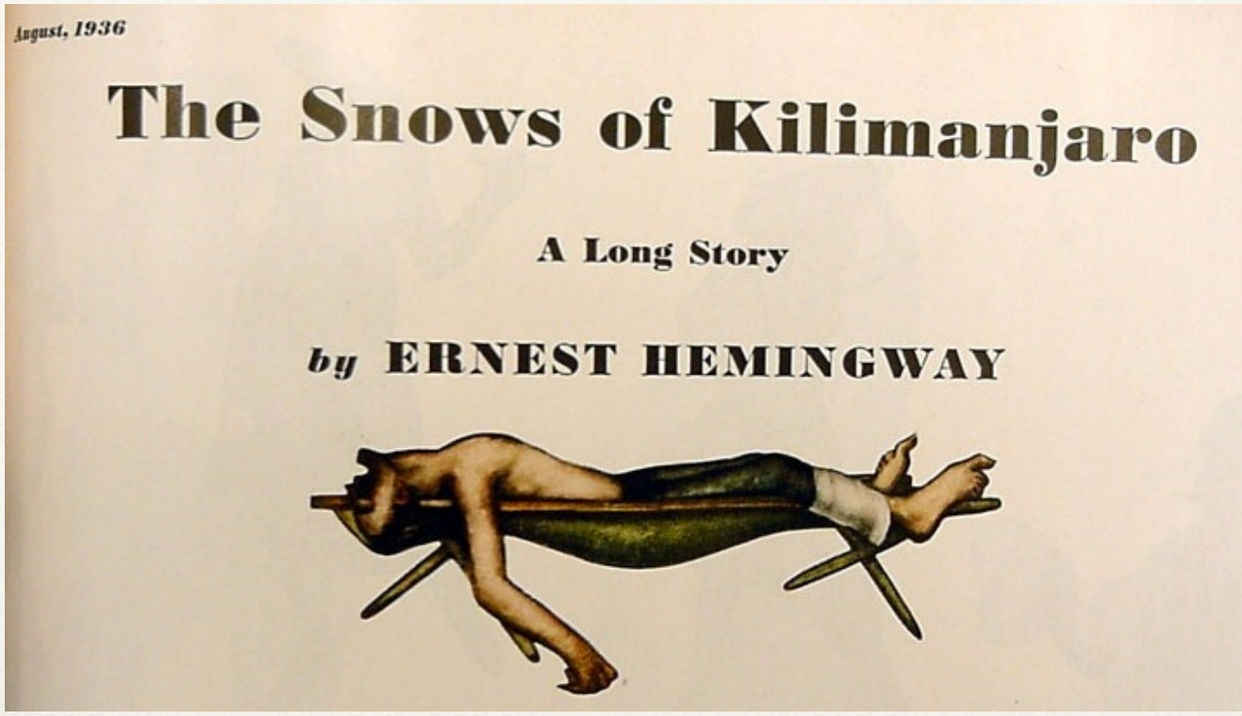

August, 1936

The Snows of Kilimanjaro

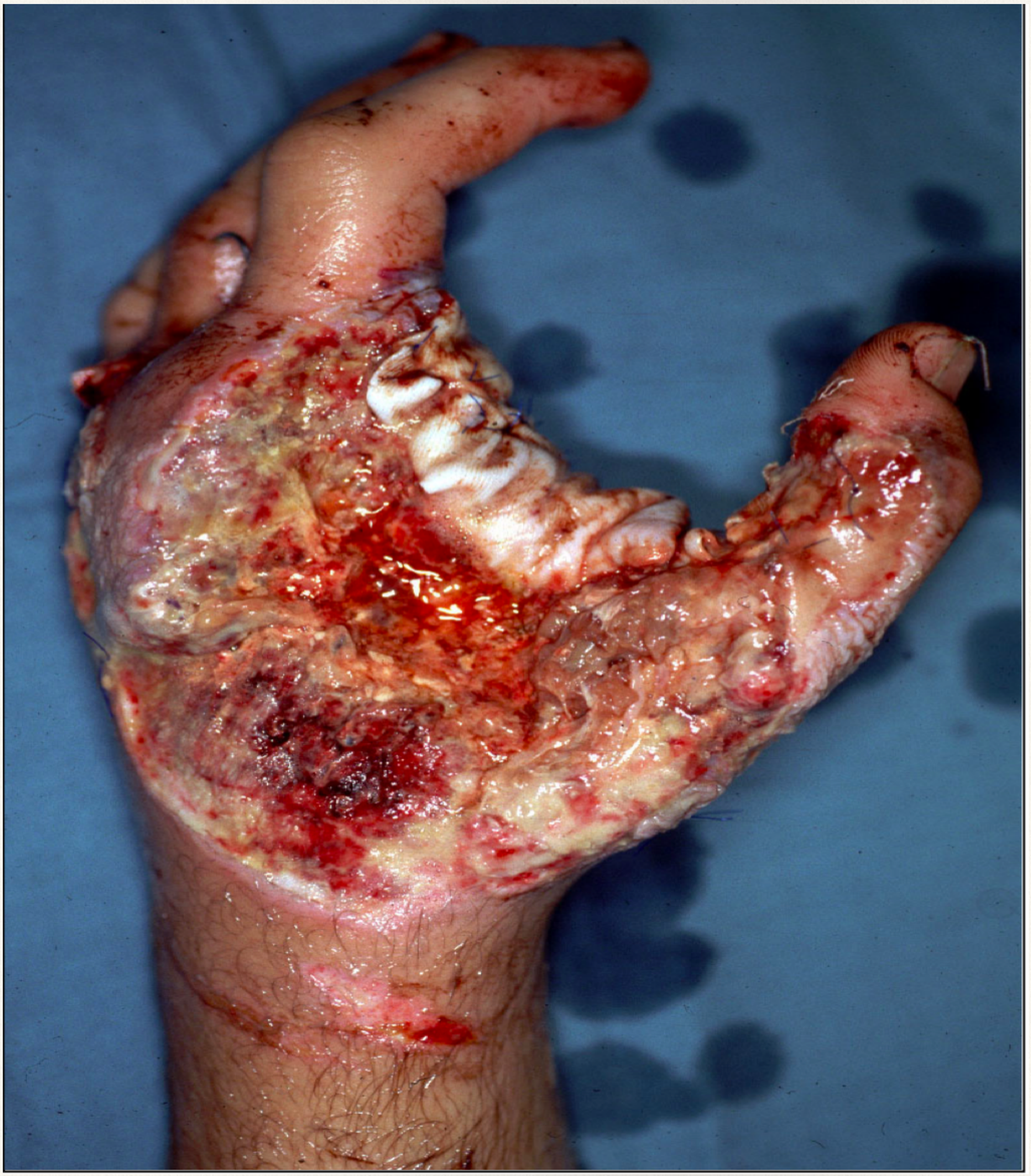
A Long Story

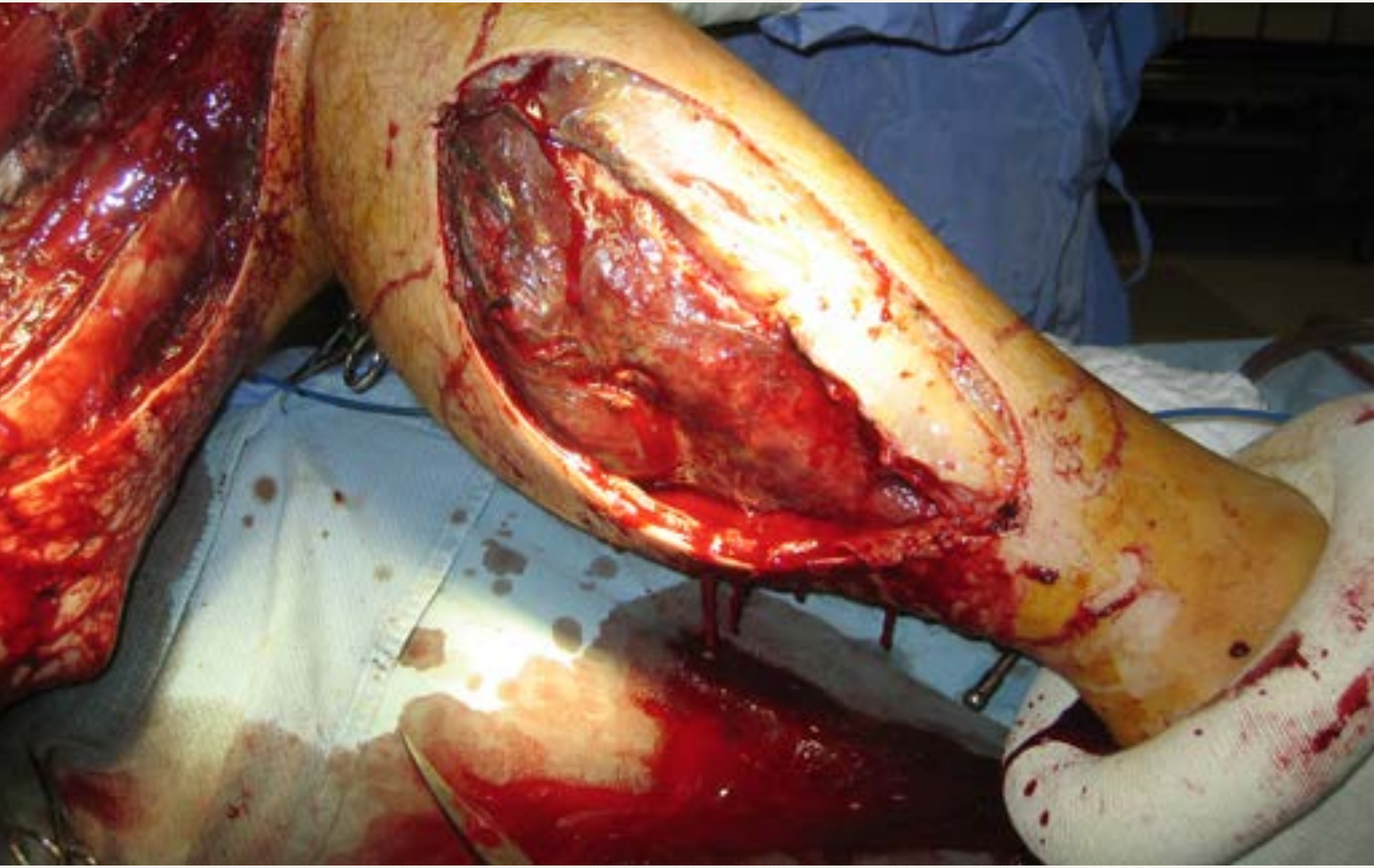
by ERNEST HEMINGWAY

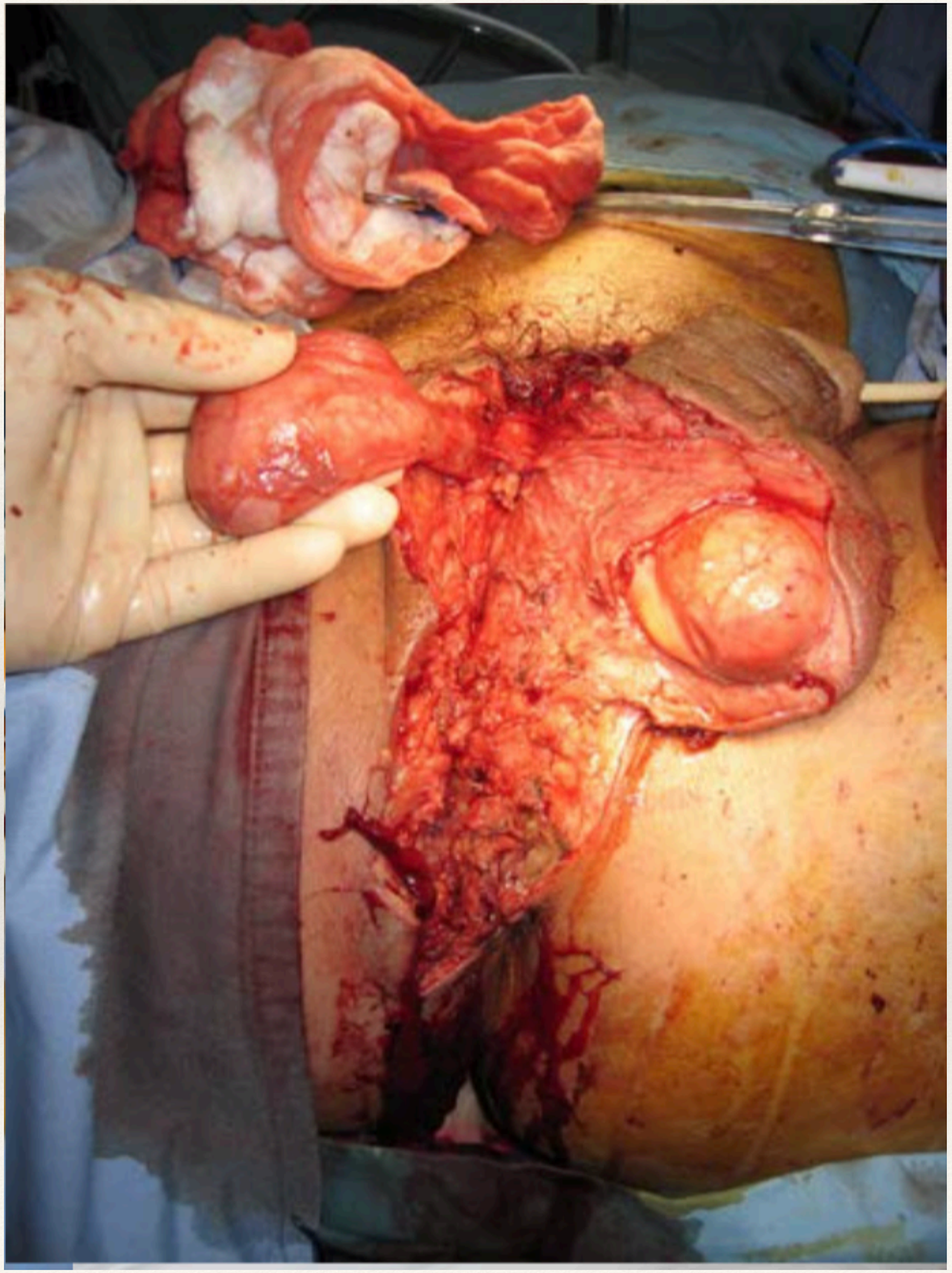
Necrotising Soft Tissue Infections

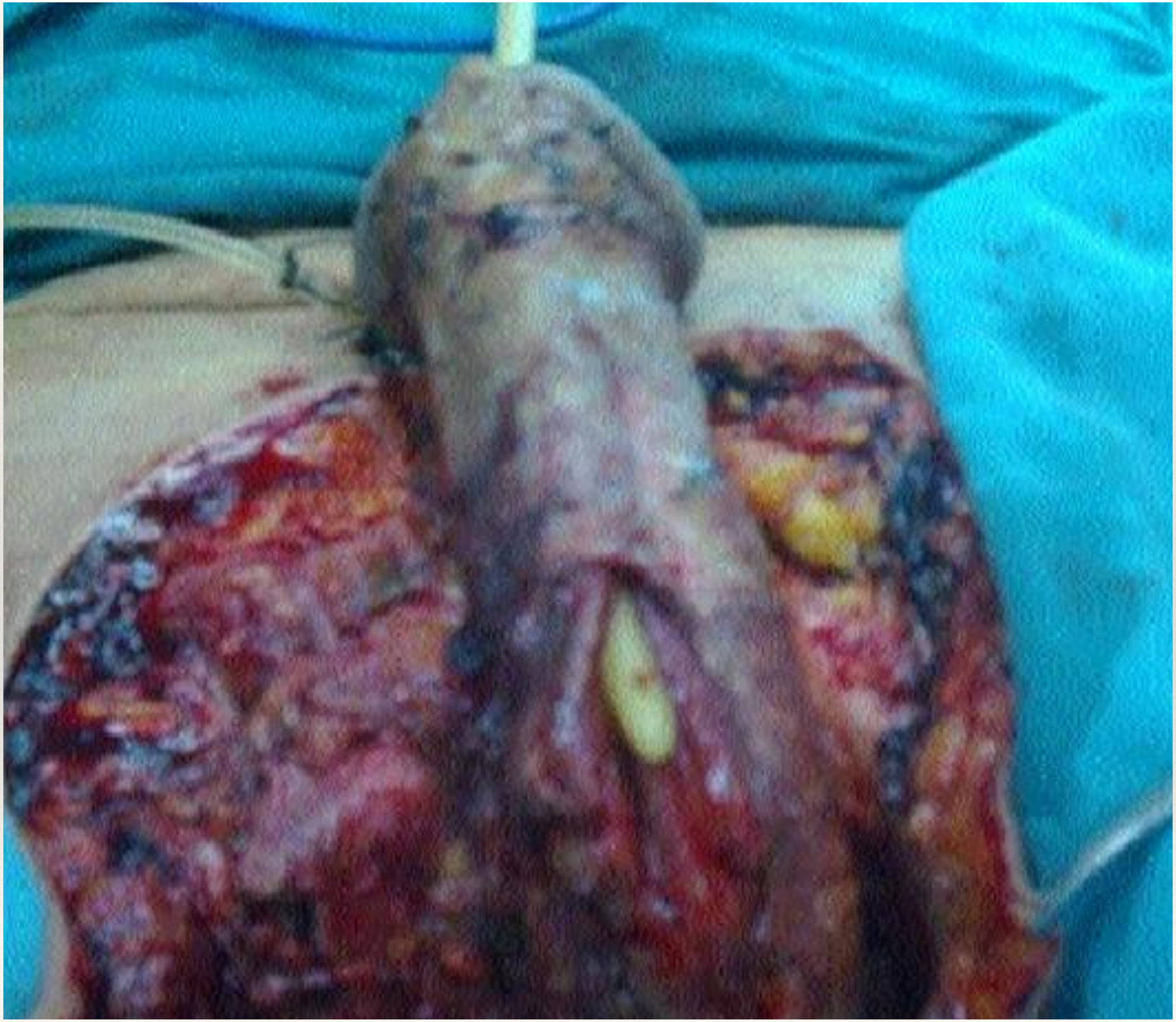
Dr John Vogel

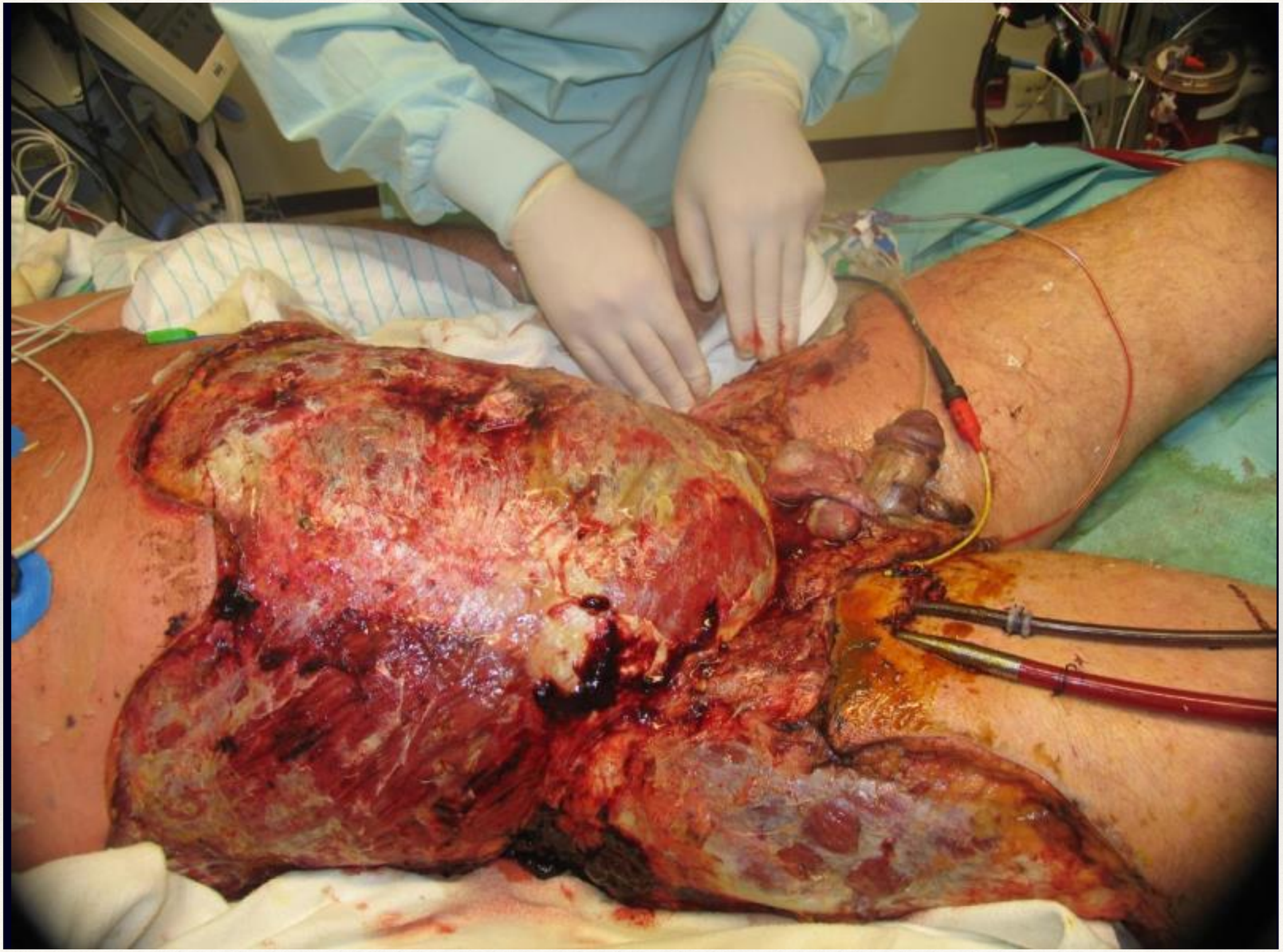
Chamber of Horrors

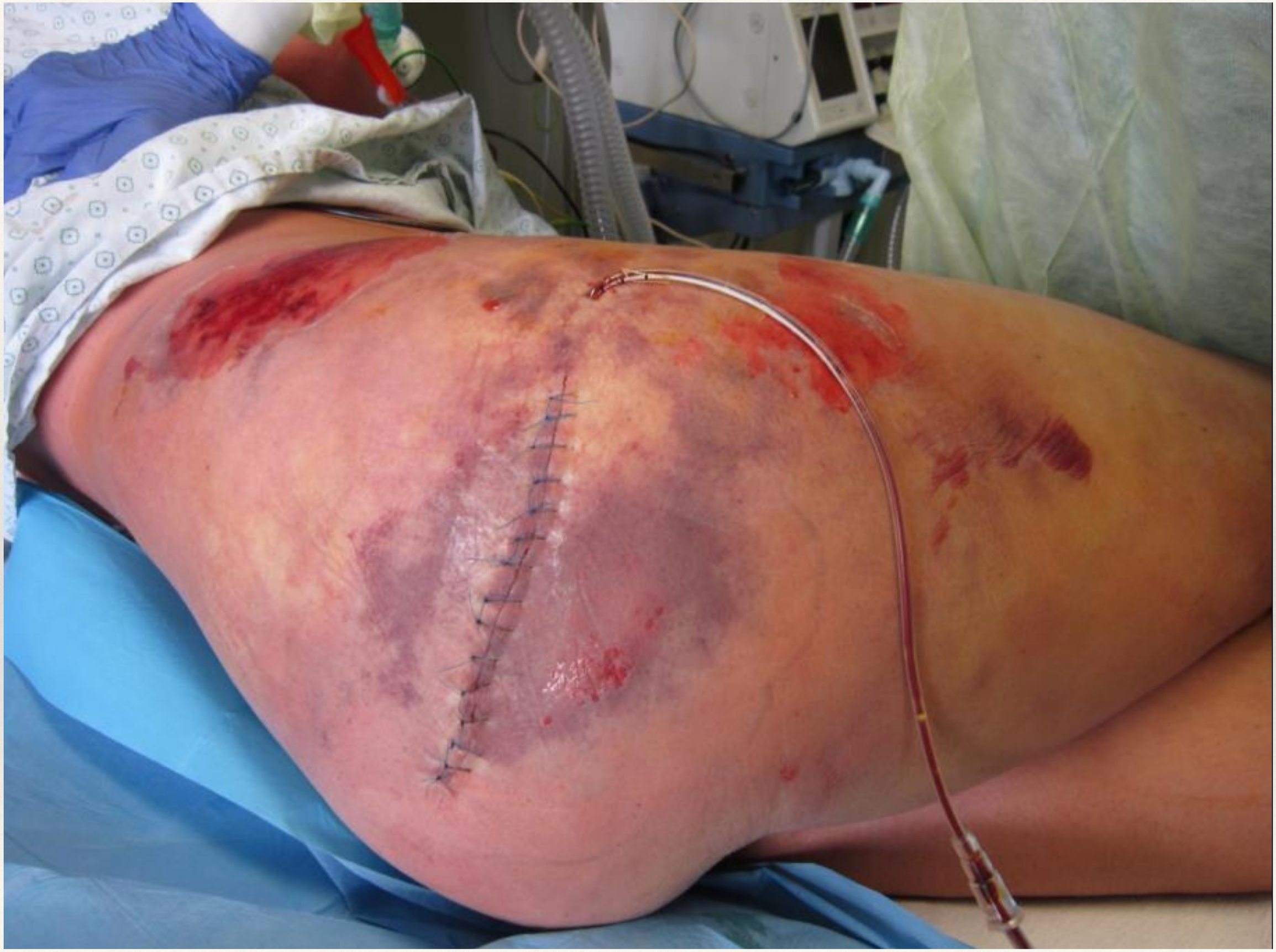


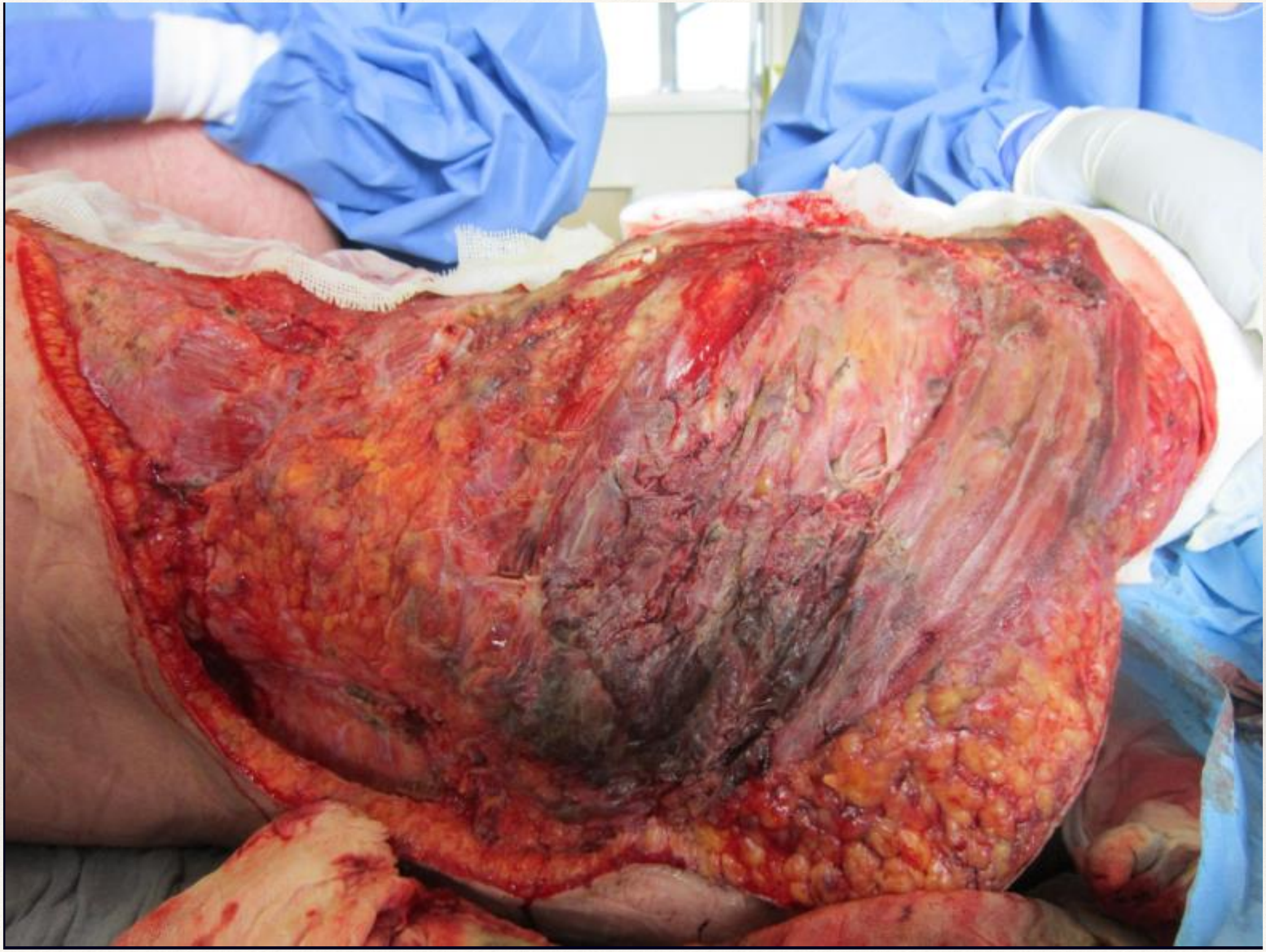




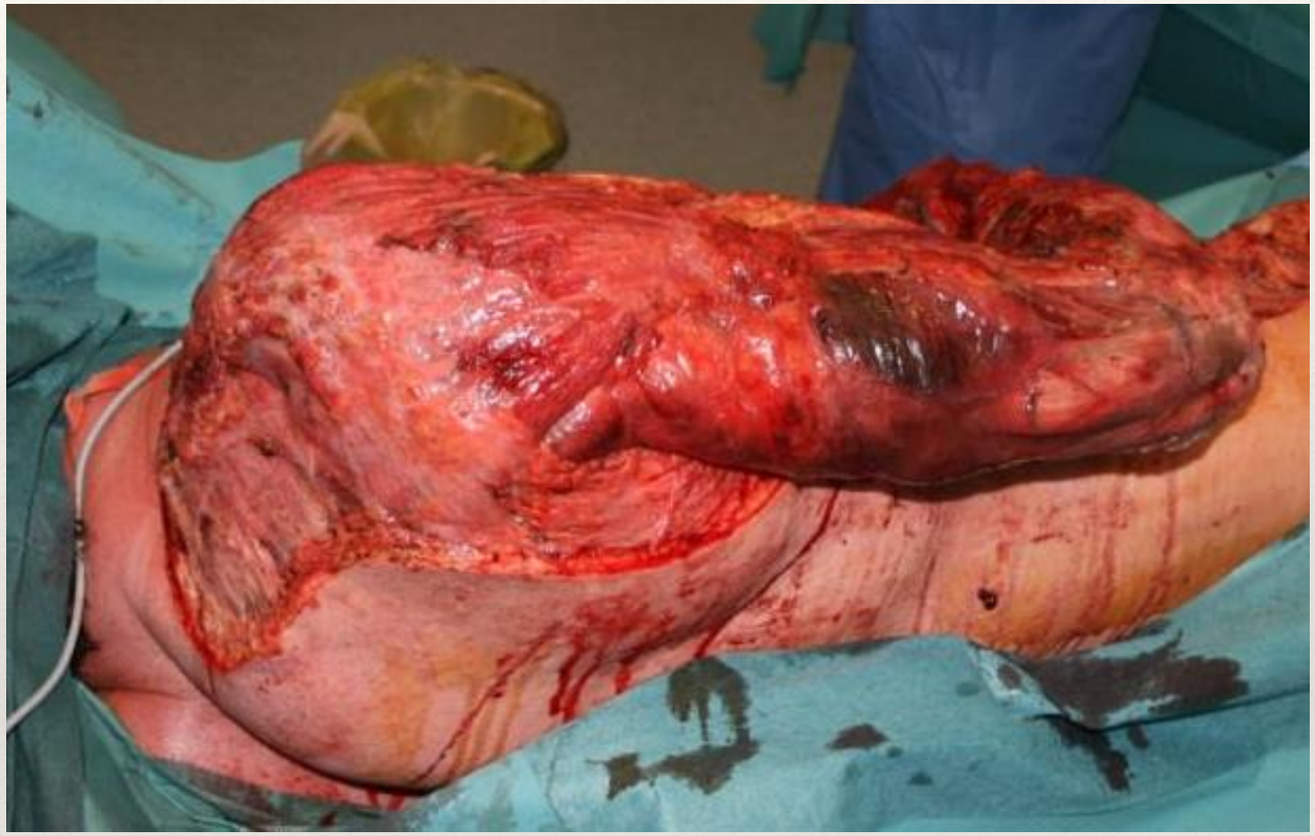








Fasciotomy or Fasciectomy



Necrotising Soft Tissue Infections are **not new**

"Many were attacked by the erysipelas **all over** the body when the cause was a **trivial accident** flesh....sinews, and bones fell away in large quantities...there were **many deaths**"

–Hippocrates, 500 BC

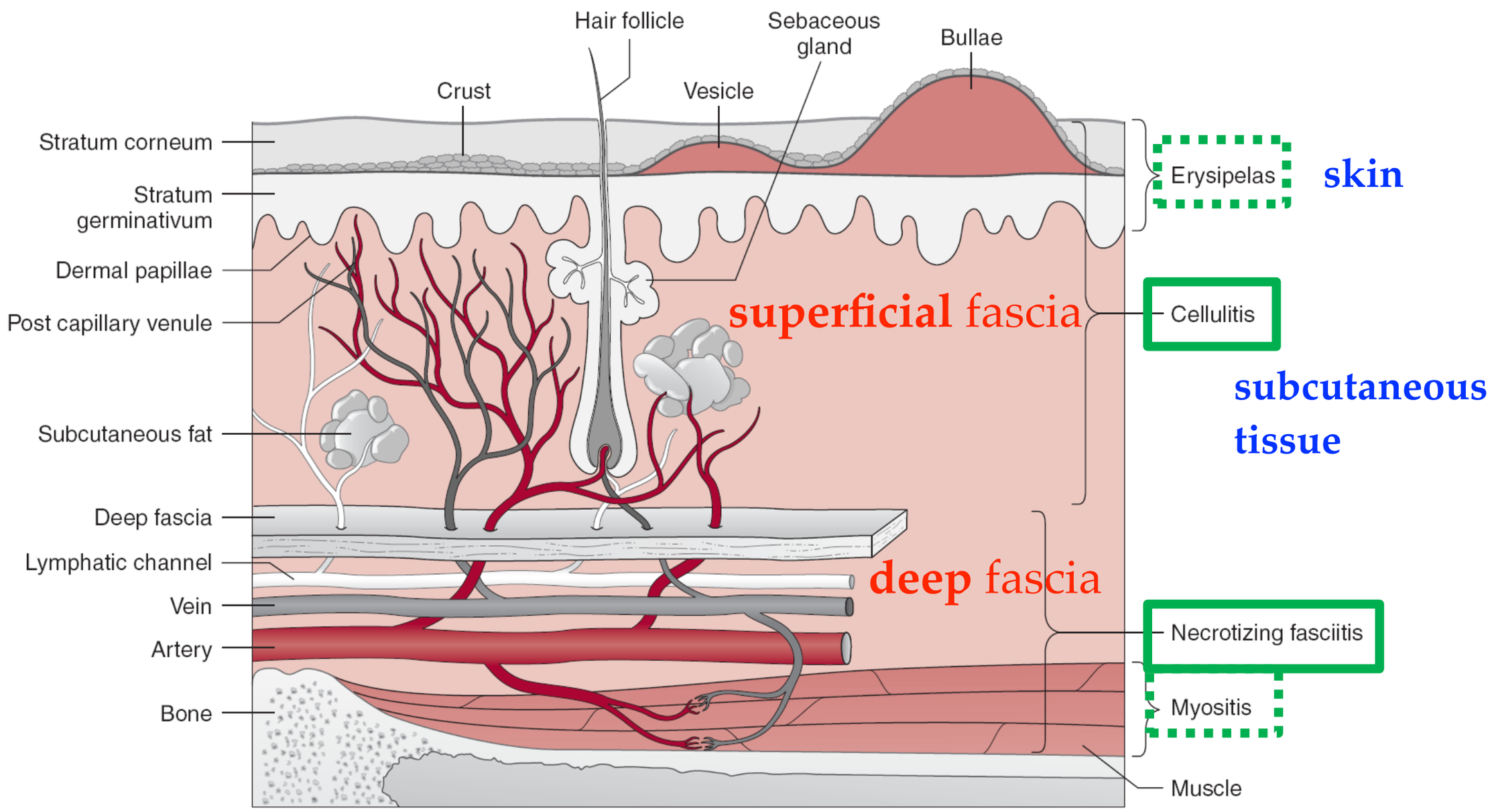
The first description of necrotising infections came during the American Civil War when a Confederate Army surgeon, Dr. Joseph Jones, reported a **mortality rate of 46%**

In the UK (1995 and 2006), ICNARC study showed necrotising fasciitis had **mortality of 42%**

"Necrotising Soft Tissue Infection" is now supplanting necrotising fasciitis as the preferred name

Critical Care 2008, 12:S1

Necrotizing fasciitis vs cellulitis



Necrotising Soft Tissue Infections are **RARE**

United Kingdom (1995 - 2006)

24/1000 of intensive care unit admissions were due to necrotising fasciitis

Ealing's ITU Experience 2009 - 2016

% of all admissions - 3/1000

Died in ITU/Hospital - 1/9

Critical Care 2008, 12:S1

Necrotising Soft Tissue Infections are Deadly

Mortality from **Myocardial Infarction**

~ 1 out of 10 die!

www.thelancet.com online January 23,2014

Mortality from **Necrotizing Soft Tissue Infection**

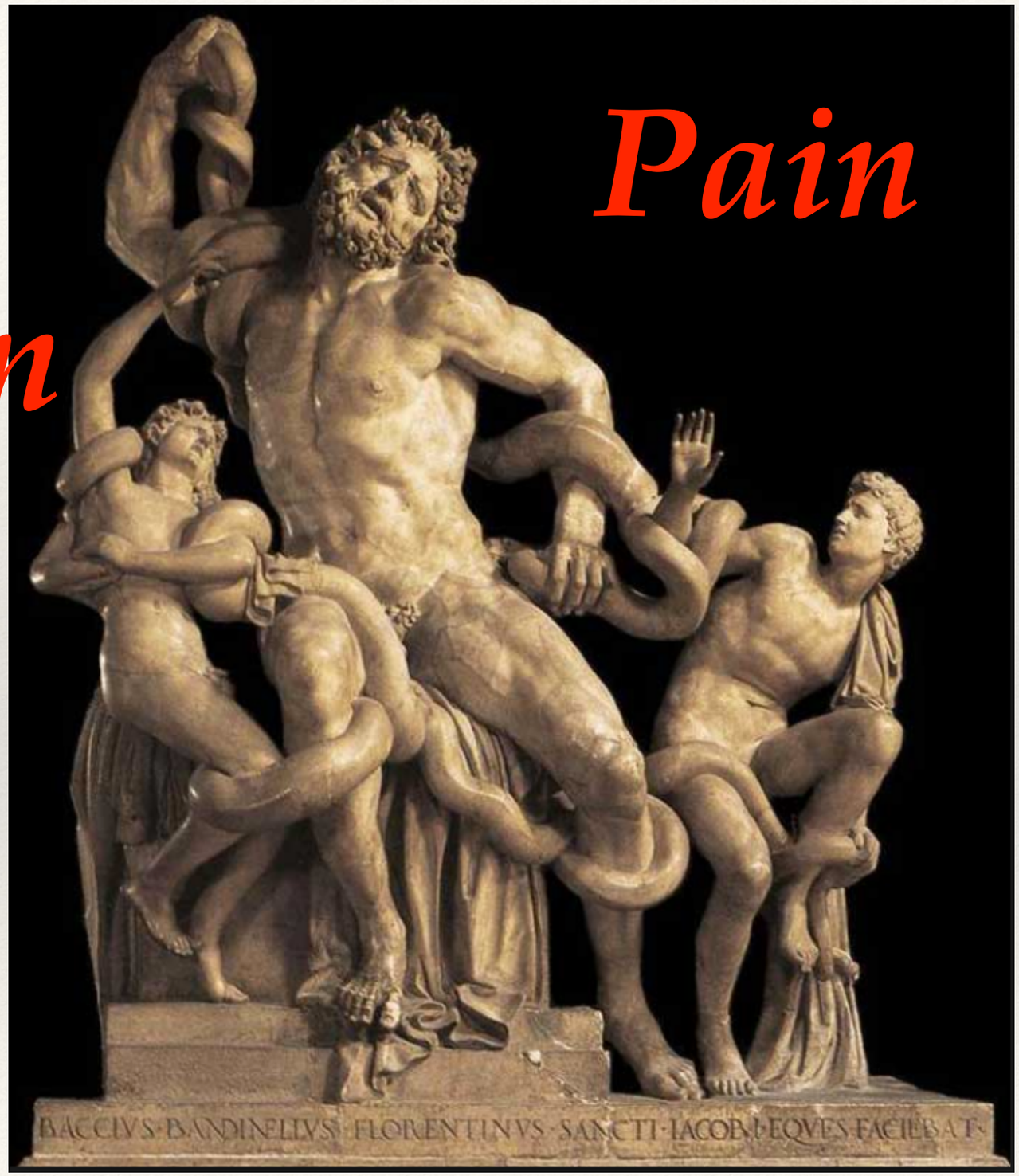
~ 4 out of 10 die!

NSTI is a killer !

Diagnosis

High index of **Suspicion**

Exquisite pain <u>out of proportion</u> to physical findings



Pain

Pain

Pain

Pain

Pain

Pain

Pain

Pain

Pain

Pain

Pain

Pain

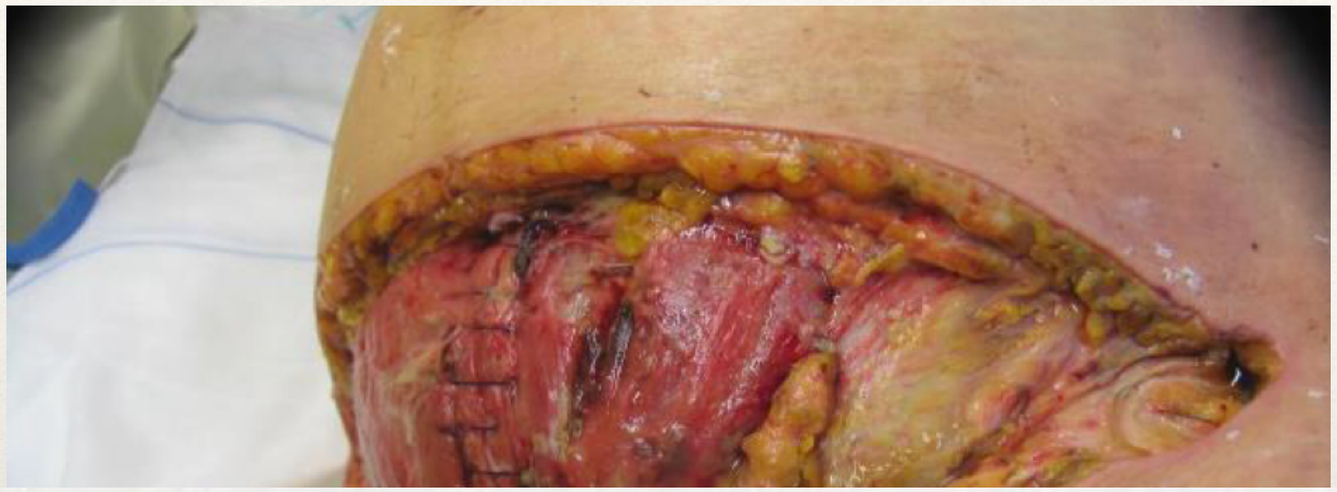
Pain

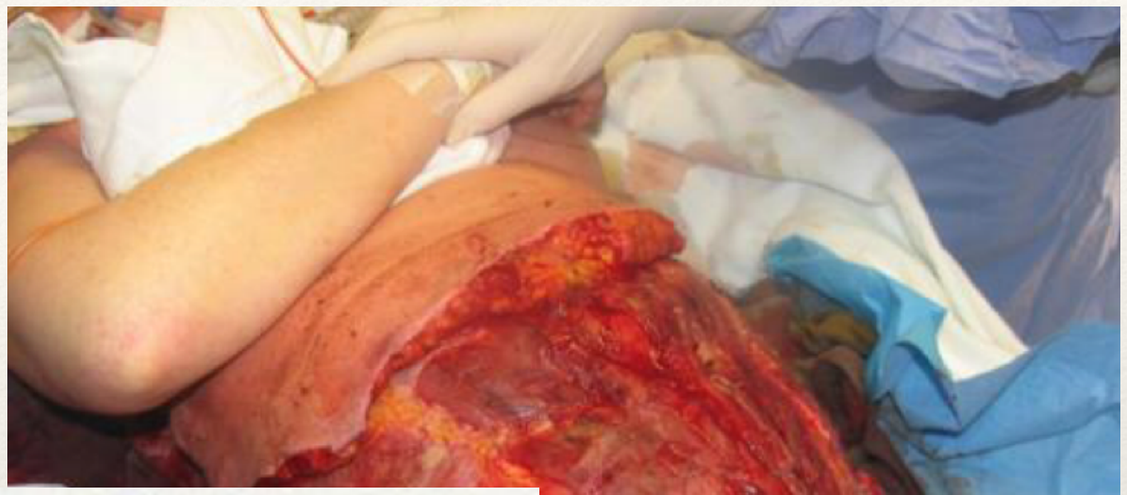
That unforgettable aroma

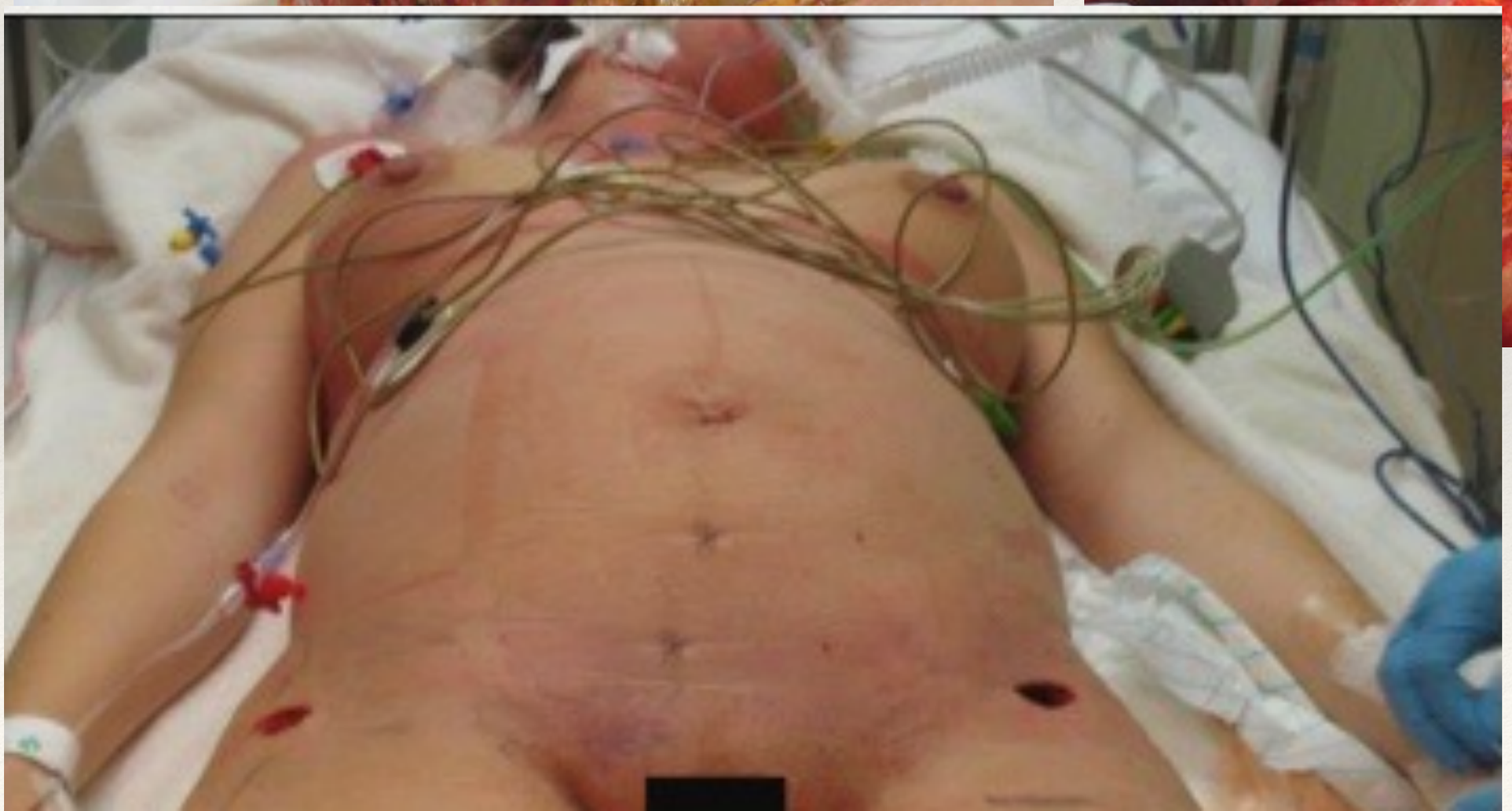
One overwhelming feature of the presentation is the strong "**repulsive, fetid odour**"

Charlie McDonald

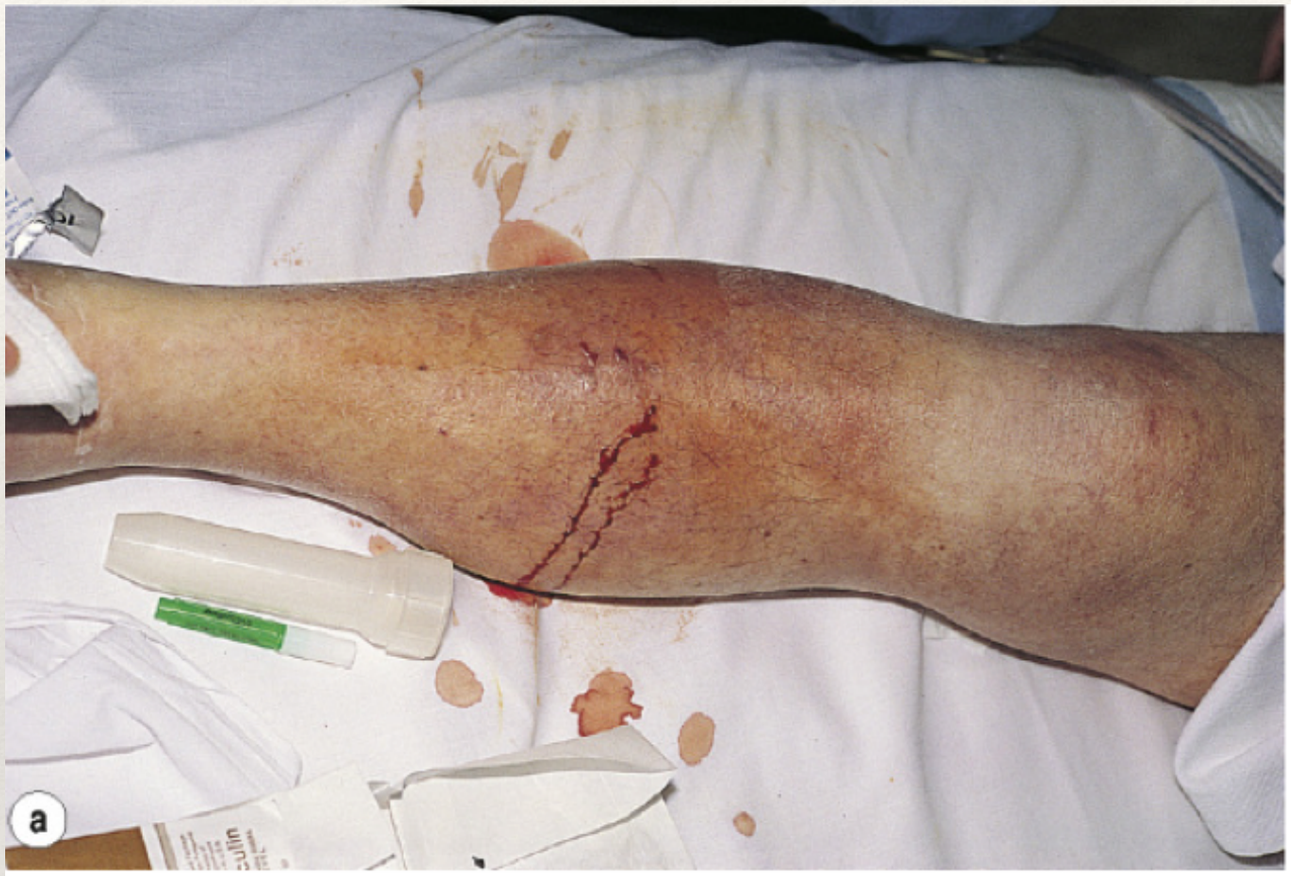
"Normal" tissue that was necrotising fasciitis when opened

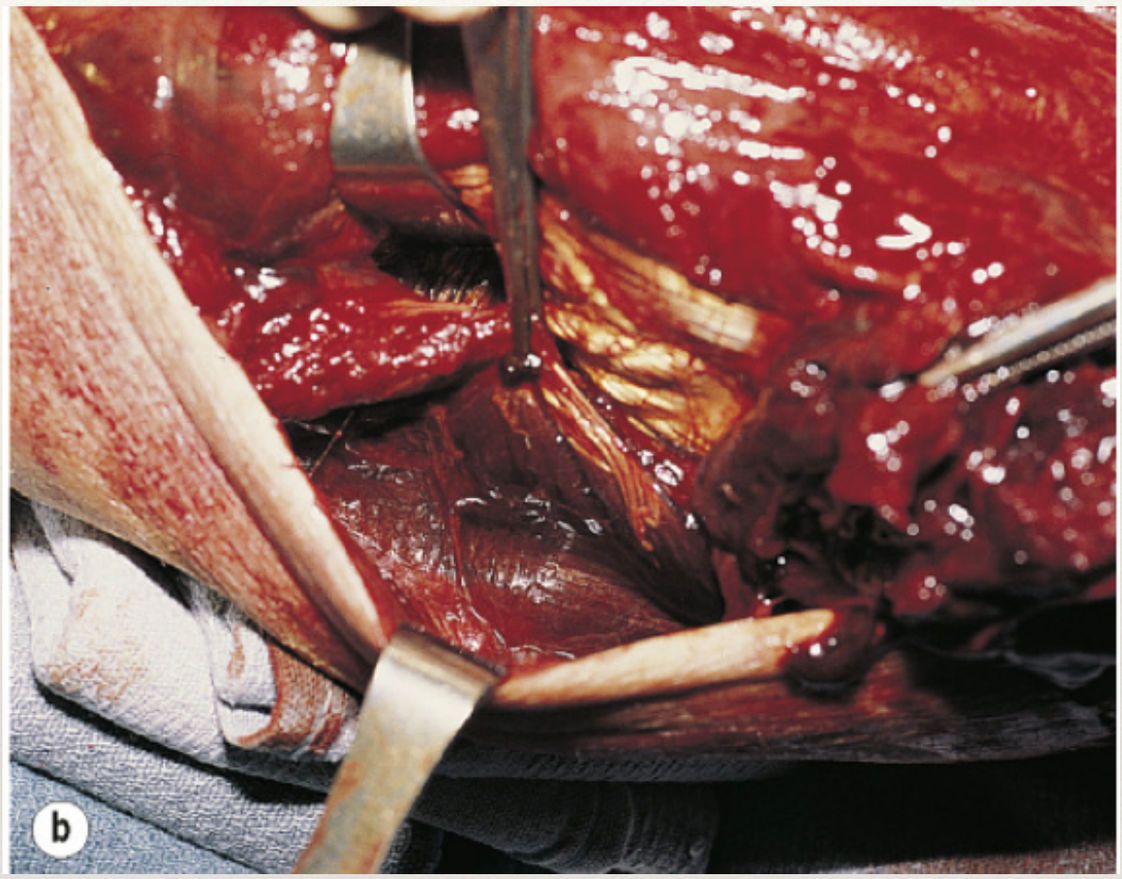






"Normal" tissue that was necrotising fasciitis when opened





Clinical findings of NSTI

- **Risk** factors
  - **Age >60**
  - **Diabetes**
  - **Obesity**
  - IV drug users
  - Malnutrition
  - CCF
  - COPD
  - PVD
  - Alcoholism
  - Immunocompromised
    - inclu. Steroids
    - **?NSAIDs**

- **Early** Physical Findings
  - **Pain** out of proportion
  - Erythema
  - Hyperthermia
  - Oedema beyond the area of erythema
  - Tachycardia
  - Fever
  - Bronzing of the skin

- **Late** Physical Findings
  - Haemorrhagic bull
  - **Foul odor**
  - "Dishwater" pus
  - Dermal gangrene
  - Crepitus
  - Rapid progression
  - SIRS
  - Sepsis
  - **Shock** and organ failure

Crit Care Med 2010 Vol. 38, No. 9 (Suppl.)

Diagnosis

Necrotizing Soft Tissue Infection: Diagnostic Accuracy of Physical Examination, Imaging, and LRINEC Score

A Systematic Review and Meta-Analysis

- "Absence of any 1 physical feature is not sufficient to rule-out NSTI.
- LRINEC had poor sensitivity, and should **not be used** to rule- out NSTI.
- Given the poor sensitivity of these tests, a **high clinical suspicion** warrants **early surgical** consultation for definitive diagnosis and management."

Annals of Surgery 2018

Treatment

Early aggressive surgery

Early aggressive surgery

Early aggressive surgery

Early aggressive surgery

Early aggressive surgery

Early aggressive surgery

Early aggressive surgery

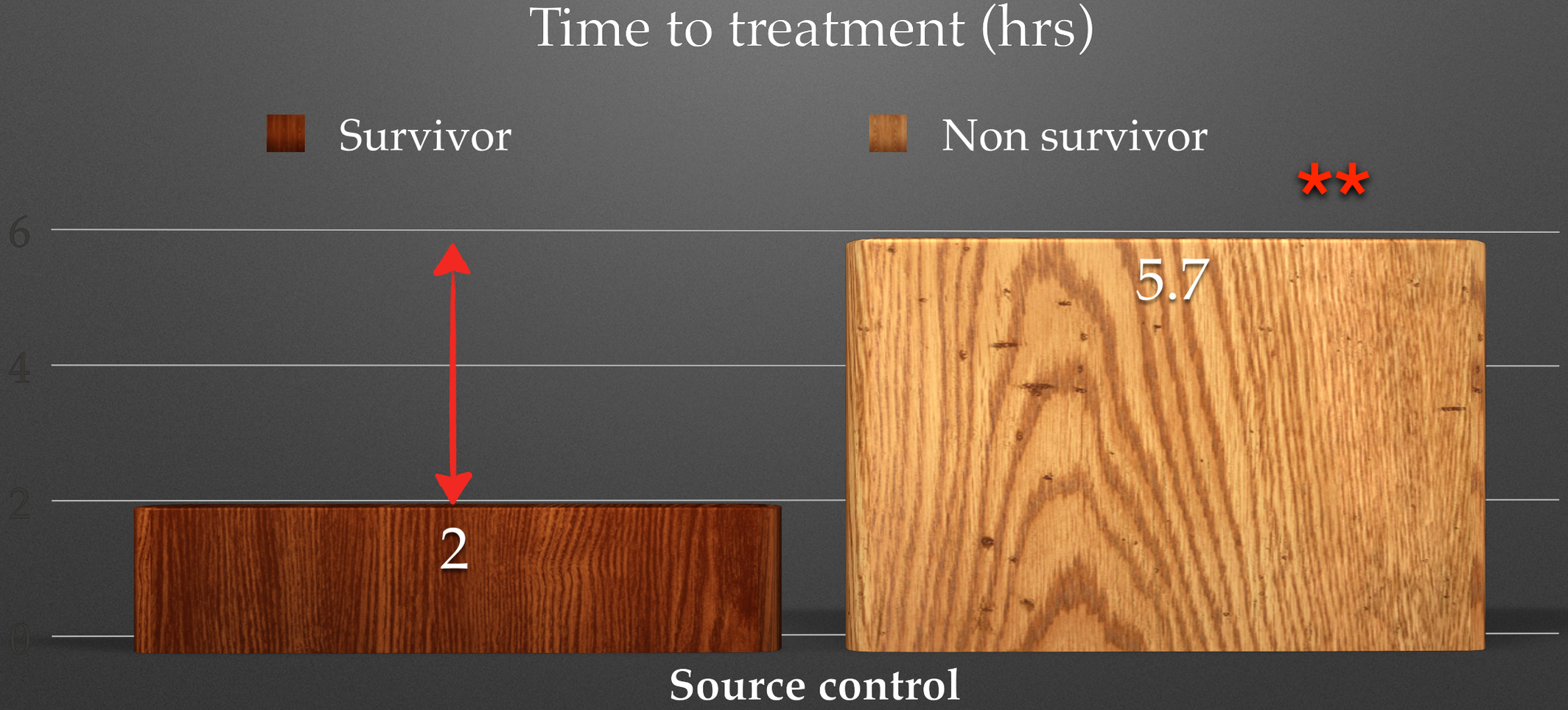
Early aggressive surgery

The clock is running !

Never delay surgery for imaging !

N Engl J Med 1996;334:1578-82

What happens if you delay surgery ?



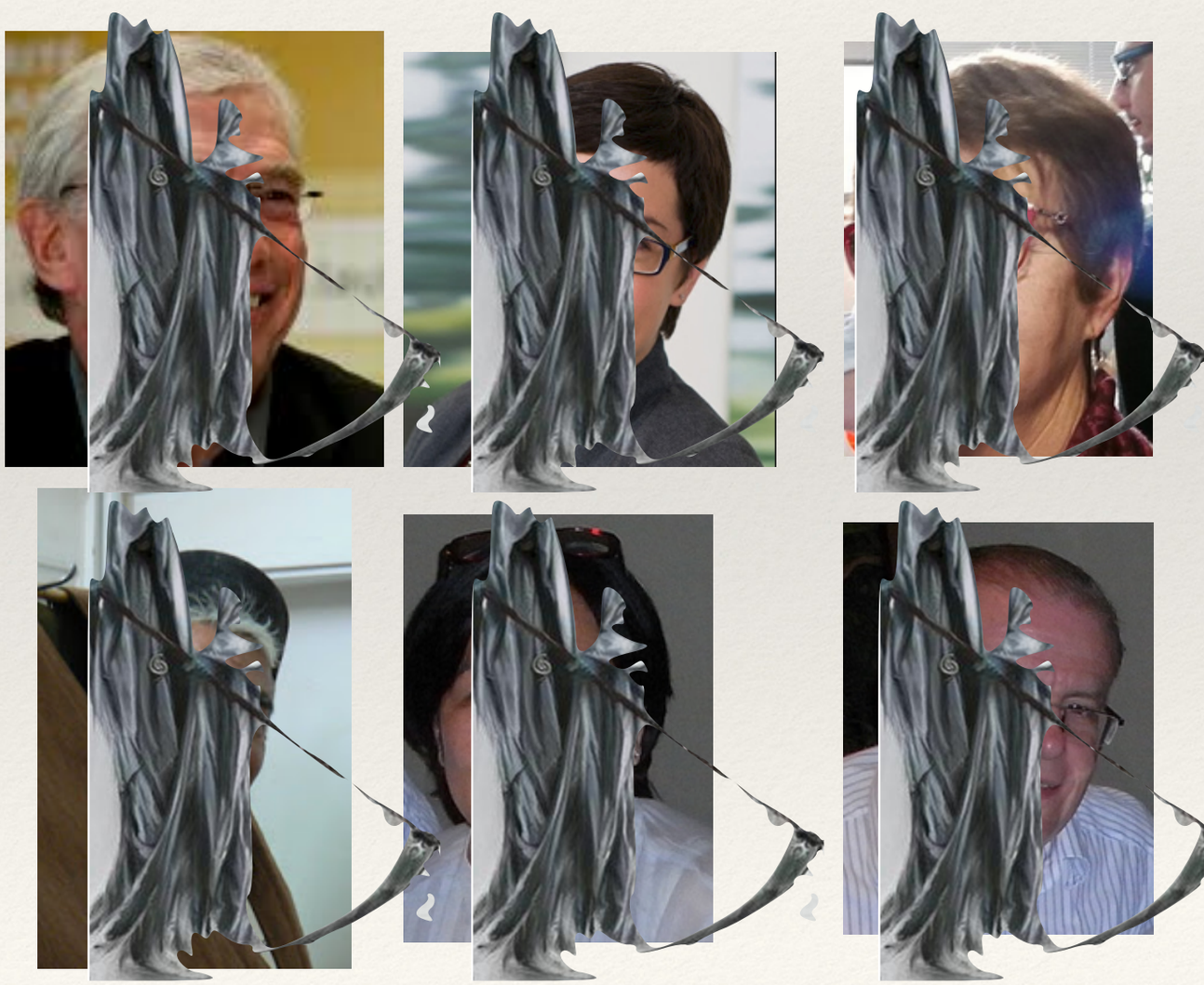
"A delay in source control **beyond 6 hours** may have a major impact on patient mortality "

Bloos et al. Critical Care 2014, 18:R42

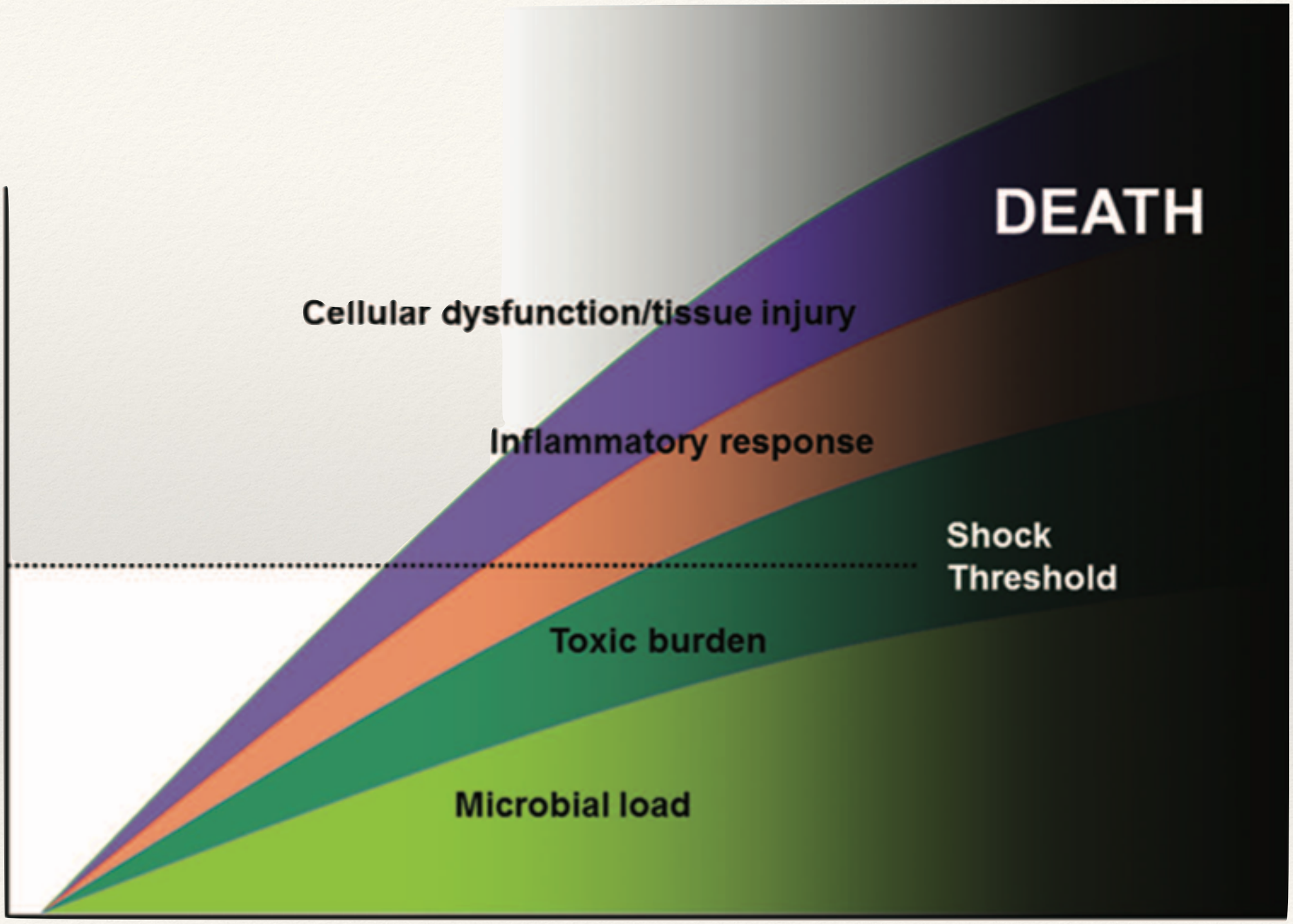
Early surgery saves lives

24 hour delay to surgery

9 X



Why early surgery saves lives



Virulence 5:1, 80-97; Jan 2014

Aggressive surgery saves lives

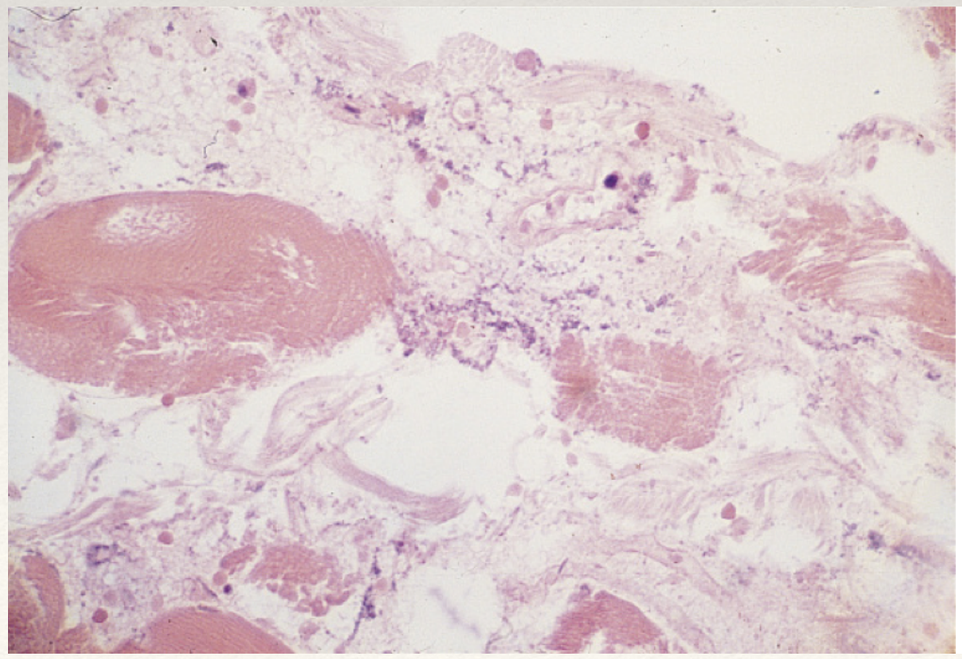
…**inadequate debridement** at the first surgical intervention increases the **risk of death**

….therapy should include **wide resection**

Chest (1996) **110**(1):219-229.
Ann. Surg. (1995) **221**(5):558-563; discussion 563-555.
Am. J. Surg. (1983) **145**(6):784-787.
Br. J. Surg. (1993) **80**(9):1190-1191.
Br. Med. J. (1994) **309**(6950):341.

Early aggressive surgery is key to survival

- Antibiotics **cannot penetrate** thrombosed necrotic tissue
- Relatively few acute inflammatory cells
- Remove toxin producing bacteria



Nb. Absence of acute inflammatory cells in area of necrosis

Adjuvant treatments

Antibiotics

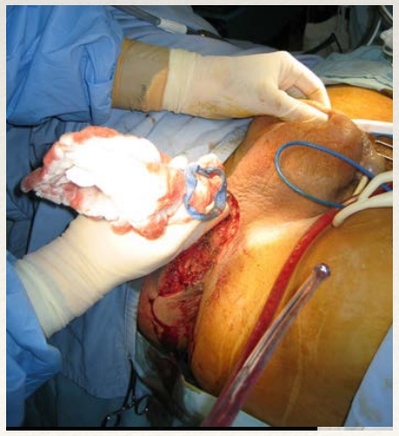
- **Adjunct** therapy to surgery
- Broad spectrum - cover Gr+ and Gr-, anaerobes, MRSA
- Toxin suppressing
  - Clindamycin (no Eagle effect)
  - Linezolid

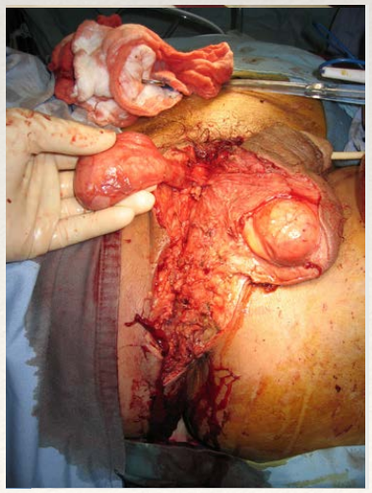
- Because of thrombosis (poor penetration) antibiotics alone will not work!

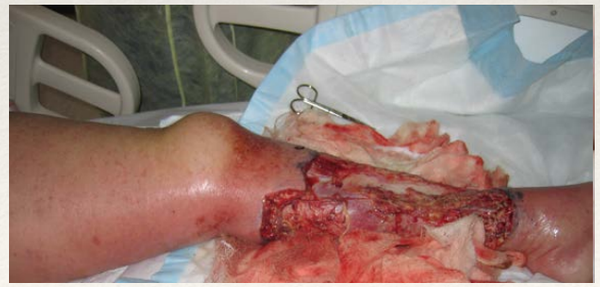
Falade et al Chest 10/15/2011

Type 1 Necrotising Soft Tissue Infection

- Polymicrobial - Gram + and -
- **Mixed** aerobes and anaerobes
- **Most common** NSTI
- Occurs after trauma or surgery
- Initial involvement of skin, S/C fat and fascia. Later into muscle
- Slower progression than GAS or clostridia but still highly lethal







Fournier's Gangrene - ex. Type 1

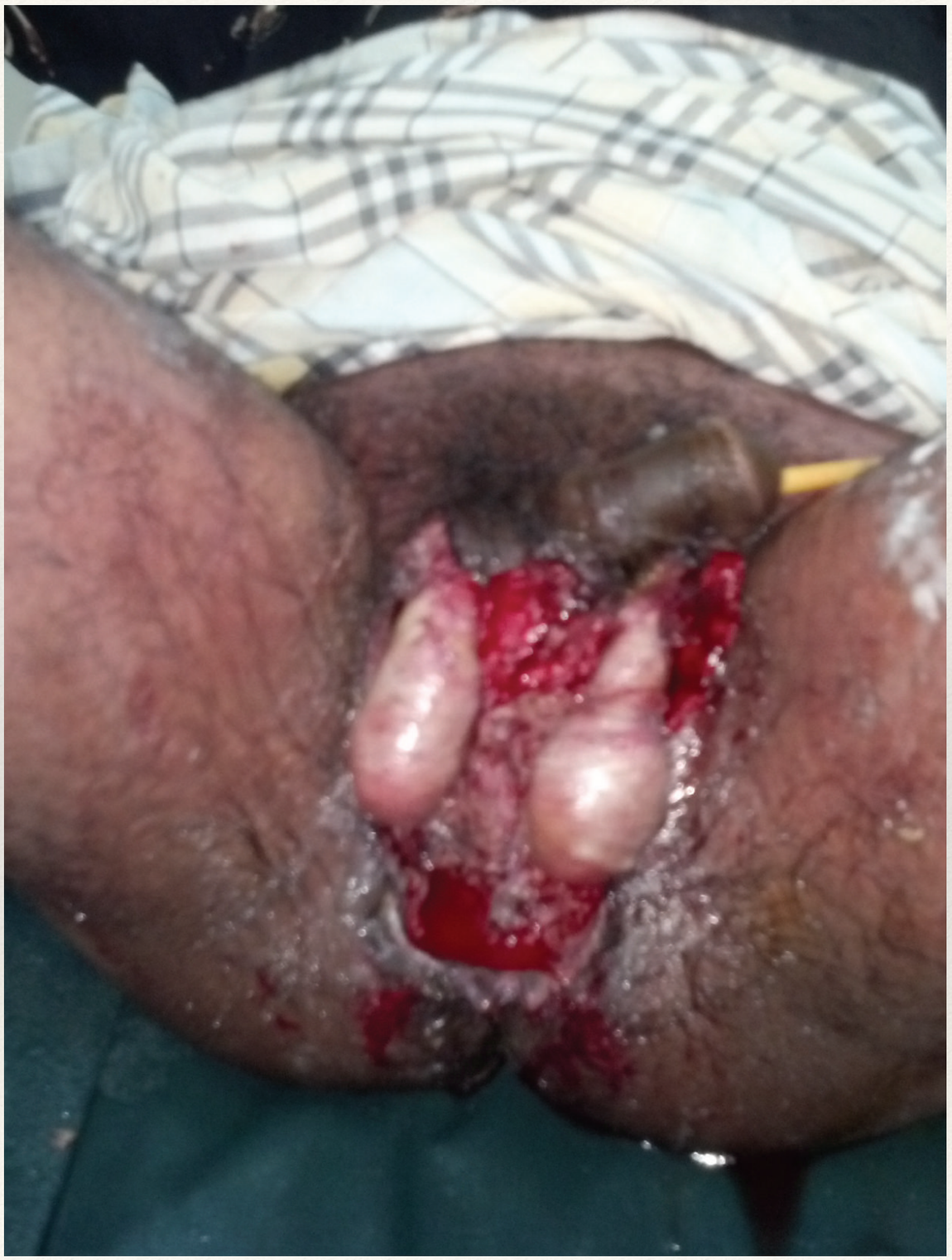


Table 1: Etiology of Fournier's gangrene.

Anorectal
Trauma
Ischiorectal, perirectal, or perianal abscesses, appendicitis, diverticulitis, colonic perforations
Perianal fistulotomy, perianal biopsy, rectal biopsy, hemorrhoidectomy, anal fissures excision
Steroid enemas for radiation proctitis
Rectal cancer
Genitourinary
Trauma
Urethral strictures with urinary extravasation
Urethral catheterization or instrumentation,
penile implantsinsertion, prostatic biopsy, vasectomy,
hydrocele aspiration,genital piercing, intracavernosal cocaine
injection Periurethral infection; chronic urinary tract infections
Epididymitis or orchitis
Penile artificial implant, foreign body
Hemipelvectomy
Cancer invasion to external genitalia
Septic abortion
Bartholin's duct abscess
Episiotomy
Dermatologic sources
Scrotal furuncle
Genital toilet (scrotum)
Blunt perineal trauma; intramuscular injections, genital piercing
Perineal or pelvic surgery/inguinal herniography.
Idiopathic

Mr C

Type 2 Necrotising Soft Tissue Infection (+/- Toxic Shock Syndrome)

- Pathogen **Group A Streptococcus** ("flesh eating bacteria") or **Staph aureus** etc
  - Virulence factors:
    - M protein (M1 and M2), inhibits complement
    - Certain alleles bind to T cells → cytokines
    - Only certain individuals express these alleles
- Staph aureus may be Panton Valentine Leukocidin (PVL) secretor

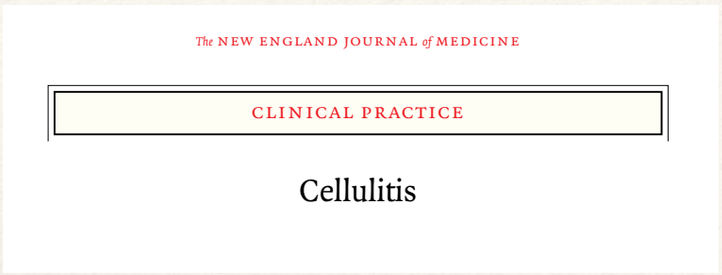
Other adjuvant treatments

- Intensive care support
- IVIG
- Hyperbaric Oxygen (controversial)

Clinical deterioration = further immediate debridement

Differential diagnosis

Diagnosis and Prognosis



NEJM 350;9; February 26, 2004

"... **difficult to differentiate cellulitis** from **necrotizing fasciitis**… **surgical exploration** ... must **not** be **delayed"**

"… requires **aggressive débridement**…

is a **true surgical emergency**"

Lancet Infect Dis **2009; 9: 281–90**

The **mortality** … from 40% **up to 80%** ..."

"…progress with a **rapidity** that, once seen, is **never forgotten**."

"...TSS has **not** achieved the **same level of awareness** among health-care professionals…"

Management of Soft tissue infections

Non purulent
Necrotizing fasciitis / Cellulitis

Severe

Emergent surgery
Rule out necrotizing / debride
Empiric antibiotics

Moderate

IV antibiotics

Purulent abscess

I & D

CID 2014: 59 (July 15)

Cytokine Storm

Mrs A C

Clinical case

- 42 yr old female leading cancer researcher (“cytokine specialist”)
- Previously healthy
- 2 day history of olecranon bursitis following banal pressure
- Rx NSAIDs
- Rapid onset of forearm swelling, redness and tenderness
- Soon followed by upper abdominal pain, diarrhoea, nausea and vomiting

Admitted to Ealing A+E

- BP 80/40; HR 115; RR 26; Temp 40◦; Sats 97%; GCS 15
- In AMU given :
  - initially fluids, Tazocin, Amikacin,
  - later Clindamycin, Noradrenaline

Transferred to ITU .....

- We find a very sick woman - "cytokine avalanche" despite appearing deceptively "well"

- Care plan organised and executed **emergently**

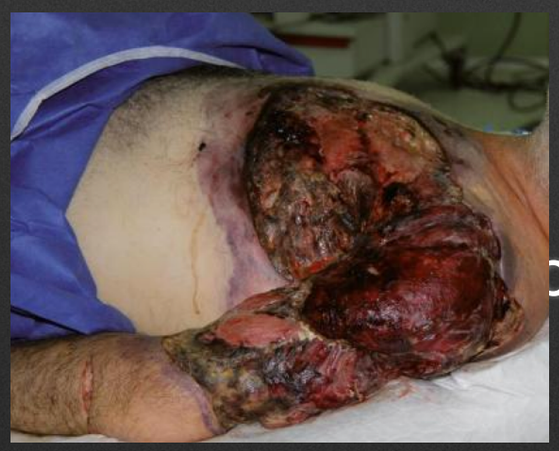
- inclu. surgical exploration for suspected soft tissue necrosis, CT

CT showed

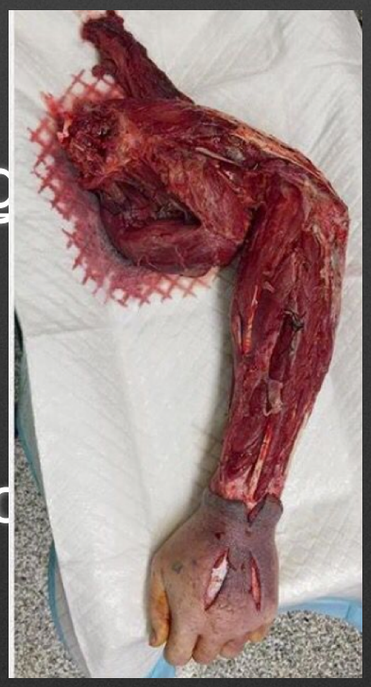
- ARDS
- “Septic abdomen" with massive 3rd spacing and a distended gall bladder
- Very oedematous arm

Where is the source?

If source not found and “controlled", she is at extremely hig

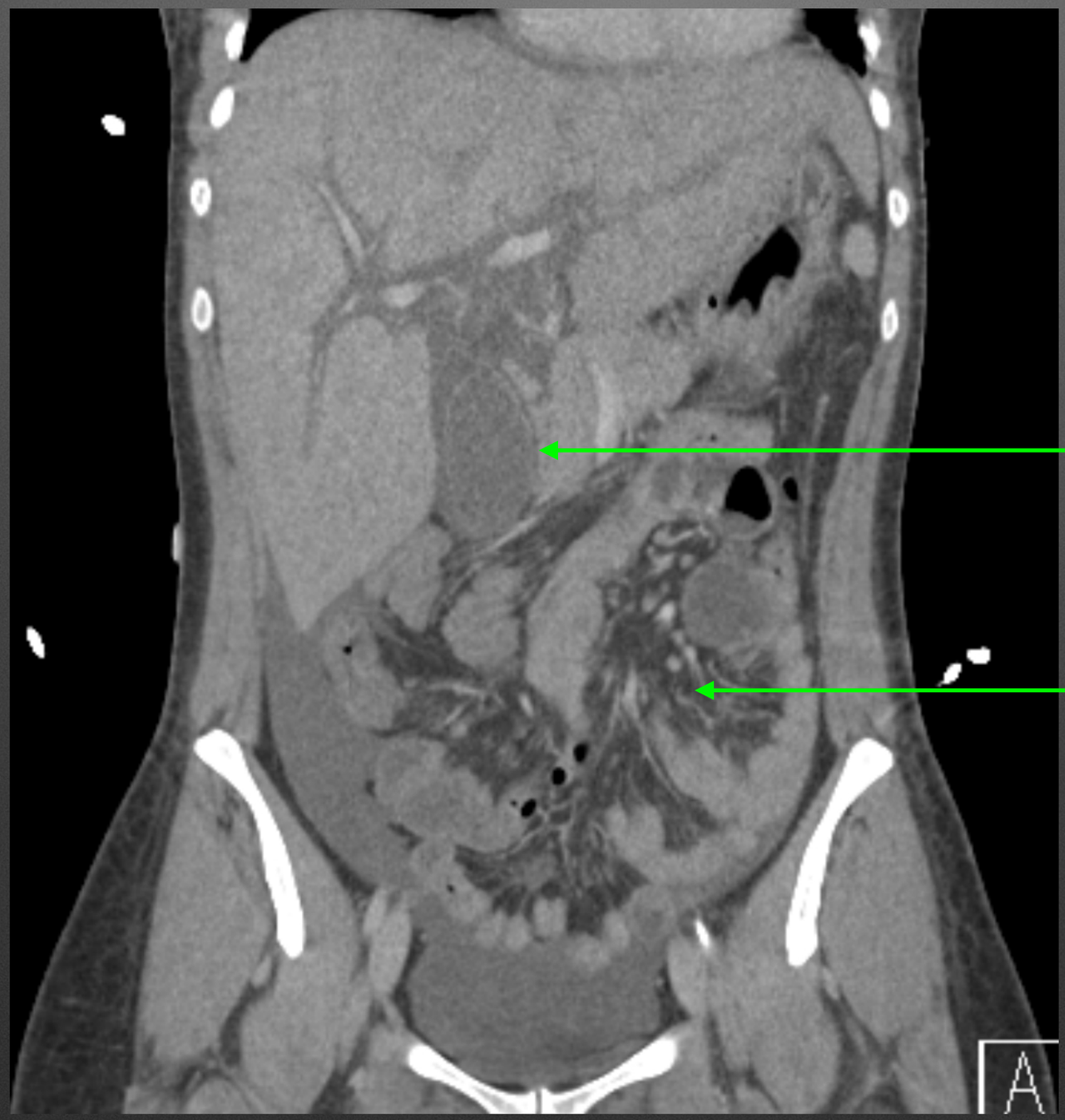


bicion of TSS: linezolid and IVIG added to clindamyc



CT showed

"Septic" swollen abdomen



Distended,
thin walled gall bladder

“Third space”
Oedema +++

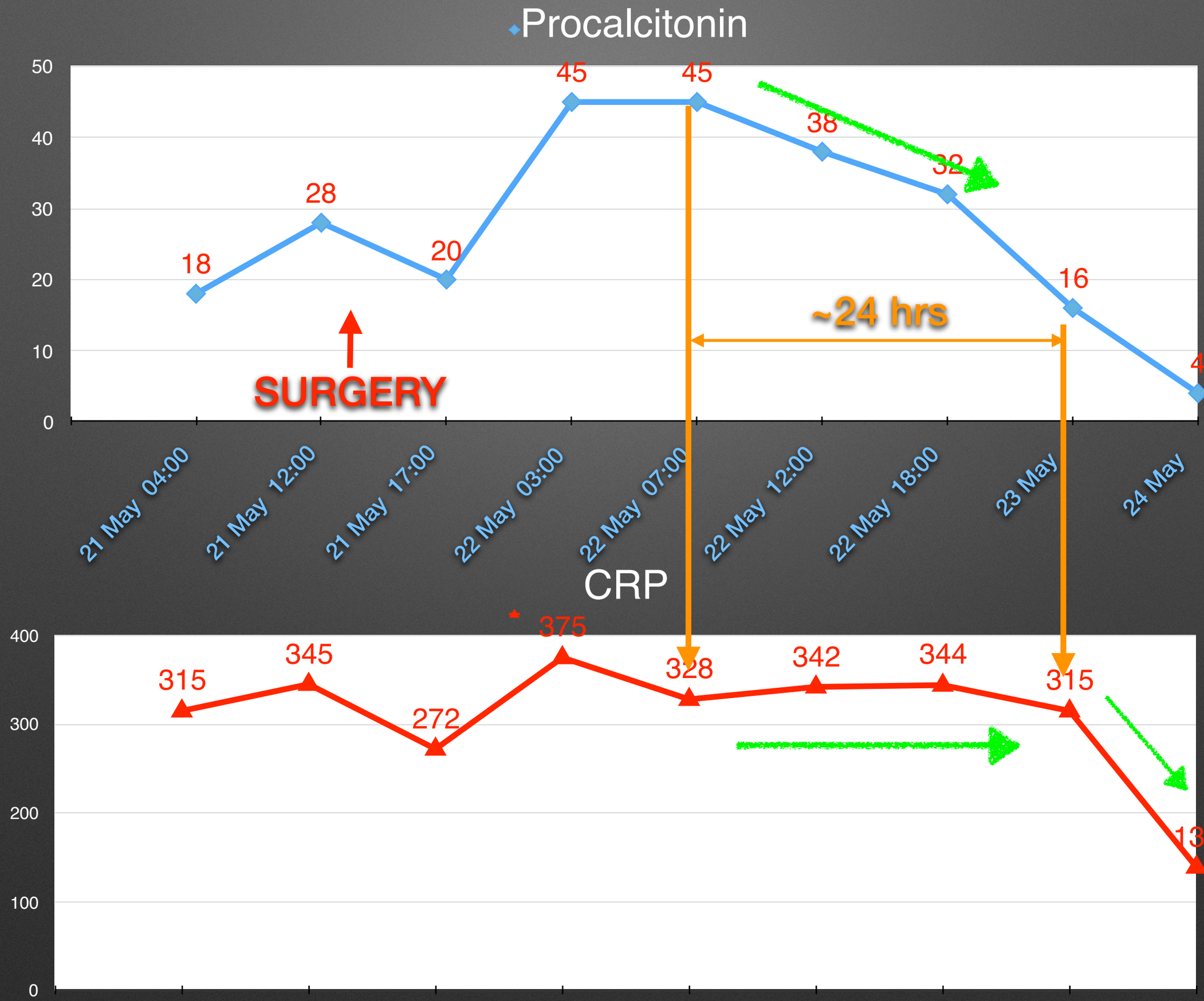
How sick?

Acid Base	pH 7.19, BD 14, HCO_3^- 12 ; lactate 4
CV	Max. Noradrenaline; BP 90/35; CI 5.1 Troponin 3,422; NT Pro BNP 17,464 ECG non specific changes
Lungs	ELWI 7 → 19
Kidney	Creatinine N - ↑181 UO 180/min
Microcirculation	CRT 10 sec
Coagulation	Platelets N → ↓103; PTT N → ↑73
ScVO2	71% → 84%
Liver	Albumin N → ↓19 Alk Phos 2.5 x N; ALT 3 x N
Infection markers	WBC 29; CRP 345; PCT 28

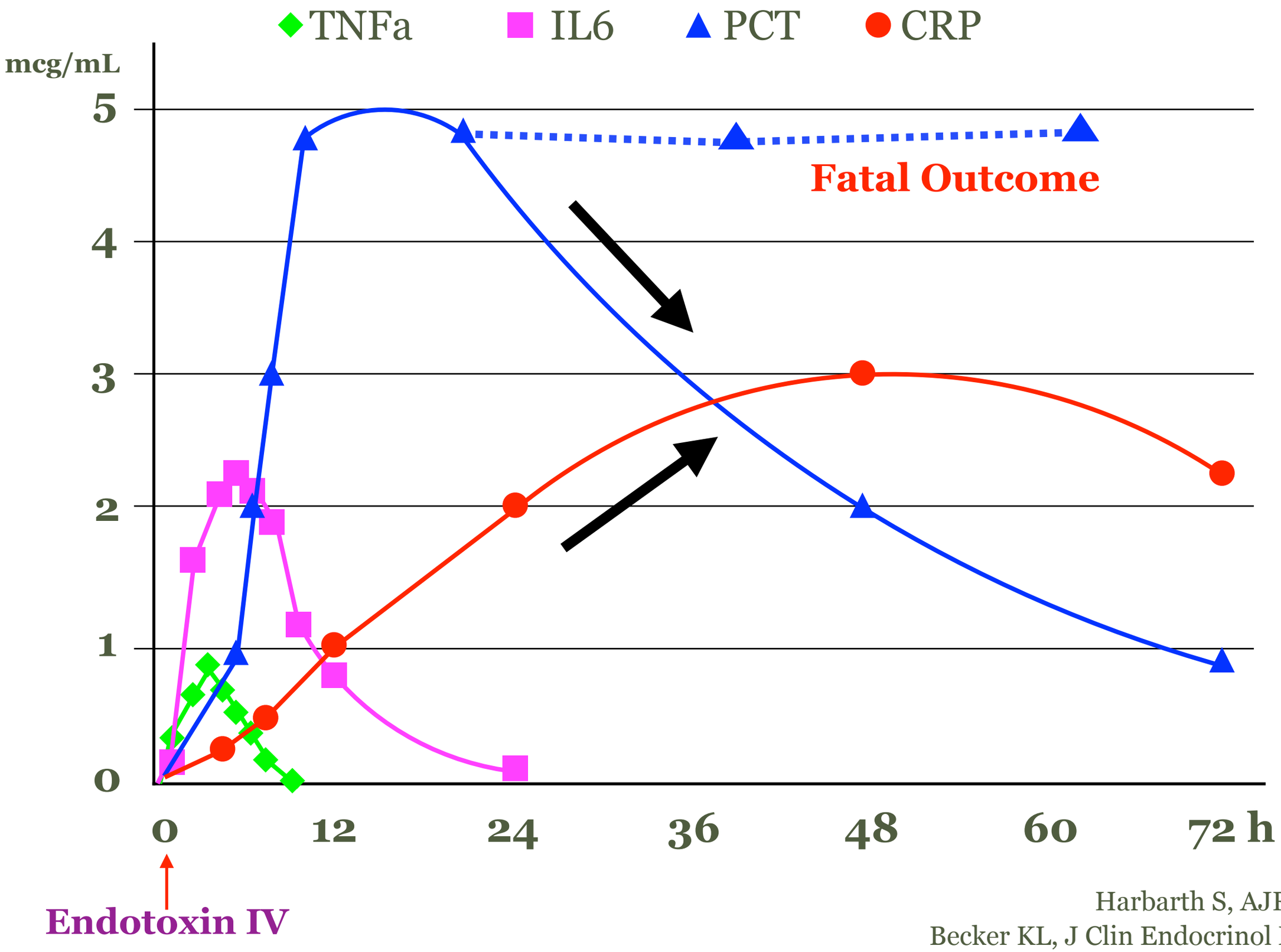
Outcome from surgery

- Surgical exploration showed very swollen but non-necrotic soft tissues
- Gynaecological exam unremarkable
- Tissue sample " motorcycled" to NWP where microscopy showed G+ cocci

  Presumed diagnosis of cellulitis with a toxin secreting m/o (GAS or Staph).


Procalcitonin
50
40
30
20
10
0
18
28
20
45
45
38
32
16
4
SURGERY
~24 hrs
21 May 04:00
21 May 12:00
21 May 17:00
22 May 03:00
22 May 07:00
22 May 12:00
22 May 18:00
23 May
24 May
CRP
400
300
200
100
0
315
345
272
375
328
342
344
315
139

Kinetics of Procalcitonin upon Infection



Harbarth S, AJRCCM 2001
Becker KL, J Clin Endocrinol Metal 2004

Final Outcome

- Micro called to confirm a Group A Strep so changed to Penicillin V and Clindamycin **("De-escalation therapy")**
- Procalcitonin was a vital component in the **life and death decision** as to whether to continue search for another "source"
- Patient extubated and discharged to ward 3 days later
- Home 10 days after that

Recap

- Soft tissue necrosis is **deadly**
- Diagnosis - **high index of suspicion**
- Treatment
  - **Surgical** source control
    - **emergent** and **aggressive**
  - Antibiotics
    - Including **toxin suppression** and IVIG
  - Intensive Care

Most importantly
there is not a moment to lose!

???

www.jvsmedicscorner.com

(Mallory / Everest2013)

Categories:

uncomplicated

such as cellulitis, simple abscesses, etc., treated with *surgical incision alone*

complicated

such as major abscesses, require *significant surgical interventions*

A more useful classifications:

non necrotizing

necrotizing infections -*require aggressive surgical management*

necrotising infections further be divided :

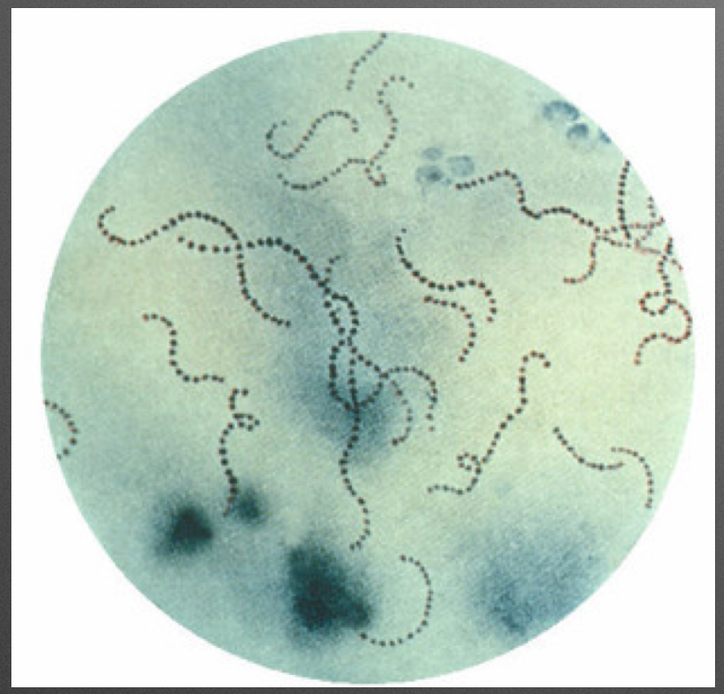
based on **anatomy** (e.g., Fournier's, Ludwig's angina),

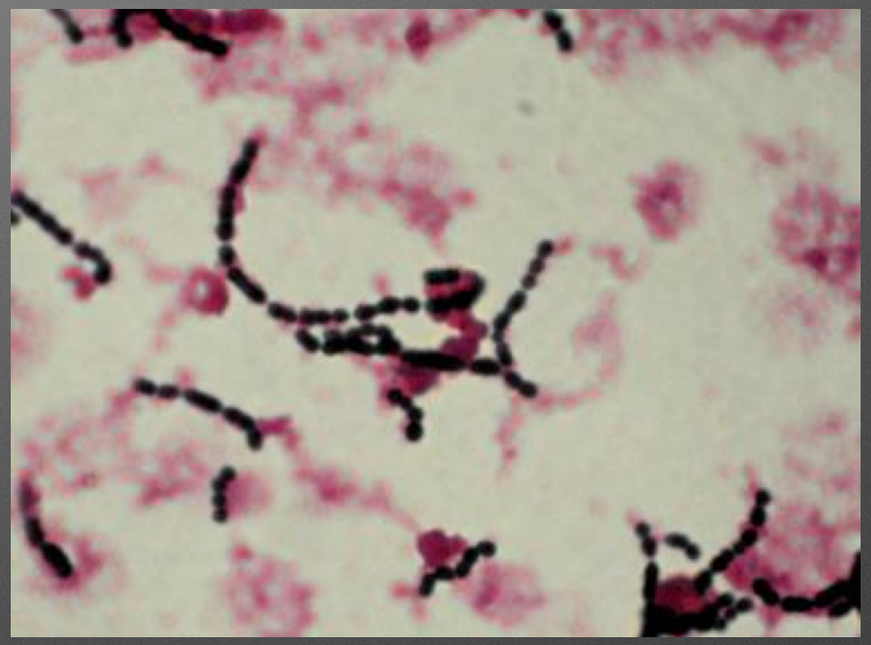
depth of involvement (e.g., necrotizing adipositis, fasciitis, or myositis),

microbial source of infection (types 1/2/3), or a combination of microbial source and depth (i.e., clostridial cellulitis, non clostridial anaerobic cellulitis).

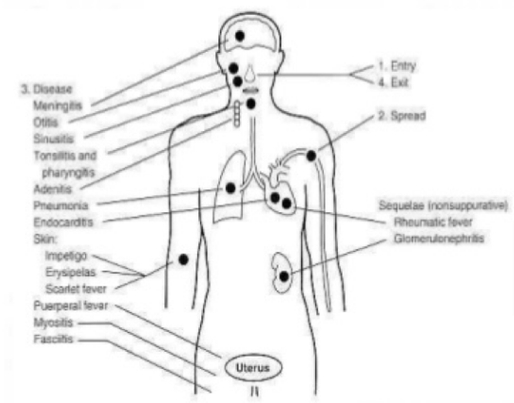
Crit Care Med 2010 Vol. 38, No. 9 (Suppl.)

Group A Streptococcus





Infections caused by *Streptococcus pyogenes* (GAS)



- Superficial diseases

pharyngitis, skin & soft tissue infⁿ, erysipelas, impetigo, vaginitis, post-partum infⁿ

- Deep infections

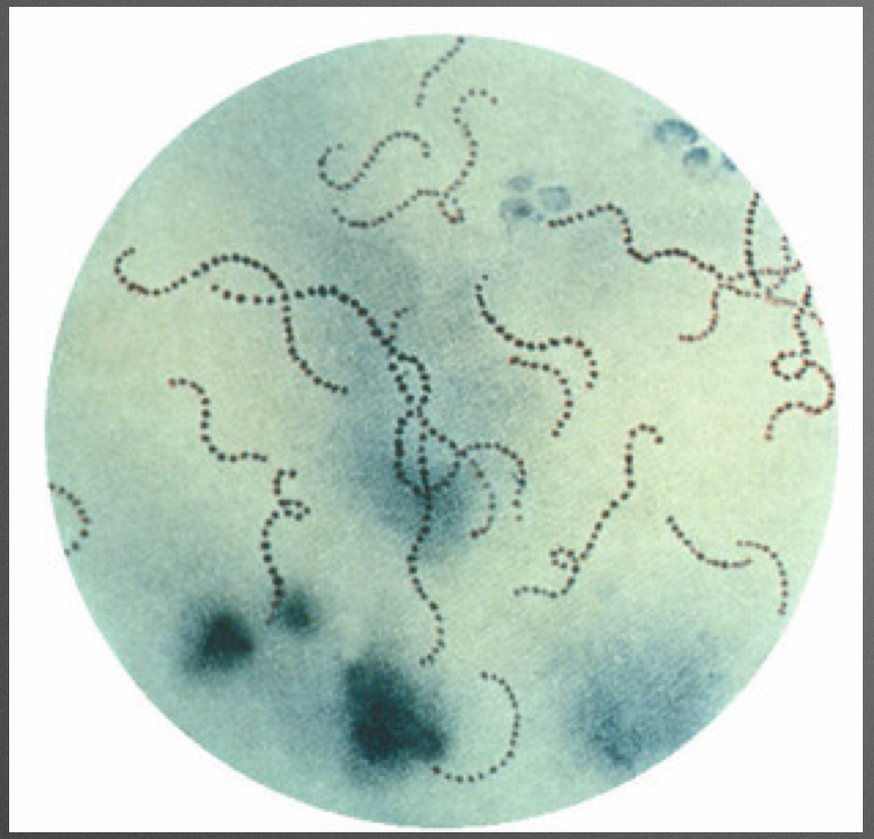
bacteraemia, necrotising fasciitis, deep soft tissue infⁿ, cellulitis, myositis, puerperal sepsis, pericarditis, meningitis, pneumonia, septic arthritis

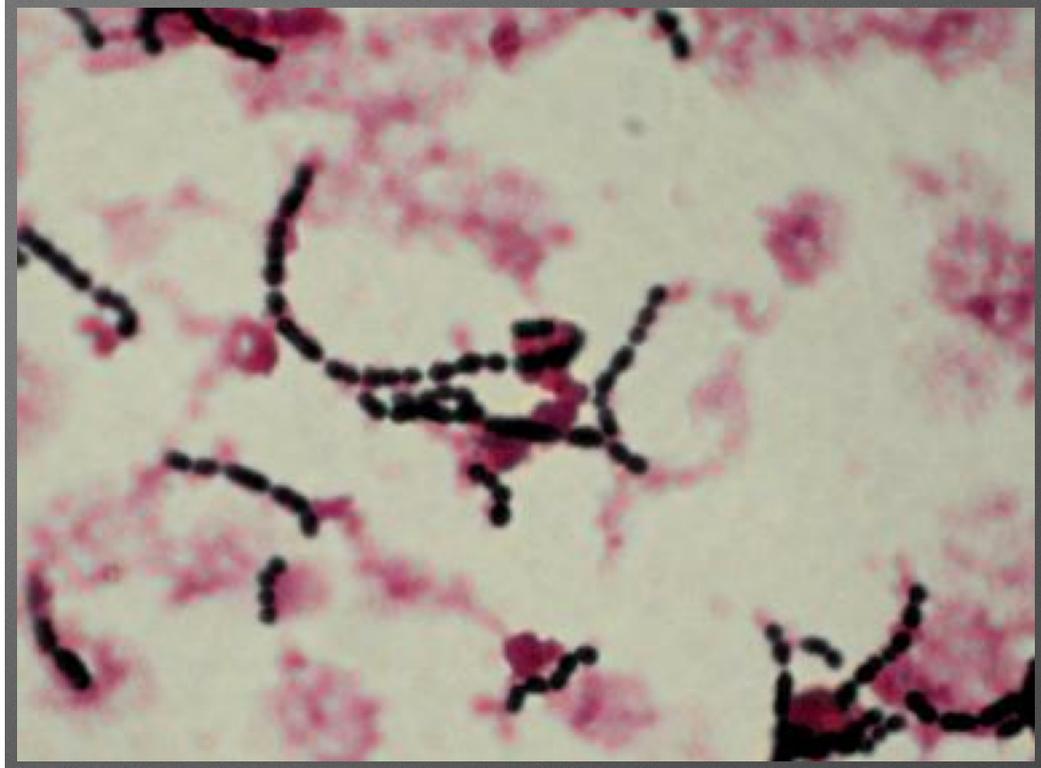
- Toxin-mediated

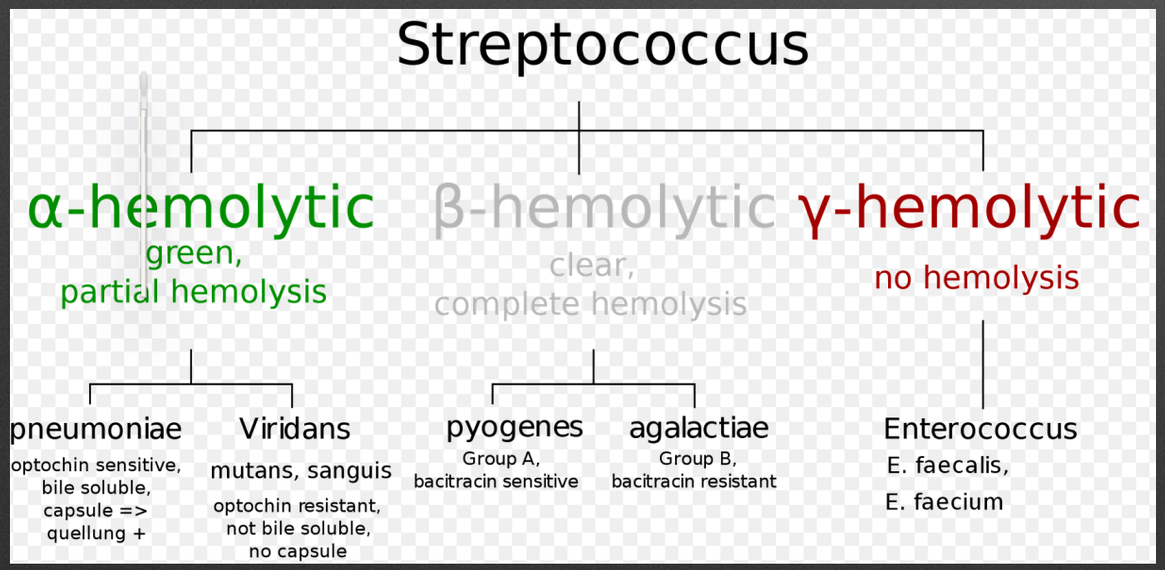
scarletina, toxic shock-like syndrome

- Immunologically mediated

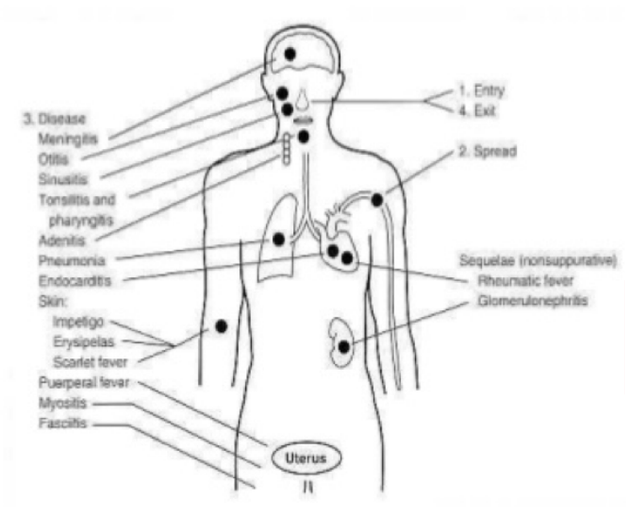
rheumatic fever, post-streptococcal GN, reactive arthritis







Infections caused by *Streptococcus pyogenes* (GAS)



- **Superficial diseases**
  pharyngitis, skin & soft tissue infⁿ, erysipelas, impetigo, vaginitis, post-partum infⁿ
- **Deep infections**
  bacteraemia, necrotising fasciitis, deep soft tissue infⁿ, cellulitis, myositis, puerperal sepsis, pericarditis, meningitis, pneumonia, septic arthritis
- **Toxin-mediated**
  scarletina, toxic shock-like syndrome
- **Immunologically mediated**
  rheumatic fever, post-streptococcal GN, reactive arthritis

Procalcitonin ratio as a predictor of successful surgical treatment of severe necrotizing soft tissue infections

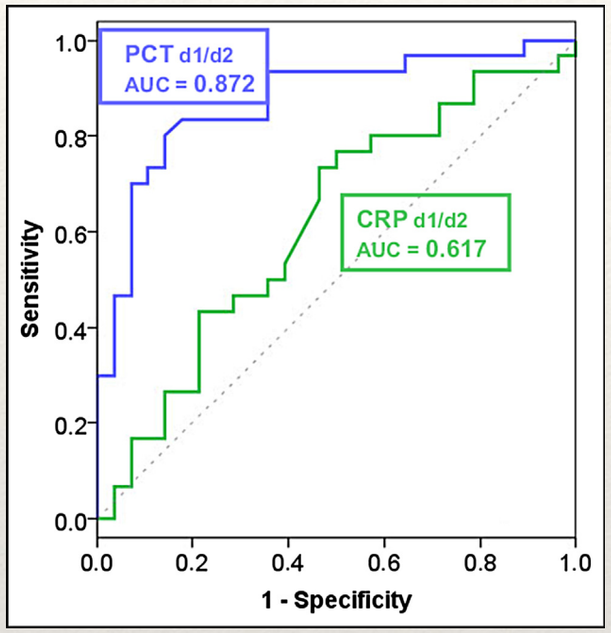


Figure 1 Receiver operating characteristic (ROC) curves of procalcitonin (PCT) and C-reactive protein (CRP) ratio of postoperative day 1 and 2 after a major surgical procedure in 38 patients with necrotizing soft tissue infection. The area under the curve (AUC) ROC for successful elimination of the infectious focus was .872 for the postoperative PCT ratio and .617 for the CRP ratio.

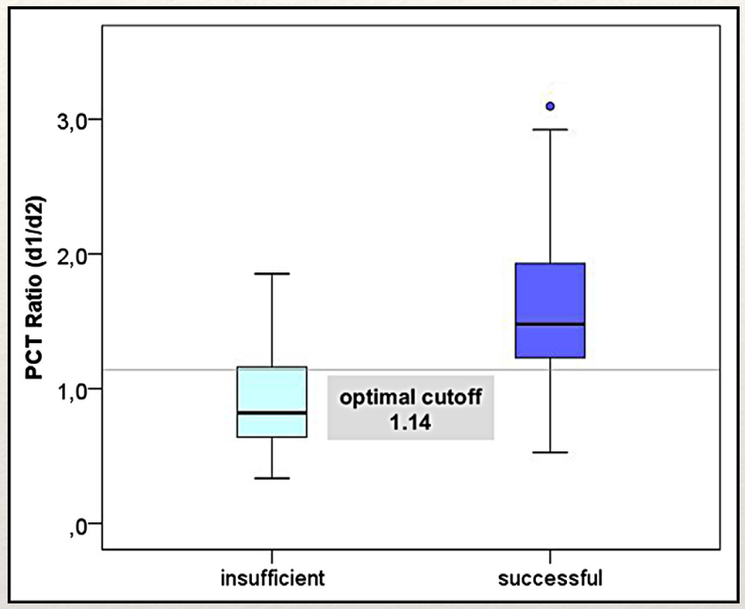


Figure 2 Cutoff value for the procalcitonin (PCT) ratio of postoperative day 1 to day 2 predicting a successful surgical eradication of the infectious focus using classification and regression tree analysis. Ratios higher than 1.14 indicate a successful elimination of the infectious source.

The diagnosis of NSTI, therefore, must be made clinically.

The single most important as- pect of managing NSTI is complete de- bridement of necrotic and infected tissues. Early operative debridement is the major determinant of outcome (51, 52 Surgical debridement should never be delayed in hope of restoration of he- modynamic stability before anesthesia in- duction, because correction of the septic state will not occur until all the in- fected and necrotic tissues have been re- moved.

A change in the fascia from a tough and shiny white appearance to a dull gray fascia that can be easily separated from the fat with blunt dissection is indicative of necrotizing infection. T classically described brownish-tan “dishwater” fluid weeping from the tissues, if present, is also highly suggestive of NSTI.

The excision margin should be healthy bleeding tissue with a normal ap- pearance.

Perineal gangrene often involves the scrotum and perianal skin. Surgical de- bridement usually involves excision of the scrotal skin and perineal skin extend- ing to the gluteal region. The testicles are usually spared and orchiectomy is rarely required.

The patient’s wound should be re-explored in the op- erating room within 24 hrs to evaluate whether the spread of infection has been stopped and if further debridement is re- quired. All newly identified necrotic tis- sue should be aggressively debrided. In patients whose clinical condition contin- ues to deteriorate, re-exploration should be considered sooner,

Surgical debridement is usually exten- sive and involves significant blood loss.

The initial IV antibiotic therapy should be broad enough to cover the di- verse and various causative agents. High- dose penicillin G or ampicillin should be used to cover for potent *Clostridium*, *Streptococcus*, and *Peptostreptococcus* infections. Penicillin G, if chosen, should be given as 18–24 million units per day for an adult.

coccus should also be covered with clin- damycin or metronidazole. Clindamycin is also effective in treating group A -he- molytic *Streptococcus* by suppressing the production of exotoxi (74). Clindamy- cin is also the drug of choice for patients allergic to penicillin. Gram-negative cov- erage can be achieved by adding an ami- noglycoside, a third- or fourth-genera- tion cephalosporin, a fluoroquinolone, or a carbapenem. Alternatively, penicillin or ampicillin can be replaced by piperacillin- tazobactam or ticarcillin-clavulanate to include Gram-negative coverage.

Selection of antimicrobials that in- hibit toxin production should be consid- ered in patients with streptococcal, clos- tridial, and staphylococcal infections, especially those with evidence o rapidly progressive or severe infections. Clinda- mycin, erythromycin, and linezolid are potential inhibitory agent

Staphylococcus-secreted peptides that recruit, activate, and lyse human neutrophils, thus eliminating a main cellular defense against staphylo- coccal infection (76). -Lactams actually enhance toxin production, whereas both clindamycin and linezolid inhibit toxin production by suppressing translation but not transcription of *S. aureus* toxin genes and directly inhibiting synthesis of group A *Streptococcus* toxins (75).

Because of the recent increase in the prevalence of community-associated MRSA necrotizing infection, vancomycin or clindamycin should be considered for use in the initial antibiotic regimen in suspected cases.

IVIG provides antibodies that can neutralize the circulating streptococcal exotoxins, thus reducing the toxin- induced tissue necrosis (87, 88). In addi- tion, IVIG may also have an effect on the circulating cytokines,

Hyperbaric oxygen (HBO) therapy has also been proposed as an adjunctive ther- apy for NSTI. This treatment modality remains controversial

n contrast, other similar series (97, 98) reported higher mortality with HBO therapy.

these patients will have an increase in caloric and protein demands due to the large protein loss through the open wounds and the hypermetabolic state.

Betadine should not be used on an open wound, as it will

cause cell damage and inhibit wound healing. Perineal wounds are especially difficult to manage, because soilage of the wound is frequent.

It is not necessary to wait for granulation tissue to fill the entire wound bed for split- thickness skin grafts, as the grafts will take as long as there is a clean and vas- cularized bed that is free from infection.

For perineal wounds that involve the scrotum, the best cosmetic result can be achieved by delayed primary closure of the wound, if it is small. If the wound is too large for primary closure, it should not be allowed to heal by secondary in- tention, as this will lead to contracture deformity of the scrotum. Several scrotal reconstruction methods have been de- scribed, including musculocutaneous flap and fasciocutaneous flaps from the thigh and the abdomen

A simple and widely used method is placement of the testicles in subcutane- ous pockets in the thigh.

Complete surgical debridement is the key to success.

Clinically, pain precedes skin changes by 24–48 h

Type I infections are the most common form of the disease. They are polymicrobial and wound tissue isolates identify on average four different organisms.

Causative microbes include a combination of Gram-positive cocci, Gram-negative rods, and anaerobes.

Type II

An infection caused by the group A streptococcus (Streptococcus pyogenes) either alone or in asso- ciation with Staphylococcus aureus,

Group A streptococci can survive and replicate in macro- phages, thereby escaping antibiotic therapy even in those tissues that remain well perfused and considered amenable to antibiotic penetration.

Type II is the only NSTI associated with toxic shock syndrome.

Bacterial growth within the superficial fascia releases a mixture of enzymes and endo- and exotoxins causing the spread of infection through this

The initial clinical skin findings underestimate the tissue infec- tion present, although thrombosis of penetrating vessels to the skin is the key feature in the pathology of NSTI.

Many patients with NF are initially misdiagnosed with cellulitis, delaying appropriate management and increasing morbidity and mortality

Unlike cellulitis where the infection begins at the junction between the dermis and superficial fascia, in NF, the infection starts at the level of subcutaneous fat and deep fascia. It is because of this sparing of the epidermal and dermal layers in the early stages of the disease that erythema and oedema of skin are not obvious,[6] and so the extent of infection clinically is not clear.

Biochemistry

Raised serum creatinine kinase indicates myositis or myonecrosis, and the effects of circulating toxins or ischaemia.[8]

Microbiology

Blood cultures are positive in 11–60% of the patients with NF caused by group A streptococci. Percutaneous needle aspiration of the advancing edge is useful but a tissue biopsy is the investigation of choice. Samples should include the advan- cing edge and central necrotic areas.

imaging is not a definitive procedure and should not delay surgery.

Surgical debridement

Several studies have shown that the most important factor affecting mortality is timing and adequacy of initial surgical debridement.[11] Delayed or inadequate debridement dramatically increases mortal- ity. Radical debridement may necessitate limb amputation. Debridement removes the source of infection and toxins, and fur- thermore, removal of infarcted tissue improves the subsequent penetration of antibiotics. The infection is rarely eradicated after a single debridement and serial debridements are almost always needed. Optimally, three debridements spaced 12 – 36 h apart

A broad-spectrum agent such as Tazocin, containing piperacillin (a penicillin which kills a wide variety of bacteria by interfering with the formation of bacterial cell walls) and tazobactam (a b-lactamase inhibitor which prevents bacteria from inactivating piperacillin leaving them sus- ceptible to attack) or a carbapenem (such as meropenem), can be combined with clindamycin. If Group A streptococcus alone is responsible, antibiotics may be rationalized to a combination of penicillin and clindamycin. Clindamycin is included in antibiotic therapy as it is known to switch off toxin production. Likewise, when MRSA is suspected, Linezolid is preferred to vancomycin as it inhibits exotoxin production.

I.V. immunoglobulin therapy

The use of i.v. immunoglobulin (IVIG) is based on the theoretical mechanism that it can bind staphylococcal- and streptococcal- derived exotoxin, so limiting the systemic cytokine release asso- ciated with systemic inflammatory response syndrome.

There is very limited evidence which suggests a decreased mor- tality

Currently, antimicrobial prophylaxis is not recommended for adults with close contact to patients with NF and group A streptococcus. However, the UK Health Protection Agency recommends increased vigilance and the seeking of early medical advice if signs and symptoms of infection develop in any such individual.

Conclusions

- Early diagnosis should yield earlier intervention and reduce mortality
  - LRINEC
  - When in doubt, explore
- Clindamycin should be incorporated into all regimens
- IVIG is a reasonable adjunct in Type 2 (streptococcal) necrotizing fasciitis.
- HBO may be of utility in Type 3 (clostridial) necrotizing fasciitis
- Plasmapheresis may benefit severe sepsis and septic shock

Table 3 Necrotizing fasciitis—pathogens and treatments by anatomical site

Anatomical location	Predominant pathogens	Empiric antimicrobial therapy
Head/neck	Anaerobes	Ampicillin/sulbactam usually sufficient, though MRSA coverage should be considered, particularly in immunosuppressed or IV drug abusers
Abdomen/perineal	Gram negative, anaerobes	Cefepime + metronidazole OR an anti-pseudomonal carbapenem OR piperacillin-tazobactam
Lower extremity	Gram negative, anaerobes, Gram positive	In MRSA prevalent areas vancomycin PLUS cefepime + metronidazole OR an anti-pseudomonal carbapenem OR piperacillin-tazobactam
Surgical site	Variable depending on surgical site	In addition to anatomic location pertinent antimicrobials, if not already included, MRSA coverage should be considered in regions with high incidence

Key slide -Add

Initial treatment

- Debridement of primary focus
- Systemic supportive care
- Antibiotics
- Single agents
  - Ampicillin/sulbactam 3gm q
  - Imipenem/cilastatin 500-75
  - Meropenem 1gm q6h
  - Piperacillin/tazobactam 4.5
- Combination therapy
  - Penicillin (4 million units Q4
  - Clindamycin (900 mg Q6 -8 hrs)
    - potent suppressor of bacterial toxin synthesis (M protein)
    - May be more effective than PCN in late infections due to stationary growth phase
- Vancomycin/Linezolid

Clindamycin is first line

- Efficacy is independent of inoculum size or growth phase: Eagle Effect
- Potent suppressor of toxin synthesis
- Subinhibitory concentrations facilitate the phagocytosis of GABS
- Reduces synthesis of PBP
- Long post-antibiotic effect β-lactams
- Suppresses TNFα synthesis

Edlich et al, *J Emerg Med*, 2009

Antibiotics

Depends on where and in which patient

Micro-organism:

- *Group A Strep*
- *Staf Aureus*

Bacteroides?

- *Pseudomonas*
- *Aeromonas*
- *Escherichia coli*
- *Enterococcus Faecium*
- *Vibriio*

- **Most common in patients without precipitating factor and in puerperal patients or recent pharingytis.**

(Com. Acquired MRSA !!!)

- *More common in compromised patients*
- *Most common in the Philippines (post abscess & Fournier)*
- *South Korea and Taiwan*

Anaya et al, Clin. Infect Dis. 2000 Salvador et al, Asian J. Surg. 2010 Goh et al BJS 2014
Chunag et al, Clin. Infect Dis. 2002

Conclusions

- *Surgical emergency requiring prompt action*
- *Repeated evaluation of wound and vital status = teamwork*
- *Risk for unexpected low cardiac output syndrome*
- *Antibiotics and Immune globulin: center and patient dependent Clindamycin and IVIG in GAS / STSS*

- *Deep shock and major repeated surgery but often young patients with good long term perspectives*

Do not give up

Be vigilant day by day and week by week

M.P.C., K.U.Leuven

Initial treatment

- Debridement
- Systemic support
- Antibiotics
- Single agent
    - Tazocin
    - Meropenem
- Combination therapy
- Penicillin (high dose)
- Linezolid
    - Toxin suppression
- Clindamycin
    - Independent of inoculum size/growth phase (Eagle effect)
    - Toxin suppression
    - Long post-antibiotic effect
    - Suppresses TNFα synthesis

Initial treatment: MRSA

Vancomycin
Linezolid
Daptomycin
Tigecycline

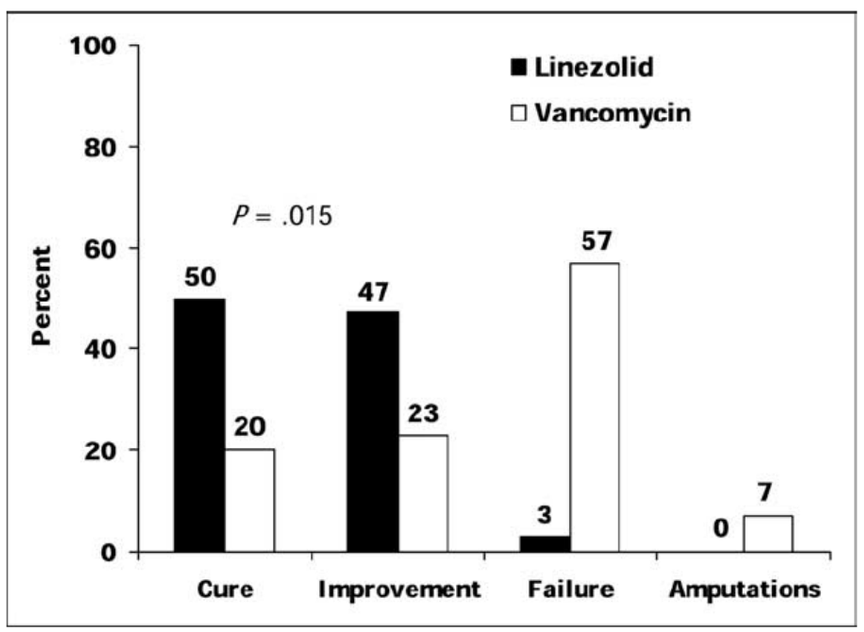


Fig. 1. Clinical outcomes with oral linezolid versus intravenous vancomycin therapy.

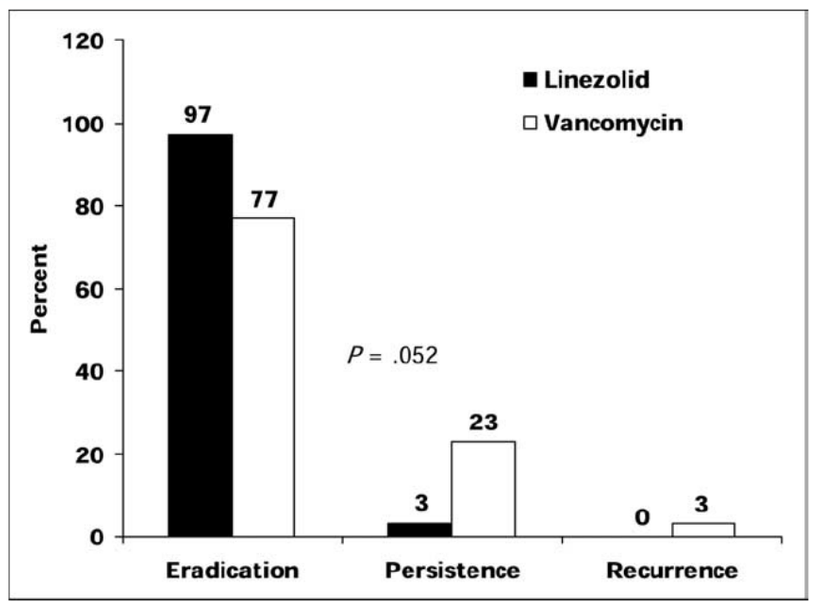


Fig. 2. Microbiological outcomes with oral linezolid versus intravenous vancomycin therapy. Eradication and persistence data include both documented and presumed cases.

Miller et al, *NEJM*, 2005

Necrotizing Soft Tissue Infections
Incidence

- CDC: ~ 500 – 1,000 new cases per year in USA
- Represents a gross underestimate, in that it refers only to Group A Streptococcus
- Increasing incidence due to Staphylococcus, and MRSA
- Amputation
  - Lower limbs > upper limbs
  - Rate of 25-50% in extremities
- Overall Mortality Rate 16-24% in good hands
- Survivors have higher likelihood of longterm death due to infection, suggesting an inherent defect in host defenses.

Ustin JS et al. *Crit Care Med* 2011

Necrotizing Soft Tissue Infections

Microbiology – 162 organisms

Organism	Case No.
Streptococcus species	31
Staphylococcus aureus	26
Klebsiella species	17
Enterococci	14
Acinetobacter baumanii	13
Escherichia coli	12
Pseudomonas aeruginosa	10
Enterobacter species	6
Proteus species	6
Bacteroides species	6
Fungi (ie, Candida)	5
Peptostreptococcus species	4
Clostridium species	2
Other	10

Wong et al*; J Bone Joint Surg Am* 2003

Conclusions

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