

Necrotizing fasciitis

Philippe Montravers, MD, PhD
Assistance Publique Hopitaux de Paris
Pole TCAUR
CHU Bichat Claude Bernard - HUPNVS
Université de Paris
Paris, France



Disclosures

- Speaker for Astra Zeneca, Basilea, MSD, The Medicines Company and Pfizer
- Advisory board membership for Astra Zeneca, Bayer, Menarini, MSD, Parexel, The Medicines Company, Pfizer and Tetraphase,

Recent guidelines for necrotizing infections

Clinical diagnosis	SIS [1]	JSC/JAID [2]	WSES [3]	IDSA [4]	KSID* [5]	ISITD [6]
Necrotizing infections	+	+	+	+	+	+
Clostridial gas gangrene		+		+		
Nonclostridial gas gangrene		+				
Myonecrosis or Pyomyositis			+	+	+	+
Necrotizing fasciitis			+	+	+	+
Synergistic gangrene						
Fournier's gangrene			+	+		+

* community-acquired cases

SIS: Surgical Infection Society

JSC/JAID: Japanese Society of Chemotherapy / Japanese Association for Infectious Diseases

WSES: World Society of Emergency Surgery

IDSA: Infectious Diseases Society of America

KSID: Korea Society of Infectious Disease

ISITD: Italian Society of Infectious and Tropical Diseases

1. May AK, et al. *Surg infect* 2009, 10:467-499.
2. *J Infect Chemother* 2011, 17 Suppl 1:72-76.
3. Sartelli M, et al. *World J Emerg Surg* 2014, 9:57.
4. Stevens DL et al. *Clin Infect Dis* 2014, 59:e10-52.
5. Kwak YG et al. *Infect Chemother* 2017;49:301-25
6. Esposito S et al. *J Chemother* 2017;29:197-214

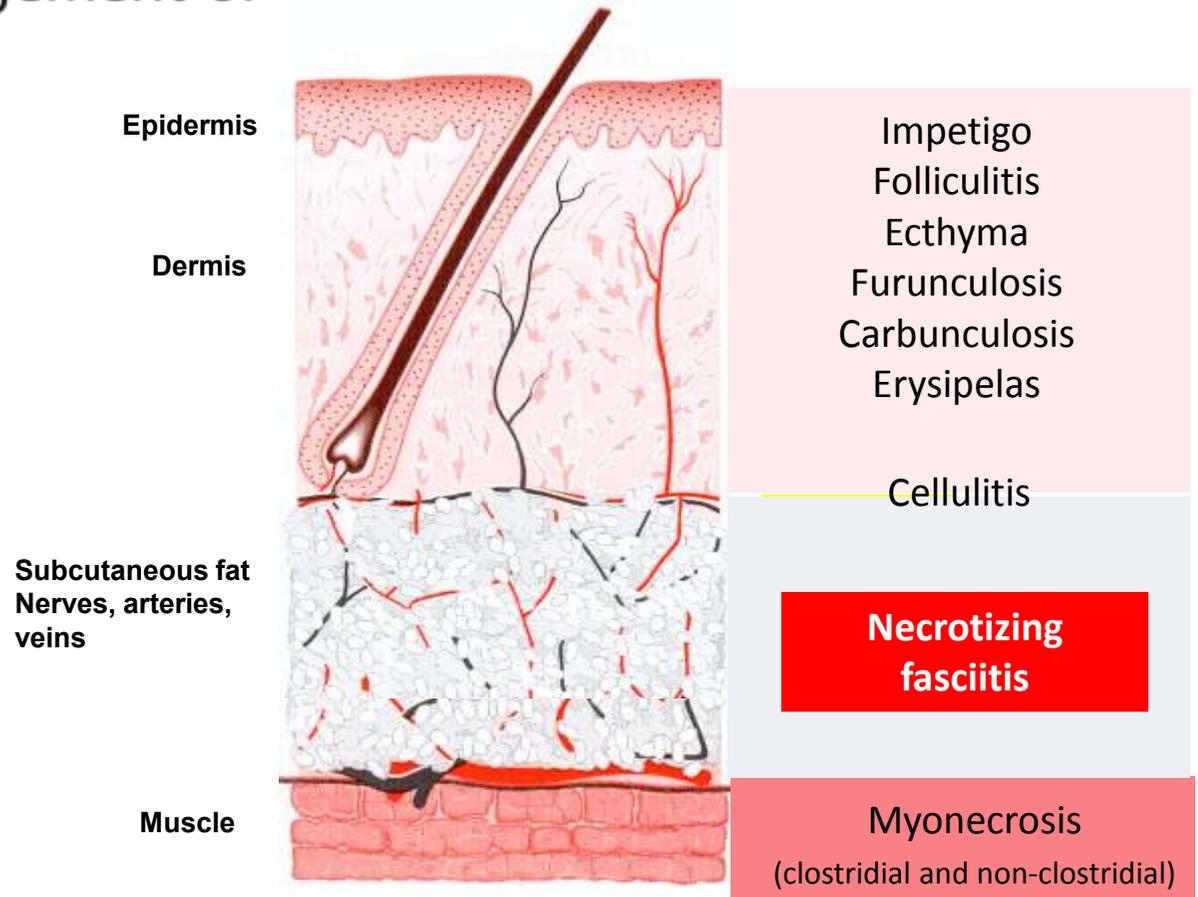
2018 WSES/SIS-E consensus conference: recommendations for the management of skin and soft-tissue infections

Sartelli et al. *World Journal of Emergency Surgery* (2018) 13:58
<https://doi.org/10.1186/s13017-018-0219-9>

Necrotizing soft-tissue infections are

- **life-threatening**
- **Invasive**
- soft-tissue infections
- with a necrotizing component
- involving **any or all layers** of the soft-tissue compartment
- from the **superficial dermis and subcutaneous tissue to the deeper fascia and muscle**

Sartelli M et al. *World J Emerg Surg* 2018;13:58



- Nichols RL et al. *Clin Infect Dis*. 2001;33(Suppl 2):S84–93;
- Stevens DL, et al. *Clin Infect Dis*. 2005;41:1373–406.



Classifications of necrotizing soft tissues infections

Examples in reviews and guidelines

Classification factor	Comment
Anatomic location	Perineum/limb/trunk/head and neck
Surgical site infection	Incisional -superficial -deep
Speed of progression	Chronic/subacute/acute
Depth of infection	Dermal and subcutaneous (Cellulitis) Fascial (Fasciitis) Muscular (Myositis) Fournier's gangrene*
Microbial cause	Type I: polymicrobial (most common) Type II: monomicrobial (staphylococci, streptococci, clostridia...) Type III*: <i>Vibrio vulnificus</i> , <i>Aeromonas hydrophilia</i> , <i>clostridia</i> ... Type IV*: candidas , zygomycetes
Clinical severity	1-Afebrile and healthy, other than cellulitis 2-Febrile and ill appearing, but not unstable comorbidities 3-Toxic appearance, or at least one unstable comorbidities, or a limb-threatening infection 4-Sepsis syndrome or life-threatening infection, e.g.necrotizing fasciitis

* not universally accepted

Eron LJ et al. *J Antimicrob Chemother* 2003;52 SupplS1:i3-i17
Hakkarainen TW et al. *Curr Prob Surg* 2014;51:344-362
Misiakos EP et al. *Front Surg* 2014;1:36

Sartelli M et al. *World J Emerg Surg* 2014, 9:57
Stevens DL and Bryant AE. *N Engl J Med* 2017;377:2253-65
Esposito S et al. *J Chemother* 2017 2017;29:197-214

Necrotizing and spreading infections in practice

- Initial presentation can be insidious
- Innocent early clinical aspect
- Major importance of underlying disease
(dermatological conditions, diabetes, chronic renal failure, hemodialysis...)
- Rapid rate of progression (a few hours)
- Delayed diagnosis and initiation of therapy
 - Frequent morbidity
 - Significant mortality rates
 - Increased fatality with delayed management

Diagnosis and Evaluation of severity

Clinical features suggestive of a necrotizing infection:

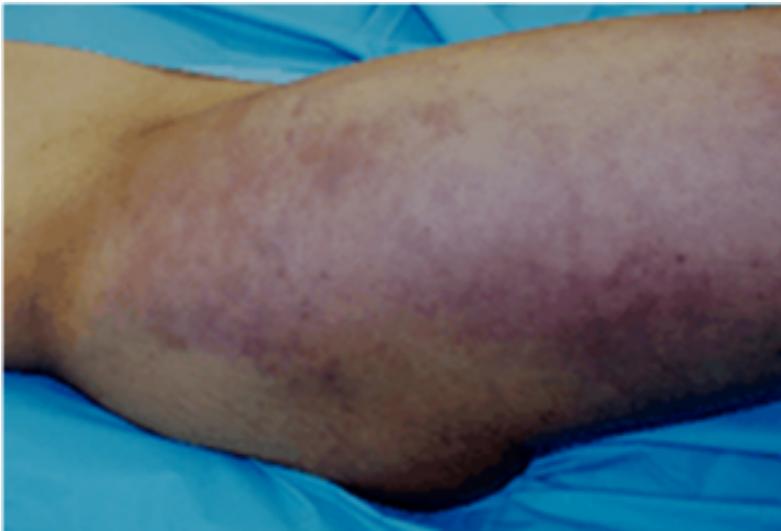
- Severe, constant pain
- Bullae (related to occlusion of deep blood vessels)



Diagnosis and Evaluation of severity

Clinical features suggestive of a necrotizing infection:

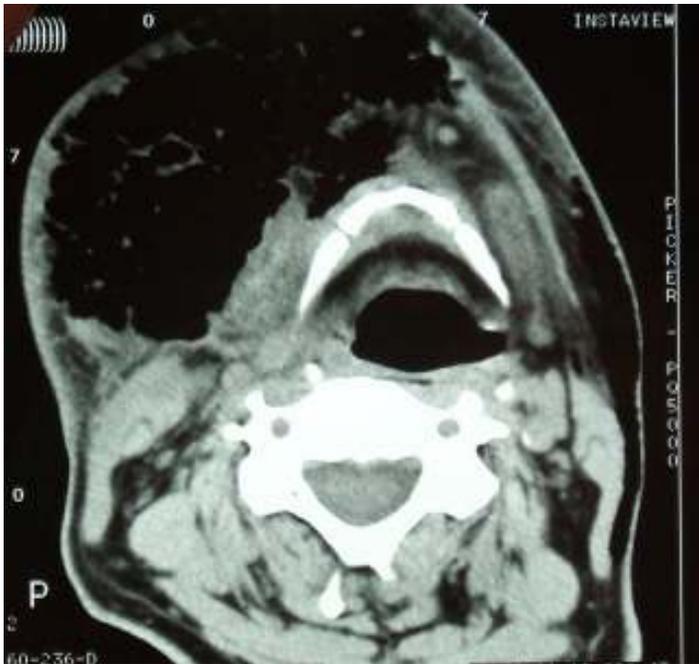
- Severe, constant pain
- Bullae (related to occlusion of deep blood vessels)
- Skin necrosis or ecchymosis (bruising) precedes skin necrosis



Diagnosis and Evaluation of severity

Clinical features suggestive of a necrotizing infection:

- Severe, constant pain
- Bullae (related to occlusion of deep blood vessels)
- Skin necrosis or ecchymosis (bruising) precedes skin necrosis
- Gas in the soft tissues, detected by palpation or imaging



Diagnosis and Evaluation of severity

Clinical features suggestive of a necrotizing infection:

- Severe, constant pain
- Bullae (related to occlusion of deep blood vessels)
- Skin necrosis or ecchymosis (bruising) precedes skin necrosis
- Gas in the soft tissues, detected by palpation or imaging
- Œdema that extends beyond the margin of erythema
- Cutaneous anaesthesia
- Sepsis or severe sepsis
- Rapid spread, especially during antibiotic therapy

How can necrotizing infections be recognized early?

- Separate patients into two categories
 - High risk of poor outcome (septic shock/ARDS/ Organ failure...)
 - Mild/moderate risk of poor outcome

What is the best timing of source control ?

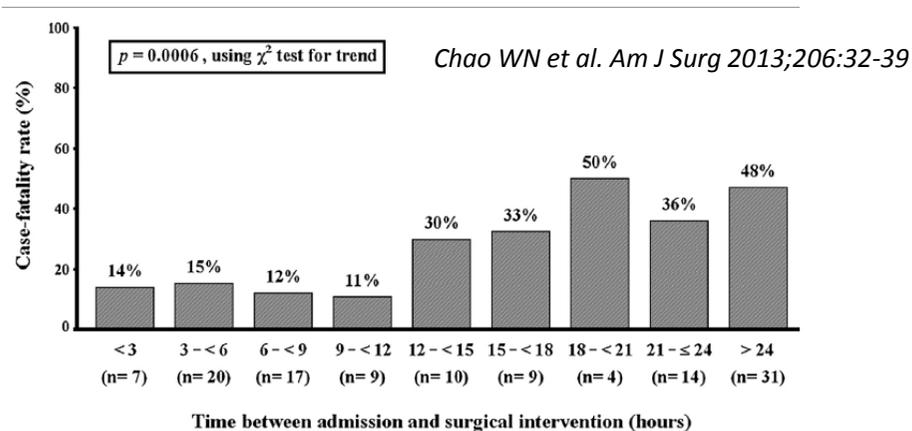
Prognosis **is dependent on timing of first surgical debridement**

Elliott DC et al. Ann Surg 1996;224:672-83
Boyer A et al. Intensive Care Med 2009;35:874-53.
Kobayashi L et al. J Trauma 2011;71:1400-5

Delayed surgical **treatment increases mortality** and number of surgical debridement needed

Kobayashi L et al. J Trauma 2011;71:1400-5

Golden period of 12-14 hrs after admission to initiate surgical debridement



McHenry R et al. Ann Surg 1995;221:558-65.
Boyer A et al. Intensive Care Med 2009;35:874-53.
Chao WN et al. Am J Surg 2013;206:32-39.

Consider to plan the first re-exploration within 12-24 h
and to repeat re-exploration(s) until the patient is free of necrosis

Sartelli M et al. World J Emerg Surg 2018;13:58

Typical surgical aspects



Brownish exudate
from the wound



Dull yellow/gray appearance
of the tissues
Extensive undermining of
surrounding tissues



Fascia is swollen
Absence of bleeding

Source control in recent guidelines

Author	Year	Prompt debrid	Re-debrid	Ostomy for Fournier	Broad spectrum AB	IV Imglobulins	HyperBaric Oxygen	VAC
May SIS-NA	2009 2011	++	++	+	++	+/- (TSS)	-	n.a.
Esposito ISID/ISC	2011	n.a.	n.a.	n.a.	++	n.a.	-	n.a.
Stevens IDSA	2014	++	++	n.a.	++	-	-	n.a.
Sartelli WSES	2014	++	++	+	++	+ (S/Str)	+	+ (after necrosis)
Misiakos Review	2014	++	++	++	++	+/-	n.a.	++
Dutch Guidelines	2017	++	++	n.a.	++	+ (Str)	+	+ (after necrosis)

++ strong recommendation, + weak recommendation,
- not recommended, n.a. not assessed

Eckmann C et al. Curr Opin Infect Dis 2016;29:139–44
<https://richtlijndatabase.nl>

Perioperative management of necrotizing infections in ICU patients

- **Consider adjuvant hyperbaric oxygen therapy** in patients with NSTI after prompt debridement (recommendation 2B).
- **Consider intravenous immunoglobulin therapy** in patients with necrotizing infections caused by Group A Streptococci (recommendation 2B).
- **Supportive treatment** in managing necrotizing infections must be early and aggressive to halt progression of the inflammatory process (recommendation 1A).
- AB103 (Reltecimod) is a new agent for modulation of inflammation after necrotizing infections. Further study is warranted to establish efficacy (no recommendation).
- Consider **negative pressure wound therapy** for wound care **after complete removal of necrosis** in necrotizing infections (recommendation 1C).

Antibiotic for necrotizing infections in ICU patients

- **Antibiotic treatment** of necrotizing infections should be **prompt and aggressive** (recommendation 1B).
- The **initial empirical antibiotic regimen** should comprise broad-spectrum drugs including **anti-MRSA and anti-Gram-negative coverage** (recommendation 1C).
- **Vancomycin** treatment should be **avoided in patients with renal impairment** and when **MRSA isolate shows a MIC for vancomycin ≥ 1.5 mg/mL** (recommendation 1B).
- **Daptomycin or linezolid** are **drugs of choice for empirical anti-MRSA** coverage. Ceftaroline, telavancin, tedizolid, and dalbavacin can be used (recommendation 2C).
- The choice of **anti-Gram-negative treatment** should be **based on local prevalence** of **ESBL-producing Enterobacteriaceae and multidrug-resistant organisms (MDROs)** non-fermenters (recommendation 1B).

Antibiotic for necrotizing infections in ICU patients

- Either **clindamycin or linezolid** should be included in the empirical antibiotic regimen as **antitoxin active drug** (recommendation 1C).
- **De-escalation** of antibiotic therapy should be based on **clinical improvement, cultured pathogens, and results of rapid diagnostic tests** where available (recommendation 1C).
- In the absence of definitive clinical trials, **antibiotic therapy** should be administered **until further debridement is no longer necessary**, the patient has **improved clinically**, and **fever has resolved for 48–72 h** (recommendation 1C).
- **Procalcitonin monitoring may be useful** to guide antimicrobial discontinuation (recommendation 2B).

Outcome of NSSTIs in recent papers

Limited prospective data

Mortality rates range from 6% to greater than 70%

May AK et al. Surg Infect 2009;10:467-499

No major changes in mortality/morbidity over the last decade

	Yilmazlar	Chia	Kuzaka	Wang	Misiakos	Narasimham	Madsen
Country	Turkey	USA	Poland	Taiwan	Greece	Australia	Scandinavia
Type of infection	Fournier N=50	Fournier N=59	Fournier N=13	NF N=115	NF N=62	NF N=98	NF N=409
Mortality (%)	26	15	0	21	18	10	18
Amputation (%)	-	15	15	7	26	-	22
Length of stay	22	19	32	25	20	24	7 (ICU)

Yilmazlar T et al. Int J Surg 2017;40:135-8
Kuzaka B et al. Med Sci Monit 2018;24:548-55
Chia L et al. J Infect 2018;76:38-43

Wang JM et al. Braz J Infect Dis 2014;18:137-43
Misiakos EP et al. Front Surg 2017;4:5
Narasimhan V et al. ANZ J Surg 2018;88:E45-49
Madsen MB et al. Intensive Care Med 2019;45:1241-51

Risk factors of death

1,392 NSSTI cases from the NSQIP database 2005-2010

30-Day Postoperative Mortality

Variable	Odds ratio	95% CI	p Value
Older than 60 years	2.47	1.72–3.55	<0.001
Dependence level			
Partially dependent	1.61	0.95–2.69	0.072
Completely dependent	2.33	1.43–3.80	0.001
Dialysis before operation	1.89	1.15–3.10	0.012
ASA class ≥ 4	3.55	2.25–5.59	<0.001
Emergent operation	1.56	1.03–2.34	0.035
Preoperative septic shock	2.35	1.55–3.56	<0.001
Platelet count			
<50,000/mm ³	3.48	1.65–7.37	0.001
<150,000/mm ³ but >50,000/mm ³	1.67	1.21–2.87	0.005

Conclusions

A **multidisciplinary team** is mandatory for the management of necrotizing SSTIs

Depending on the time line, various specialities are involved (e.g; emergency department, surgeon, intensivist, Infectious disease specialist, microbiologist, physiotherapist, pain management, nutritionist, plastic surgeon...)

Delayed recognition and management of these patients are **key issues** to improve the prognosis

Source control and adequate anti-infective therapy and management of organ dysfunctions are the first therapeutic goals for the intensivist