

SALA CONCORDIA B

INFEZIONI E SEPSI

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La gestione delle infezioni della cute e dei tessuti molli



Disclosures

- ABBVIE
- GILEAD
- VIIV
- MSD
- JANNSEN-CILAG
- ANGELINI
- PFIZER
- MENARINI

Topic

- Acute bacterial infections involving the skin and underlying tissues are becoming a growing and challenging problem
- Significant healthcare cost and important amount of hospital stays
- This is the reason why the medical research is looking for new strategies to resolve this major problem

Topic

- Hospital admission may be required to provide appropriate care for ABSSSI patients with septic shock, complicating comorbid conditions, or those at risk of acute deterioration.
- However, unnecessary hospitalizations place patients at increased risk for adverse events and hospital-acquired infections, are economically burdensome, and may not be associated with optimal outcomes

SSTIs

Uncomplicated

- Superficial infections, such as:
 - Simple abscesses
 - Impetiginous lesions
-  Furuncles
-  Cellulitis
- Can be treated by surgical incision alone

Complicated

- Deep soft tissue, requires significant surgical intervention
- Infected ulcers
- Infected burns
- Major abscesses
- Significant underlying disease state that complicates response to treatment

Non-Necrotizing

- Impetigo
- Furunculous and carbuncles
- Animal and human bites
- Infected pressure ulcers

Necrotizing

- Pyomiositis
- Necrotizing fasciitis
- Clostridial myonecrosis
- Fournier's Gangrene

- SSTIs
- Differentiation of necrotizing soft tissue infections (NSTIs) from non-necrotizing infections.
- This differentiation is critical, because necrotizing infections warrant prompt aggressive surgical debridement



Diagnosis of necrotizing soft tissue infections

Skin findings

- Erythema
- Tense edema
- Gray or discolored wound drainage
- Vesicles or bullae
- Skin necrosis
- Ulcers
- Crepitus

Systemic features

- Severe pain out of proportion to physical findings
- Pain that extends past margin of apparent skin infection
- Fever
- Tachycardia, tachypnea
- Diaphoresis
- Delirium

“Hard Clinical Signs”

- **Bullae**
- **Crepitus**
- **Gas on radiograph**
- **Hypotension with systolic blood pressure less than 90 mm Hg**
- **Skin necrosis**

FDA 2013

Acute Bacterial Skin and Skin Structure Infections (ABSSSI)

- **Subset of complicated SSTIs**
 - **cellulitis/erysipelas**
 - **wound infections**
 - **major cutaneous abscess**
- an ABSSSI is defined as a bacterial infection of the skin with a lesion size area of ≥ 75 cm² (lesion size measured by the area of redness, oedema or induration)
- the primary response criteria are defined as a 20% reduction in lesion size with resolution of fever after 48–72 h in patients who are alive and did not receive rescue therapy

Acute Bacterial Skin and Skin Structure Infections (ABSSSI)



Major Cutaneous Abscess

Infection characterized by a collection of pus within the dermis or deeper that is accompanied by redness, edema, and/or induration



Cellulitis/Erysipelas

Diffuse skin infection characterized by spreading areas of redness, edema, and/or induration



Wound infection

Infection characterized by purulent drainage from a wound with surrounding redness, edema, and/or induration

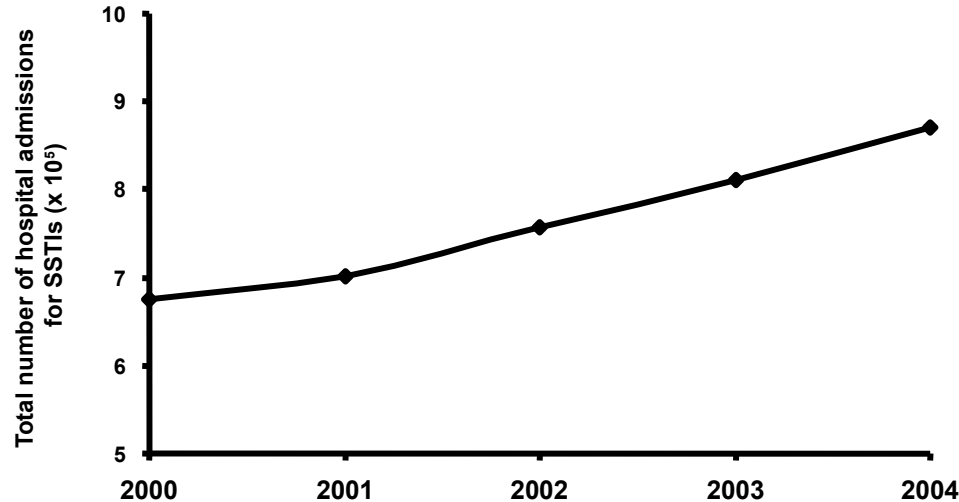
Minimum lesion surface area of approx. 75 cm²

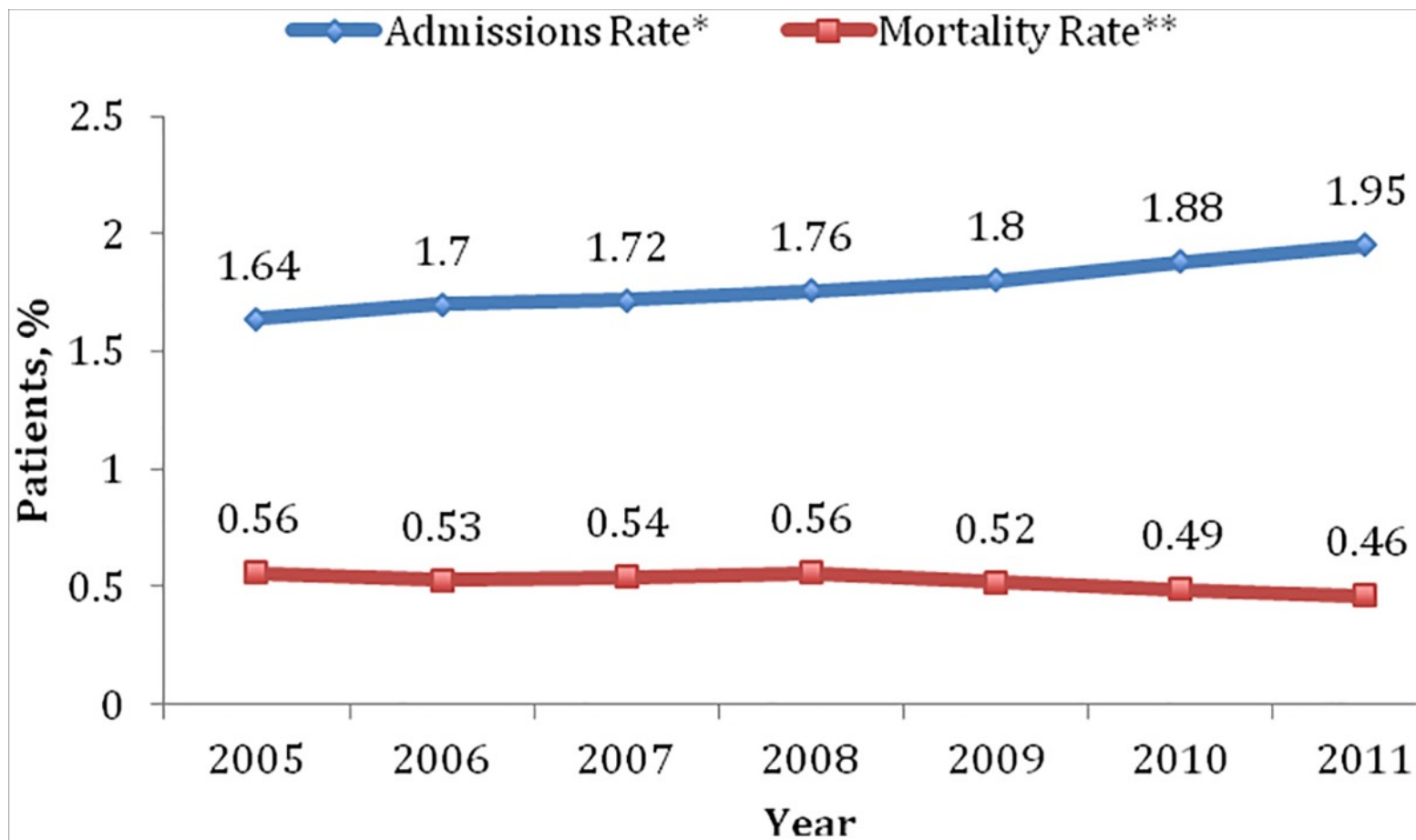
ABSSSI = acute bacterial skin and skin structure infection

1. <http://www.anshudentalcare.com/Access-Drainage-surgery-in-Jaipur.html>.
2. <http://www.bestonlinemd.com/cellulitis-can-worsen-if-you-have-diabetes/>.
3. FDA Briefing Presentation. Anti-infective Drugs Advisory Committee Meeting. March 31, 2014. NDA 21-883.
4. FDA. Guidance for Industry. October 2013, <https://www.fda.gov/downloads/Drugs/Guidances/ucm071185.pdf>

Hospital admissions due to skin and soft tissue infections have been increasing

- US Healthcare Cost and Utilization Project National Inpatient Samples show hospital admission for skin and soft tissue infections increased by 29% from 2000 to 2004





Keith S Kaye, Plos One 2015



Contents lists available at ScienceDirect

Journal of Global Antimicrobial Resistance

journal homepage: www.elsevier.com/locate/jgar



Frequency and antimicrobial susceptibility of bacterial isolates from patients hospitalised with community-acquired skin and skin-structure infection in Europe, Asia and Latin America

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S. aureus was the most common ABSSSI organism in all regions, and represented 43.3% of the overall collection.

Impact of Outpatient vs Inpatient ABSSSI Treatment on Outcomes: A Retrospective Observational Analysis of Medical Charts Across US Emergency Departments

P. Brandon Bookstaver,¹ Timothy C. Jenkins,² Edward Stenehjem,³ Shira Doron,⁴ Jack Brown,⁵ Shannon H. Goldwater,^{6,a} Carlos Lopes,^{6,d} Angela Haynes,^{6,b} Chuka Udeze,^{6,c} Yifan Mo,⁶ Patrick Gillard,⁷ Yan Liu,⁶ and Katelyn Keyloun⁷

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⁵Wegmans School of Pharmacy, St John Fisher College, Rochester, New York; ⁶Allergan plc, Madison, New Jersey; ⁷Allergan plc, Irvine, California

Results. Records from 1527 ED visits for ABSSSI from 40 centers were reviewed (admitted, n = 578 [38%]; nonadmitted, n = 949 [62%]). [redacted] were typically [redacted] (mean age, 52.2 years vs 43.0 years), more likely to be morbidly obese (body mass index > 40 kg/m²; 17.3% vs 9.1%), and had [redacted] (Charlson Comorbidity Index ≥ 4; 24.4% vs 6.8%) compared with those not admitted. In the primary analysis, adjusted logistic regression, controlling for comorbidities and severity of illness, demonstrated that there was a similar likelihood of all-cause unplanned ED visits or readmissions between admitted and nonadmitted patients (odds ratio, 1.03; 95% confidence interval, 0.74–1.43; P = .87).

Determinants of SSTI complicated

- Patient
 - Immunosuppression (IV drug user, steroids, DM)
 - Acute deterioration (Sepsis, shock)
- Wound
 - Large size ($> 75\text{cm}^2$), deep invasion, rapid progression, virulent bacteria, resistant bacteria
- Therapy
 - In-hospital treatment, surgical intervention, IV antibiotic therapy, failure of initial Abtx

Determinants of prognosis of cSSTs

Comorbidity

Obesity
diabetes mellitus
Peripheral vasculopathy

Local lesion

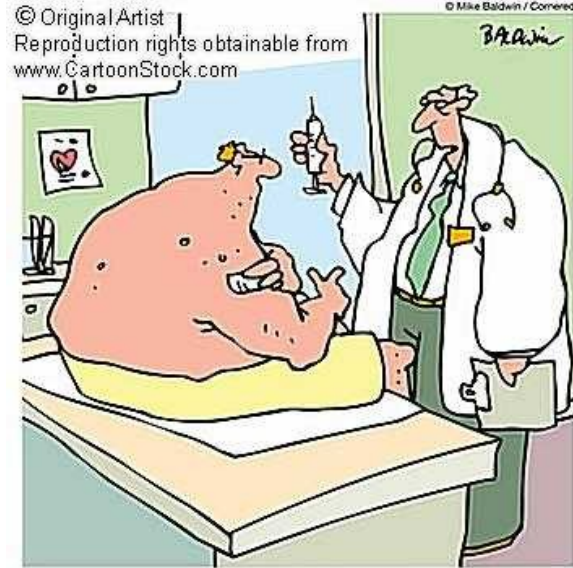
Edema
Deepness
Necrosis

Systemic signs

Fever
SIRS
Shock

Comorbidità Casistica 449 paz.

- ✓ 36 % patologia cardiaca e vascolare periferica
- ✓ 15% diabete
- ✓ 8% obesità grave
- ✓ 7,3% degli episodi diagnosi di infezione in altro sito
- ✓ 2,2% degli episodi si è complicato con gangrena.



"It wasn't really insulin. You don't have diabetes yet. It was just a warning shot."

ABSSSI treatment

- **Outpatient setting**
- **Inpatient setting**
- **Emergency department**

ABSSSI treatment

Outpatient setting

- **Advantages**

- Reduced hospital stays and costs
- Satisfactory for patients

- **Disadvantages**

- Adherence issues
 - Elderly
 - Cognitive impairment
 - IV Drug user

ABSSSI treatment

Inpatient setting

- **Advantages**

- Close monitoring adherence, clinical outcome and laboratory follow-up

- **Disadvantages**

- Hospital costs
- Adverse effects correlated with hospitalization

Emergency department

- More than 2 million patients are seen for SSTIs in US emergency departments every year
- Community-acquired methicillin-resistant *Staphylococcus aureus* is the primary cause in more than 60% of cases
- up to 50% of patients with SSTIs suffer from recurrences

ABSSSI treatment Emergency department

- **Advantages**

- Reduced hospital stays and associated costs
- Treatment adherence ensured

- **Disadvantages**

- Proper selection of patients
- Organization issues

- Mower et al. (Ann Emerg Med. 2019) reported that among 2,923 patients seen in three EDs for SSTI, only 84 (2.9%) required intensive care unit (ICU) admission or operating room intervention or died.
- Talan et al. (West J Emerg Med. 2015) found that among patients with SSTIs presenting to a U.S. network of 11 U.S. EDs, administration of parenteral antibiotics was the only reason for hospital admission in approximately 40% of patients, suggesting that outpatient care would be feasible in many patients if parenteral antibiotic treatment could be provided.

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ORIGINAL CONTRIBUTION

CME



Pathway with single-dose long-acting intravenous antibiotic reduces emergency department hospitalizations of patients with skin infections

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Submit an article

Journal homepage

284

Views

27

CrossRef
citations to date

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Altmetric

Clinical Focus: Infectious Diseases

Hospital admission patterns in adult patients with skin and soft tissue infections: Identification of potentially avoidable hospital admissions through a retrospective database analysis

Thomas P. Lodise , Weihong Fan & Katherine A. Sulham

Pages 137-143 | Received 18 Jun 2015, Accepted 22 Jul 2015, Published online: 30 Jul 2015

 Download citation

 <https://doi.org/10.1080/21548331.2015.1076325>



The mortality rate is low among ABSSSI patients with no comorbidities, and effective outpatient treatment should be encouraged in order to reduce unnecessary costs and the healthcare burden on hospitals

Caso Clinico

- ✓ M.B.M. donna 34 anni giunge al DEA trasferita da altro nosocomio per comparsa da alcune ore di:
 - Iperpiressia (TC 40 °C)
 - Spiccata dolorabilità arto inferiore dx
 - Alvo diarroico
- ✓ APR: non eventi patologici di rilievo. Non allergie a farmaci
- ✓ Significativa familiarità per diabete mellito



Condizioni generali gravissime

- Iperpiressia (TC 40°C)
- Vigile, sofferente, anurica
 - Diarrea profusa
- Ipotensione (85/40 mmHg)
 - Tachipnea (FR 40 °C)
 - Tachicardia (FC 120 bpm)
- SatO2 93% in aria ambiente
 - IRA (anuria)

The laboratory risk indicator for necrotizing fasciitis score (LRINEC score)

<u>Variable,Units</u>	<u>Score</u>	<u>Variable,Units</u>	<u>Score</u>
C-reactive protein, mg/L		Sodium, mmol/L	
<150	0	≥135	0
≥150	4	<135	2
Total white cell count, per mm ³		Creatinine, μmol/L	
<15	0	≤141	0
15–25	1	>141	2
>25	2		
Hemoglobin, g/dL		Glucose, mmol/L	
>13.5	0	≤10	0
11–13.5	1	>10	1
<11	2		

Risk of NSTI

LRINEC score	Risk category	Probability of NSTI
≤ 5	Low	$< 50\%$
6–7	Intermediate	50%–75%
≥ 8	High	$> 75\%$

Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score

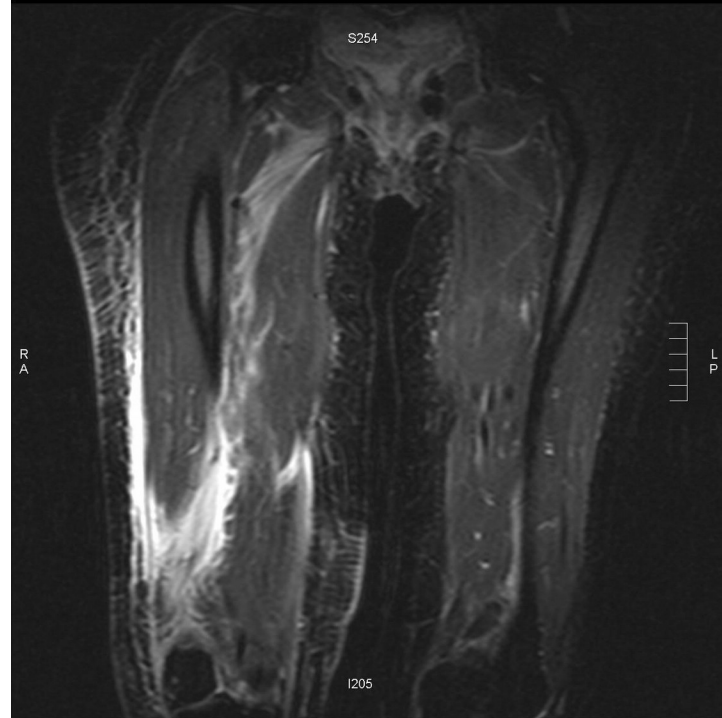
Variable, Units	β	Score
C-Reactive Protein, mg/L		
<150	0	0
≥ 150	3.5	4
Total white cell count, per mm ³		
<15	0	0
15–25	0.5	1
>25	2.1	2
Hemoglobin, g/dL		
>13.5	0	0
11–13.5	0.6	1
<11	1.8	2
Sodium, mmol/L		
≥ 135	0	0
<135	1.8	2
Creatinine, $\mu\text{mol/L}$		
≤ 141	0	0
>141	1.8	2
Glucose, mmol/L		
≤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

Final model constructed using factors found to be independently predictive of necrotizing fasciitis on multivariate analysis. β values are the regression coefficients of our model after adjusting for a shrinkage factor of .89. The maximum score is 13; a score of ≥ 6 should raise the suspicion of necrotizing fasciitis and a score of ≥ 8 is strongly predictive of this disease. To convert the values of glucose to mg/dL, multiply by 18.015. To convert the values of creatinine to mg/dL, multiply by 0.01131.

SCORE della pz: 8

ACCES#752341
359383
30-May-73
035Y
F

SE:3
IM:8
11:56:12



COSCIA DESTRA-GAMBA DESTRA
t2_tirm_cor
RM DELLA COSCIA DESTRA

ACCES#752341
359383
30-May-73
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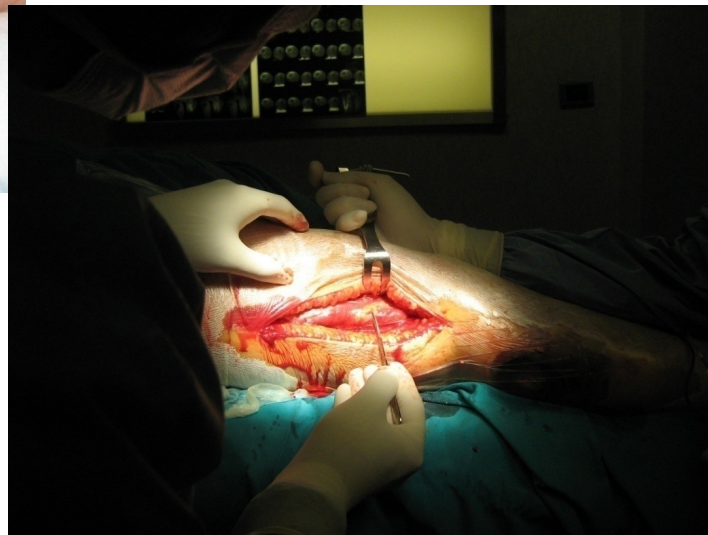
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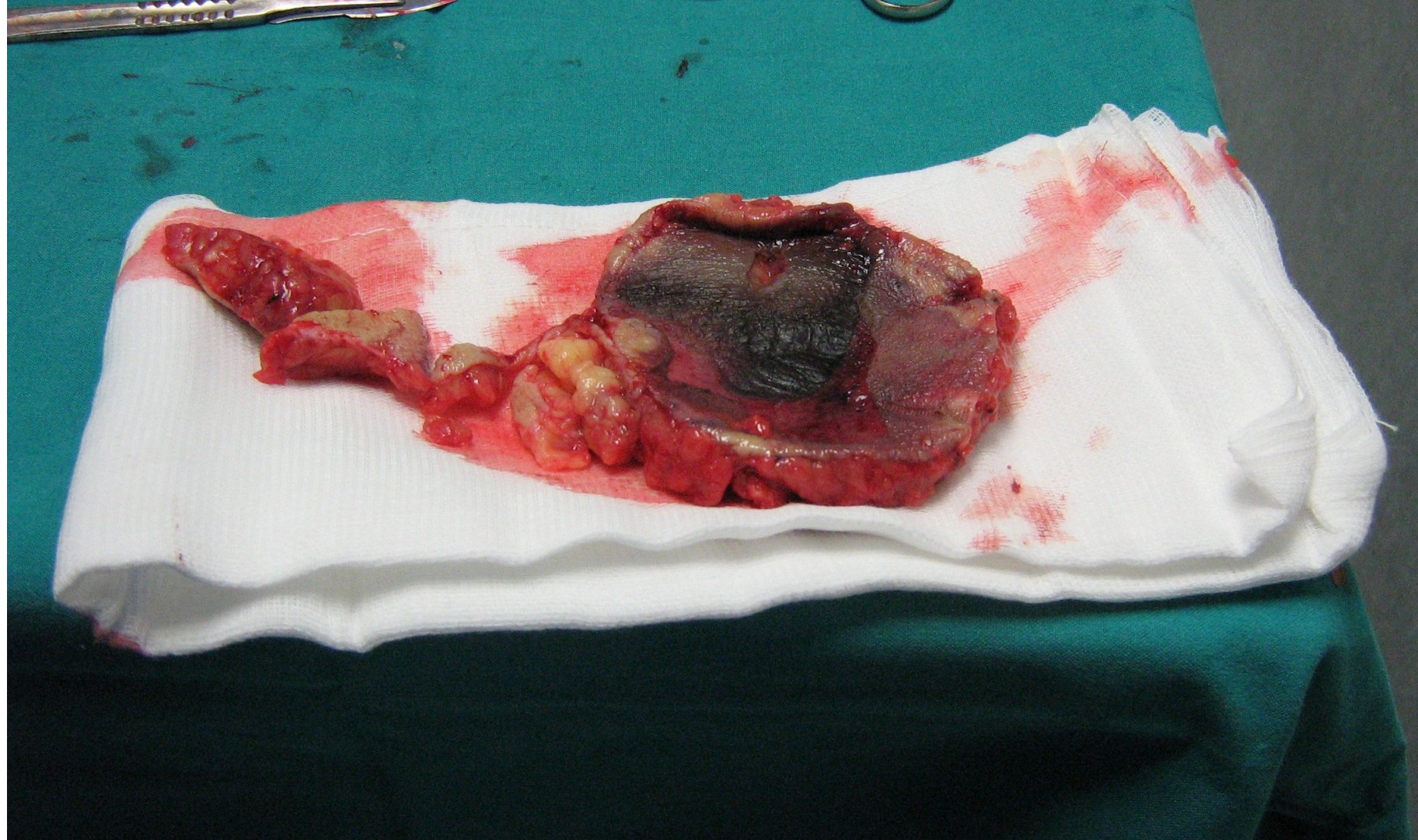


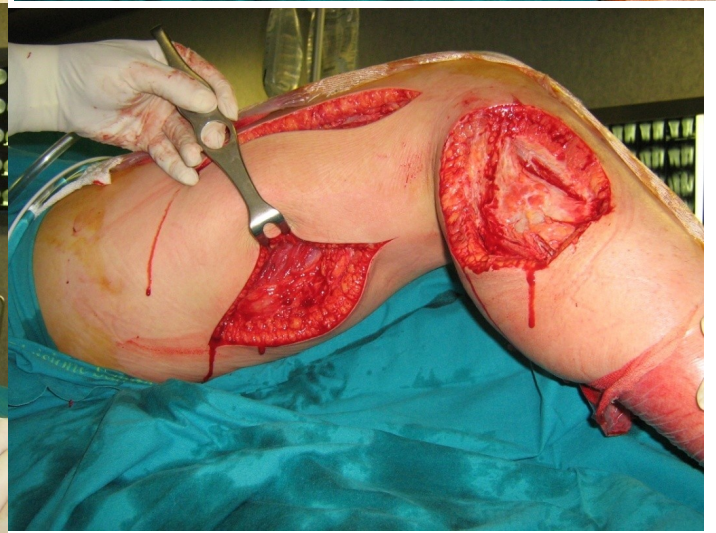
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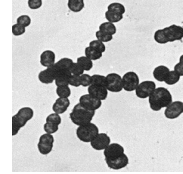
fasciotomia allargata







Esami microbiologici



- Tampone Intraoperatorio
 - Esame colturale
- Ricerca DNA batterico



**STREPTOCOCCO β emolitico
di gruppo A**

Caso clinico



- Uomo di 50 anni, TD attivo, HCV positivo
- Riferisce circa una settimana fa un'iniezione fuori vena a carico del braccio sx con successiva tumefazione e fuoriuscita di materiale purulento.
- Giunge in PS per il peggioramento del quadro clinico nonostante terapia antibiotica con ceftriaxone
- Esami ematici con leucocitosi neutrofila
- PCR 7, 50 mg/dl.

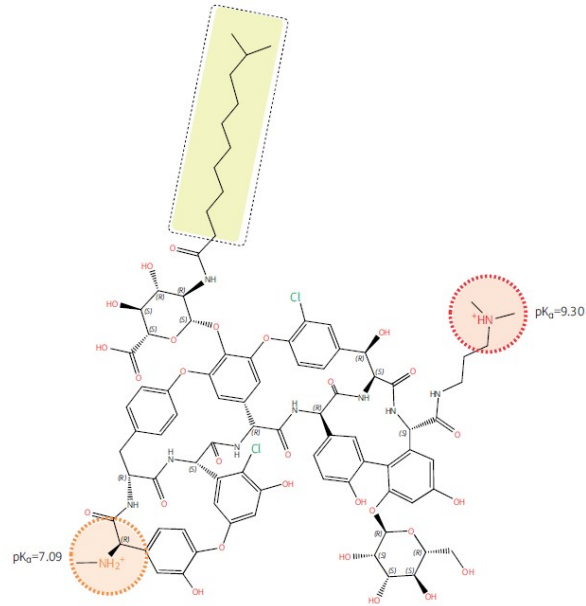


- Al fine di evitare il ricovero si decide di somministrare dalbavancina 1500mg/die presso il DEA.
- Successivo controllo ambulatoriale dopo 72 ore con netto miglioramento del quadro clinico.

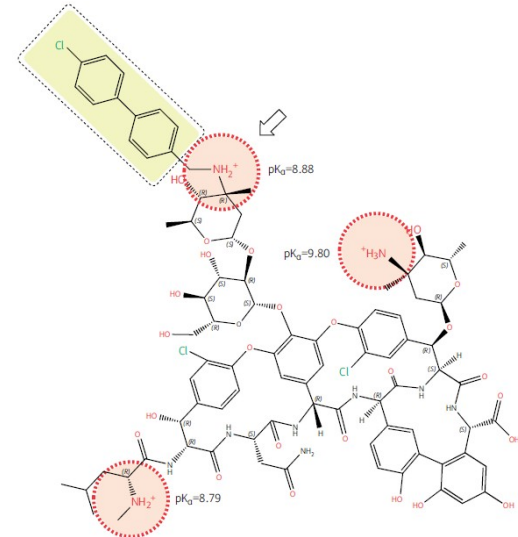


The role of long-acting lipoglycopeptide antibiotics

Dalbavancin

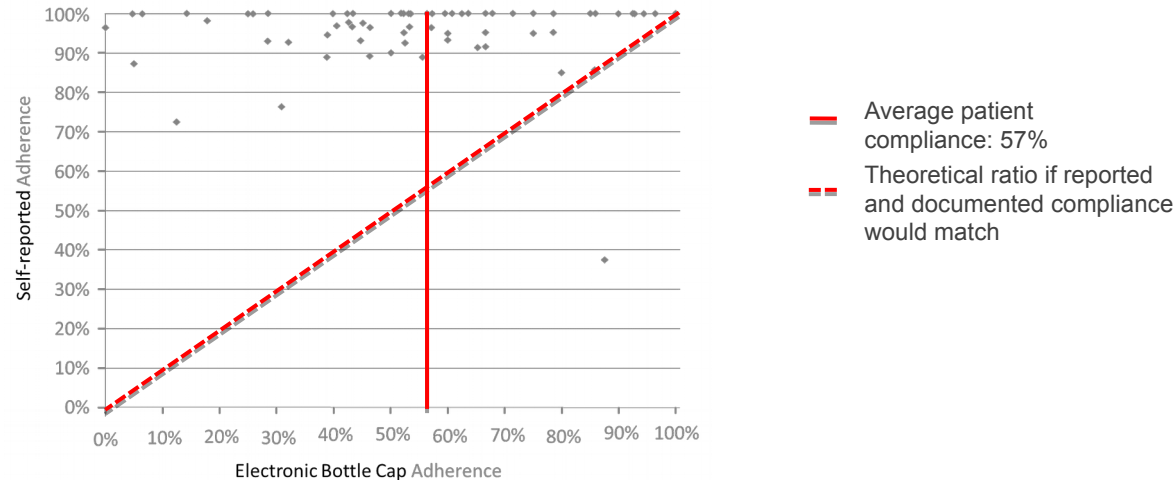


Oritavancin



Patient Compliance is variable with oral medication in ABSSSI*

Reported patient compliance does not match documented therapy adherence (96% versus 57%; $P < 0.0001$)



Low patient adherence was an independent predictor of poor clinical response at 30 days ($p < 0.05$)

*US study enrolling 188 adult patients hospitalized with uncomplicated skin and soft tissue infections caused by *Staphylococcus aureus* who were being discharged with oral antibiotics to complete therapy

Advantages of Long acting therapy

- **Intravenous treatment is needed but:**
 - a) vascular access is limited (IDVU, recurrent phlebitis)
 - b) possible misuse of an indwelling venous access
- **The patient can be treated at home but:**
 - a) we expect a low adherence to oral available drugs (old people, IVDU)