# Gas Gangrene Infections of the Small Intestine, Colon and Rectum*

CLAUDE R. HITCHCOCK, M.D., PH.D., MELVIN P. BUBRICK, M.D.

*From the Minneapolis Medical Research Foundation, Inc., and the Department of Surgery, Hennepin County Medical Center, Minneapolis, Minnesota 55415*

GAS GANGRENE INFECTION has historically been associated with military surgery, and its incidence in civilian practice has been considered to be exceedingly low.[16] Since construction of hyperbaric chamber facility in 1964, the Hennepin County Medical Center has served as a referral center for 133 patients having bacteriologically proved gas gangrene infections. Forty-one per cent of the infections were secondary to an elective surgical procedure or were "primary" in nature (42 cases following elective surgery, 22 "primary" cases), and 58 per cent were complications following trauma. As a result of our experience over the past decade, we now regard gas gangrene as an infection posing a constant threat to patients undergoing many types of elective surgery, and a disease process that is invariably lethal if diagnosis is delayed or if treatment is inadequate. This paper is based on 33 of our cases of gas gangrene in which the infection originated in the small bowel, colon, or rectum.

## Pathogenesis of Gas Gangrene Infection

The first anaerobic bacterium of the group of 90 species of bacteria known as "clostridia" was described in 1861 by Louis Pasteur, who reported an organism that uniquely produced butyric acid in culture (*Clostridium butylicum*). In 1891 Achalme described an organism of this group that subsequently was named *welchii* following the work of Welch and Nuttall in 1892. The name *perfringens* for this species was introduced by Veillon and Zuber in 1897, and current authors favor the use of *perfringens* to designate this most virulent species of the clostridia group.

Once started, the pathologic process of true gas gangrene can be so fulminating and rapid that death often occurs within 30–48 hours. Regrettably, some patients in America die each month of gas gangrene with the diagnosis totally unsuspected, or established too late for effective treatment. Only two factors are needed to initiate infection with this anaerobic organism, contamination of tissue with clostridia, and "hypoxia." From our clinical material it is obvious that transient localized hypoxia can stimulate germination of spores (often from the human gastrointestinal tract during surgical procedures), and bacterial growth progresses rapidly to produce violent changes in local tissues. Exotoxins produced by the organisms destroy, liquefy, and dissect surrounding tissue, producing a fulminating and rapid spread of the disease.

Intense and "woody hard" edema develops quickly in the area of infection and frequently causes occlusion of the micro-

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Address reprint requests to Dr. Hitchcock: Chief of Surgery, Hennepin County Medical Center, Fifth and Portland South, Minneapolis, Minnesota 55415.

circulation (arteriole–capillary–venule circuit) in tissues encased in fascial compartments or even the tight skin of the trunk or neck. Interference with adequate microcirculation by the intense edema fosters further hypoxia of tissues, which further enhances growth of the organisms. Thrombosis of local vessels occurs, and with the appearance of hydrogen sulfide and carbon dioxide gases dissecting along tissue planes, a virtually self-perpetuating and widely disseminating infection is established within a matter of hours. In our experience, in as short a time as 12–20 hours, the defense mechanisms of the host can be completely overwhelmed, phagocytic responses fail, and the patient succumbs from his disease. Under these conditions all organs of the body show the effects of the exotoxins. The kidneys are pale and grey, the liver is pale and soft, the brain has color changes and softening indicating the distant effects of these devastatingly toxic materials.

The alpha exotoxin is a lecithinase C and is highly lethal; it hemolyzes and necroses all tissues. The theta toxin is a hemolysin that necroses tissue and is highly lethal due to a specific cardiotoxic effect. The kappa toxin, a collagenase, is lethal due to its ability to lyse proteins. Nu toxin, a hyaluronidase, acts as a "spreading factor." Mu toxin affects the DNA of cells all over the body. Fibrinolysin is produced and lyses fibrin. Neuraminidase destroys the immunologic receptors on erythrocytes. Hemagglutinin inactivates the group factor A on erythrocytes, and the "circulating factor" inhibits phagocytosis.

## Classification

In our classification of this disease we refer to clostridial myositis, either localized or diffuse and spreading in type—or cellulitis, localized or diffuse and spreading in type. The term "cellulitis" in our classification is used to indicate involvement of all tissues in the true sense of cellular disease and includes infection of fascia, fat, nerve sheaths, peritoneum, connective tissues generally, etc.

TABLE 1. *Age Distribution*

| Age Range (Years) | Number of Patients |
|---|---|
| 0–9 | 0 |
| 10–19 | 3 |
| 20–29 | 5 |
| 30–39 | 2 |
| 40–49 | 2 |
| 50–59 | 4 |
| 60–69 | 9 |
| 70–79 | 6 |
| 80–89 | 2 |
| TOTAL | 33 |

Most previous investigators have had a misconception that only the patient with "diffuse spreading myositis" (*i.e.*, excessive muscle necrosis) had a truly serious gas gangrene infection.[1] Nothing could be further from the truth! Many of our patients had minimal involvement of muscle but extensive and ultimately lethal involvement of fascia, fat, skin, nerve sheaths, peritoneum, pleura, in fact virtually all tissues other than muscle.

In clinical practice we have found that therapy and prognosis are based more often on the aggressiveness of the infection, rather than on its origin as a subcutaneous cellulitis or subfascial myositis. Accordingly, in this study the distinction whether the infarction is localized or spreading and diffuse, rather than whether it is cellulitis or myositis, is emphasized.

## Early Recognition of the Disease

Constant awareness of the possibility of this infection will lead the alert physician to watch for early signs, such as pain out of proportion to the problem at hand, apprehension on the part of the patient with anxiety and restlessness, early onset of rap-

TABLE 2. *Etiologies of Infection*

| Operation or Infection | Number of Patients | Number of Deaths | Mortality (Per Cent) |
|---|---|---|---|
| Elective bowel resection | 12 | 7 | 58.3 |
| Perirectal abscess | 10 | 5 | 50.0 |
| Perforated bowel | 5 | 1 | 20.0 |
| Appendectomy | 3 | 0 | 0 |
| Colostomy | 2 | 1 | 50.0 |
| Small bowel resection for strangulated hernia | 1 | 0 | 0 |
| TOTAL | 33 | 14 | 42.4 |

TABLE 3. *Types of Infection*

| Type of Infection | Number of Patients | Number of Deaths | Mortality (Per Cent) |
|---|---|---|---|
| Localized disease | | | |
| Cellulitis | 7 | 3 | 42.9 |
| Myositis | 5 | 2 | 40.0 |
| TOTAL | 12 | 5 | 41.7 |
| Spreading diffuse disease | | | |
| Cellulitis | 9 | 3 | 33.3 |
| Myositis | 12 | 6 | 50.0 |
| TOTAL | 21 | 9 | 42.9 |

idly progressive edema of extreme degree, crepitation of the tissues in the area of the wound, and characteristic bronze color changes of the skin. Early x-ray examination of soft tissues can often demonstrate gas, which is presumptive evidence of a clostridial infection. The infected wound first drains a thin, watery type material, which shortly changes to a foul, putrid pus some hours later. A gram-stained smear of the exudate from the wound usually will aid in establishing the diagnosis by demonstrating large gram-positive rods which, again, are presumptive evidence of the infection. We believe all of these organisms should be grown in culture and the species determined. However, vigorous full-scale therapy should be applied immediately upon early suspicion of the disease.

## Clinical Material

**Age and Sex:** There were 21 male and female patients. The average age was 52.8 years, with a range of 15–84 years. About two-thirds of the patients were more than 50 years old (Table 1).

**Etiology of Infection:** (Table 2) In more than a third of the cases, the clostridial infection developed following an elective bowel resection. Ten cases originated as primary perirectal infections, and the remainder followed acute intra-abdominal inflammatory processes.

**Type of Infection:** Table 3 lists the types of infections involved. The disease was localized in 12 cases, and 21 cases were of the diffuse spreading type.

**Bacteriology:** Positive clostridial broth cultures were obtained from tissue juice

and muscle in all cases. The highly toxigenic *Clostridium perfringens* was by far the most common species cultured, being present in 29 of the 33 cases (Table 4).

All wounds were found to be contaminated with at least one secondary organism, with an average of 2.7 secondary organisms cultured from each wound. Alpha-hemolytic streptococcus and *Escherichia coli* were the organisms most frequently found (Table 5).

**Incubation Period:** The average incubation period was 3.8 days from the time of initial surgery or inflammation, with a range of seven hours to 14 days (Table 6). There was no significant difference between the incubation periods in the group with localized disease and the group with spreading diffuse disease.

## Treatment

**Initial Evaluation:** On each patient's arrival at the Hennepin County Medical Center, the history from the referring hospital was reviewed and the patient was thoroughly examined, with emphasis placed on the status of the infection and the associated disease processes present, particularly cardiopulmonary and renal disease. Bacteriologic studies, including wound smears and tissue cultures, were obtained on admission. Fluid-and-electrolyte resuscitation was initiated at once, and vigorous pulmonary care was instituted as indicated.

**Antibiotics:** All patients were treated with intravenous aqueous sodium penicillin G in doses of 12–24 million units per day, unless a history of penicillin allergy was present, in which case cephalothin or tetracycline was substituted as the primary antimicrobial agent. A second broad-spectrum antibiotic, generally cephalothin, tetracycline, or chloramphenicol, was used in all cases, and this was modified in accord with the sensitivity patterns of the secondary organisms cultured from the wounds.

TABLE 4. *Predominant Organisms Cultured*

| Organism | Number of Patients |
|---|---|
| *Clostridium perfringens* | 29 |
| *Clostridium tertium* | 1 |
| *Clostridium septicum* | 1 |
| *Clostridium capitovale* | 1 |
| Species undetermined | 1 |
| TOTAL | 33 |

TABLE 5. *Secondary Organisms Cultured*

| Organism | Number of Patients |
|---|---|
| Alpha-hemolytic streptococcus | 20 |
| *Escherichia coli* | 19 |
| Staphylococcus, coagulase-negative | 8 |
| *Klebsiella–Enterobacter* | 7 |
| *Proteus* | 6 |
| *Pseudomonas* | 6 |
| Diphtheroids | 5 |
| *Candida albicans* | 4 |
| *Bacteroides* | 3 |
| Beta-hemolytic streptococcus | 3 |
| Staphylococcus, coagulase-positive | 2 |
| *Peptococcus* | 2 |
| *Paracolobactrum* | 2 |
| *Serratia* | 2 |
| *Aerobacter* | 1 |
| TOTAL | 90 |

TABLE 6. *Incubation Periods*

| Type of Infection | Number of Patients | Average Incubation Period (Days) |
|---|---|---|
| Localized disease | | |
| Cellulitis | 7 | 3.7 |
| Myositis | 5 | 3.0 |
| TOTAL | 12 | 3.4 |
| Spreading diffuse disease | | |
| Cellulitis | 9 | 4.0 |
| Myositis | 12 | 4.0 |
| TOTAL | 21 | 4.0 |

TABLE 7. *Number of Treatments with Hyperbaric Oxygen*

| Number of Treatments | Number of Patients |
|---|---|
| 1 | 1 |
| 2 | 2 |
| 3 | 0 |
| 4 | 2 |
| 5 | 6 |
| 6 | 6 |
| 7 | 2 |

TABLE 8. *Control of Infection*

| Type of Infection | Number of Patients | Infection Controlled |
|---|---|---|
| Localized disease | | |
| Cellulitis | 7 | 6 |
| Myositis | 5 | 5 |
| TOTAL | 12 | 11 (91.7 per cent) |
| Spreading diffuse disease | | |
| Cellulitis | 9 | 9 |
| Myositis | 12 | 6 |
| TOTAL | 21 | 15 (71.4 per cent) |

**Antitoxin:** Only four patients in this study group had been given gas gangrene antitoxin by the primary referring physician. Previous data from our institution have failed to show any effectivness from the use of antitoxin.[6, 7]

**Surgery:** Following initial evaluation, fluid resuscitation, and antibiotic administration, the patients were taken to the operating room, where a full assessment of the extent of infection was made. All frankly devitalized and necrotic tissue was debrided. Our experience with the use of hyperbaric oxygen as supportive therapy has led us to be conservative in the debridement of marginally viable tissue, and accordingly, the need to remove tissue of questionable viability at the time of initial debridement has been eliminated.

**Hyperbaric Oxygen Therapy:** It has been our policy to employ hyperbaric oxygen therapy (HBO) when diffuse spreading myositis or cellulitis is present. We have also used HBO for localized disease in cases where there is a question as to the advancing nature of the disease process, providing no active pulmonary disease that might impose a serious risk to the development of pulmonary oxygen toxicity (Lorrain-Smith syndrome of progressive pulmonary fibrosis) is present.

HBO is administered by giving oxygen through a tight-fitting oronasal mask equipped with a demand valve. A respirator is used to deliver the oxygen if an endotracheal tube or tracheostomy tube is in place. The "bottom" time is two hours at 3 ATA (atmosphere absolute), after which decompression is started. All patients are accompanied by a physician during each chamber run.

The standard treatment schedule consists of three treatments in the first 24 hours, two treatments in the second 24 hours, and one treatment in the third 24 hours. This schedule is modified according to the response of the patient or the development of pulmonary or cerebral signs of oxygen toxicity. Nineteen patients in the series were treated with hyperbaric oxygen, with an average of 4.9 treatments per patient (Table 7).

## Results

**Control of Infection (Table 8):** The infection was controlled in 11 of the 12 patients who had localized disease (91.7 per cent). The one case in which the infection was not controlled involved a 57-year-old diabetic man who was moribund with severe congestive heart failure and renal failure; a perirectal abscess developed as a terminal event, and the patient died before treatment could be instituted.

The infection was controlled in 15 of 21 patients who had diffuse spreading disease

(71.4 per cent). The septic process was controlled in all nine patients with diffuse spreading cellulitis and in six of the 12 patients with diffuse spreading myositis. Of the six patients in the latter group in whom the infection was not controlled, three were moribund on initial evaluation and died within a few hours of admission.

**Mortality:** The overall mortality rate for the 33 patients in the series was 42.4 per cent. Mortality was highest for infections following elective bowel resection (Table 2).

The mortality rates were 41.7 per cent for the 12 patients who had localized disease and 42.9 per cent for the 21 patients with spreading diffuse disease (Table 3). None of the deaths among the patients with localized disease was attributable to lack of control of the infection, but rather death was secondary to the severe associated disease processes present (Table 9). Among the nine deaths in patients with diffuse spreading disease, six were directly related to uncontrolled infection although, as noted, three of these patients were terminally ill at the time of initial evaluation (Table 10).

Among both groups of patients, pneumonia, renal failure, and gastrointestinal hemorrhage were the leading factors contributing to death.

TABLE 9. *Causes of Death, Localized Disease*

| Patient | Cause of Death |
|---|---|
| 1 | Renal failure |
| 2 | GI hemorrhage<br>Renal failure<br>Hepatic failure |
| 3 | GI hemorrhage<br>Pulmonary insufficiency |
| 4 | Pulmonary embolism<br>Hepatic failure |
| 5 | Localized cellulitis – uncontrolled*<br>Congestive heart failure<br>Renal failure |

* Patient moribund on admission.

TABLE 10. *Causes of Death, Spreading Diffuse Disease*

| Patient | Cause of Death |
|---|---|
| 1 | Spreading, diffuse myositis – uncontrolled<br>Myocardial infarction<br>Pneumonia<br>Renal failure |
| 2 | Spreading, diffuse myositis – uncontrolled* |
| 3 | Pneumonia and oxygen toxicity |
| 4 | Pneumonia<br>GI hemorrhage<br>Renal failure |
| 5 | Spreading, diffuse myositis – uncontrolled<br>Pneumonia and pulmonary emboli<br>Renal failure |
| 6 | Spreading, diffuse myositis – uncontrolled* |
| 7 | Spreading, diffuse myositis – uncontrolled<br>Congestive heart failure |
| 8 | Spreading, diffuse myositis – uncontrolled*<br>Pneumonia |
| 9 | Pneumonia |

* Patient moribund on admission.

**Results of Hyperbaric Oxygen Therapy (Table 11):** HBO therapy was used in treatment of only three of the patients who had localized disease. Of the 21 patients with diffuse spreading disease, 16 were treated with HBO, and ten survived (37.5 per cent mortality) compared with two survivors among the other five patients treated without HBO (60.0 per cent mortality).

## Discussion

The clostridia are ubiquitous organisms occurring naturally in man, animals, and soil.[12] Although gas gangrene is not common, the uniform presence of clostridia, particularly the highly toxigenic *Clostridium perfringens*, in the intestinal tract of man makes infection with this organism an ever-present danger following surgery or inflammation about the gastrointestinal tract.

TABLE 11. *Results of Hyperbaric Oxygen Therapy*

| Type of Infection | Treatment Including HBO | | | Treatment Not Including HBO | | |
|---|---|---|---|---|---|---|
| | Number of Patients | Number of Deaths | Mortality (Per Cent) | Number of Patients | Number of Deaths | Mortality (Per Cent) |
| Localized disease | | | | | | |
| Cellulitis | 1 | 0 | 0 | 6 | 3 | 50.0 |
| Myositis | 2 | 1 | 50.0 | 3 | 1 | 33.3 |
| TOTAL | 3 | 1 | 33.3 | 9 | 4 | 44.4 |
| Spreading diffuse disease | | | | | | |
| Cellulitis | 8 | 3 | 37.5 | 1 | 0 | 0 |
| Myositis | 8 | 3 | 37.5 | 4 | 3 | 75.0 |
| TOTAL | 16 | 6 | 37.5 | 5 | 3 | 60.0 |

Survival following different types of clostridial infections has been difficult to assess in the surgical literature. Several small series of cases of clostridial sepsis of the abdominal wall and clostridial infections developing after abdominal surgery have been reported, with combined mortality rates in the range of 35 per cent.[4, 10, 11, 14] Fromm and Silen[4] reviewed the literature on 111 cases of postoperative clostridial sepsis of the abdominal wall and found a mean mortality rate of 60 per cent. Isenberg[8] reviewed 25 cases of clostridial infection from one institution and found an overall survival rate of 36 per cent, yet only three of 13 patients with postoperative infection survived and all patients who had gas gangrene of the abdominal wall died. Reporting from a referral center in Amsterdam similar to our own, Roding *et al.*[13] recently reviewed 130 cases of gas gangrene, of which 31 cases developed after operation; the mortality rate was 45.2 per cent in the latter group.

Although surgery and antibiotics are well established as the keystone to the therapy of gas gangrene, there has been continued controversy over the use of hyperbaric oxygen therapy during the past decade. The successful use of HBO in the treatment of gas gangrene was first reported by Brummelkamp *et al.*[2] in 1961. Since that time, other investigators have confirmed the efficiency of HBO as additive therapy for clostridial infections,[6, 7, 9, 13, 15, 16] although still others have questioned its value.[1, 5]

In a controlled study from our research laboratories, Demello *et al.*[3] used heat-shocked spores of *C. perfringens* to produce a characteristic gas gangrene infection in dogs. There were no survivors among 70 untreated controls. There were also no survivors among dogs treated by HBO only, surgery only, or HBO and surgery together. Survival was 50 per cent when antibiotics were used, 70 per cent when antibiotics and surgery was employed together, and 95 per cent when triple therapy consisting of antibiotics, surgery, and HBO was employed. These results confirmed the supportive value of hyperbaric oxygen therapy when used in conjunction with surgery and antibiotics.

The mortality rates reported for localized and diffuse spreading disease in this series are still distressingly high. The deaths among patients who had localized disease were no doubt more directly related to the more serious associated disease processes than to the clostridial infections. However, it would appear that among the

patients with diffuse, spreading disease particularly these cases developing after elective surgery, earlier diagnosis and treatment could have greatly improved survival.

## Summary

Thirty-three cases of gas gangrene infections originating from the small bowel, colon, and rectum are reviewed. The distinction between localized and diffuse, spreading, types of infection is made. The overall mortality rate was 42.4 per cent and mortality was highest for infections following elective bowel resections.

Treatment consisted of antibiotics and surgical debridement, with hyperbaric oxygen used as adjunctive therapy for the more serious cases. The importance of early recognition of clostridial infection is stressed as the key to improved survival.

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