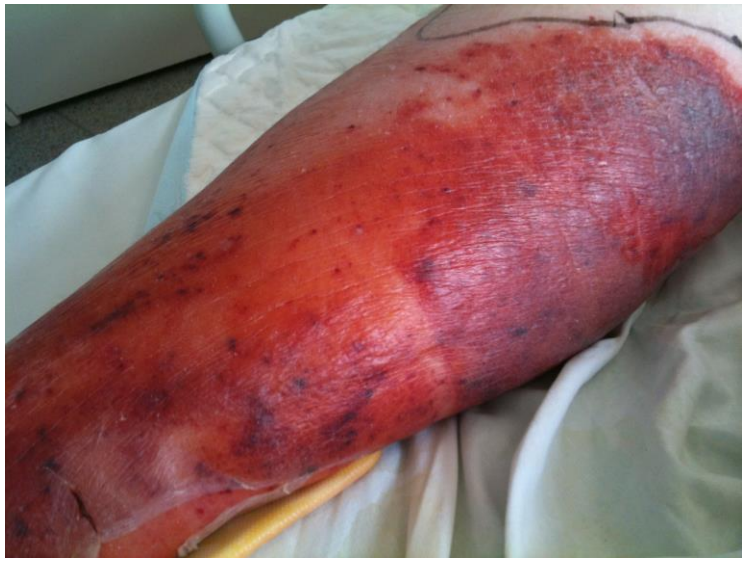
TRAITEMENT ANTI-INFECTIEUX SUPPRESSIF

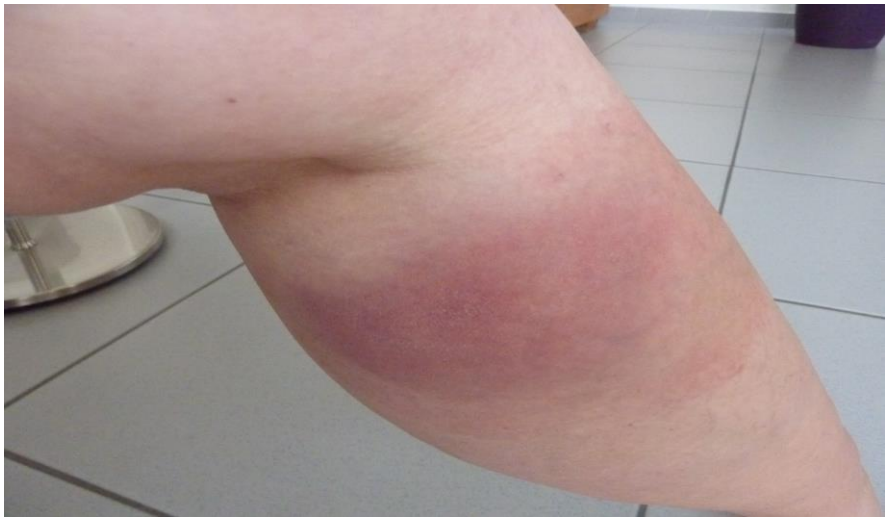
INFECTION CUTANÉE

Isabelle Alcaraz Morelle
Service Universitaire des Maladies Infectieuses CH Tourcoing

JRPI 10/10/2017

Dermohypodermite aiguë bactérienne





DERMOHYPODERMITE AIGUE BACTERIENNE

Pourquoi proposer un traitement suppressif?

- 10% à 50% récidivent selon les séries
- Lymphoedème > érysipèle > lymphoedème
- ERYSIPÈLE: Streptocoque A β hémolytique

Société de Pathologie Infectieuse de Langue Française
et Société Française de Dermatologie
Conférence de consensus.
Erysipèle et fasciite nécrosante : prise en charge.
Méd Mal Infect 2000; 30: 241-5

- Pénicilline V (Phénoxyméthylpénicilline) = 2 à 4 MUI/ j
- Benzathine Benzyl Pénicilline IM: 2,4 MUI/ 2 à 3 semaines
- Allergie: Macrolide

Antimicrobial Prophylaxis in Adults

MARK J. ENZLER, MD; ELIE BERBARI, MD; AND DOUGLAS R. OSMON, MD, MPH

Mayo Clin Proc. 2011;86(7):686-701

TABLE 1. **Selected Nonsurgical Antimicrobial Prophylaxis Regimens for Adults**[a,b]

Recurrent cellulitis in conjunction with upper or lower extremity lymphedema or erysipelas[5-7]	Penicillin V	250-1000 mg orally twice daily[f]
	or Penicillin G benzathine	1.2 million U IM every 2 to 4 wk
	Penicillin allergy	
	Erythromycin	250-500 mg orally twice daily

IDSA GUIDELINE

Clinical Infectious Diseases 2014;59(2):e10–52

Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America

Dennis L. Stevens,[1] Alan L. Bisno,[2] Henry F. Chambers,[3] E. Patchen Dellinger,[4] Ellie J. C. Goldstein,[5] Sherwood L. Gorbach,[6] Jan V. Hirschmann,[7] Sheldon L. Kaplan,[8] Jose G. Montoya,[9] and James C. Wade[10]

[1]Division of Infectious Diseases, Department of Veterans Affairs, Boise, Idaho; [2]Medical Service, Miami Veterans Affairs Health Care System, Florida; [3]San Francisco General Hospital, University of California; [4]Division of General Surgery, University of Washington, Seattle; [5]University of California, Los Angeles, School of Medicine, and R. M. Alden Research Laboratory, Santa Monica, California; [6]Department of Community Health, Tufts University, Boston, Massachusetts; [7]Medical Service, Puget Sound Veterans Affairs Medical Center, Seattle, Washington; [8]Department of Pediatrics, Baylor College of Medicine, Houston, Texas; [9]Department of Medicine, Stanford University, California; and [10]Geisinger Health System, Geisinger Cancer Institute, Danville, Pennsylvania

A panel of national experts was convened by the Infectious Diseases Society of America (IDSA) to update the 2005 guidelines for the treatment of skin and soft tissue infections (SSTIs). The panel's recommendations were developed to be concordant with the recently published IDSA guidelines for the treatment of methicillin-resistant *Staphylococcus aureus* infections. The focus of this guideline is the diagnosis and appropriate treatment of diverse SSTIs ranging from minor superficial infections to life-threatening infections such as necrotizing fasciitis. In addition, because of an increasing number of immunocompromised hosts worldwide, the guideline addresses the wide array of SSTIs that occur in this population. These guidelines emphasize the importance of clinical skills in promptly diagnosing SSTIs, identifying the pathogen, and administering effective treatments in a timely fashion.

- Péni V / Erythromycine / Benzathine Benzyl Pénicilline

Quel bénéfice en attendre?

Cochrane Database Syst Rev. 2017 Jun

Interventions for the prevention of recurrent erysipelas and cellulitis.

Dalal A[1], Eskin-Schwartz M, Mimouni D, Ray S, Days W, Hodak E, Leibovici L, Paul M.

- UK, Sweden, Tunisia, Israel, and Austria.
- 6 études randomisées : 5 AB, 1 sélénium
- 573 patients
- 1 à 4 épisodes préalables
- 481 péni / 32 érythro, 6 à 18 mois de traitement
- Suivi pour deux études 18 et 24 mois après fin de l'AB

- Risque de récurrence diminué de 69% /placebo

  RR: 0.31, 95% (CI) 0.13 -0.72, p= 0.007
- Pas de bénéfice démontré après arrêt de l'antibiothérapie
- EI mineures
- résistances?

Journal of Infection 2014; 69:26-34 RR: 0,46 , IC 95 % [0,26-0,79].

Table 1 Characteristics of included studies.

Study	Population	Intervention	Control	Outcome	Follow-up time
Kremer 1991.[22] Israel.	≥2 previous episodes of soft tissue infection (cellulitis or erysipelas).	Erythromycin. 250 mg, tablets, b.i.d., 18 months. Patients allergic to erythromycin given penicillin V-K, 250 mg b.i.d. *N* = 20.	No medication. *N* = 20.	Number of patients with recurrences; number of recurrences; adverse events.	18 months.
Chakroun 1994.[21] France.	Infectious cellulitis. Most had prior antibiotics.	Penicillin G. 1.2 million units (~720 mg), intramuscular injection, every 15 days, unclear duration. *N* = 24. Note: 77.8% had prior antibiotics.	Unclear. *N* = 34. Note: 29.4% had prior antibiotics.	Patients with recurrences.	11.6 months average follow-up.
Sjoblom 1993.[23] Sweden.	≥2 episodes of erysipelas during the last 3 years.	Phenoxymethylpenicillin. 1 g for BW <90 kg. 1 g + 2 g for BW 90–120 kg. 2 g for BW >120 kg. Tablets, b.i.d., unclear duration. Patients allergic to penicillin were given erythromycin: 0.25 g b.i.d. for BW <90 kg. 0.25 + 0.5 g b.i.d. for BW 90–120 kg. 0.5 g b.i.d. for BW >120 kg. *N* = 20.	No treatment. *N* = 20.	Number of patients with recurrences; adverse events.	Follow-up time possibly varied.
PATCH 1 2012.[26] UK.	≥2 episodes of cellulitis. Within 3 years of index occurrence.	Penicillin VK. 250 mg, tablets, b.i.d., 12 months. *N* = 136.	Placebo tablets, b.i.d., 12 months. *N* = 138.	Number of patients with recurrences; number of recurrences; adverse events; time to next episode.	36 months.
PATCH II 2012.[25] UK.	≥1 episode of cellulitis. Index episode diagnosed within last 12 weeks.	Penicillin VK. 250 mg, tablets, b.i.d., 6 months. *N* = 60.	Placebo tablets, b.i.d., 6 months. *N* = 63.	Number of patients with recurrences; number of recurrences; adverse events; time to next episode.	36 months.

PATCH II

Britisjh Journal of Dermatology 2012

- Étude randomisée en double aveugle,
- 1 épisode ds les 12 semaines de dermohypodermite (ulcère exclu)
- 20 hôpitaux
- 129 participants: 2 bras :250mg Péni V bid /placebo

MANQUE DE PUISSANCE

- 6 mois de traitement
- 3 ans de suivi
- RÉCURRENCES: Péni: 20% / Placebo: 33%
- HR: 0,53 > réduction de 47% du risque de récurrence

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Penicillin to Prevent Recurrent Leg Cellulitis

Kim S. Thomas, Ph.D., Angela M. Crook, Ph.D., Andrew J. Nunn, M.Sc., Katharine A. Foster, Ph.D., James M. Mason, D.Phil., Joanne R. Chalmers, Ph.D., Ibrahim S. Nasr, M.Sc., Richard J. Brindle, D.M., John English, M.B., B.S., Sarah K. Meredith, F.F.P.H., Nicholas J. Reynolds, M.D., F.R.C.P., David de Berker, M.D., F.R.C.P., Peter S. Mortimer, M.D., F.R.C.P., and Hywel C. Williams, Ph.D., F.R.C.P., for the U.K. Dermatology Clinical Trials Network's PATCH I Trial Team*

N Engl J Med 2013;368:1695-703

- Essai randomisé en double aveugle
- Atcd de récurrence dans les 6 mois précédents
- 274 patients/ 28 hôpitaux

	Péni V 250 mg bid 12 mois	**Placebo 12 mois**
Médiane de temps de récidive	626 jours	532 jours
% patient faisant une récidive	22%	37% (HR: 0,55 p= 001)

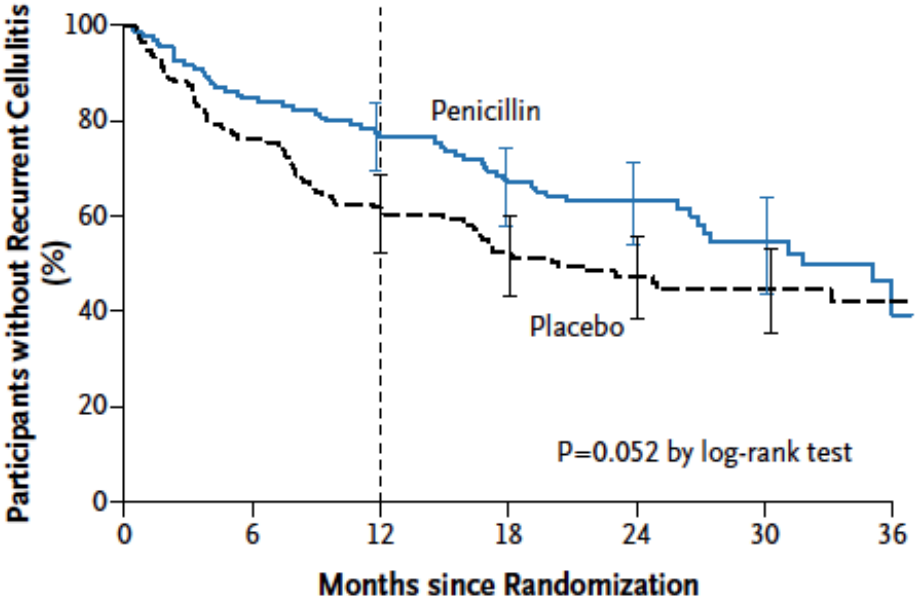
Table 2. Hazard Ratios for Confirmed Recurrence of Cellulitis in the Penicillin Group as Compared with the Placebo Group.

Variable	Recurrence of Cellulitis	Percentage-Point Difference (95% CI)	Hazard Ratio (95% CI)	P Value
	*no. of events/total no. of patients (%)**			
Primary analysis: prophylaxis phase, year 1				
Penicillin	30/136 (22)	–15 (–26 to –4)	0.55 (0.35 to 0.86)	0.01
Placebo	51/138 (37)			
Secondary analysis: follow-up phase, years 2 and 3†				
Penicillin	26/97 (27)	0 (–14 to 12)	1.08 (0.61 to 1.93)	0.78
Placebo	22/81 (27)			

* The proportion of patients with a recurrence of cellulitis was a prespecified secondary end point. Proportions are presented as percentages, not person-time event rates.

† The secondary analysis for years 2 and 3 was postrandomization. As a result, the groups may not have been balanced at the start of this period.

N Engl J Med 2013;368:1695-703



No. at Risk							
Penicillin	136	107	97	80	44	25	11
Placebo	138	101	81	68	36	25	17

Figure 2. Proportion of Participants Who Remained Recurrence-free over Time.
The I bars represent 95% confidence intervals.

Pourquoi ces échecs?

- Non compliance

- Facteurs favorisants liés au terrain
  - Lymphoedème
  - Porte d'entrée persistante

- Facteurs liés au protocole AB
  - Choix de l'AB/ germe
  - Dose
  - rythme

Echecs
Facteurs favorisants / terrain

- Lymphoedème

  - 171 patients 47% récurrences, 46% oedème chronique (p: 0002)

    Br J Dermatol 2006 Nov;155(5): 947-50

  - 115 patients: prophylaxie efficace **uniquement** en l'absence de lymphoedème

    Clinical Infectious Diseases 1997; 25:685 – 9

Echecs
Facteurs favorisants / terrain

- Intertrigo:

  - 66% pour 167 érysipèles – 294 contrôles: *Roujeau J-C et al. Risk factors for erysipelas of the leg (cellulitis): case–control study. BMJ 1999; 318:591–4.*

Table 2 Multivariate analysis of risk factors for erysipelas of the leg

Risk factor	Odds ratio* (95% CI)
Lymphoedema	71.2 (5.6 to 908)
Site of entry	23.8 (10.7 to 52.5)
Leg oedema†	2.5 (1.2 to 5.1)
Venous insufficiency	2.9 (1.0 to 8.7)
Overweight	2 (1.1 to 3.7)

*Adjusted for age, sex, hospital, and variables in table.
†Excluding oedema related to venous insufficiency.

N Engl J Med 2013;368:1695-703

Table 3. Factors Predictive of Prophylaxis Failure.*

Factor	Odds Ratio (95% CI)†	P Value
No. of previous cellulitis episodes		
≥3	3.23 (1.82–5.73)	<0.001
<3	1	
Edema		
Preexisting edema	1.83 (0.97–3.47)	0.06
No evidence of edema	1	
BMI		
≥33	2.05 (1.16–3.64)	0.01
<33	1	

* Failure of prophylaxis was defined as at least one confirmed episode of cellulitis during the prophylaxis phase.
† All effects were included in the model; data for two patients were not included owing to a missing value for BMI.

Echecs
Facteurs / protocole AB

- Antibiotique
  - Quelle sensibilité pour autres germes que Strepto A ?

    Njim et al. BMC Infectious Diseases ***(2017) 17:418:*** 50,6 % Strepto A
  - Macrolides et résistance
  - Pas de différence démontrée Péni V et BenzathineBenzylPénicilline

- Doses et rythme?

  - 250 mg Péni V , Erythro bid > trop faible ? ou suffisant/ CMI
  - 1,2 MUI BBP trop faible ? > plutôt 2,4 MUI
  - récidives souvent à 3 semaines > toutes les 2 semaines????

- Durée ?

  - minimum 6 mois, <u>plutôt un an et plus</u>

Koster - The Netherland Journal of Medicine 2007
analyse les échecs (117 patients) et les réponses

- Autre germe ? **<u>Choix de l'antibiotique</u>**

  > succès de la Clindamycine 300mg X 4/ J
  !! Large spectre Risque digestif !!

- **Délai**: Benzathine benzyl penicilline 1,2 MUI, toutes les 4 à 3 semaines > succès si toutes les 2 semaines

- **Dose**: > clarithromycine 250 mg X 2/j

Et si le patient est allergique à la pénicilline?

- On le teste!

Allergie aux bétalactamines > Macrolides

- ERYTHROMYCINE ???

Journal of Infection (199l) 22, 37-40

- 36 patients
- Erythromycine 250 mg X2 / aucune prophylaxie (18 mois)
- Récidive: 0/ 8
- Intolérance digestive: 3

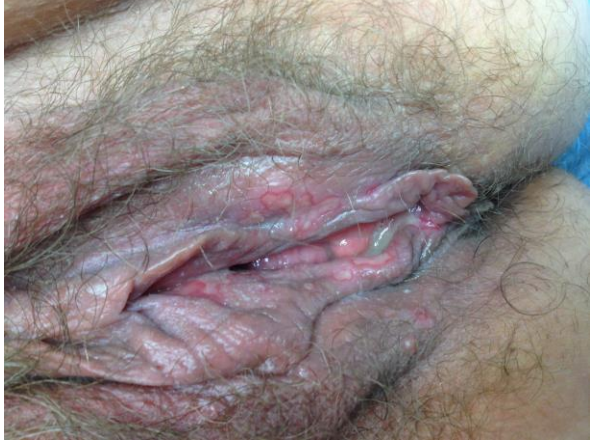
Résistance du Streptocoque béta hémolytique / groupe MLS:

- Erythromycine: 4% en 2015 (CNR streptocoque)
- groupe MLS : 5% en 2010

En résumé
Prophylaxie des érysipèles récurrents

- Péni V 1 MUI X 2/ j ou Amoxicilline 500mg X 2 (voire 500mg) (SFD)
- BBP: 2,4 MUI / 3 semaines (petits poids 1,2 MUI ?)
- Durée ? : Des années
- Eviter les macrolides
- Traiter la porte d'entrée (intertrigo)
- Lutte contre le lymphoedème: pas de jambe pendante, Contention précoce +++

Traitement suppressif de l'HERPES RECURRENT



6 récurrences annuelles ou plus d'herpès génital

- VALACYCLOVIR 500 mg: 1 cp/j , à réévaluer annuellement *(JAD 2007)*
  si ID: 500mg X 2/j

  - Réduit les poussée de 70% à 80% *Sex Transm Dis 2003;30:226–31*

  - Excellente tolérance *Goldberg LH,. Arch Dermatol 1993;129:582–7.*
    Fife KH, J Infect Dis 1994;169:1338–41.

  - Effet prolongé après l'arrêt

HERPES GENITAL

J Infect Dis 2005 July 1; 192(1): 156–16

- Très peu de résistance / « immunocompétent »
- Peu de transmission dans population non ID

Recurrent herpetic keratitis despite antiviral prophylaxis: A virological and pharmacological study

Antoine Rousseau [a, b], David Boutolleau [c, d], Karine Titier [e], Tristan Bourcier [f],

Antiviral Research 146 (2017) 205–212

Traitement suppressif de l'HERPES RECURRENT

ECHECS: que faire ?

- Doubler la dose (CDC)
- Génotype ? Résistance < 1% chez l'ID (R croisée acyclovir / valacyclovir)
- Javaly K, Wohlfeiler M, Kalayjian R, et al. Treatment of mucocutaneous herpes simplex virus infections unresponsive to acyclovir with topical foscarnet cream in AIDS patients: a phase I/II study. J Acquir Immune Defic Syndr 1999; 21:301–306.
- **Imiquimod 5-percent** cream does not alter the natural history of recurrent herpes genitalis: a phase II, randomized, double-blind, placebo-controlled study. ANTIMICROBIAL AGENTS AND CHEMOTHERAPY Oct. 2002: 3243–3248
- Prise en charge du terrain

MICROBIOME

Antimicrobials from human skin commensal bacteria protect against *Staphylococcus aureus* and are deficient in atopic dermatitis

Teruaki Nakatsuji,[1] Tiffany H. Chen,[1] Saisindhu Narala,[1] Kimberly A. Chun,[1] Aimee M. Two,[1]

Nakatsuji *et al.*, *Sci. Transl. Med.* **9**, eaah4680 (2017) 22 February 2017

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