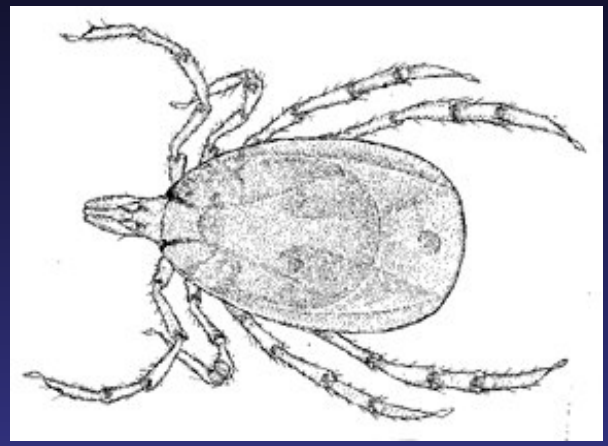
SBIMC-BVIKM



LYME DISEASE

TREATMENT OPTIONS

Adults and children

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23 may 2002

CID 2000;31:1-14

- Table 4. Recommended therapy for patients with Lyme disease.

Indication	Treatment	Duration	
Tick bite	None recommended	observe	
Erythema migrans	Oral regimen[a]	14-21	A-I
Acute neurological disease			
Meningitis or radiculopathy	Parenteral regimen[a]	14-28	B-II/A-I
Cranial-nerve palsy	Oral regimen	14-21	
Cardiac disease			
1st or 2d degree heart block	Oral regimen	14-21	B-II
3d degree heart block	Parenteral regimen[a]	14-21	B-III
Late disease			
Arthritis without neurological disease	Oral regimen	28	B-II
Recurrent arthritis after oral regimen	Oral regimen or	28	B-III
	parenteral regimen	14-28	
Persistent arthritis after 2 courses of antibiotics	Symptomatic therapy		B-II
CNS or peripheral nervous system disease	Parenteral regimen	14-28	B-II
Chronic Lyme disease or postLyme disease syndrome	Symptomatic therapy		

CID 2000;31:1-14

- **Table 1.** Categories indicating the strength of each recommendation for or against use.

Category	Definition
A	Good evidence to support a recommendation for use
B	Moderate evidence to support a recommendation for use
C	Poor evidence to support a recommendation for or against use
D	Moderate evidence to support a recommendation against use
E	Good evidence to support a recommendation against use

- **Table 2.** Grades indicating the quality of evidence on which recommendations are based.

Grade	Definition
I	Evidence from at least 1 properly randomized, controlled trial
II	Evidence from at least 1 well-designed clinical trial without randomization, from cohort or case-controlled analytic studies (preferably from >1 center), from multiple time-series studies, or from dramatic results of uncontrolled experiments
III	Evidence from opinions of respected authorities that is based on clinical experience, descriptive studies, or reports of expert committees

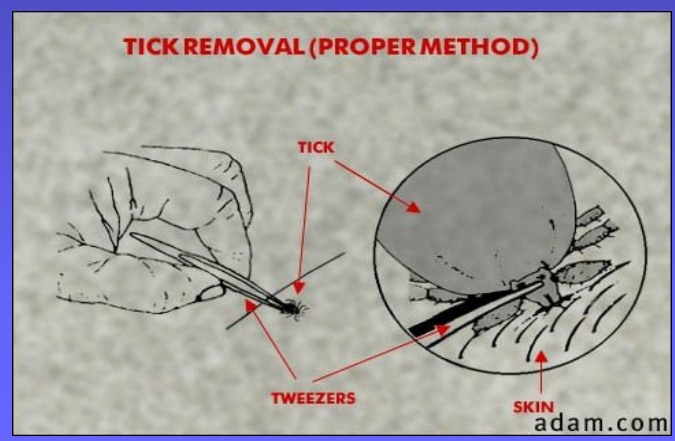
TREATMENT OPTIONS
Randomised controlled trials

- **Few RCTs, few patients/study** (error type II)
- **Few RCTs including children**
- **Heterogeneity (inclusions criteria and end-points)**
- **Different lengths of follow-up**
- **2 Meta-analysis: prophylaxis, chronic LD**
- **USA/Europe:** **prophylaxis: USA**
  ECM: 9 Europe/5USA
  arthritis: >> USA
  neuroborreliosis: >> Europe

LYME DISEASE
PREVENTION

- ***JCM 1987;25:557:*** **Experimental transmission to rodent requires tick attachement for ≥ 24h.**
- ***JID 1997;175:996*: Higher risk to develop infection when ticks removed ≥ 72h (p=0,008).**

- **Avoid vector tick exposure**
- **Protective clothes, ticks repellents, daily checking the body for ticks, prompt removal of attached ticks.**



ANTIMICROBIAL PROPHYLAXIS (AMP)

- **4 RCTs** (USA)
  - *NEJM 1992;327:1769*. (double-blind, 387 pts, 1y. follow-up)
    - » 344 deer ticks analyzed, 15% infected
    - » Risk of infection in placebo group: 1,2% vs 0 in amoxi. (NS)
  - *NEJM 2001;345:79* : (double-blind, 482 pts, 6 weeks follow up)
    - » risk of infection 3,2% placebo vs 0,4% doxy 1 dose 200 mg → > 72h, *I. scapularis* at nymphal stage, engorged tick.
- **1 meta-analysis** (96)
  - 600 adults and children, follow-up 6m-3y.
  - Peni/ampi/tetra (10d) vs placebo
  - Pooled rate of infection in placebo 1,4% vs 0% (NS)
  - **Low incidence of reported events :** the addition of 1 event could influence the results.
  - Risk of AB related adverse events > cases of early LD prevented, not cost-effective.

ANTIMICROBIAL PROPHYLAXIS

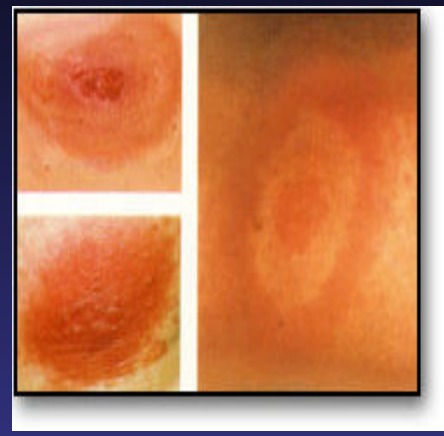
CONCLUSIONS

- **Low rate of LD after tick bite in endemic area**
  (Higher rate of asymptomatic infection in Europe)
- **No evidence for a benefit of prophylaxis**
- **If attached ticks " 48-72h: No clear data**
  - **Dependent of species, stage, infection status of the tick and probability of transmission of infection**

Routine use of AMP not recommended

Prospective surveillance

ERYTHEMA MIGRANS



- 14 RCTs, no meta-analysis
  - 2 studies enrolled > 200 patients
    - Amoxi 20d vs azithro 7d: lower cure rate and more relapses in azithro. (p=0,02)
    - Cefurox.ax vs doxy 20d: as effective, more related adverse events in doxy. (p=0,041)
  - 1 study interrupted after 19 patients analyzed: 5/9 failure in roxithro. vs 0/10 in peni V

- cefurox.ax=peni V
  peniV=mino*
  azithro=amoxi+probenecid=doxy*
  azithro=peniV*

  azythro=doxy
  amoxy+probenecid=doxy
  cefurox.ax=doxy
  ceftriax=peniV
  azithro=peniV

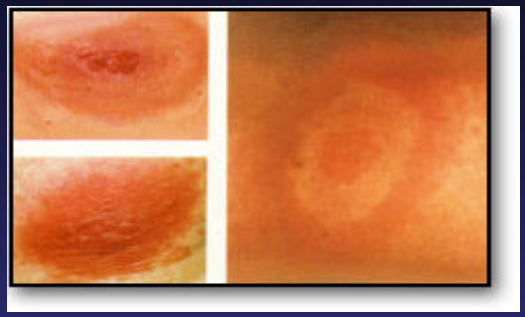
ERYTHEMA MIGRANS

- **Duration of treatment: no RCT**
  - **Standard durations: 10-21 d, azithro 5-7d.**
  - **1 retrospective study (57 pts): doxy 14d = 21d**
- **Adverse events: Variable rates**
  - **Amoxi, peniV: eruption**
  - **Doxy: photosensitivity (> 8y., pregnancy)**
  - **Cefurox.ax.: diarrheae, Jarish-Herxheimer reaction**
- **Rare cases of late complications with each medication (< 10%)**

ERYTHEMA MIGRANS

- **Dosage**: no RCT

	Adults	Children
amoxi	500 mg tid	50mg/kg/d div 3
doxy	100 mg bid	1-2 mg/kg bid
cefurox	500 mg bid	30 mg/kg/d div 2
azithro	500 mg od	5 mg/kg od (10mg/kg, 1th dose)



ERYTHEMA MIGRANS

- **First choice:**
  - **Amoxi tid** (13E) **or doxy bid** (19E)
  - **For 14-21d**
- **Second choice:**
  - **cefurox.ax.: more expensive** (**46 E**)
- **Other alternatives:**
  - **Macrolides (lower cure rate)** (**7d. azithro 500 mg:34 E**)
  - **No data on clometocilline**

Amoxi tid or doxy bid
For 14-21d

ARTHRITIS

5 RCTs, few children, USA

- **Peni 20MiU/d 10d vs ceftriax 2g iv 14d**
  - Ceftriax > peni (23pts, end-points !)
  - Additionnal 31 pts (non RCT): ceftriax. 2g = 4g. (Corticosteroids !)
- **Ceftriax 2g od 2 weeks = 4 weeks.** (76%-70% of cure)
- **Doxy vs amoxi+probenecid for 30 d** (38 pts).
  - 80% complete resolution at 3 months, 1 neuroborreliosis subsequently.
  - No resolution after a second course with ceftriax. 14d (HLA).
- **Stage 3 mixed** (arthritis + CNS)
  - Cefotax 2g tid > peni G10 MIU bid (60 pts) (40% J-H reaction in cefotax)

ARTHRITIS

No good level of evidence !

- **No neurological symptoms associated: oral therapy (cost/effectiveness)**

  First choice:

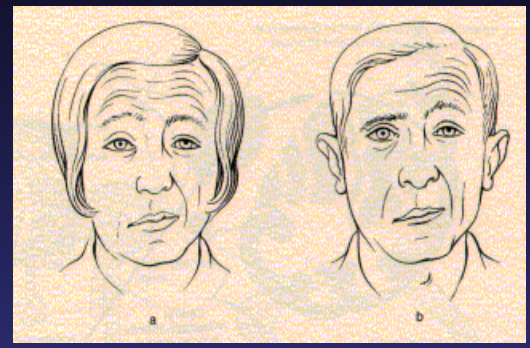
  - Doxy bid (37 E)
  - Amoxi tid (26 E)
  - for 4 weeks
  - Slow resolution

  Second choice:

  - Ceftriaxone 2g od for 2 weeks. (548,66 E) (75-100mg/kg od)

- **Recurrence (> 6-12 months):**
  - second course of treatment. (po or iv ceftriax. 2 weeks)
  - no response: symptomatic/synovectomy (HLA, T cells response to OspA)

NEUROBORRELIOSIS



Acute-subacute: meningitis or radiculopathy

- Spontaneous resolution of facial palsy.
- Studies
  - PeniG 5MiU qid = po doxy 200mg od for 14d.(n=54)
  - PeniG 5MiU qid = po doxy 200mg od for 14d.(n=46)
  - PeniG 5MiU qid = iv doxy 200 mg od (n=75)
  - Ceftriax 2g od = cefotax 2g tid 14d.(n=33)
  - PeniG 5MiU qid = cefotax 2g tid 10d.(n=21)
  - Ceftriax 50-90mg/kg od = peniG 80-120.000UI/kg qid 14d.(n=75)
  - PeniG 80-120.000 UI/kg qid = ceftriax 75-90mg/kg od 14d.(n=23)

- Non RCT: Facial palsy + meningitis: 29 pts, doxy 200mg bid 9-17d (90% cure at 6 months)

NEUROBORRELIOSIS

- Acute-subacute neuroborreliosis

	ceftriax	peni G	doxy
Adults	2g od	4- 5Miu qid	100-200 mg bid
Children	75-100 mg/kg od	80-120.000 Ui/kg qid	-

For 14d. minimum

Slow resolution in 30%, bilateral facial palsy

NEUROBORRELIOSIS

- Late neuroborreliosis:
  - Inclusions criteria, stage 3 mixed …
  - Ceftriax od or cefotaxime tid seem better
  - Duration: 14-30d.
  - Typically slow response to treatment (months)

OTHERS

- CARDITIS
  - No RCT or controlled studies

    Antibiotic efficacy ?

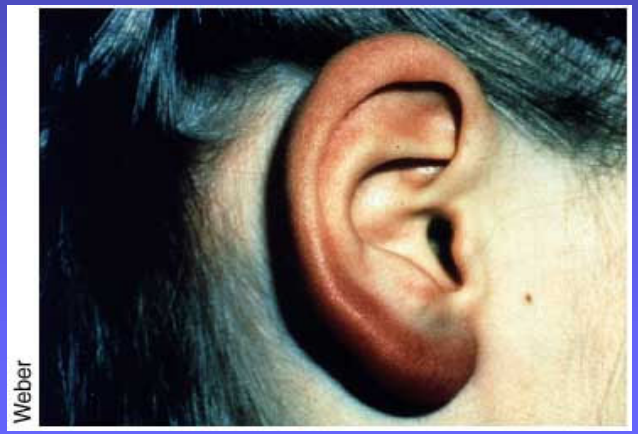
    BAV1-2: oral treatment: amoxi or doxy

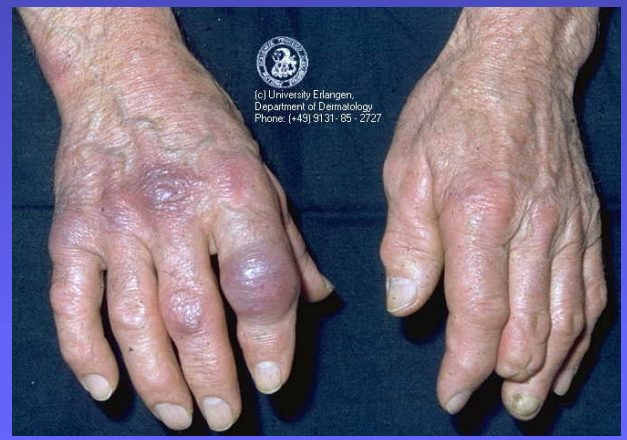
    BAV 3: parenteral therapy: ceftriax (corticosteroids ?)

    Duration 14-21d.

OTHERS

- ACRODERMATITIS CHRONICA ATROPHICANS
- LYMPHOCYTOMA
  - case series
  - oral amoxi or doxy for 14-28d.

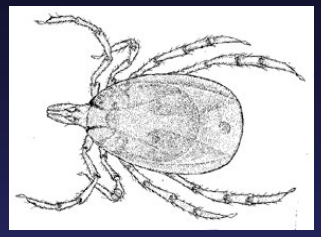




OTHERS

Chronic Lyme Disease or Post-Lyme Disease syndrome

- Poorly defined entities
- 2 RCTs:
  - 129 pts, ceftriax 30d then doxy 60d vs placebo
  - No difference between the 2 groups
- 1 meta-analysis: Cost/effectiveness of empirical parenteral therapy for patients with fibromyalgia and positive serology (endemic area): incidence of false + serology >> the incidence of true + in patients with nonclassical infection. More side effects: risk and cost>> benefits.



LYME DISEASE TREATMENT OPTIONS

- **Antibiotic treatment of LD** (excepted CLD)
  - Global efficacy
  - Few long term complications if early and good treatment

BUT:

Low level of evidence for type, dose and duration of antibiotic therapy !