) died. Death was sudden in three cases with the clinical features of pulmonary embolism, and gradual in three with progressive toxaemia. The remaining patient was found at laparotomy to have secondary carcinomatosis.

In six later patients, extensive radical excision of the necrotic fascia and overlying skin was performed.
as soon as the diagnosis was established. Two patients died. In one patient who received OHP for 2 days, the lesion was arrested but this patient died from bronchopneumonia. The other patient developed necrotizing fasciitis 48 hr after negative diagnostic laparotomy for weight-loss and anaemia. Radical excision was performed (Fig. 3a and b). The lesion was completely arrested but this patient died later and post-mortem examination revealed carcinoma of the head of pancreas. In all six patients the excised skin was defatted and preserved and used for later grafting. A detailed account of two of the patients in this group is reported elsewhere (Tehrani et al., 1976).

The role of hyperbaric oxygen in the treatment of this condition remains to be determined. In most patients with gas gangrene treated in this centre, OHP combined with simple incision has usually been associated with rapid cessation of the primary condition. Encouraging results have also been reported (Grainger, MacKenzie and McLachlin, 1967) in the treatment of patients with synergistic bacterial gangrene. The authors have not gained evidence of a comparable beneficial effect in the treatment of necrotizing fasciitis. Certainly hyperbaric oxygen did not halt the spread of the necrotic process in the majority of their patients. Present experience would suggest that the high mortality associated with necrotizing fasciitis could further be reduced by earlier recognition and radical surgical treatment. OHP should not be regarded as a substitute for aggressive surgical intervention. The preservation and use of the excised overlying skin which has a normal appearance in the early stages of the disease process, not only prevents later skin gangrene but has the advantage of economy in the use of donor areas for subsequent grafting. There is the additional benefit of a reduction in the duration of in-patient hospital treatment.

References


Necrotizing fasciitis.

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