Skin and soft tissue infections (SSTI): classification & management

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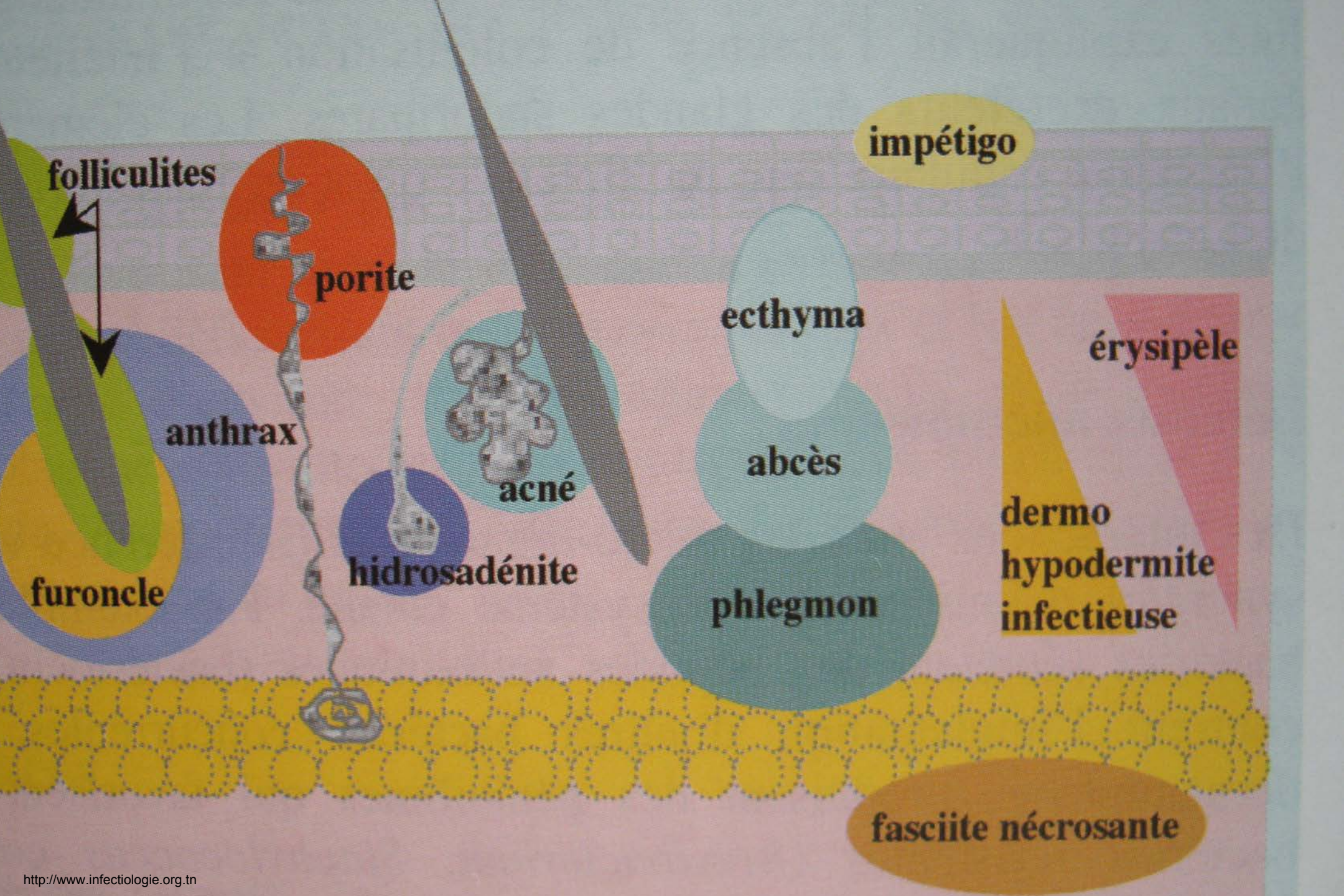
Potential links of Interest

- In the past 4 years, I (or my department) have received honoraria from some **pharmaceutical companies** for
  - lectures on SSTI (**Pfizer),** & STDs (**BMS)**
  - participation in advisory boards on HPV (**Sanofi)**, TBE (**Baxter)**, and KS (**Gallen**)
  - CME programs (**Janssen)**.

I am the Editor in Chief of the Journal of Travel Medicine (IF = 1.47)



SSTI in returning travellers I (n = 48)

- **Impetigo : 19 (39%)**

[12 (63%) related to arthropod bite or sting]

- *S aureus* (40%)
- *Streptococcus sp* (20%)
- *S.aureus* + st (20%)
- negative (20%)

- **Erysipela : 9 (18%)**
- **Ecthyma : 8 (16%)**
- **Abcess : 4 (8%)**
- **Furuncle : 4 (8%)**
- **Intertrigo : 2 (4%)**
- **Folliculitis : 1 (2%)**
- **Cellulitis : 1 (2%)**

Caumes et al - Clin Inf Dis 1995;20:542-548

SSTI in returning travellers II (N=60)

SSTI	N (%)	% culture +	MSSa	GAS	Both
Impetigo	21 (35%)	76%	31%	38%	31%
Abcess	14 (23%)	57%	100%	0	0
Ecthyma	11 (19%)	91%	10%	60%	30%
Cellulitis	11 (19%)	0	NA	0	0
Folliculitis	3 (5%)	33%	100%	0	0

Hochedez P et al. Am J Trop Med Hyg 2009; 80: 431-4

Superficial SSTI = skin infections = pyoderma

- Impetigo
  - Bullous (*Staphylococcus aureus*)
  - Non bullous (*Sa* >> GAS except in developing countries)
- Ecthyma (GAS >> *Sa*)
- Folliculitis (Sa)
  - superficial,
  - deep, furuncle,
  - carbuncle
- Paronychia

Deep SSTI = soft tissue infections

- Erysipelas
- Cellulitis
- Necrotizing cellulitis
- Gangrene
- Myonecrosis

GAS

- Lymphangitis
- Abcess (subcutaneous) (*S.aureus*)

Clinical presentation is correlated with the culprit microbial agent

Strept. pyogenes	Staph. aureus
Impetigo	Impetigo
Echtyma	Folliculitis (superficial), orgelet
Lymphangitis	Folliculitis (deep), sycosis
Erysipela	Furoncle, carbuncle
Cellulitis	Panaris, phlegmon, abcess
	Surinfection
	Cellulitis (if PVL positive Sa)

Antibiotic treatment / culprit agent

Staphylococcus sp	*Streptococcus sp*
Pénicilline M, Csp I, II	**Pénicilline** G**, A,** Csp
MLSK	MLSK
Fusidic acid	**TMP-SMX**
Rifamycines (RMP-RFB)	Rifamycines
Linezolide	Linezolide
Fosfomycine IV	Fosfomycine IV
Vancomycine IV	Vancomycine IV
Tigécycline IV	Tigécycline IV

Bullous **Impetigo (S.aureus)**


Bullous Impetigo plus
Infectious cellulitis
Impetigo plus
Ecthyma (S.aureus)
http://www.infectiologie.org.tn

Courtesy Pascal delGiudice (Fréjus, France)

Secondary SSTI : impetigo of the scalp

Treatment of pyoderma in Mali
Erythromycine versus Amoxicilline

-Randomized comparative open trial

-Criteria of inclusion : « severe pyoderma » (i.e., pyoderma severe enough to require antibiotherapy) in persons > 1 year

- Need to include : 128 malades (≠ 20%)

- Patients randomly selected (Ery or Amoxi) plus polyvidone iodine, during 8 days

- Criteria of judgement at day 8: clinical cure (photo external evaluation)

Faye O et al. Int J Dermatol 2007; 46:19-22

Treatment of pyoderma

-132 patients included, lost to follow up = 2 A, 1 E

-Mean age = 8 years old (SD=10 years)

-80% of the cases are secondary SSTI (impetiginization)

-« Intent to treat » and « per protocole »

-Clinical cure : amoxicillin = erythromycin = 89 ± 8 % (NS)

-Side effects : Ery (11/65) >>> Amoxi (2/64)

→ **Amoxicilline = Erythromycine**

Faye O et al. Int J Dermatol 2007; 46:19-22

Abcess (*S.aureus*)

Impact of antibiotherapy on the outcome of SARM related « uncSSTI »

	Adapted	Not adpated	OR (CI 95)
N =	312	219	
HCA	105 (34%)	75 (34%)	1.03
Abcess	**209 (67%)**	**152 (69%)**	**1.12**
Low limb	114 (37%)	82 (37%)	1.04
I + D	**249 (80%)**	**178 (81%)**	**0.9**
Failure	**16 (5%)**	**29 (13%)**	**2.8 (1.4-5.3)**

« patients with SARM ..uncSSTI could benefitiate of adapted AB-therapy »

Ruhe JJ et al. Clin Inf Dis 2007 ; 44 : 777-84

Abcess management

- « Ubi pus, Ibi evacuata »

Still true since Hippocrate

Am J Med 1876; 6: 226

Infectious cellulitis : Broad spectrum Going from Erysipela to necrotizing Cellulitis GAS, GAS and GAS

Clinical spectrum of infectious cellulitis

Erysipela	Cellulitis	Necrotizing cellulitis

Monomicrobial =GAS e	Plurimicrobial

Medicine	Surgery

Erysipela vs infectious cellulitis

Erysipela vs infectious cellulitis

- Peripheral surelevated borderline
- Clear borderline with surrounding tissues

Bisno AL. N Engl J Med 1996; 334:240-245

« In practice, distinguishing between cellulitis and erysipelas clinically may be difficult…. »

Stevens DL. Clin Infect Dis 2005; 41: 1373-1406

Criteria of severity when facing an infectious cellulitis

- No clinical response to antibiotherapy
- Intense and constant pain (+++)
- Cutaneous oedema reaching surrounding tissues
- Cutaneous necrosis (blue, white then black)
- Gaz (crepitation, Xray)
- Loss of cutaneous sensitivity (+++)
- Having clinical signs of severe infections

Stevens DL. Clin Inf Dis 2005; 41: 1373-1406

Erysipela : physiopathology

- More toxinic than suppurative
- Low density of bacteria involved
- Hypersentivity to streptococcal antigens (immune process) ?
- **Always** due to Streptoccus spp.
  - Either *Streptococcus pyogenes* (GAS)
  - But other species can be involved : G = 22% in a case-series of 90 patients en Finland (Siljander T et al. Clin Infect Dis 2008; 46: 855-61)

Infectious cellulitis

Risk factor erysipela in Tunisia

114 cases vs 208 controls	**OR**	**CI 95 %**
Obesity	1.3	0.6-2.9
History of leg surgery	5.2	0.8-34
Rupture of the cutaneous barrier	**13.6**	**6.3-31**
Veinous insufficiency	0.7	0.3-1.6
Lymphoedema	**19.1**	**1.1-331**

Mokni M et al. Dermatology 2006; 212:1416-1422

Risk factor erysipela in France

129 cases vs 294 controls	OR	CI 95 %
Obesity	2,0	1,1 - 3,7
Leg oedema*	2,5	1,2 - 5,1
Portal of entry	23,8	10,7 - 52,5
Veinous insufficiency	2,9	1,0 - 8,7
Lymphoedema	71,2	5,6 - 908

***leg oedema not associated to veinous insufficiencey**

Dupuy A et al. BMJ 1999;318:1591-4

Potential portal of entry

	Case	Control	OR	CI95%	PCA*
Intertrigo	**66 %**	**23 %**	**13,9**	**7,2 - 27,0**	**61 %**
Ulcer	**14 %**	**1 %**	**62,5**	**7,0 - 556**	**14 %**
Wound	**38 %**	**8 %**	**10,7**	**4,8 - 23,8**	**35 %**
Eschar	4 %	1 %	14,3	0,9 - 220	
Dermatosis	9 %	3 %	1,8	0,4 - 7,0	

* PCA : Proportion of attributable cases

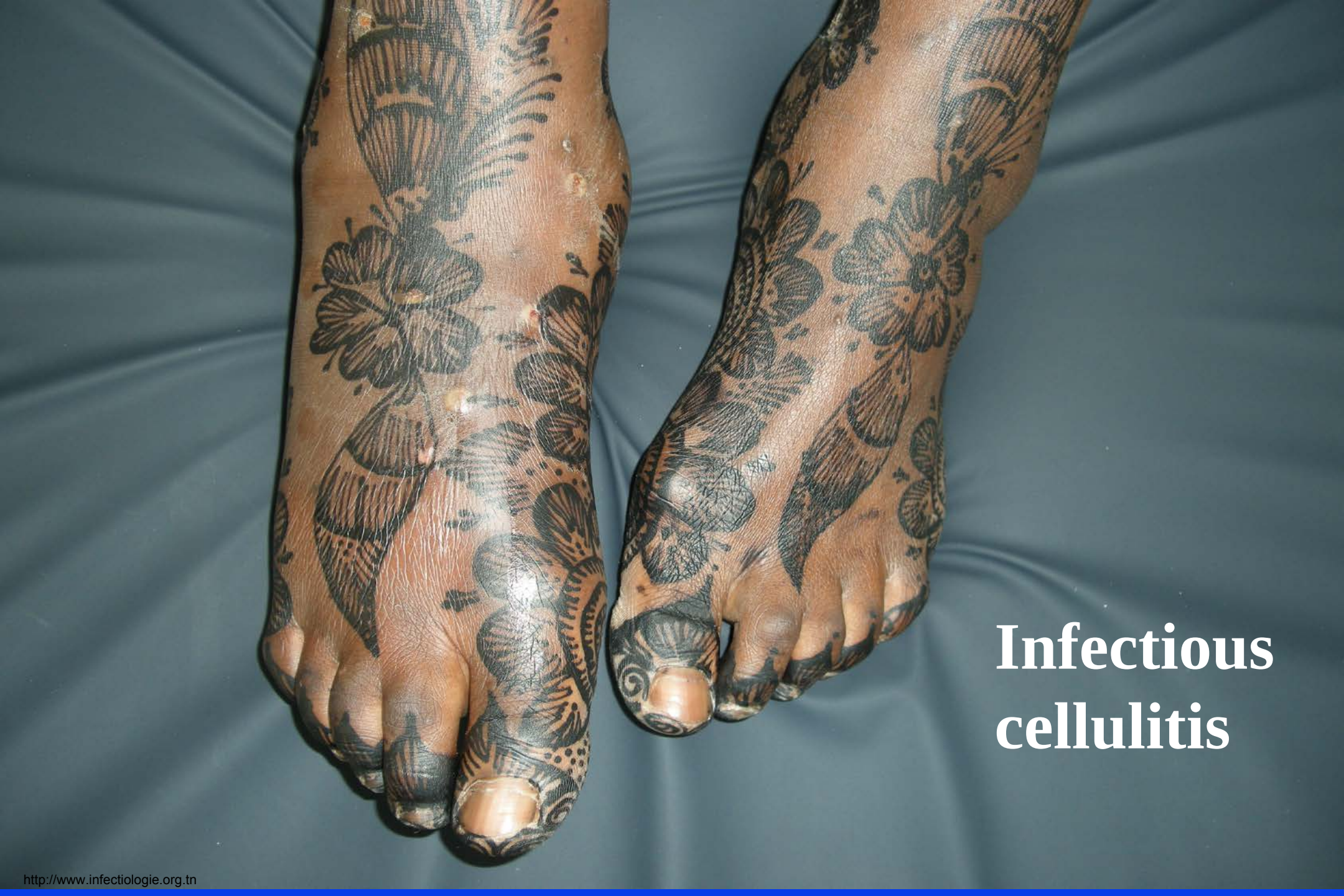
Dupuy A et al. BMJ 1999; 318:1591-4

Potential role of cutaneous mycosis as a portal of entry (univariate analysis)

	OR	IC 95%
Cutaneous mycosis	2,4	1,7-3,3
Toe Intertrigo*	2,8	1,9-4,2
Plantar involvement	1,7	1,2-2,4
Nail involvement	2,2	1,5-3,3

*Still significant after multivariate analysis

Roujeau JC et al. Dermatology 2004;209:301-7


Infectious
cellulitis

Breast cellulitis (right side)

Necrotizing cellulitis : epidemiology

- Norway : < 4 cases/100.000 persons/year
- United Kingdom: 25 cases/6 first months of 1994
- USA: 3.5 cases of life threatening Strep (36% with cutaneous signs) /100.000/ 2000- 2004;
- France: 1.7 life threatening Strep /100 000 (2002) & 2.7/100.000 (2004)
- Australia: 2.7/100 000/year (95% CI = 2.3-3.2)

Chelsom J et al. Lancet 1994;344:1111-5.
Burge TS et al. Br Med J 1994;308:1453-4.
Davies HD et al. N Engl J Med 1996;335:547-54.
Loughlin R et al. CID 2007;45:853-62
O'Grady KA et al. Med J Aust 2007;186:565-9

Necrotizing cellulitis : epidemiology

- 1991 - 1995: 77 cases of necrotizing cellulitis in Ontario (Canada)
- 0.085/100 000 to 0.40/100.000 (p < 0,001)
- Mean age: 57 years old
- 79% Community acquired
- 47% with toxic shok syndrom

Kaul R et al. Am J Med 1997;103:18-24

Necrotizing cellulitis : risk factors

- **Underlying medical conditions (62%)**
  - chronic disease (30%), diabetis (30%), alcoholism (17%)
  - immunosuppression (13%), IV drug addiction (8%), ongoing treatment for cancer (4%)
- **Local factors**
  - surgery (7%), varicella (5%), chronic dermatose (13%)
  - cutaneous wound (49%)

Kaul R et al. Am J Med 1997;103:18-24

Necrotizing cellulitis : risk factors for death

- Death : 34%, multivariate analysis
  - older age (p = 0,003)
  - hypotension (p = 0,002)
  - bacteriemia (p = 0,04)
- Serotypes most commonly involved : M1 (35%), M3 (25%); 41% des souches avec gène de la *spe*A, 30% *spe*C. Outcome was not associated with sérotype ou *spe*

Kaul R et al. Am J Med 1997;103:18-24

Secondary SSTI : necrotizing cellulitis of the scalp

Necrotizing cellulitis of the leg (GAS)

Necrotizing cellulitis : etiologies

- Gram positif rods (80% of 128 proven cases)
  - *Streptococcus spp*, mostly GAS,
  - +/- *Staphylococcus aureus*
- Gram negative bacilli
  - alone or in association with other species
  - *Escherichia coli*, *Klebsiella pneumoniae*, bacille pyocyanique, *Pasteurella multocida*, *Neisseria*, *X. maltophilia*, *V. vulnificus*, *Aeromonas sp*, *Proteus* ....
  ----> diabète, immunosuppression, cirrhosis
- Anaerobes

Carratalà J et al. Eur J Clin Microbiol Infect Dis 2003;22:151-7

Community acquired infections in France: Sensibility of *Staphylococcus aureus to AB*

	Pristinamycine	**F**usidic acid	Mupirocine	**Total**
PéniS	32 (100)	31 (97)	32 (100)	**32(15%)**
PeniR, MetiS	165 (100)	148 (89,7)	165 (100**)**	**165(80%)**
MetiR	8 (100)	6 (75)	8 (100)	**8 (4%)**

Lorette. Ann Dermatol Venereol 2003;130:723-728

Community acquired infections in France : microbial agents (259), AB sensibility

	Peni G	Peni M	Fusidic acid*	Pristinamycine
S.aureus (56%)	15%	96%	90%	100%
S.pyogenes (6%)	100%	NT	I/	100%

***MIC 50-90 S.a = 0,12-0,25 vs S.p = 8-8**

Lorette. Eur J Acad Dermatol Venereol 2009; 23: 1423-6

S.pyogenes macrolides R in USA

	S. pyogenes	Macrolides R
Total	**1885**	**129 (6.8%)**
Throat	**1598**	**99 (6.2%)**
Skin	**146**	**16 (10.9 %)***
Blood	**66**	**6 (9%)**
Lungs	**32**	**7 (21.9%)****

* p = 0.06

** p = 0.002

Richter S et al. Clin Inf Dis 2005 ; 41:599-658

Erysipela : antibiotic treatment

- Adaptation : weight, renal
- penicilline G IV high doses in hospitalisation,
- Importance of oral route +++
  - amoxicillin (3-4,5 g/d, 3 times per day) better than peni V (absorption)
  - macrolides : roxithromycine ? (old tiral) but you have to know the % strepto erythro-R,
  - synergistines : pristinamycine (3 g/d)
  - lincosamides : clindamycine 600 mg x 3/j

Cochrane: Treatment erysipela

- 25 trials, 2488 patients, AB familly oriented
- Macrolides/streptogramines vs penicillines: RR = 0.84 ($CI_{95\%}$ 0.73 – 0.97), 2 trials oral vs IV: RR = 0.85 ($CI_{95\%}$ 0.73 – 0.98)
- « We cannot define the best treatment for cellulitis and most recommendations are made on single trials. There is a need for trials to evaluate the efficacy of oral antibiotics in the community setting as there are service implications for cost and comfort »

Killburn SA et al. Cochrane Database of Systematic Review 2010, Issue 6. Art. No;:CD004299

Necrotizing cellulitis : antibiotic treatment

- Not at risk of MRSA: piperacilline-tazobactam 4g x 4/d + gentamycine 3 mg/kg/d +/- metronidazole 500 mg x 3/d (si anaerobes) OR clindamycine (if toxinic presentation)
- At risk of MRSA: vancomycine + clindamycine OR Linezolide OR Fusidic acid
- Face/Neck localisation : amoxicilline-acide clavulanique (2 g x 3/d) + gentamycine ou amoxicilline 100 mg/kg/d) + clindamycine (600 mg x 4/j)

Cesari-Giordani JF et al. Réanimation 2003;12:265s
Swartz MN. NEJM 2004;350:904-12
Legat FJ et al. AAC 2005;49:4368-71

Nosocomial : antibiotic treatment

- vancomycine (or linezolide) + ceftazidime (1-2 g x 3 /day) + amikacine + métronidazole
- vancomycine (or linezolide) + piperacilline-tazobactam ou imipenem + amikacine (± metronidazole) + clindamycine (up to 600 mg x 4/d) if toxinic signs

Cesari-Giordani JF et al. Réanimation 2003;12:265s
Swartz MN. NEJM 2004;350:904-12

Treatment of infectious cellulitis in case of severe allergy to penicillins

- Tigecycline IV
- Linezolide PO/IV or ceftobiprole or daptomycine
- Antistreptococcal Fluoroquinolones : moxifloxacine + clindamycine + aminoside
- Ceftriaxone or imipenem (10% of allergic cross reaction with other beta-lactam) + aminoside

Necrotizing cellulitis : surgical indications

- **What I have learned** :
  - early = prognosis vital (8/21 vs 2/47, p = 0.0007)
  - difficult = well stabilized patient
  - large (and debilitating)
  - daily dressings, skin graft
  - important sequellae

Bilton BD et al. Am Surg 1998;64:397-400

- **What I teach** now:
  - the key point : control the infection and the sepsis
  - when the infection is controled, there is no emergency
  - better to have an experienced surgeon
  - better to wait for the necrosis to be well delimited

SSTI = cutaneous bacterial infections

- **Large clinical spectrum, potentially life threatening**
- ***S. pyogenes* or *S.aureus***
- **At risk persons, portal of entry**
- **Amoxicillin, cloxacillin, fusidic acid pristinamycin, clindamycin,**


Merci pour votre attention
www.medecine-voyages.fr
http://www.infectiologie.org.fr