Infections cutanées graves

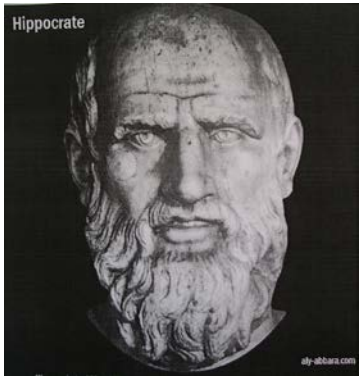
Bactériologie et Traitement Antibiotique

B. Guery
CHRU Lille

Liens d’intérêts

- ✓ Aucun lien d’intérêt sur la thématique présentée

Définition



- ✓ The erysipelas would quickly spread widely in all directions. Flesh, sinews and bones fell away in large quantities. . . .
- ✓ Fever was sometimes present and sometimes absent. . . . There were many deaths.
- ✓ The course of the disease was the same to whatever part of the body it spread.

Hippocrate….

Infections cutanées bactériennes

- ✓ Très fréquentes dans la pratique quotidienne
- ✓ Formes cliniques nombreuses
  - Furoncle, anthrax
  - Folliculite
  - Panaris/phlegmon
  - Impétigo
  - Dermatose érosive/prurigineuse surinfectée
  - Dermo-hypodermite, érysipèle
  - Dermo-hypodermite nécrosante, Fasciite nécrosante

Impetigo

Folliculite

Ecthyma

Erysipèle

Cellulite

Fasciite nécrosante

Fasciite

Myonécrose

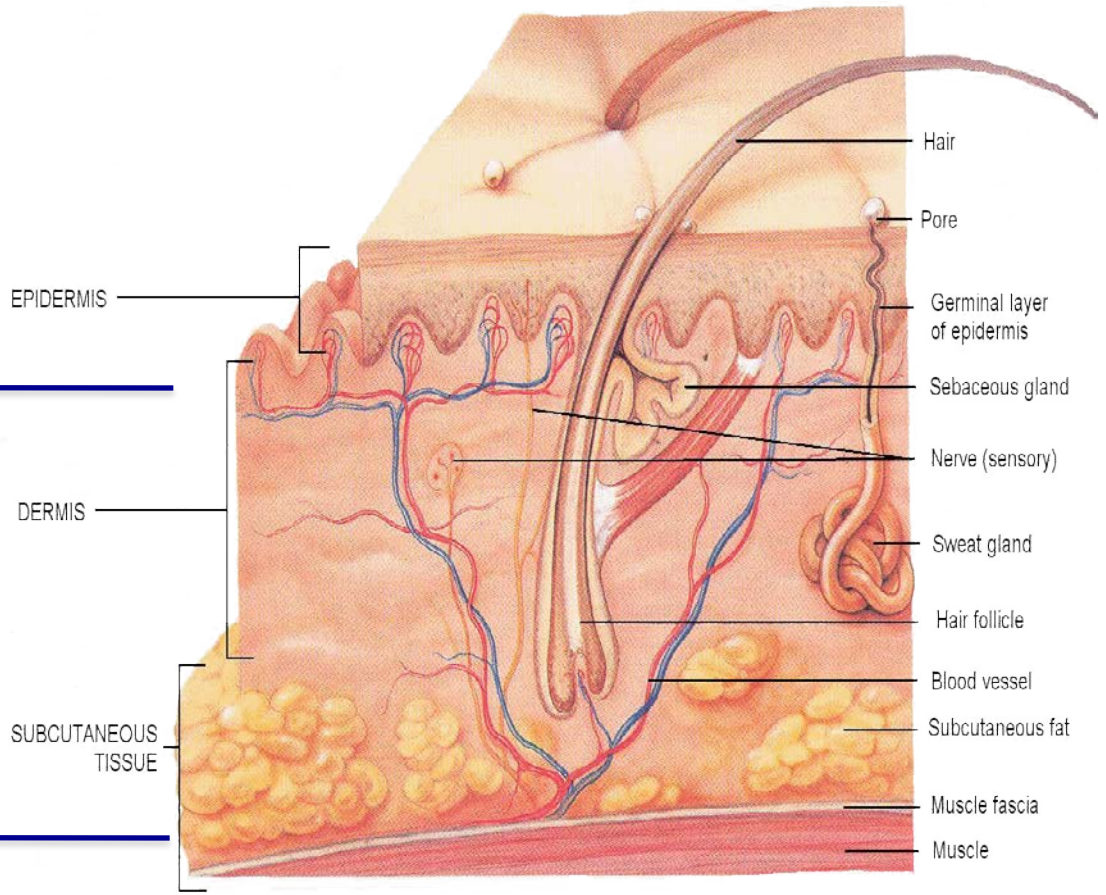


Table 1 Risk factors for erysipelas and necrotizing fasciitis [1,3–5,6•,7]

Erysipelas	Necrotizing fasciitis
Overweight	Diabetes
Edema, lymphedema	Immunosuppression
Prior leg surgery, especially saphenectomy	Alcoholism
History of erysipelas	Chickenpox
Leg ulcer	Arteritis
Toe web intertrigo	Traumatism

Gallibot-Carré M, Rougeau JM Curr Opin Infect Dis 2007

Necrotising fasciitis

Helen Yasmin Sultan *consultant* [1], Adrian A Boyle *consultant*[2], Nicholas Sheppard *specialist registrar*[3]

Study and country	Severe pain	Fever	Tachycardia (with or without hypotension)	Skin erythema	Skin oedema	Skin tenderness	Blistering or bullae	Ecchymosis or skin discoloration	Crepitus
Wong et al [12] (n=89), Singapore	98	53	74 (18)	100	92	98	45	No data	14
Childers et al[11] (n=162), United States	100	70	No data	95	82	No data	16	49	25
Frazee et al[16] (n=122), United States	No data	44	59 (21)	80	66	54	12	No data	7
Angoules et al[17] (n=451), United Kingdom	63	15	(12)	73	49	No data	15	No data	7

BMJ 2012;345:e4274 doi: 10.1136/bmj.e4274 (Published 20 July 2012)

Necrotizing fasciitis

Rukshini Puvanendran MMed FCFP MBBS Jason Chan Meng Huey MBBS Shanker Pasupathy FRCS MBBS

Box 1. Risk factors for necrotizing fasciitis

- Diabetes
- Chronic disease
- Immunosuppressive drugs (eg, prednisolone)
- Malnutrition
- Age >60 years
- Intravenous drug misuse
- Peripheral vascular disease
- Renal failure
- Underlying malignancy
- Obesity

Table 4. Laboratory risk indicator for NF: *A score of ≤5 points indicates a low risk (<50% probability) of NF; 6-7 points indicate an intermediate risk (50%-75% probability) of NF; 8 points or more indicate a high risk (>75% probability) of NF.*

INVESTIGATION	SCORE
Serum C-reactive protein ≥150 mg/L	4 points
White blood cell count	
• 15000/μL-25000/μL	1 point
• >25000/μL	2 points
Hemoglobin	
• 11.0-13.5 g/dL	1 point
• <11 g/dL	2 points
Serum sodium <135 mEq/L	2 points
Serum creatinine >1.6 mg/dL (141 mmol/L)	2 points
Serum glucose >180 mg/dL (10 mmol/L)	1 point

NF—necrotizing fasciitis.

Table 3. Clinical features suggestive of necrotizing soft tissue infections

SKIN	PAIN	GENERAL
Erythema with ill-defined margins	Pain that extends past margin of apparent infection	Fever with toxic appearance
Tense edema with grayish or brown discharge	Severe pain that appears disproportionate to physical findings	Altered mental state
Lack of lymphangitis or lymphadenopathy	Decreased pain or anesthesia at apparent site of infection	Tachycardia
Vesicles or bullae, hemorrhagic bullae		Tachypnea due to acidosis
Necrosis		Presentation with DKA or HHNK
Crepitus		

DKA—diabetic ketoacidosis, HHNK—hyperosmolar hyperglycemic non-ketotic acidosis.

Can Fam Physician 2009;55:981-7

Necrotizing Fasciitis

Taro Shimizu[1] and Yasuharu Tokuda[2]

- ✓ NF is caused by infection, and the predisposing factors include
  - drugs, hypersensitivity, vascular problems, burn, insect bite, needle stick injury, and trauma
- ✓ NF can lead to severe sepsis, specifically in patients with
  - immunosuppression, diabetes, malignancy, drug abuse, and chronic kidney disease
- ✓ Several reports also indicate that intravenous drug use is a leading risk factor for NF

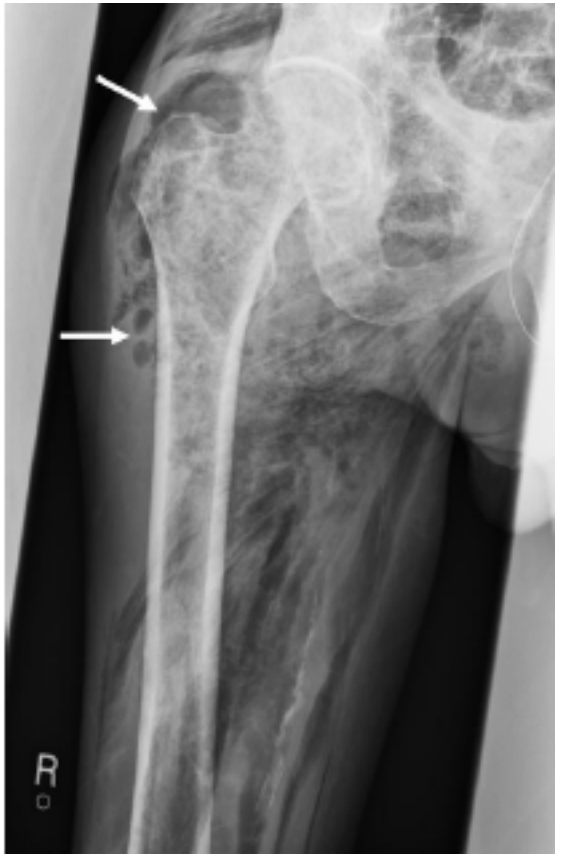
Inter Med 49: 1051-1057, 2010


I WANT YOU!

Necrotizing soft-tissue infections

Jeffrey S. Ustin, MS, MD; Mark A. Malangoni, MD, FACS

- ✓ The Food and Drug Administration classification of skin and soft tissues infections
  - An uncomplicated infection responds to a simple course of antibiotics or incision and drainage.
  - Complicated infections involve deeper tissues and generally require surgical intervention



Crit Care Med 2011 Vol. 39, No. 9

Necrotizing Fasciitis

Taro Shimizu[1] and Yasuharu Tokuda[2]

Table 1. Causative Bacteria of Type 1 and Type 2 Necrotizing Fasciitis

type 1
polymicrobial infections including anaerobes.
type 2
Streptococcus pyogenes (Group A Streptococcus)
Staphylococcus aureus, including methicillin-sensitive and resistant
Other microbiological etiologies
Vibrio vulnificus
Aeromonas hydrophila
Enterobacteriaceae (*Escherichia coli*, *Pseudomonas* spp., and *Klebsiella* spp)

Inter Med 49: 1051-1057, 2010

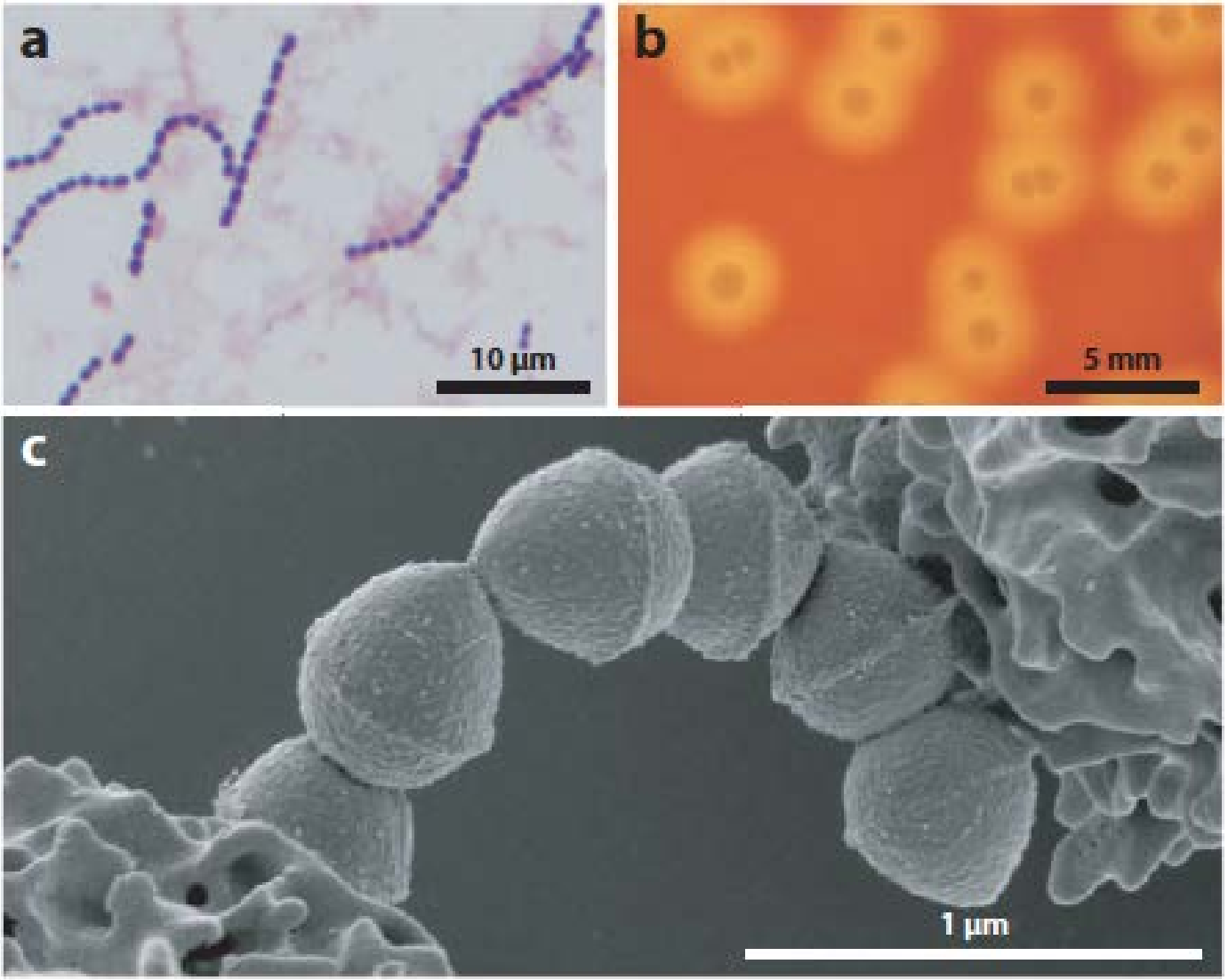
Type 1

- ✓ Polymicrobien
  - 80%
  - Aérobies: Strepto-Staph-BGN….
  - Anaérobies: *Bacteroides* dans 50% des cas, *Peptostreptococci* dans 1/3 des cas
- ✓ Terrain:
  - diabète, obsésité, polyvasculaire, insuffisance rénale, exogénose
- ✓ Dénomination spécifique
  - Fournier: génito-urin, colorectal,…
  - Ludwig: moins de pathogènes (*Fusobacterium*, *Peptostrepto*). 40% extension médiastinale avec surmortalité

Type 2

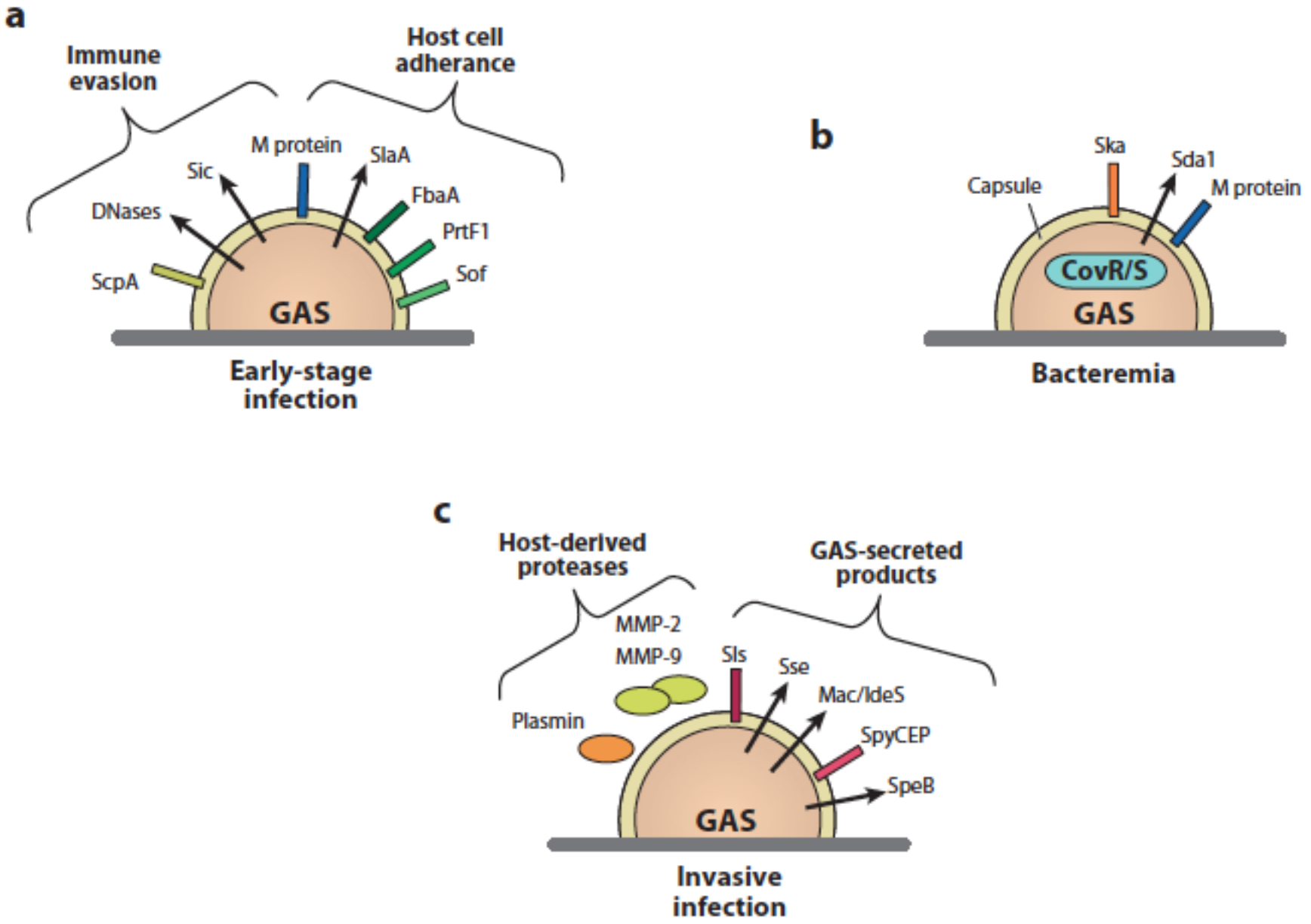
- ✓ Monomicrobien
  - 10-15%
  - SGA+++
  - SARM en augmentation +/- Strepto
- ✓ Porte d'entrée « minime »
  - Diffusion hématogène
- ✓ Facteurs favorisants: AINS
- ✓ Facteurs de virulence
  - SGA: Proteine M,F , inhibiteur du complément, proteinases, …
  - Staph: PVL, hémolysine….

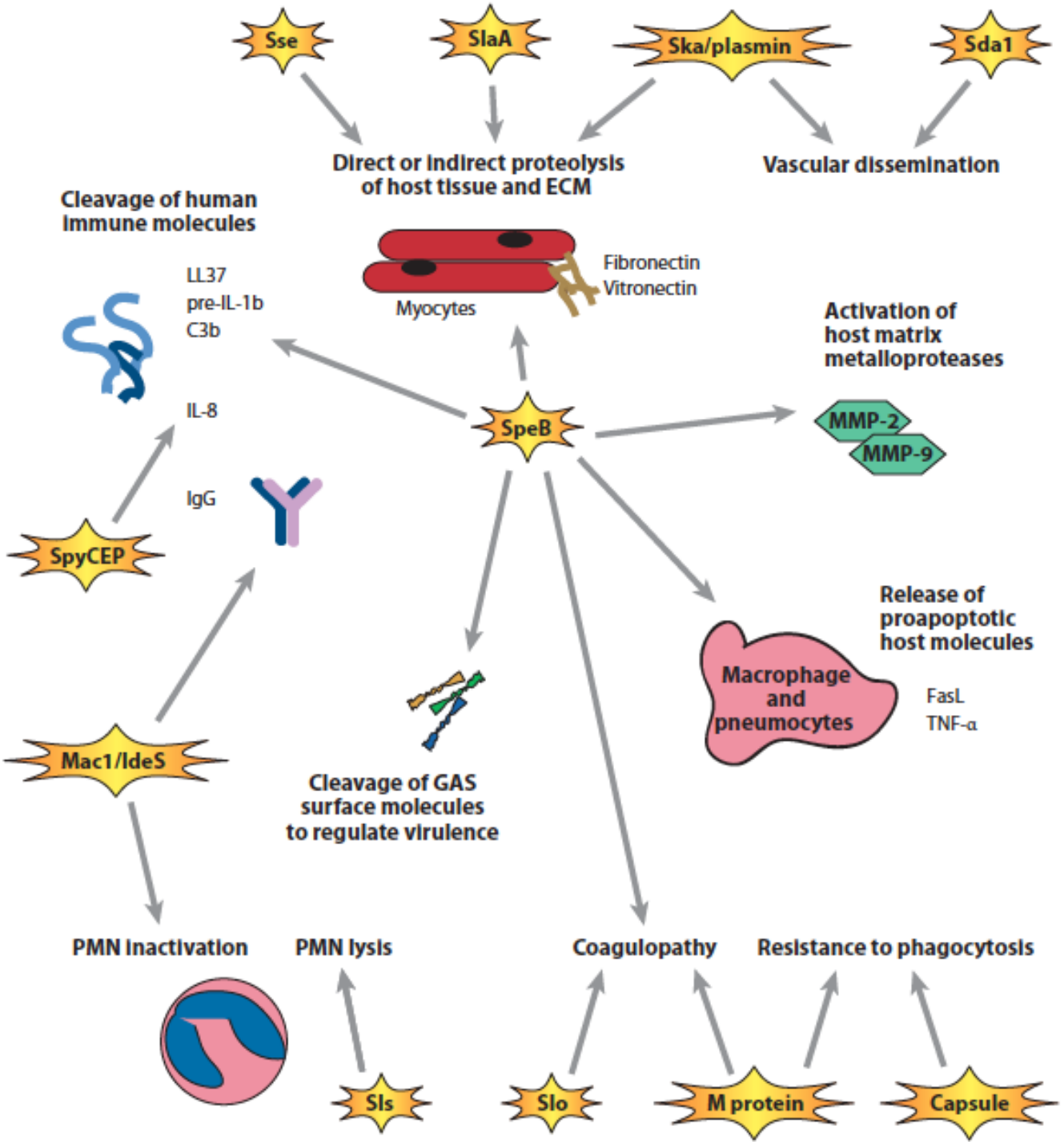
GAS are gram-positive cocci that grow in pairs and chains.



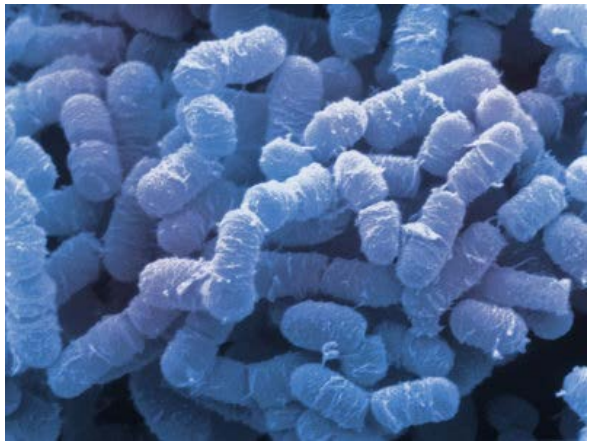
Scanning electron micrograph of GAS organisms interacting with human neutrophils

Annu. Rev. Pathol. Mech. Dis. 2010. 5:1–31


a
Immune evasion
Host cell adherance
M protein
SlaA
Sic
FbaA
DNases
PrtF1
ScpA
Sof
GAS
Early-stage infection
b
Ska
Sda1
Capsule
M protein
CovR/S
GAS
Bacteremia
c
Host-derived proteases
GAS-secreted products
MMP-2
MMP-9
Sls
Sse
Mac/IdeS
Plasmin
SpyCEP
SpeB
GAS
Invasive infection


Sse
SlaA
Ska/plasmin
Sda1
Direct or indirect proteolysis of host tissue and ECM
Vascular dissemination
Cleavage of human immune molecules
LL37
pre-IL-1b
C3b
IL-8
IgG
SpyCEP
Myocytes
Fibronectin
Vitronectin
SpeB
Activation of host matrix metalloproteases
MMP-2
MMP-9
Release of proapoptotic host molecules
Macrophage and pneumocytes
FasL
TNF-α
Mac1/IdeS
Cleavage of GAS surface molecules to regulate virulence
PMN inactivation
PMN lysis
Coagulopathy
Resistance to phagocytosis
Sls
Slo
M protein
Capsule

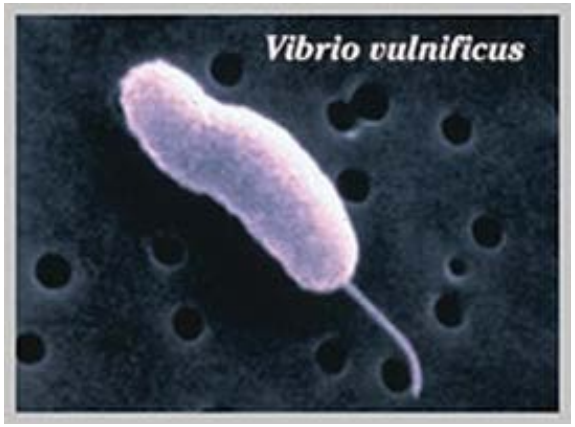
Type 3

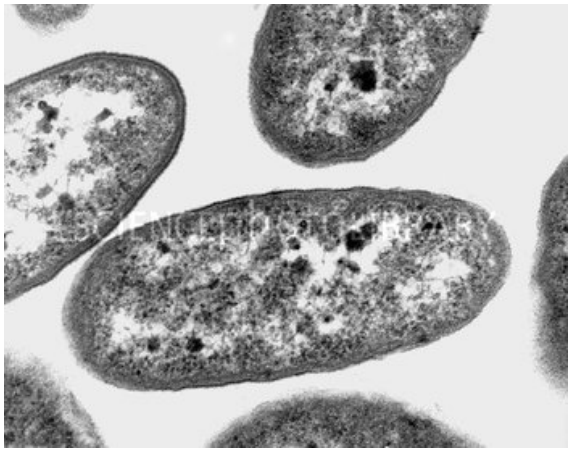


- ✓ Myonécrose à *Clostridium*
  - <5%
  - *C. perfringens, C. septicum*
- ✓ Contexte:
  - Trauma:
    - Plaies pénétrantes, écrasements, dévascularisation
  - Chirurgie digestive, héroine « black tar », post obstétrical
  - Hémato-oncologie:
    - Myonécrose spontanée
    - *C. septicum*
- ✓ Clinique
  - Progression très rapide 2cm/h
  - Paralysie réponse de l'hôte
  - Toxines (α-toxine,…)

Type 4

- ✓ Infections « water-borne »
  - *Vibrio vulnificus*:
    - fruits de mer, activité récréatives
    - Terrain sous jacent: cirrhose, hépatite chronique, hemochromatose
    - Virulence: toxine induisant la production de ROS
  - *Aeromonas hydrophilia*
    - Post Tsunami
- ✓ Plus rare fongique
  - Rhizopus, Mucor, Rhizomucor
  - Diabète, immunosuppression





Epidémiologie

- ✓ 10.000 cas d'infection invasive à SGA/an aux USA
  - Mortalité peut atteindre 50%
- ✓ 0.24-0.4/100 000 hbts au Royaume Uni
- ✓ Fasciite nécrosante
  - SGA prédominant
  - *S. aureus* moins fréquent (problème des PVL)
  - Associations: SGA et *S. aureus* avec
    - Streptocoques alpha hémolytiques
    - *S. epidermidis*
  - Gram négatifs
    - *E. coli*
    - *Bacteroides fragilis*
    - *Clostridium spp*

PRISE EN CHARGE ANTIBIOTIQUE

Severity assessment of skin and soft tissue infections: cohort study of management and outcomes for hospitalized patients

Charis Marwick[1]*, Janice Broomhall[1], Colin McCowan[1], Gabby Phillips[2], Sebastian Gonzalez-McQuire[3]†, Kasem Akhras[4]‡, Sanjay Merchant[4], Dilip Nathwani[5] and Peter Davey[1]

CREST

- ✓Class I:
  - no recorded significant co-morbidity, no sepsis and SEWS<4.
- ✓Class II:
  - documentation of one or more significant co-morbidities (peripheral vascular disease, chronic venous insufficiency or morbid obesity) but no sepsis and SEWS<4.
- ✓Class III:
  - sepsis but SEWS<4.
- ✓Class IV:
  - sepsis with SEWS≥4.

J Antimicrob Chemother 2011; **66**: 387–397

Table 1. SEWS parameters and scoring systems (adapted from Jorup-Ronstrom *et al.*[20])

	Score						
Parameter	3	2	1	0	1	2	3
Respiratory rate (breaths/min)	≤8			9–20	21–30	31–35	≥36
Oxygen saturation (%)	<85	85–89	90–92	≥93			
Temperature (°C)	<34	34–34.9	35–35.9	36–37.9	38–38.4	≥38.5	
Systolic blood pressure (mmHg)	≤69	70–79	80–99	100–199		≥200	
Heart rate (beats/min)	≤29	30–39	40–49	50–99	100–109	110–129	≥130
AVPU response (stimulus required to induce response)	unresponsive	pain	verbal	alert			

AVPU, alert, verbal, pain, unresponsive (category of stimulus required to generate patient response).
Case example, patient with SSTI and sepsis: respiratory rate=26; oxygen saturation=94%; temperature=38.4; blood pressure=84/62; heart rate=107; AVPU response=alert; SEWS=4; and urgent medical review is mandated.

Table 5. Multivariable analysis for death within 30 days of start of treatment for SSTI (all odds ratios were calculated with data from the 189 patients with complete information about antibiotic treatment)

	Unadjusted odds ratio	95% CI	*P* value	Adjusted[a] odds ratio	95% CI	*P* value
Severity class						
I	1.0			1.0		
II	4.33	0.44–42.61	0.209	6.51	0.51–83.12	0.149
III	18.83	2.18–162.91	0.008	32.39	2.80–374.49	0.005
IV	45.50	4.53–457.20	0.001	167.88	5.30–5319.54	0.004
Initial treatment						
appropriate	1.0			1.0		
over-treatment	0.60	0.12–3.11	0.545	1.02	0.14–7.72	0.981
under-treatment	2.51	0.63–10.02	0.194	0.57	0.09–3.51	0.545

Table 4. Appropriateness of initial antibiotic therapy by severity class for 189 hospital inpatients with SSTI

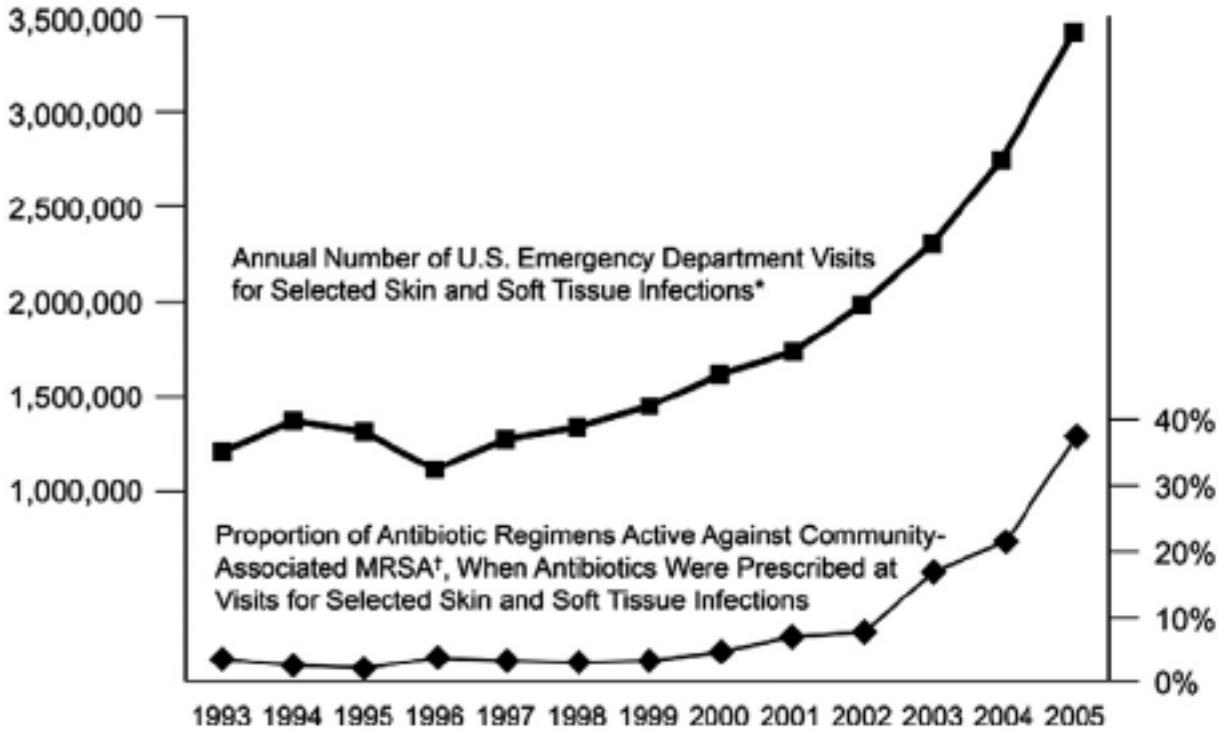
Severity class	Total no. patients	Treatment classification by comparison with UK guidance, *N* (%)[5]		
		appropriate treatment	over-treatment	under-treatment
I	88	19 (22)	57 (65)	12 (14)
II	56	20 (36)	14 (25)	22 (39)
III	33	10 (30)	10 (30)	13 (39)
IV	12	1 (8)	0	11 (92)
All	189	50 (26)	81 (43)	58 (31)

In this cohort of 205 patients, no less than 35 different antibiotic regimens, some of which were **not appropriate** for the respective condition

J Antimicrob Chemother 2011; **66**: 387–397

No. of patients	Antibiotic 1	Route 1	Antibiotic 2	Route 2	Antibiotic 3	Route 3	Consensus appropriate	Initial disagreement
Severity class I								
5	clindamycin	po					appropriate	0
2	flucloxacillin	po	penicillin V	po			appropriate	0
12	flucloxacillin	po					appropriate	0
9	benzylpenicillin	iv	flucloxacillin	iv			over	0
1	ceftazidime	iv	metroi					
2	ceftriaxone	iv						
2	cefuroxime	iv	metroi					
2	cefuroxime	iv						
1	ciprofloxacin	po	clindai					
2	ciprofloxacin	po	clindai					
5	clindamycin	iv						
1	co-amoxiclav	iv	fluclox					
1	co-amoxiclav	iv	metroi					
5	co-amoxiclav	po						
9	co-amoxiclav	iv						
16	flucloxacillin	iv						
1	piperacillin/tazobactam	iv						
3	cefalexin	po						
1	ciprofloxacin	iv						
7	ciprofloxacin	po						
1	metronidazole	po						
Severity class II								
2	benzylpenicillin	iv	fluclox					
1	ceftriaxone	iv						
2	clindamycin	iv						
2	clindamycin	po						
12	flucloxacillin	iv						
1	vancomycin	iv						
1	ceftriaxone	iv	fluclox					
2	cefuroxime	iv						
1	ciprofloxacin	po	clindai					
1	ciprofloxacin	iv	clindai					

patients	Antibiotic 1	Route 1	Antibiotic 2	Route 2	Antibiotic 3	Route 3	appropriate	disagreemen
3	ciprofloxacin	po	clindamycin	po			over	1
2	ciprofloxacin	po	flucloxacillin	iv			over	1
1	clindamycin	iv	flucloxacillin	iv			over	0
2	co-amoxiclav	iv					over	1
1	gentamicin	iv	piperacillin/tazobactam	iv			over	0
1	amoxicillin	po					under	0
1	ciprofloxacin	po	rifampicin	po			under	0
2	ciprofloxacin	po					under	0
1	clarithromycin	po					under	0
1	co-amoxiclav	po	flucloxacillin	po			under	0
1	co-amoxiclav	po	metronidazole	po			under	0
1	co-amoxiclav	po					under	0
1	erythromycin	iv					under	1
1	flucloxacillin	po	penicillin V	po			under	0
7	flucloxacillin	po					under	0
1	fusidic acid	po					under	0
1	gentamicin	iv					under	0
1	norfloxacin	po					under	0
2	rifampicin	po	trimethoprim	po			under	0
Severity class III								
1	benzylpenicillin	iv	flucloxacillin	iv			appropriate	0
1	ceftriaxone	iv					appropriate	0
1	clarithromycin	iv					appropriate	1
1	clindamycin	iv					appropriate	0
5	flucloxacillin	iv					appropriate	0
1	vancomycin	iv					appropriate	0
1	cefuroxime	iv	metronidazole	iv			over	0
1	ciprofloxacin	po	flucloxacillin	iv			over	1
1	co-amoxiclav	iv	flucloxacillin	iv			over	1
6	co-amoxiclav	iv					over	1
1	piperacillin/tazobactam	iv					over	0
1	benzylpenicillin	iv	metronidazole	iv			under	0
1	benzylpenicillin	iv					under	0
1	ciprofloxacin	po					under	0
1	clarithromycin	po					under	0
4	clindamycin	po					under	0
1	co-amoxiclav	po	metronidazole	po			under	0
2	co-amoxiclav	po					under	0
1	levofloxacin	iv					under	0
1	metronidazole	iv					under	0


3,500,000
3,000,000
2,500,000
2,000,000
1,500,000
1,000,000
Annual Number of U.S. Emergency Department Visits for Selected Skin and Soft Tissue Infections*
Proportion of Antibiotic Regimens Active Against Community-Associated MRSA†, When Antibiotics Were Prescribed at Visits for Selected Skin and Soft Tissue Infections
40%
30%
20%
10%
0%
1993 1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005

Practice Guidelines for the Diagnosis and Management of Skin and Soft-Tissue Infections

Dennis L. Stevens,[1,3] Alan L. Bisno,[5] Henry F. Chambers,[6,7] E. Dale Everett,[13] Patchen Dellinger,[2] Ellie J. C. Goldstein,[8,9] Sherwood L. Gorbach,[14] Jan V. Hirschmann,[3,4] Edward L. Kaplan,[15,16] Jose G. Montoya,[10,11,12] and James C. Wade[17]

Clinical Infectious Diseases 2005; 41:1373–406

Table 5. Treatment of necrotizing infections of the skin, fascia, and muscle.

First-line antimicrobial agent, by infection type	Adult dosage	Antimicrobial agent(s) for patients with severe penicillin hypersensitivity
Mixed infection		
Ampicillin-sulbactam	1.5–3.0 g every 6–8 h iv	Clindamycin or metronidazole[a] with an aminoglycoside or fluoroquinolone
or		
piperacillin-tazobactam	3.37 g every 6–8 h iv	
plus		
clindamycin	600–900 mg/kg every 8 h iv	
plus		
ciprofloxacin	400 mg every 12 h iv	
Imipenem/cilastatin	1 g every 6–8 h iv	…
Meropenem	1 g every 8 h iv	…
Ertapenem	1 g every day iv	…
Cefotaxime	2 g every 6 h iv	…
plus		
metronidazole	500 mg every 6 h iv	
or		
clindamycin	600–900 mg/kg every 8 h iv	
Streptococcus infection		
Penicillin	2–4 MU every 4–6 h iv (adults)	Vancomycin, linezolid, quinupristin/dalfopristin, or daptomycin
plus		
clindamycin	600–900 mg/kg every 8 h iv	
S. aureus infection		
Nafcillin	1–2 g every 4 h iv	Vancomycin, linezolid, quinupristin/dalfopristin, daptomycin
Oxacillin	1–2 g every 4 h iv	…
Cefazolin	1 g every 8 h iv	…
Vancomycin (for resistant strains)	30 mg/kg/day in 2 divided doses iv	…
Clindamycin	600–900 mg/kg every 8 h iv	Bacteriostatic; potential of cross-resistance and emergence of resistance in erythromycin-resistant strains; inducible resistance in methicillin-resistant *S. aureus*
Clostridium infection		
Clindamycin	600–900 mg/kg every 8 h iv	…
Penicillin	2–4 MU every 4–6 h iv	…

[a] If *Staphylococcus* infection is present or suspected, add an appropriate agent. iv, intravenously.

Necrotizing soft-tissue infections

Jeffrey S. Ustin, MS, MD; Mark A. Malangoni, MD, FACS

Drug Regimen by Type of Infection	Adult Dose (Intravenous)
Type I Infections (Mixed)	
Piperacillin-tazobactam	3.375 gm q6h
Plus	
Clindamycin	600–900 mg q6–8h
Plus	
Ciprofloxacin	400 mg q12h
Imipenem-cilastatin	500–1000 mg q6h
Meropenem	1 gm q8h
Type II Infections	
Clindamycin	600–900 mg q6–8h
Plus	
Penicillin	2–4 million units q4–6h
Or	
Linezolid (if allergic to penicillin)	600 mg q12h
Or	
Vancomycin (if allergic to penicillin)	30 mg/kg/day in 2 divided doses
Type III Infections	
Clindamycin	600–900 mg q6–8h
Plus	
Penicillin	2–4 million units q4–6h
Vibrio or *Aeromonas* Infections	
Doxycycline	1 gm q12h

Clinical Practice Guidelines by the Infectious Diseases Society of America for the Treatment of Methicillin-Resistant *Staphylococcus aureus* Infections in Adults and Children

Catherine Liu,[1] Arnold Bayer,[3,5] Sara E. Cosgrove,[6] Robert S. Daum,[7] Scott K. Fridkin,[8] Rachel J. Gorwitz,[9] Sheldon L. Kaplan,[10] Adolf W. Karchmer,[11] Donald P. Levine,[12] Barbara E. Murray,[14] Michael J. Rybak,[12,13] David A. Talan,[4,5] and Henry F. Chambers[1,2]

- ✓ Antibiotiques recommandés
  - Pathologie sévère et extensive
  - Comorbidités, immunosuppression, age, zone difficile à drainer (face, main, génital)
- ✓ Ambulatoire
  - CAMRSA: Clindamycine, TMP-SMX, cycline, linezolide
  - CAMRSA + Strepto:
    - β-lactamine + Clindamycine, TMP-SMX, tetracycline
    - Linezolide

Clinical Infectious Diseases 2011;52(3):e18–e55

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- ✓ Hospitalisé
  - Vancomycine IV
  - Linezolide PO ou IV
  - Daptomycine
  - Telavancine
  - Clindamycine

Clinical Infectious Diseases 2011;52(3):e18–e55

Review

Diagnosis and management of necrotising fasciitis: a multiparametric approach

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- ✓ Pas de guidelines « evidence-based »
- ✓ Pathogènes en phase stationnaire
  - Inactivité des molécules avec activité de paroi
- ✓ Clindamycine
  - Switch off la production de toxines
  - Gain en mortalité (OR 13)
- ✓ Associations recommandées
  - Peni Clinda
  - Imipénème Clinda
- ✓ Si suspicion de SARM
  - Linezolide ou dapto préféré à vanco

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Conclusion

- ✓ Problème de définition
- ✓ Hétérogénéité de prise en charge
- ✓ Traitement multidisciplinaire
- ✓ Nécessité de travaux prospectifs, d’intégration dans les définitions existantes
- ✓ Guidelines