Place de l'antibiothérapie préventive après piqure de tique

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Webinaire CRMVT Grand Est

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Conflits d’intérêts

- I received lecture fees and/or travel fees from the following entities in the last three years:
  - ViiV Healthcare, Gilead Science, MSD, Sanofi, Pfizer

- Participation to scientific board:
  - Gilead Science

Introduction

- Recommandation 2006

L'antibioprophylaxie systématique après piqûre de tique n'est pas recommandée.

En zone d'endémie, l'antibioprophylaxie peut être discutée au cas par cas dans des situations à haut risque de contamination (piqûres multiples, long délai d'attachement, fort taux d'infestation connu) : doxycycline PO en monodose (200 mg) (grade A) ou amoxicilline PO (3 g/j pendant 10 à 14 jours) (grade B). Trois situations

- Quel rationnel pour quelles recommandations aujourd'hui ?

Quels bénéfices potentiels ?

Table 1 Characteristics of randomized clinical trials included in meta-analysis

	Area	Age	Males (%)	Antibiotic	Oral or topical	Daily dose (mg)	Duration (d)	Follow-up (m)
Costello et al. 1989 [20]	USA	Adults and children	35.7	Penicillin	Oral	1000	10	
Shapiro et al. 1992 [21]	USA	Adults and children	42.6	Amoxicillin	Oral	750	10	12[b]
Agre et al. 1993 [22]	USA	Children	49.2	Penicillin or tetracycline[a]	Oral	1000	10	12–36
Nadelman et al. 2001 [23]	USA	Adults and children	53.3	Doxycycline	Oral	200	1	1.5
Schwameis et al. 2016 [3]	Germany and Austria	Adults	48.7	Azithromyci	Topical	–	3	2
Harms et al. 2021 [9]	Netherlands	Adults and children	50.0	Doxycycline	Oral	200	1	6

[a] Patients older than 9 years received tetracycline and those younger than 9 years received penicillin

[b] Visit follow-up for 3 months, and telephone follow-up for 12 months

Quels bénéfices potentiels ?

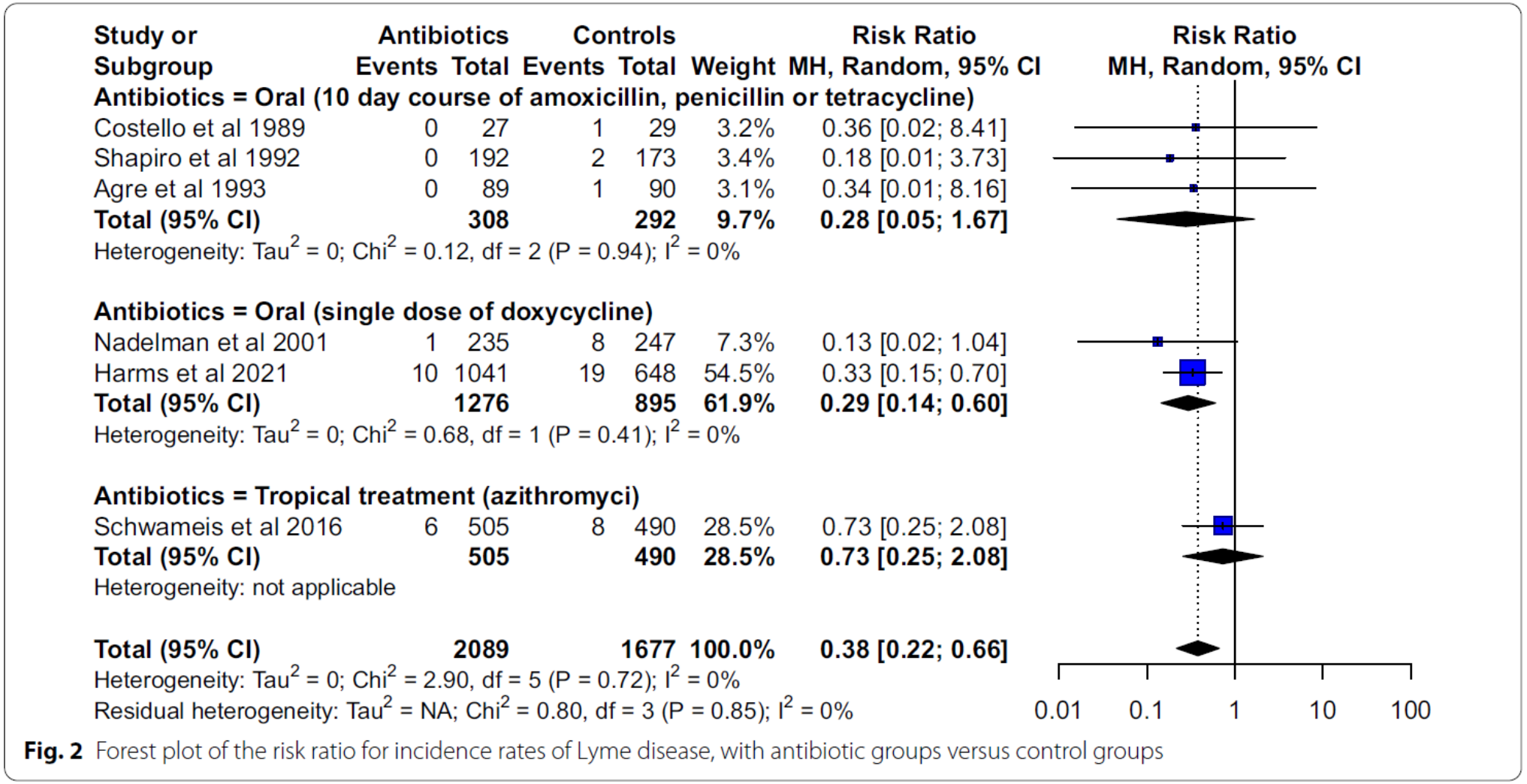


Fig. 2 Forest plot of the risk ratio for incidence rates of Lyme disease, with antibiotic groups versus control groups

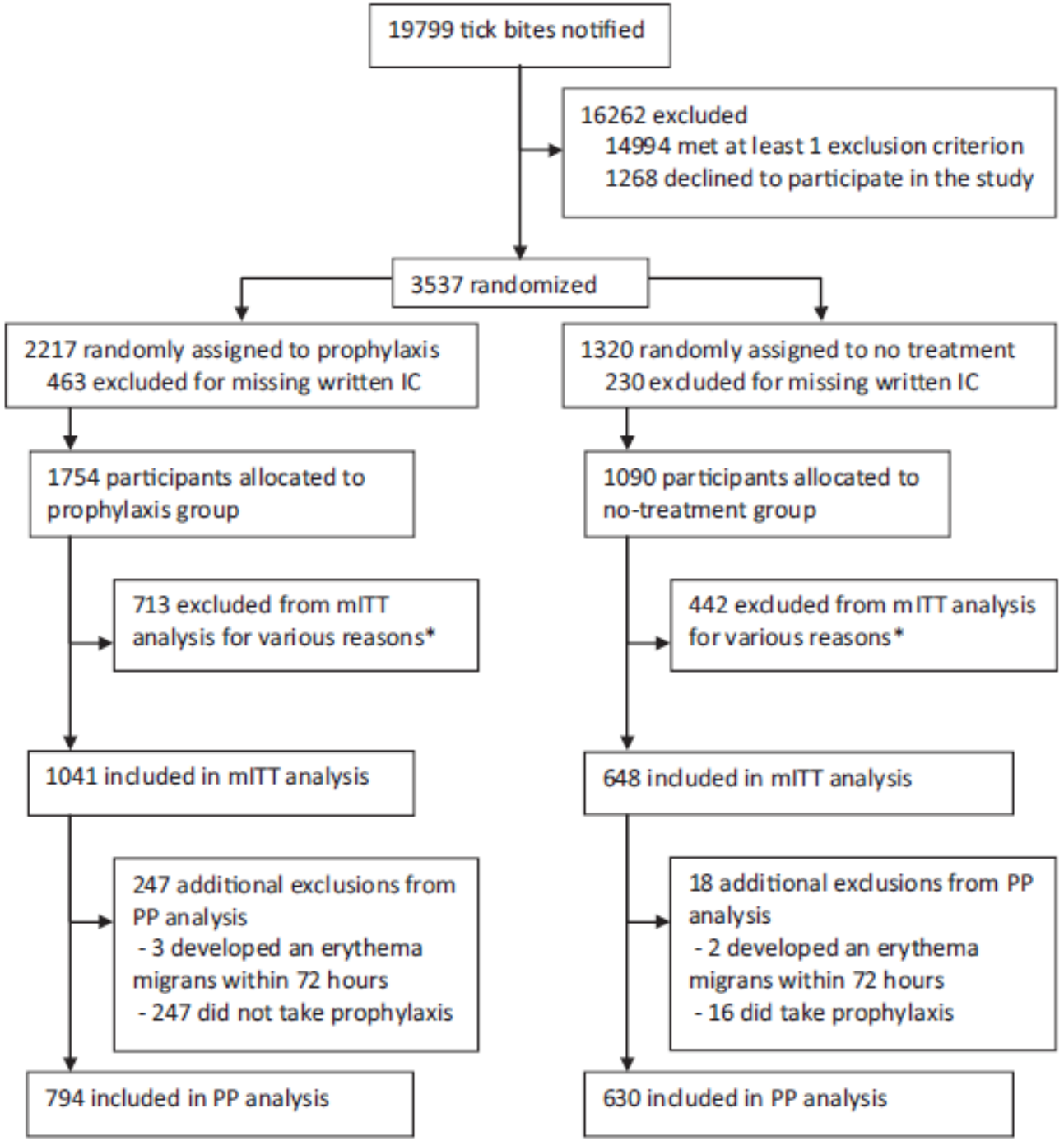
- Zhou G et al. BMC Infect Dis 2021

Quels bénéfices potentiels ?

Table 2
Differences between study groups for modified-intention-to-treat analysis and per-protocol analysis as calculated as absolute risk, relative risk reduction, number-needed-to-treat and relative risk, for all study participants as well as several subsets of participants as characterized by their individual characteristics.

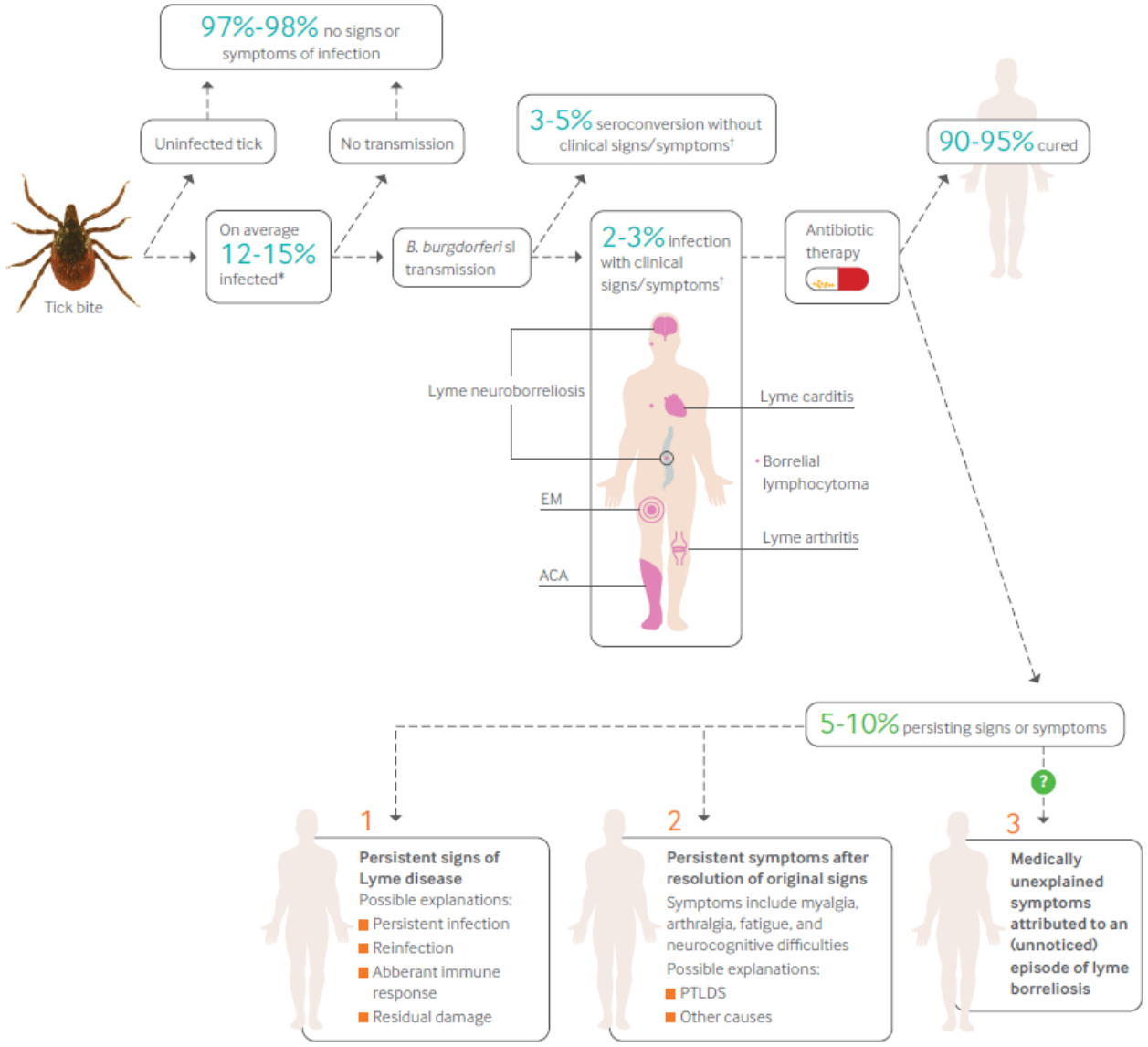
	prophylaxis group			no-treatment group				relative risk	relative risk reduction	number-needed-to-treat
	n	events	absolute risk (%)	n	events	absolute risk (%)	p-value	estimate (95% CI)	estimate (95% CI)	estimate (95% CI)
All participants										
modified-intention-to-treat	1041	10	0.96	648	19	2.93	0.003	3.05 (1.43 - 6.52)	67% (31% - 84%)	51 (29 - 180)
per-protocol	794	5	0.63	630	17	2.70	0.002	4.29 (1.59 - 11.55)	77% (39% - 91%)	48 (28 - 150)
Subset of participants sending in an engorged tick (Engorgement category 1+2+3, see Table 1)										
modified-intention-to-treat	566	7	1.24	363	14	3.86	0.010	3.12 (1.27 - 7.65)	68% (23% - 87%)	38 (20 - 224)
per-protocol	427	3	0.70	353	14	3.97	0.002	5.65 (1.64 - 19.49)	82% (43% - 95%)	31 (18 - 99)
Subset of participants sending in a *B. burgdorferi* s.l. positive tick										
modified-intention-to-treat	216	3	1.39	126	14	11.11	<0.001	8 (2.34 - 27.30)	88% (60% - 96%)	10 (6 - 25)
per-protocol	150	0	0.00	121	13	10.74	<0.001		100% (77% - 100%)	9 (6 - 20)
Subset of participants sending in an engorged (Engorgement category 1+2+3, see Table 1) and *B. burgdorferi* s.l. positive tick										
modified-intention-to-treat	102	2	1.96	61	11	18.03	<0.001	9.20 (2.11 - 40.11)	89% (58% - 97%)	6 (4 - 17)
per-protocol	65	0	0.00	59	11	18.64	<0.001		100% (70% - 100%)	5 (4 - 13)
Subset of participants reporting an attachment time of >24 h										
modified-intention-to-treat	345	4	1.16	193	6	3.11	0.173	2.68 (0.77 - 9.39)		
per-protocol	268	1	0.37	183	6	3.28	0.018	8.79 (1.07 - 72.38)	89% (29% - 98%)	34 (17 - 913)
Only cases caused by *B. burgdorferi* s.l. positive ticks										
modified-intention-to-treat	1034	3	0.29	643	14	2.18	<0.001	7.5 (2.17 - 26.01)	87% (57% - 96%)	53 (32 - 140)
per-protocol	789	0	0.00	626	13	2.08	<0.001		100% (77% - 100%)	48 (31 - 109)

- ES bénins, 5-30% des patients
- Si symptômes : 97% ECM, 1% Lyme disséminé
- Harms MG et al. J Infect 2021 ; Zhou G et al. BMC Infect Dis 2021



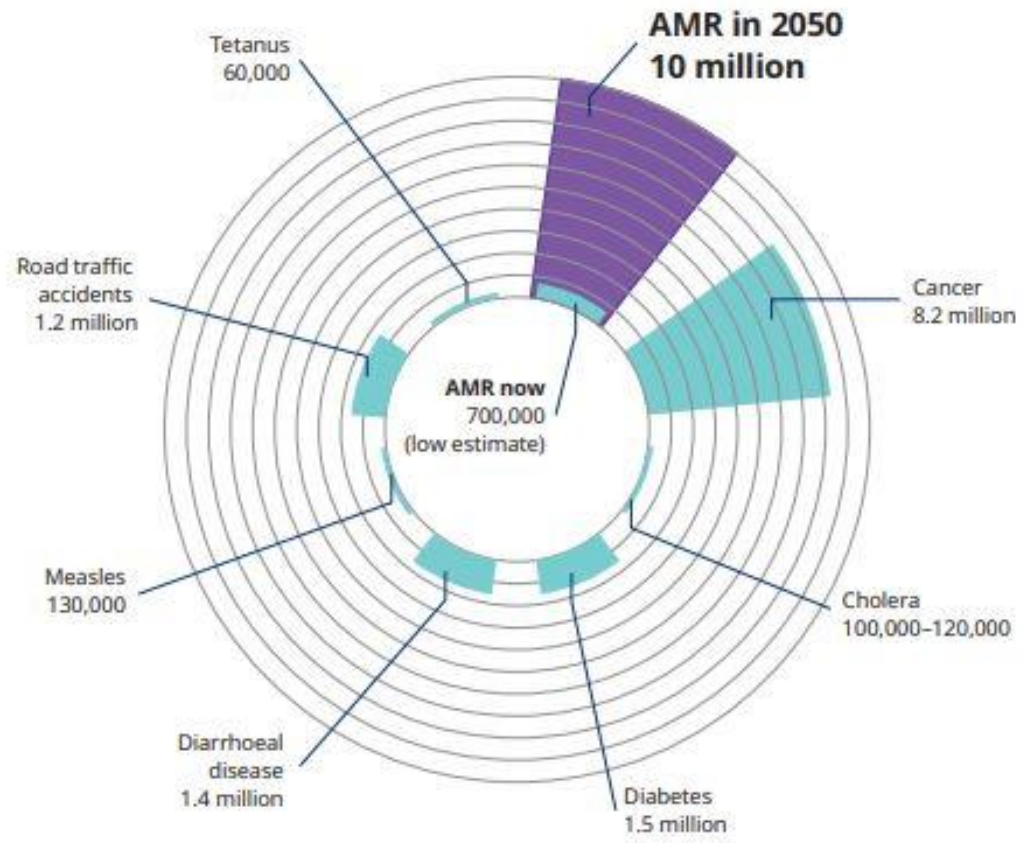
- Harms MG et al. J Infect 2021

Quel risque veut-on réellement prévenir ?



- Kullberg BJ et al. BMJ 2020

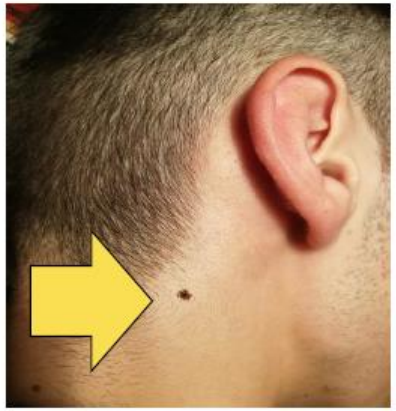
De l’importance du bon usage



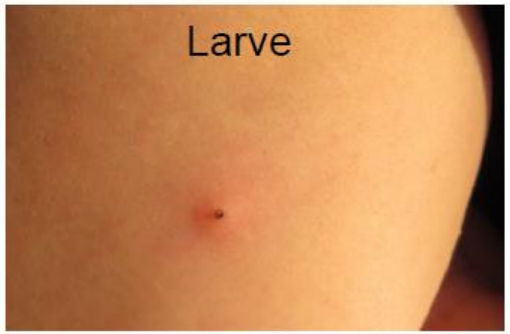
Source: O'Neill Review, May 2016

Que recommande-t-on après une exposition aux piqûres de tique ?

- Inspection corporelle minutieuse, sans oublier le cuir chevelu - grade AE
- Le jour même et le lendemain - grade AE



Les piqûres d'*Ixodes ricinus*



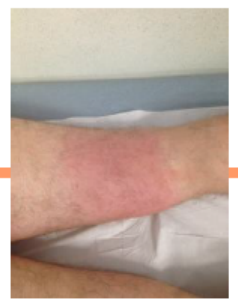
Nymphe d'*Ixodes ricinus*, gorgée et non gorgée

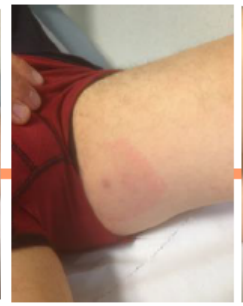
Que recommande-t-on après piquure de tique ?

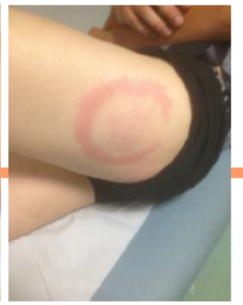
- Retirer la tique : extraction mécanique - grade AE
  - Crochet à tique
  - Pince fine

- Désinfecter la peau & se laver les mains - grade AE

- Auto/hétéro-surveillance pendant 4 semaines après piquure de tique - grade AE
  - Lésion cutanée ?
  - Fièvre ?







En 2019, il n'est plus/pas recommandé :

- de prescrire une antibioprophylaxie - grade B

(quel que soit le terrain, le nombre de tiques retirées, la durée d'attachement, le niveau de gorgement et la stase de la tique)

- de prescrire une sérologie en l'absence de symptômes évocateurs (borréliose de Lyme ou autre MVT) - grade A

- de pratiquer un auto-test - grade A

- d'envoyer la tique dans un laboratoire (ou de tester la tique à l'aide d'un test rapide) pour détection d'agents infectieux, dans l'objectif de prescrire une antibiothérapie à la personne piquée - grade A

Recommandation SPILF 2019

The risk of developing Lyme borreliosis after a tick bite is < 5%, even in high-endemicity areas and following prolonged attachment of the tick [11]. Consequently, after a tick bite sustained in France:

- serodiagnosis [12] or a self-performed test is not recommended (grade A);
- performing tests on the extracted tick to look for infectious agents is not recommended (grade A);
- initiating an antibiotic therapy is not recommended, irrespective of the patient's age, of the attachment duration, and of the stage of development of the extracted tick (grade B).

Recommandation HAS 2018

Conduite à tenir en cas de piqûre

L'abstention thérapeutique avec une surveillance rapprochée est recommandée à la condition expresse de l'absence d'érythème migrant ou d'autres symptômes liés à des MVT.

- Aucun risque infectieux supplémentaire n'a été démontré chez la femme enceinte.
- Aucun risque infectieux supplémentaire n'a été démontré chez l'enfant de moins de 8 ans.
- Chez le patient immunodéprimé, il existe un risque accru d'autres MVT.

Il n'y a pas de recommandation spécifique dans ces trois cas particuliers, mais un avis spécialisé peut être demandé auprès d'un infectiologue, d'un gynécologue-obstétricien ou d'un pédiatre.

Recommandation IDSA 2020

III. Who should receive antibiotic prophylaxis to prevent Lyme disease following presentation with a tick bite?

Recommendation

1. We recommend that prophylactic antibiotic therapy be given only to adults and children within 72 hours of removal of an identified high-risk tick bite, but not for bites that are equivocal risk or low risk *(strong recommendation, high-quality evidence)*. **Comment:** If a tick bite cannot be classified with a high level of certainty as a high-risk bite, a wait-and-watch approach is recommended. A tick bite is considered to be high-risk only if it meets the following three criteria: the tick bite was from (a) an identified *Ixodes* spp. vector species, (b) it occurred in a highly endemic area, and (c) the tick was attached for ≥36 hours.

- https://www.idsociety.org/practice-guideline/lyme-disease/#FullRecommendationsforthePrevention,Diagnosis,andTreatmentofLymeDisease

Recommandation IDSA 2020

Rationale for Recommendation

For high-risk tick bites, we have weighed the likelihood of disease and the effectiveness of prophylactic doxycycline therapy to be higher than the potential risks of the antibiotic. For ticks that have not been identified as an *Ixodes* spp. vector species or are *Ixodes* spp. but do not meet high-risk criteria, the risk of adverse reactions from antibiotic exposure may not be matched by a likely benefit. Because of uncertainty about the safety of doxycycline in pregnancy, we advise pregnant women to have an informed discussion with their physicians about the risks, benefits, and uncertainties of antibiotic treatment versus observation.

Regardless of whether antibiotic prophylaxis is given, clinicians should counsel patients about the symptoms and signs of local *Ixodes* spp.-borne infections. First, prophylaxis with doxycycline does not guarantee infection avoidance. For instance, data from a laboratory animal study [149] suggest that mitigation of transmission by oral doxycycline is most successful when taken soon after tick removal. Thus, patients should be advised to seek medical attention if they develop an expanding erythematous lesion at the site of the tick bite or other skin sites, fever, or any other unexplained illnesses, particularly within 30 days of the tick bite. Second, *I. scapularis* ticks may transmit pathogens causing other diseases, including anaplasmosis, babesiosis, and ehrlichiosis, for which systematic data supporting postexposure antibiotic prophylaxis currently do not exist.

- https://www.idsociety.org/practice-guideline/lyme-disease/#FullRecommendationsforthePrevention,Diagnosis,andTreatmentofLymeDisease

Quel avenir ?

- Arriver à identifier les situations à haut risque de transmission pour diminuer le nombre de sujets à traiter pour éviter un évènement ?
  - Scores cliniques
  - PCR sur tiques
    - Mais échecs antérieurs de point-of care test

Hofhuis A et al. Plos One 2017

Sprong H et al. Parasit Vectors 2013

- Traitement topique pour limiter le risque iatrogénique ?
  - Mais niveau de preuve insuffisant à ce jour

Zhou G et al. BMC Infect Dis 2021
Schwameis M et al. Lancet ID 2017

Merci de votre attention

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