Recognising necrotising fasciitis

Necrotising fasciitis is a blanket term that is used to describe skin and soft tissue infections caused by one or a number of bacterial species (Schwartz and Kapila, 2004). In many cases, the disease progresses rapidly, causing large areas of soft tissue damage, extreme pain for the patient, and systemic sepsis if left untreated. Early diagnosis and prompt treatment are essential to halt the progress of the disease. This article examines a variety of presentations of necrotising fasciitis with the aim of assisting the clinician in achieving prompt recognition and providing appropriate treatment.

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KEY WORDS
Necrotising fasciitis
Monomicrobial
Polymicrobial
Streptococcus pyogenes
Prompt recognition
Appropriate treatment

Necrotising fasciitis is a relatively rare infection that is said to affect between 500–1500 individuals in the US annually (Wong et al, 2003), with the reported incidence of 0.40 cases per 1000000 population (Poromanski, 2004). It is a potentially life-threatening disorder, in which bacterial toxins invade and destroy large areas of host tissue. The infection has been attributed to a variety of organisms.

The most well known of these is the Group A haemolytic streptococcus commonly referred to as *Streptococcus pyogenes*. It is, however, important to recognise that this bacterium is often not the only one responsible for necrotising soft tissue infection.

Three distinct types of necrotising infection have been identified:

- Type 1: Refers to a polymicrobial synergistic infection which may or may not include *S. pyogenes* (Wong et al, 2003; Levine and Manders, 2005)
- Type 2: Refers to a monomicrobial infection usually caused by *S. pyogenes* (Loudon, 1994), involving about 10% of all cases (Levine and Manders, 2005). Identification of type 2 is often confused due to the ability of other organisms to cause significant tissue destruction once the initial infection has taken hold. Other organisms reported to cause this type of infection include Group B Streptococci (Gardam et al, 1983) and *Klebsiella* spp. (Wong et al, 2003)
- Type 3: Refers to tissue infection caused by Clostridial organism which causes myonecrosis (Ray et al, 2003; Perry and Floyd, 2004). In such cases, the presentation may be termed clostridial myonecrosis (Kramer and Doering, 2001) and is attributable to a virulent alpha toxin (O'Brien and Melville, 2004; Sakurai et al, 2004).

Aetiology

Many of the studies carried out disagree as to the exact organisms responsible for causing necrotising fasciitis. Despite many infections being identified as monomicrobial, some studies have highlighted a number of polymicrobial infections. In such cases, a number of organisms work synergistically to destroy tissue by similar means to a monomicrobial streptococcal infection.

In a study by Elliott et al (2000), only 28 of 182 patients (approximately 15%) with necrotising skin infections had an infection caused by a single pathogen. The remaining 154 patients had polymicrobial infection, with an average of 4.4 different causative organisms present on culture. The most common organism found in this study, in both the monomicrobial and polymicrobial infections, was *S. pyogenes*.

In another study by Childers et al (2002), of 145 patients with necrotising infection, only 29% were found to be monomicrobial; the remaining 71% had up to six different organisms present. In a similar study, Wong et al (2002) found that 25 out of 89 patients (28.1%) had monomicrobial infection compared with 48 patients (53.9%) having polymicrobial infections. In these patients the organisms found included *streptococcal* spp., *staphylococcal* spp., enterococci and *enterobacteriaceae*, such as *Escherichia coli, Pseudomonas* and *Klebsiella* (Wong et al, 2003).

A common finding across all the studies is the low number of clostridium isolates in cases where the primary infecting organism is *S. pyogenes* (Childers et al, 2002; Elliott et al, 2002; Wong et al, 2003).

Streptococcus pyogenes

S. pyogenes is a gram-positive, non-spore forming coccus that occurs in

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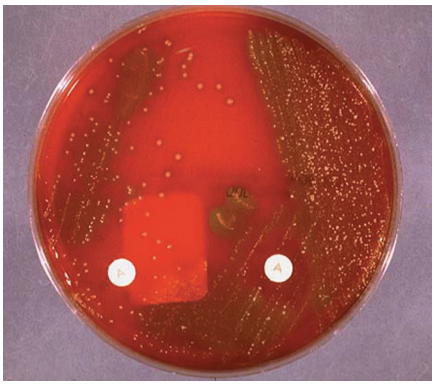


Figure 1. The lysing effect of *Streptococcus pyogenes* on blood agar.

chains or in pairs. This organism is one of the most frequent pathogens of humans and is believed to be present in 5%–15% of the population, normally occuring in the respiratory tract (Todar, 2002).

When the bacteria are introduced or transferred to vulnerable areas, suppurative infection may ensue. Puerperal fever (post-childbirth sepsis) was largely attributed to the presence of *S. pyogenes* during the last century. Historically, soft tissue infection of the groin/pelvic region was referred to as Fournier's Gangrene (Headley, 2003). Acute episodes of *S. pyogenes* infection may present as pharyngitis, impetigo, cellulitis, toxic shock syndrome, and, necrotising fasciitis (Hackett and Stevens, 1993).

In-vitro, the bacteria requires an enriched medium containing blood in which to grow. The streptococcal organism has largely been classified using agar plating to note the type of haemolytic reaction displayed (*Figure 1*). The reaction of Group A haemolytic streptococcus on agar is the complete lysis of the red blood cells present, compared with the haemolysis reaction of some bacteria which results in only partial haemolysis of the red blood cells leaving a green residue on the plate (Sleigh and Timbury, 1994).

Pathophysiology

S. pyogenes may enter the body through either long-standing chronic wounds or through an acute wound entry site.

Some strains of *S. pyogenes* form a capsule composed of hyaluronic acid (HA). This mimics the HA-rich connective tissue of the host dermis and, for this reason, the capsule is non-immunogenic. This results in the reduced functioning of polymorphonuclear leucocytes allowing greater proliferation of the organism (Caputo et al, 1997; Poromanski et al, 2004).

Beneath the capsule is the cell wall, which contains the group- and type-specific antigens of *S. pyogenes*. Three type-specific protein antigens have been identified:

- M protein: a major antigen and virulence determinant associated with virulent streptococci, it protects the bacteria against phagocytosis and also prevents interaction with complement. In the absence of M protein, streptococci are not infectious
- T protein: an important epidemiological marker
- F protein: mediates adherence to epithelial host cells.

The virulence of *S. pyogenes* is determined by a variety of elaborate toxins and enzymes, and once established within the host cell, the bacteria begins to release them. They have been identified by Sleigh and Timbury (1994) as:

- Streptokinase: a protease which breaks down fibrin
- Hyaluronidase: an enzyme which attacks and breaks down HA in the host dermis, and also in the capsule surrounding the organism in order to enable replication
- Proteases (invasins): which contribute to tissue necrosis
- Nicotenamide adenine dinucleotidase: which destroys host leucocytes
- Haemolysins: 'lyse' or break down erythrocytes
- Streptococcal pyrogenic exotoxins (Erythrogenic toxins): have a variety of important effects, including enhancement of delayed hypersensitvity and susceptibility to endotoxin, cytotoxicity, and immunosuppression of B-lymphocyte function. They also stimulate T cells to release massive amounts of cytokines which creates signs of shock, fever, rash and hypotension. They are also responsible for the erythematous rash visible in scarlet fever
- Streptolysins: Streptolysin O is an oxygen-labile enzyme which is leucotoxic causing leucocyte malfunction (Darenberg et al, 2003). Streptolysin S can lyse erthrocytes, leucocytes and platelets following direct cell contact
- DNAase: reduces the viscosity of abscess material thereby facilitating spread of the organism. It also assists in the evasion of the innate immune system.

It is thought that the combination of theses enzymes and toxins contribute greatly to the local and systemic damaging effects of *S. pyogenes*.

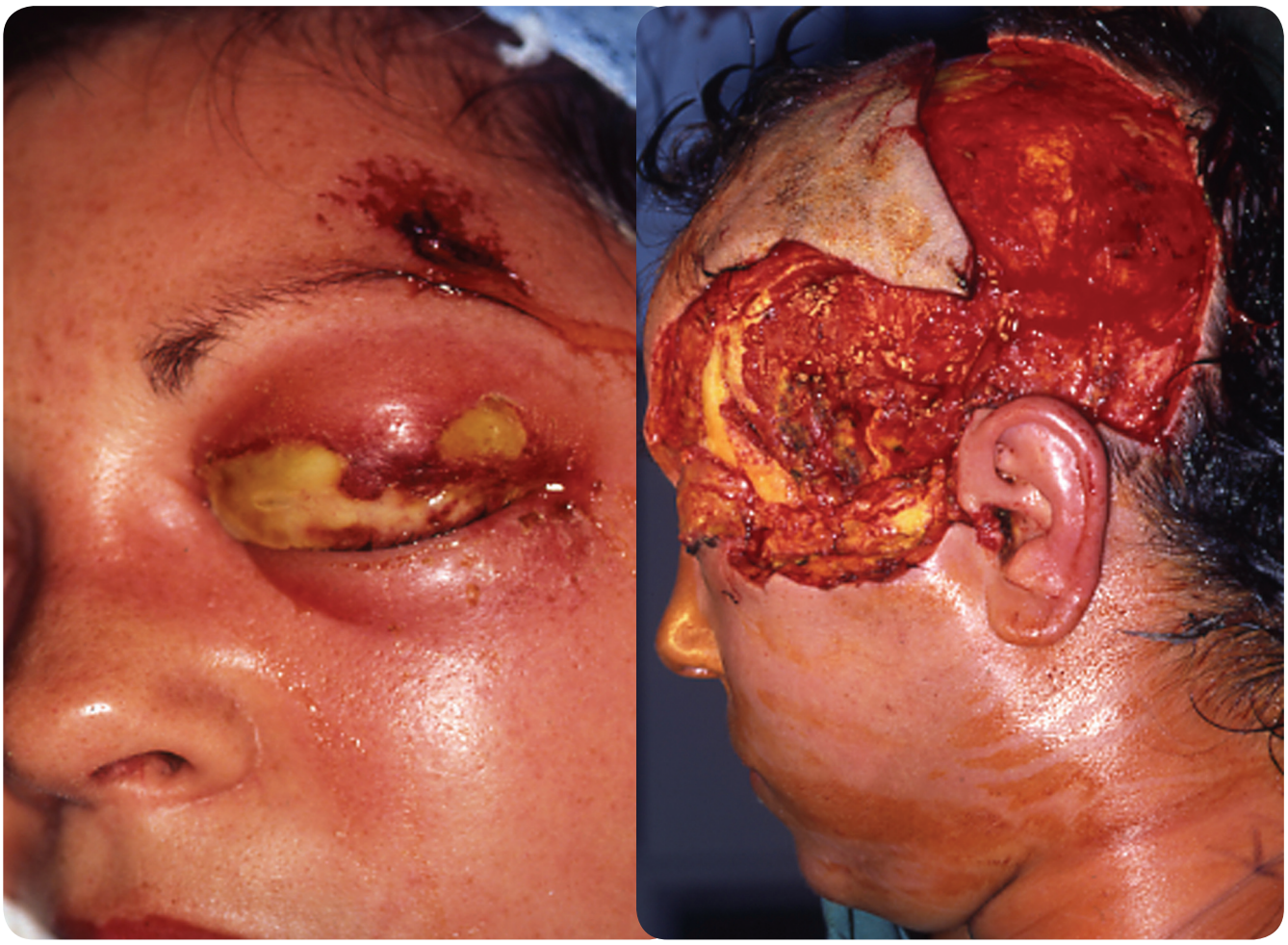
As a result of tissue and microvascular destruction, a reduction in blood supply causes secondary tissue ischaemia. Clotting and thrombosis occur within the vessels, thereby affecting the local tissues which become ischaemic and die. This results in the killing of host cells, provoking a further and potentially damaging inflammatory response. The histamine reaction that follows causes fluid to leak out of the local capillaries into the extravascular space (Fink and De Luca, 2002).

The toxins released by *S. pyogenes* may also lead to abcesses and eventual organ failure. Other complications include disseminated intravascular coagulopathy and multi-system organ failure.

Presentation and clinical features

Schwartz and Kapila (2004) and Wong and Wang (2005) suggested the following clinical features as being linked with necrotising infection:

- Rapid progression
- Poor therapeutic response
- Blistering necrosis



Figures 2a and b. These photographs of a young female patient clearly show that the initial injury above the left eye and the ensuing infection of the surrounding tissue, the eye itself being closed due to the local oedema. A large area of tissue had to be excised in order to arrest the progress of the infection.

- Cyanosis
- Extreme localised tenderness
- Pyrexia
- Tachycardia
- Hypotension
- Altered level of consciousness.

To complement these features, the demographic, clinical, biochemical and radiographic data have been summarised (Wong et al, 2003).

The presentation of necrotising fasciitis varies, depending on the site and also the presence or absence of a chronic wound from which the infection propagates. The history may therefore reflect recent trauma (*Figures 2a and b; 3, 4*) or surgery (*Figure 5*) or in the case of chronic wounds, the patient may already be known to the healthcare team (*Table 1*).

In some cases, there is little evidence of trauma or skin damage before the development of symptoms (*Figure 6*) (Headley, 2003). This can make early diagnosis difficult, however, there are a number of key characteristics that may be observed (Poromanski et al, 2004).

In cases of acute infection of previously unbroken skin, the time from injury to development of severe symptoms can be very short (0–2 hours in some cases). Clinically, necrotising fasciitis often begins with pain disproportinate to skin signs. In long-standing wounds, an increase in pain, possibly associated with an increase in exudate levels may indicate a change in the bioburden of a wound and may precipitate an acute streptococcal infection.

Studies report patients experiencing pain beyond that which would be associated with 'normal' wound pain, therefore, this may be a useful clinical indication (Childers et al, 2002). It must be added, however, that diabetic patients with neuropathy may not experience pain to this degree making diagnosis more difficult (Caputo et al, 1997). There is little evidence relating to the initial clinical findings, such as pain and fever in diabetic patients, with necrotising disease.

The pain then changes to swelling and soft tissue erythema that does not respond to antibiotics. Rapid progress to a pathognomic gray-blue skin is followed by necrosis (*Figure 3*). Where crepitance is detected (in about 30% cases), it is associated with polymicrobial infection.

In some patients, violaceous bullae can be noted on the skin surface, and these are often filled with foul smelling 'dish water pus'. Left untreated, the lesion may spread and a systemic toxic reaction may follow once the toxins enter the bloodstream (Headley, 2003). Shock and tachycardia follow.

Pyrexia is common but not always present, and temperature should be monitored as soon as infection is suspected. Some studies report a temperature of greater than 38°C as indicative of more severe systemic infection (Childers et al, 2002).

Risk factors

Although there are no conclusive studies which describe all the risk factors for the development of necrotising fasciitis, most authors agree that there are certain factors which, if present, may predispose a patient to a necrotising infection (*Table 1*). Most studies carried out to date have been presentations of retrospective data, highlighting the key, common factors, which were present in a group of patients over a given period of time. These studies, despite agreeing on many of the key risk factors, show very different rates of occurrence when comparing the risk factors involved. Childers et al (2002) examined retrospective data for a group of 163 patients and found that 58% of the patients were smokers, 35% had diabetes, and 27% were intravenous drug users.

Wong et al (2003) found that among the 89 patients involved, 63 (70.8%) had diabetes, 20 (22.5%) had peripheral vascular disease, and chronic liver disease and cancer were also implicated in this study with only 12 subjects (13.5%) having no co-morbid factors. Significantly, mortality was adversely affected by an increase in the length of time from onset of symptoms to diagnosis, and then time to operation (Wong et al, 2003).

The speed at which the disease can progress, and its severity, has implications for practitioners in both primary and acute care settings. Awareness of the risk factors and also of early disease presentation is therefore essential to prevent complications and to ensure swift treatment.

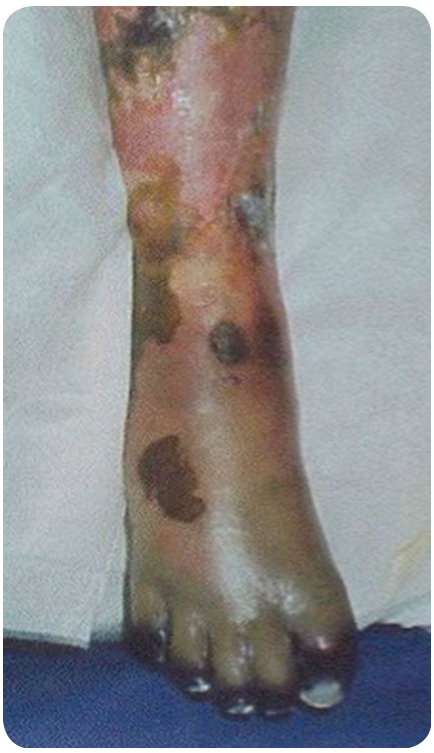


Figure 3. A 30-year-old female with Streptococcal infection of the lower leg, believed to have followed on from initial injury to hand. A rapidly spreading cellulitis and swelling of tissue is noted, which moves from red to dusky blue as the local vascular network is destroyed.

Diagnosis

The early diagnosis of necrotising infection is often delayed due to the lack of early signs of infection (Wong et al, 2003; Wong and Wang, 2005). While an awareness of the risk factors asociated with necrotising fasciiitis may aid diagnosis, some patients present with no predisposing factors. Wong et al (2003; *Table 2*) have listed physical findings noted on presentation. In cases in which a chronic wound is present, the practitioner may suspect a change in the wound status or in the overall patient condition (*Table 1*). Although diagnosis is primarily clinical, a variety of investigations are of value; these include aspiration for microbial culture, frozen section histopathology and radiography. The latter may be used to expedite surgical intervention (Levine and Manders, 2005). A diagnostic tool has been developed;

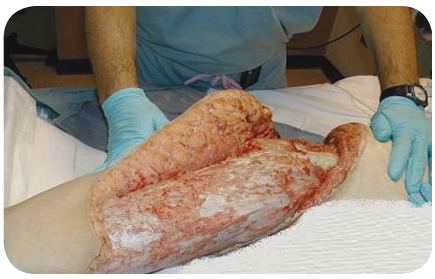


Figure 4. The leg of a 36-year-old female undergoing surgical debridement for necrotising fasciitis following initial trauma to the knee.

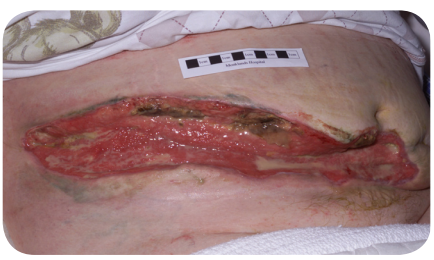


Figure 5. Female post-abdominal surgery with polymicrobial wound infection.

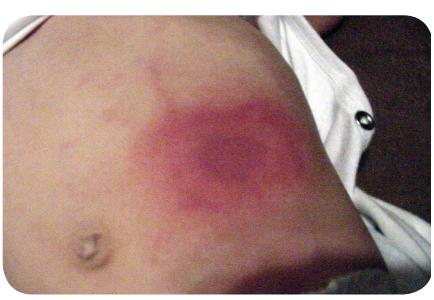


Figure 6. This image highlights the initial presentation of a young child following Herpes zoster infection, possibly from itching a chicken pox lesion.

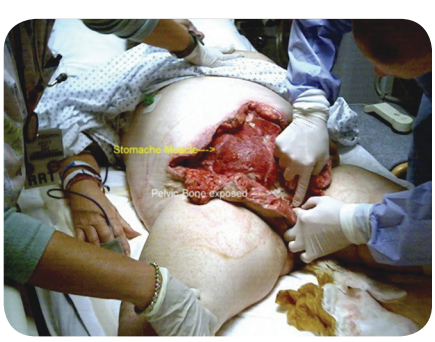


Figure 7. Surgical debridement of the abdomen of a 58-year-old female with Fournier's gangrene.

Table 1

Risk factors for necrotising soft tissue infection and possible presentations

Risk factor	Presentation
Age (greater than fifty)	Pain (usually greater than site implies)
Atherosclerosis	Erythema
Presence of chronic wound	Pyrexia
Cancer or immunocompromised	Bullae
Alcoholic liver disease	Apparent bruising
Corticosteroid use	Extensive necrosis
Diabetes mellitus	Swelling
Hypoalbuminaemia	Signs of organ failure (late diagnosis)
Intravenous drug abuse	Sweating
Renal failure	Tachycardia
Trauma	Toxic delirium
Obesity	
Malnutrition	
Occult diverticulitis	
Post-operative infection	
Peripheral vascular disease	
Strangulated femoral hernia	
Use of non-steroidal medication (inconclusive)	

Table adapted from Timmons (2004)

Table 2

Physical findings on admission (Wong et al, 2003)

Physical finding	Patient (%)
Tenderness	97.8
Erythema	100
Warm skin	96.6
Bullae	45
Crepitus	13.5
Necrosis of skin	13.5
Hypotension	18
Fever (temp over 38°C)	52.8
Tachycardia (pulse over 100bpm)	74.2

this is based on patient information such as medical history, clinical signs and symptoms, and tests (Poromanski et al, 2004). The findings obtained were broadly similar to those reported by Wong et al (2003) and listed in *Table 2*.

Differential diagnoses include cellulitis, trauma with haematoma, and deep vein thrombosis (File and Tan, 2000). A feature that distinguishes cellulitis is the disproportinate pain seen in necrotising fasciitis. This feature forms part of a Laboratory Risk Indicator for Necrotizing Fasciitis, a robust score capable of detecting even early cases (LRINEC; Wong et al, 2004).

Treatment

Any delay in treatment is associated with an increase in mortality of the condition (Aronoff and Bloch 2003; Headley, 2003).

Pharmacological

Intravenous antibiotics should be administered as soon as is possible in order to attempt to slow the progress of the organism. It is recommended that penicillin, in the form of benzyl penicillin, should be used to treat the streptococcal components and it must be kept in mind that a number of these infections are polymicrobial so further treatment with broad-spectrum agents is often necessary. Clindamycin, gentamycin and metronidazole are commonly required (Fink and De Luca, 2002; Headley, 2003).

Surgical

Aggressive surgical debridement is essential to minimise the effects of this condition. The non-viable tissue is removed, leaving a wide margin of unaffected tissue in order to minimise the risk of recurrence. This explains the large excision margins that surgeons leave (*Figures 2b, 4, 7*).

Psychological

Patients may be surprised by the results post-operatively, as the initial wound will not be representative of the final wound that the surgeon creates to excise wide margins around the lesion.

Adequate psychological preparation is necessary in the preoperative phase; although this may prove difficult given the speed of the disease process. Caring for relatives is also essential, however, there are few studies which examine the before and after care of this patient group in sufficient depth as to examine the psychological responses of patient and relative.

Future developments

The role of hyperbaric oxygen has also been used to some effect in some studies, with the increase in oxygen in the wound assisting in faster wound healing and also a reduction in bacterial numbers. The results are inconclusive and this therapy should only be used as an adjunct to surgery and antibiotics, not a replacement (Bissett, 2002).

Conclusion

The rapid progression of the symptoms of necrotising skin infection make prompt diagnosis and treatment a priority. The rare occurrence of this condition may also result in misdiagnosis due to a lack of experience of the clinician involved. It is essential that staff in all areas are aware of the presentation of this disease and the risk status of the patient.

Failure to identify necrotising fasciitis can result in extensive tissue loss or death. Given its infrequency, it is vital that practitioners remain alert to its existence.

Most of the research to date has been retrospective and therefore fails to

answer some of the questions, such as which systemic treatments are most beneficial, and which topical treatments can produce the most desirable patient outcomes following debridement.

The key message from this article is that all staff should consider necrotising skin infection as a potential factor in any case which presents with the signs and symptoms mentioned. By doing so, this will maximise the patient's chance of survival and reduce the level of tissue damage caused by the organism. WUK

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Key Points

- Necrotising fasciitis is a relatively rare and life-threatening disorder, in which bacterial toxins invade and destroy large areas of host tissue.
- The rapid progression of necrotising skin infection make prompt diagnosis and treatment a priority.
- Failure to identify necrotising fasciitis can result in extensive tissue loss or death.
- Given its infrequency, it is vital that all practitioners remain alert to its existence.
- By considering necrotising fasciitis, the patient's chance of survival will be maximised, and the level of damge caused by the organism(s) reduced.

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