NECROTISING SOFT TISSUE INFECTIONS

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Introduction

- Described by Hippocrates 500BC as “erysipilas all over body from trivial accident resulting in many deaths
- Hospital gangrene described by the British and American military especially Joseph Jones(1871) with 46% mortality
- Jean Alfred Fournier (1883) described perineal gangrene in men
- Meleney (1924) described haemolytic streptococcal gangrene
- Wilson (1952) proposed the term necrotising fasciitis
- Current consensus prefers necrotising soft tissue infection (NSTI)
- Mortality still remain high (up to 26%) even in advanced health care environment principally because of delayed surgical intervention.

CLINICAL PRESENTATION OF NSTI

Clinical presentation of NSTI is insidious and nonspecific and is usually mistaken for cellulitis or myositis.

Table 3. Symptoms/Signs Associated with Necrotizing Soft-Tissue Infection at the Time of Admission

Finding	Percent of patients[6] (n = 89)	Percent of patients[31] (n = 192)	Percent of patients[32] (n = 22)
Erythema	100	66	95
Pain or tenderness beyond margins of erythema	98	73	95
Swelling	92	75	86
Crepitus or skin necrosis	13	31	0
Induration	12	45	
Bullae	45	23	41
Fluctuance	11		
Fever	53	32	
Hypotension	18	11	

(Sarani 2009)

Pathology of NSTI

- Rapidly spreading subcutaneous infection primarily for superfical fascia and fat
- Characterised by “thin pus” – dishwashing fluid
- Secondary vessel thrombosis → skin and muscle ischaemic necrosis

Anatomic Distribution of NSTI [4]

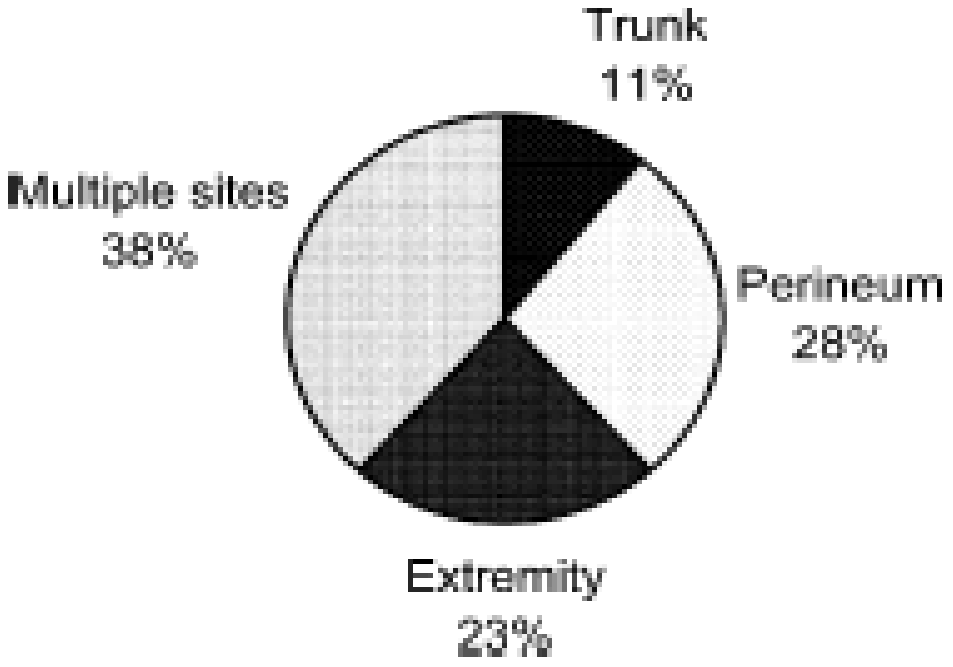


Fig. 1. Site of necrotizing soft-tissue infection.

(Endorf 2005)

Polymicrobial infections characterise Type I NSTI

Table 2. CAUSATIVE ORGANISMS FOR 45 POLYMICROBIC NSTIs (n = 127)

Aerobes (gram-positive)	51 (40%)
Enterococci	21
Streptococcal species*	11
Coagulase negative staphylococci	10
Staphylococcus aureus	6
Bacillus species	3
Aerobes (gram-negative)	54 (43%)
Escherichia coli	15
Pseudomonas aeruginosa	13
Enterobacter cloacae	5
Klebsiella species	5
Proteus species	4
Serratia species	4
Acinetobacter calcoaceticus	3
Others†	4
Anaerobes	19 (15%)
Bacteroides species	12
Clostridium species	4
Others‡	5
Fungi§	3 (2%)

* Includes Group B streptococcus (3), gamma streptococcus (non faecalis) (3), alpha streptococcus (2), *S. milleri* (1), and *S. pyogenes* (2).
† Includes *Citrobacter freundi* (2), *Xanthomonas maltophilia* (1), *Eikinella corrodens* (1), and *Aeromonas hydrophilia* (1).
‡ Includes Peptostreptococcus (2) and diptheroids (1).
§ Includes *Candida tropicalis* (2) and *Candida albicans* (1).

(McHenry 1995)

Monomicrobial Infections are characteristic of Type II NSTI

Table 3. CAUSATIVE ORGANISMS FOR THE 19 MONOMICROBIC NSTIs

Streptococcus pyogenes	10
Clostridium perfringens	2
Staphylococcus aureus	2
Pseudomonas aeruginosa	1
Escherichia coli	1
Serratia marscesans	1
Gamma-*streptococcus*, not enterococcus	1
Candida glabrata	1

(McHenry 1995)

Type III NSTI are due to marine vibrio ssp infection.
Note.
Group A β-Haemolytic Streptococcus
Community acquired MRSA

Predisposing Associated factors in NSTI

Vascular insufficiency

- Diabetes mellitus
- Peripheral arterial vascular disease
- Post-radiation arteriosclerosis

Immunosupressions

- HIV/AIDS
- Chronic steroid use
- Chemo/radiation therapy
- Immunosuppressive therapy
- Diabetes Mellitus

Metabolic Disorders

- Diabetes mellitus
- End-stage renal failure
- Liver cirrhosis
- Obesity
- Alcoholism
- Malnutrition and debility
- *Intravenous drug abuse*

Malingant neoplastic disease especially lymphoma and colorectal carcinoma

Hypertension

TABLE 1 *Risk Factors for NF Identified in Study Patients*

Risk Factor	Survivors	Nonsurvivors
Age > 50 yr	7	4
Diabetes mellitus	7	5
Malnutrition	10	4
Hypertension	3	3
Intravenous drug abuse	5	2
Total	32	18

When patient had 3 or more risk factors the mortality rate was more than 56%

(Francis 1993)

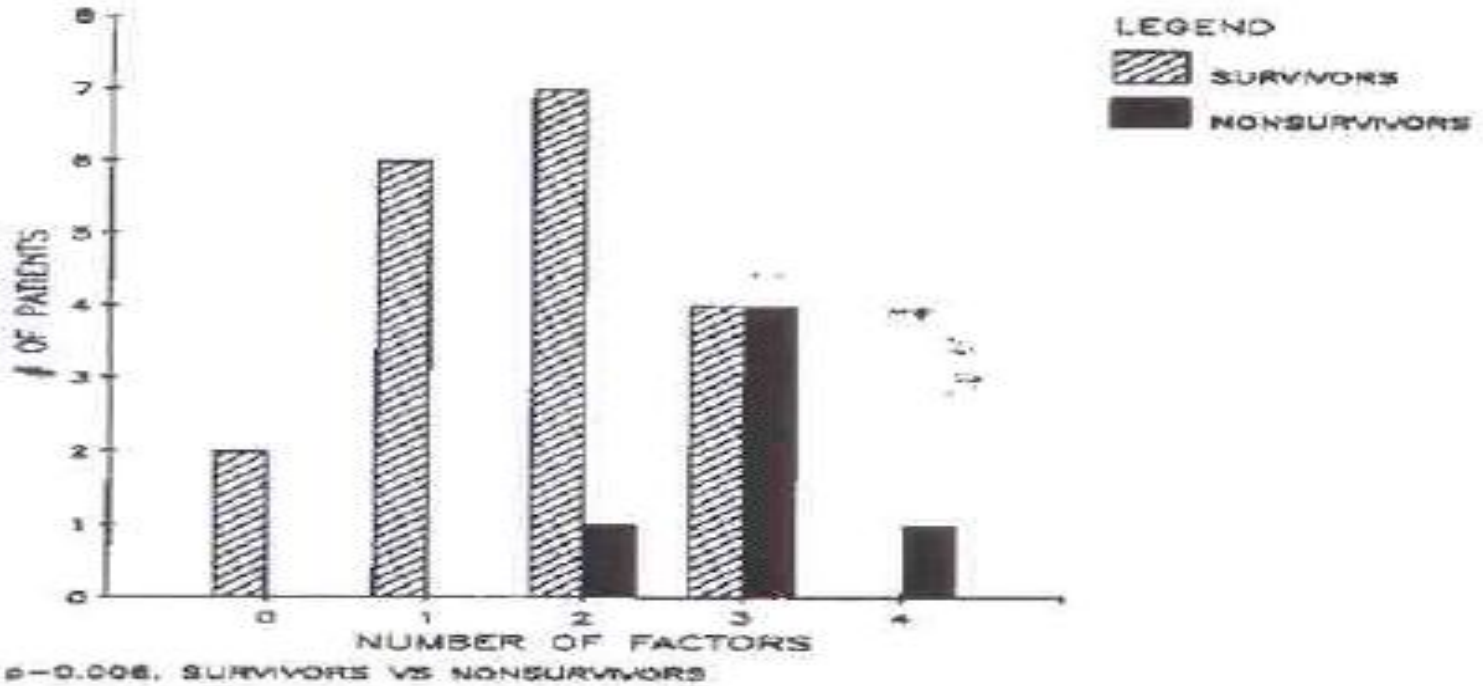


FIG. 1. Risk factors for survival in necrotizing fasciitis. Nonsurvivors had significantly more risk factors than the survivors. If a patient had three or more risk factors, the mortality rate was 56 per cent.

(Francis 1993)

Classification of NSTI

Type I

- Older patients with predisposing co-morbidity
- Polymicrobial (synergistic) infections
- No trauma

Type II

- Younger patient
- Monomicrobial infection
  - Group A Streptococcal pyogenes
  - Staphylococcus aureus especially MRSA
  - Associated trauma
  - IV drug abuse

Type III

- Marine vibrio spp [6]
- Warm seaside locations
- Very fulminant course

Pathophysiology

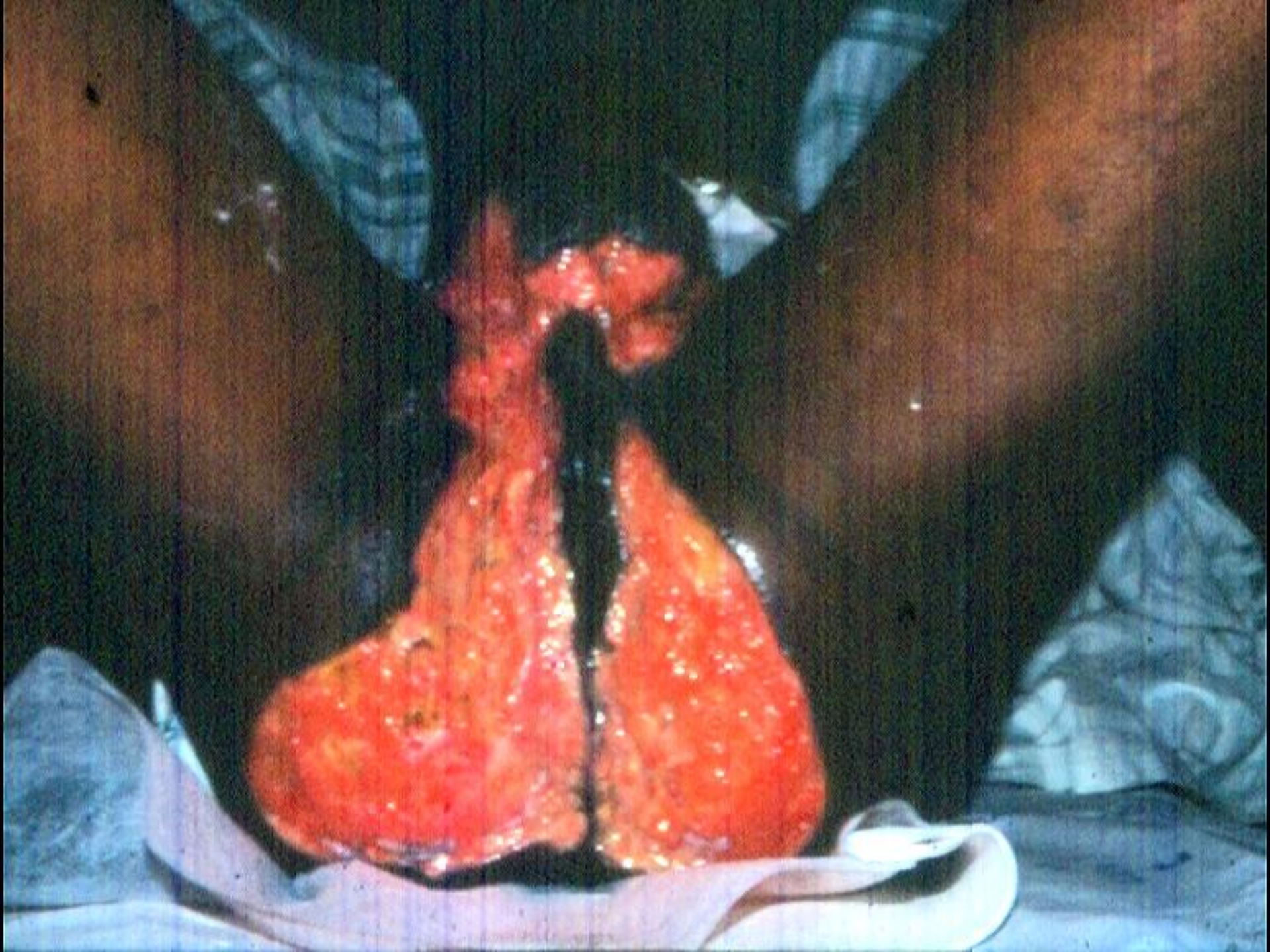
- Exotoxin aid in rapid spread of infection eg. streptokinase, coagulase, hyaluronidase, streptodornase, streptolyin O and exotoxin A, B, C.
- M-protein on surface of strep and staph pyogeneg are superantigens which bind V_{β} portion of T-Cell receptor
- Induces a deluge of pro-inflammatory cytokine release e.g. IL-1, IL-6, and TNF$\propto$. (SIRS),
  - widespread thrombosis which causes ischaemic necrosis and further hampers immune response!
- Bacterial fimbriae contain lipoteichoic acid (LTA) which promotes adhesion to host epithelium and fibronectin.
  - This results in resistance to clearance by inflammatory fluid and phagocystosis
- Streptokinase O and S damage neutrophils which degranulate releasing lysozymes and proteases.

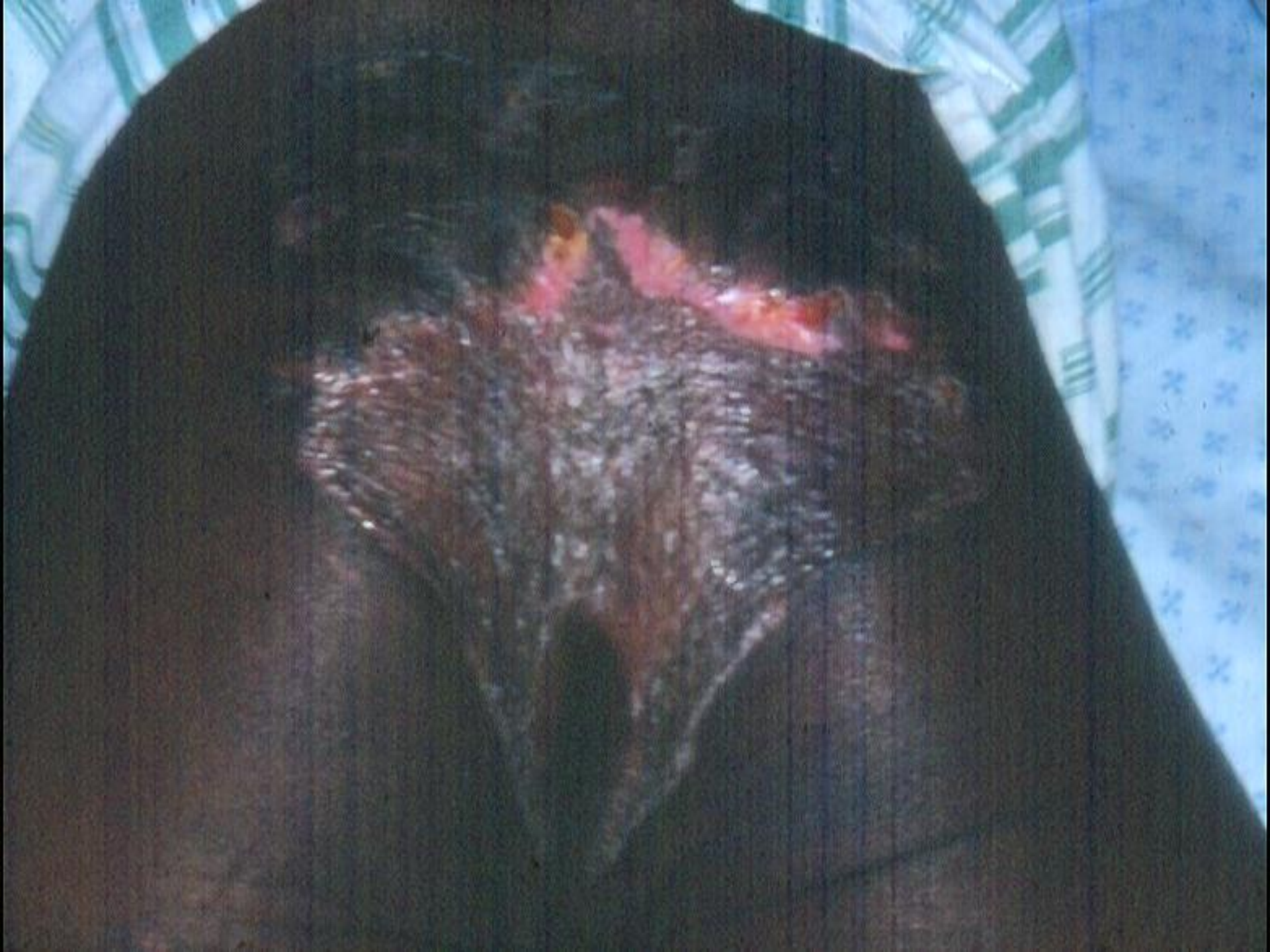
Diagnostic Investigation in NBTI

- There is no single specific diagnostic tool for NSTI
- Imaging with plain radiograph or CT scan may show interstitial gas (12-20%) or oedema in the subcutaneum on CT Scan.
- Frozen Section intra-operatively does not add much to direct observation
- Pre-op biopsy only acts to delay operative exploration and debridement.

Management Approach

- Admit to high dependency treatment unit
- Active resuscitation should use blood products early
- Early use of antibiotic empirically until culture and sensitivity directs to specific antibiotics.
- Early aggressive surgical debridement for infective source control:
  - Planned repeated debridement 12-36hrly until infection is controlled.
  - Surgical exploration should be used early even as a diagnostic tool.
  - Planned debridement used until there is No necrosis or No patient
- Active nutrition support, preferably enteral whenever possible.
- Multiple organ support, especially respiratory, cardiac and renal.
- Hyperbaric oxygen therapy is controversial.
- Pooled human IgG is not widely used
  - benefit in streptococcal infection.





Laboratory Risk Indicator for Necrotising Fasciitis [7]

Table 2. Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score

Variable, Units	β	Score
C-Reactive Protein, mg/L		
<150	0	0
≥150	3.5	4
Total white cell count, per mm^3		
<15	0	0
15–25	0.5	1
>25	2.1	2
Hemoglobin, g/dL		
>13.5	0	0
11–13.5	0.6	1
<11	1.8	2
Sodium, mmol/L		
≥135	0	0
<135	1.8	2
Creatinine, μmol/L		
≤141	0	0
>141	1.8	2
Glucose, mmol/L		
≤10	0	0
>10	1.2	1

(Wong 2004)

Wong's LRINEC score of 8 or more in strongly predictive, 6 or 7 should raise suspicion

PREDICTORS OF OUTCOME [3,8]

Table 5 Adjusted odd ratios for predictors of mortality of necrotizing fasciitis (N = 128)

Predictor	Adjusted odds ratio (95% confidence interval)	*P*
Cancer	46.54 (5.76-376.03)	<.0001
Band form WBC ≥10%	5.61 (1.48-21.30)	.011
Hypotension	6.62 (1.52-28.77)	.012
Aeromonas infection	10.22 (1.34-77.96)	.025
Vibrio infection	7.03 (1.21-41.03)	.030
Presence of hemorrhagic bullae	0.16 (0.03-0.93)	.042

Hsiao 2008)

An additional strong predictor of mortality is delay from admission to operation. [5]

Retroperitoneal NST [9,10,11]

- Retroperitoneal/extraperitoneal location of NSTI is scarcely recognised .
- Vigilant for retroperitoneal necrotising fasciitis when dealing with perineal sepsis
- in high risk patients e.g. diabetics, HIV/AIDS or cancer with perineal sepsis
-
- in patients with gynaecologic problems such as intra-uterine instrumentation including illicit abortion.
- When the testis is gangrenous in a case of Fourniers gangrene [13]
- Extraluminal gas on plain radiograph is diagnostic but its absence does not exclude retroperitoneal NSTI.
- Abdominal CT scan may reveal the retroperitoneal necrosis [14]

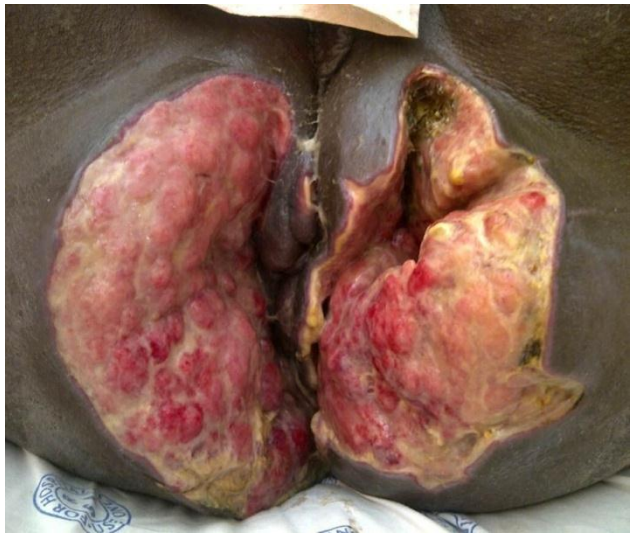
TABLE I. PRE-OPERATIVE CLINICAL FINDINGS IN 10 PATIENTS WITH RNF

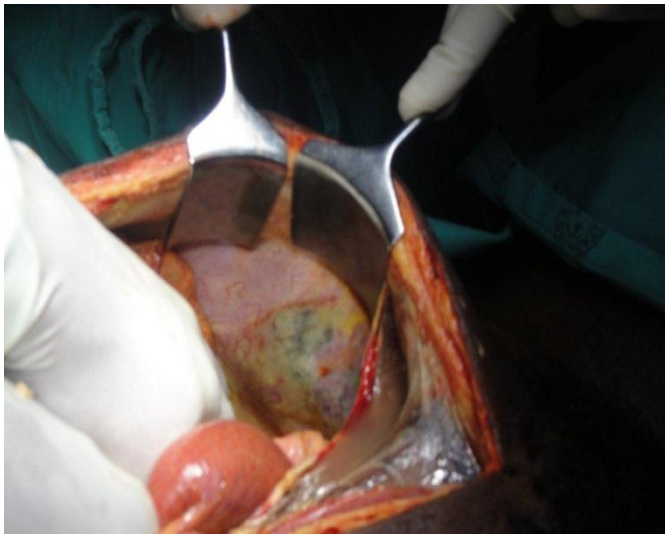
Initiating incident	No. of patients	APACHE II	Av. interval to 1st op.	Reason for referral/review
Perineal sepsis	2	6, 15	18 h	Abdominal tenderness
C/S for obstructed labour	3	13, 8, 8	7 d	Necrosis C/S wound (2), postpartum uterine infection (1)
Intra-uterine instrumentation	3	14, 9, 10	7 d*	Gangrene uterus (2), intra-uterine sepsis (1)
Abdominal trauma	2	3, 12	5 d	Failed non-op. management (1), late post-laparotomy precipitous deterioration (1)

Because of wide variation, individual patients' APACHE II scores are given.
Figures in parentheses denote number of patients.
* If 1 patient with 19 d delay is excluded, then average for the other 2 = 16 h.
Av. = average; C/S = caesarean section.

Mokoena 1993

RETROPERITONEAL NECROTISING FASCIITIS





Retroperitoneal NSTI carries very high mortality [10]

- Management of retroperitoneal NSTI follows the general principles of treating NSTI.

- Aggressive planned repeated laparotomy and debridement improves mortality [11]

Use of Clindamycin [12]

- Empirical antibiotics should be guided by local anti-microbial sensitivity spectrum.
- Community acquired MRSA is increasing in USA and elsewhere.
- Therefore the choice of antibiotic must factor MRSA.
- Clindamycin is:

i. effective choice for MRSA,
ii. it also inhibits expression of M-protein superantigens which otherwise elicit copious cytokine secretion by T-cells,
iii. inhibits LTA expression which suppresses bacterial adhesion,
iv. suppresses ∝-toxin production by clostridium perfingens, and
v. suppresses E coli LPS-induced production of pro-inflammatory cytokine TNF-∝ by monocytes.

Admission of NSTI to Burn Centre ([4,15])

- Treatment of NSTI include operative resuscitation and management of the wound
- skin grafting, nutritional support, physiotherapy and rehabilitation.
- Burn centres are possessed of multidisciplinary teams and are increasingly being used to manage NSTI.

Conclusion

- NSTI are rare therefore clinicians only see few in practising lifetime
- Presentation insiduous and nonspecific
  - Mistaken for cellulitis or myositis
  - Demand clinician vigilance in at risk patients
- Wong Laboratory Risk indicator for Necrotising Fascitis (LRINEC) score is a new promising diagnostic tool
- Management entails aggressive approach:
  - Resuscitation with blood products
  - Early empirical antibiotics
  - Aggressive surgical debridement until no sepsis or no patient
  - Early surgical exploration should be take as diagnostic, therefore negative exploration acceptable.
- Retroperitoneal NSTI scarely described
  - Missed because peritoneal membrane usually intact
  - Any patient with perineal sepsis who develops abdominal distension or ileus must raise suspicion
  - planned repeated laparotomy and debridement only hope
- Increasingly NSTI are being admitted to Burns Centres

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