

Lyme disease

The bacteria and clinical symptoms

Lecture
on 8.1.2013
at
Nutech Mediworld
(Medical Director:
Geeta Shroff, MD)
New Dehli



**Here we are: The tick family (*Ixodes ricinus*)
Larva- Nymph - adult female and male tick, all
transmitter of *Borrelia* s.l.**



„Honeymoon“ before mating



Foto: Frau Polack

I am hungry and
patiently waiting for a
host to grab and adhere
to.....



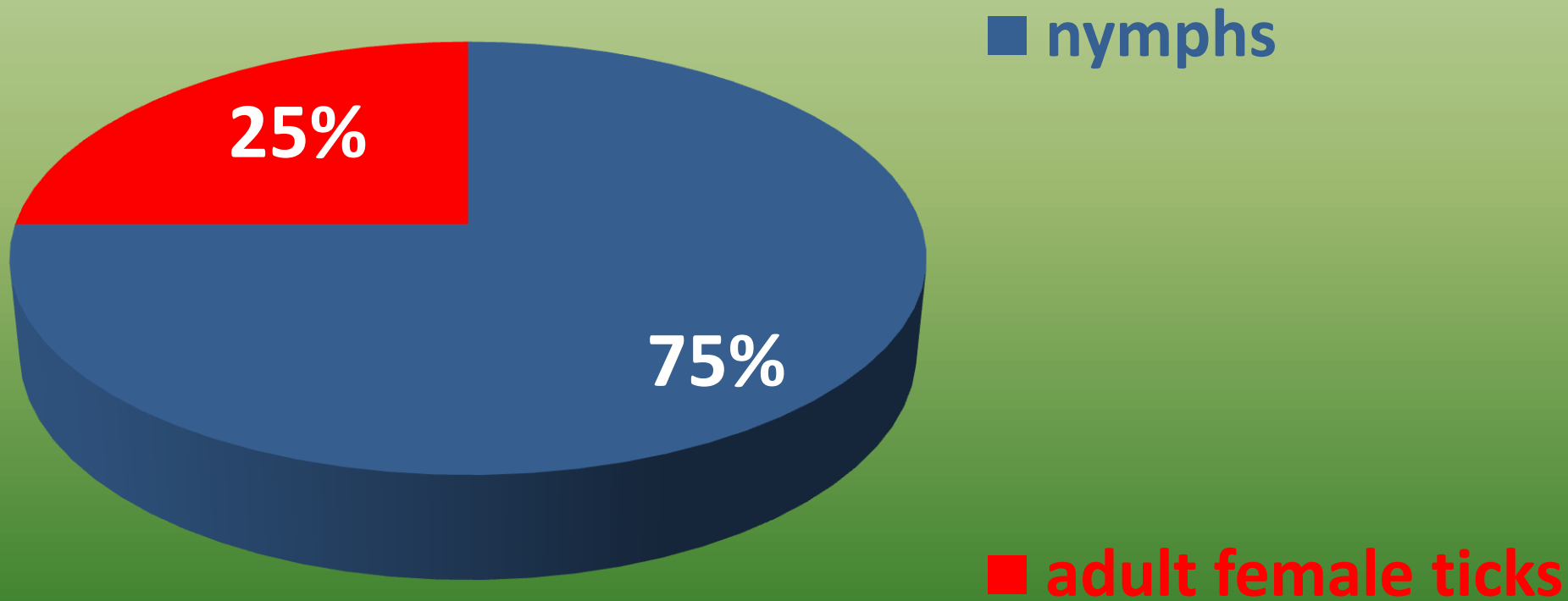
Foto: Frau Polack

The tiny tick nymph is mostly transmitting *Borrelia s.l.*



Foto: Frau Heidi Polack

Transmission rate from nymphs and adult female ticks to humans





**Adult female tick
firmly attached to a human host**

Foto: Frau Polack

Symptoms in early stage of infection with *Borrelia burgdorferi* s.l.

Contact
with a tick
after
1-2 weeks



Flu-like
symptoms

with or without
Erythema migrans

with or without fever

with or without
musculo-skeletal pain

generally with a great
deal of exhaustion

there is mostly a change in the general
condition for the worse or there is a
„silent period“ without any clinical sign)

Typical bull`s eye rash (Erythema migrans)



...but 13 days after the tick bite the same rash can easily be overlooked



Foto privat

A rash (EM) 10 days after a tick bite`s infection with *Borrelia s.l.*



Erythema migrans (EM), vaguely edged out



Lymphocytoma, typical for children



EM, 4 days after a tick bite, quite similar to the efflorescences of a beginning herpes zoster, but with intense back pain



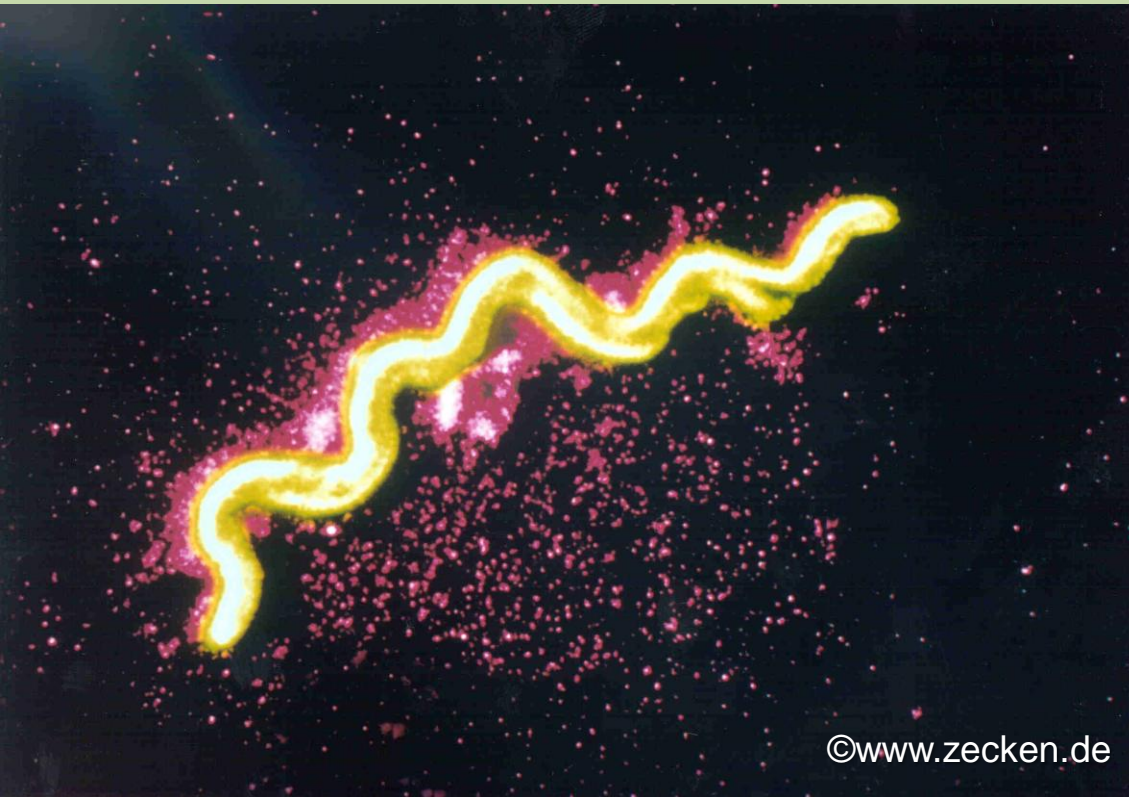
Chronic EM, after 7 years of local treatment with Corticoid cremes



The same EM, 4 weeks after Minocyclin treatment



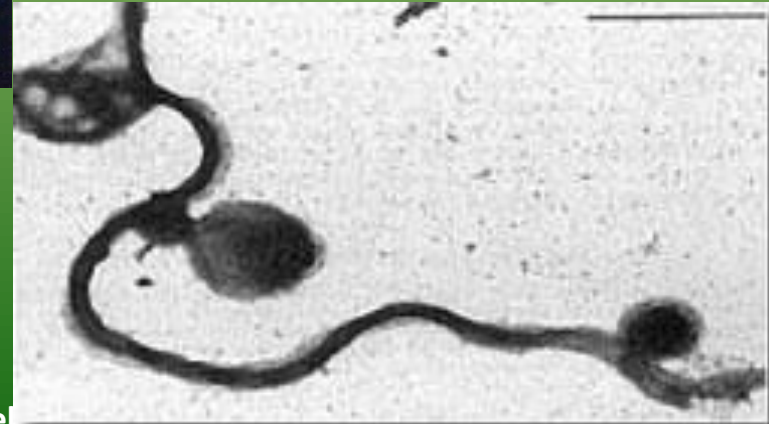
What happens after an infection with *Borrelia s.l.*



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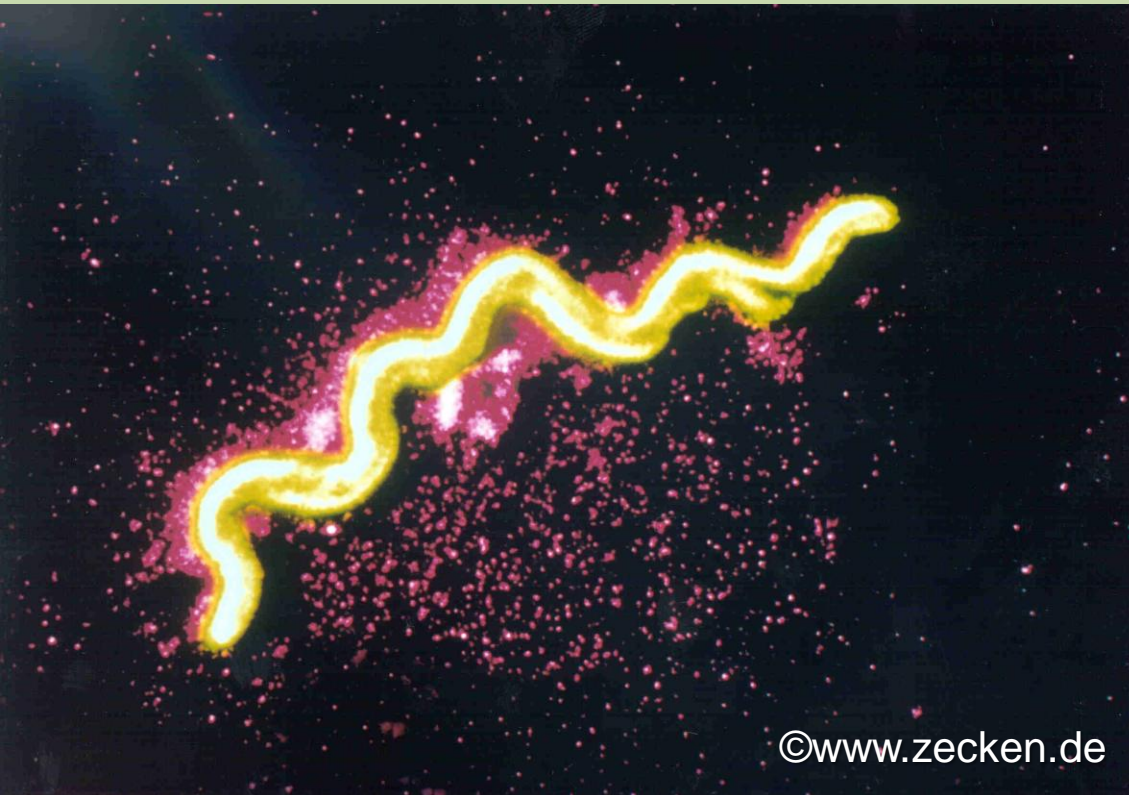
The spirochetes divide themselves every 12-24 hrs starting immediately after the host's infection. They rebuild their cell wall continuously. The lipopolysaccharides of the cell wall have an antigen effect and therefore the host's immunsystem forms antibodies

Borrelia are able to build persistent forms, the so-called round bodies (blebs, cysts, L-forms) and biofilms. They stimulate Th 1-cytokines like TNF-alpha, IFN gamma, IL 1 beta with the consequence of a chronic persistent infection.



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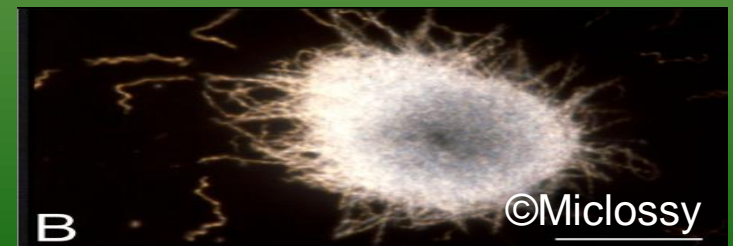
The different stages of viable *Borrelia* s.l. demand adequate treatment regimes



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All the intracellular persister forms can be treated with Tetracyclines (best Minocyclin), with Makrolides (Clarithromycin, Azithromycin), but always in combination with Tinidazol (Fasigyn®) or Rifampicin

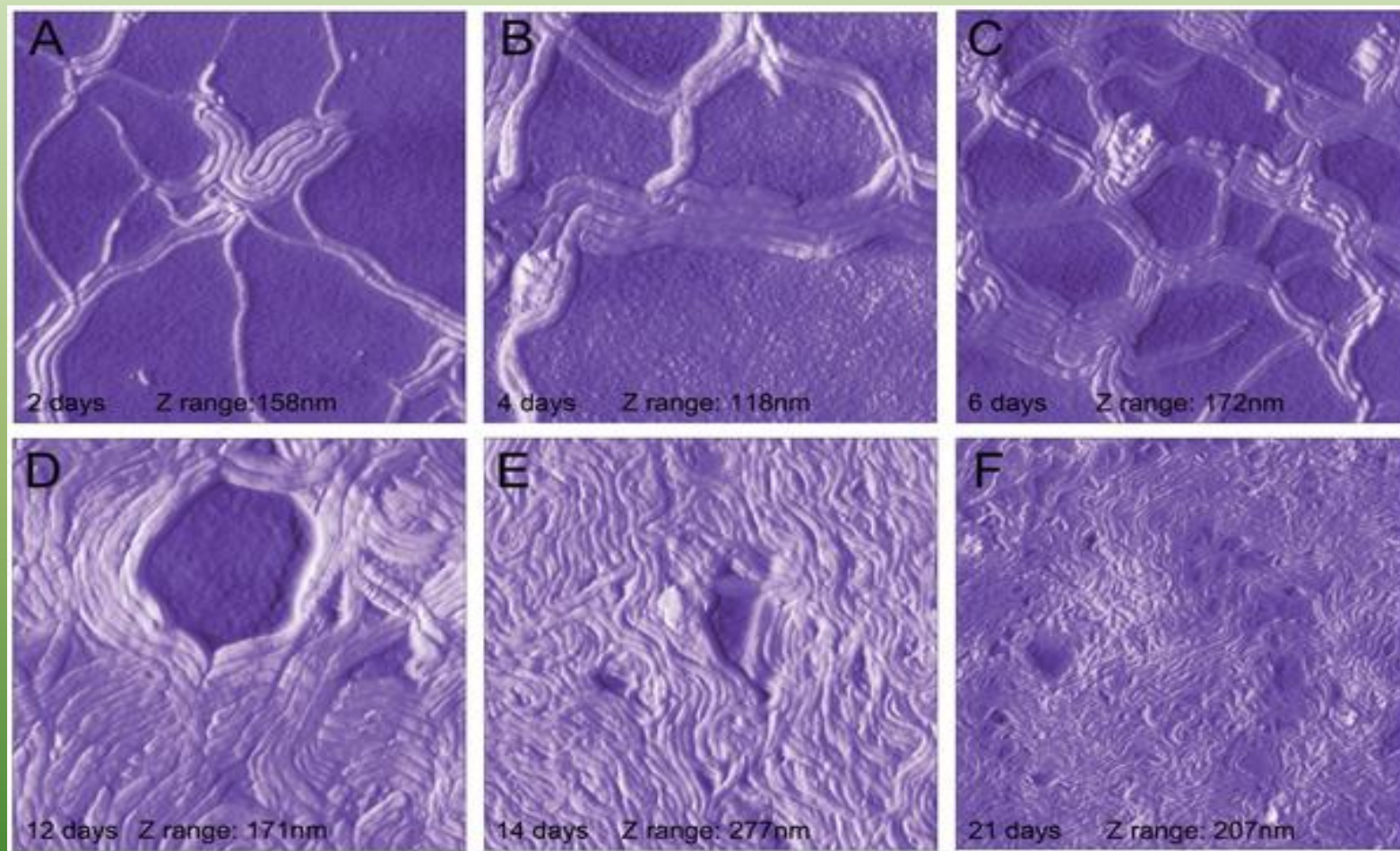
As long as the spirochetes divide themselves they can be treated with cell wall synthesis inhibitors like Cephalosporines (Amoxicillin®, Cefuroxim®) or Betalactames (Ceftriaxon®, Cefotaxim®) or Tetracyclines (Minocyclin or Doxycyclin)



B

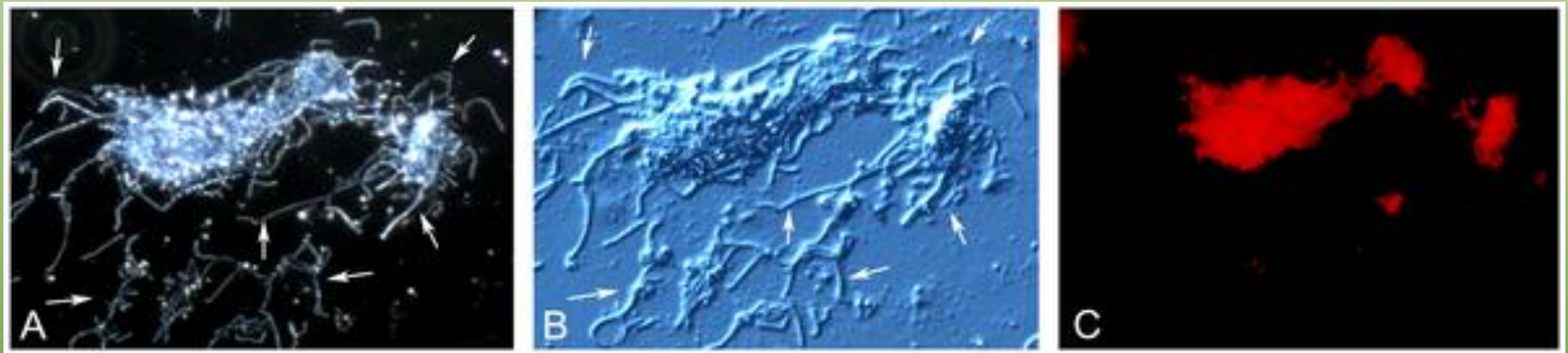
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Figure 2. Three-dimensional AFM images of aggregate development of *Borrelia burgdorferi* B31 strain on agarose substrate after 2 days (A), 4 days (B), 6 days (C) 12 days (D) 14 days (E) and 21 days (F).



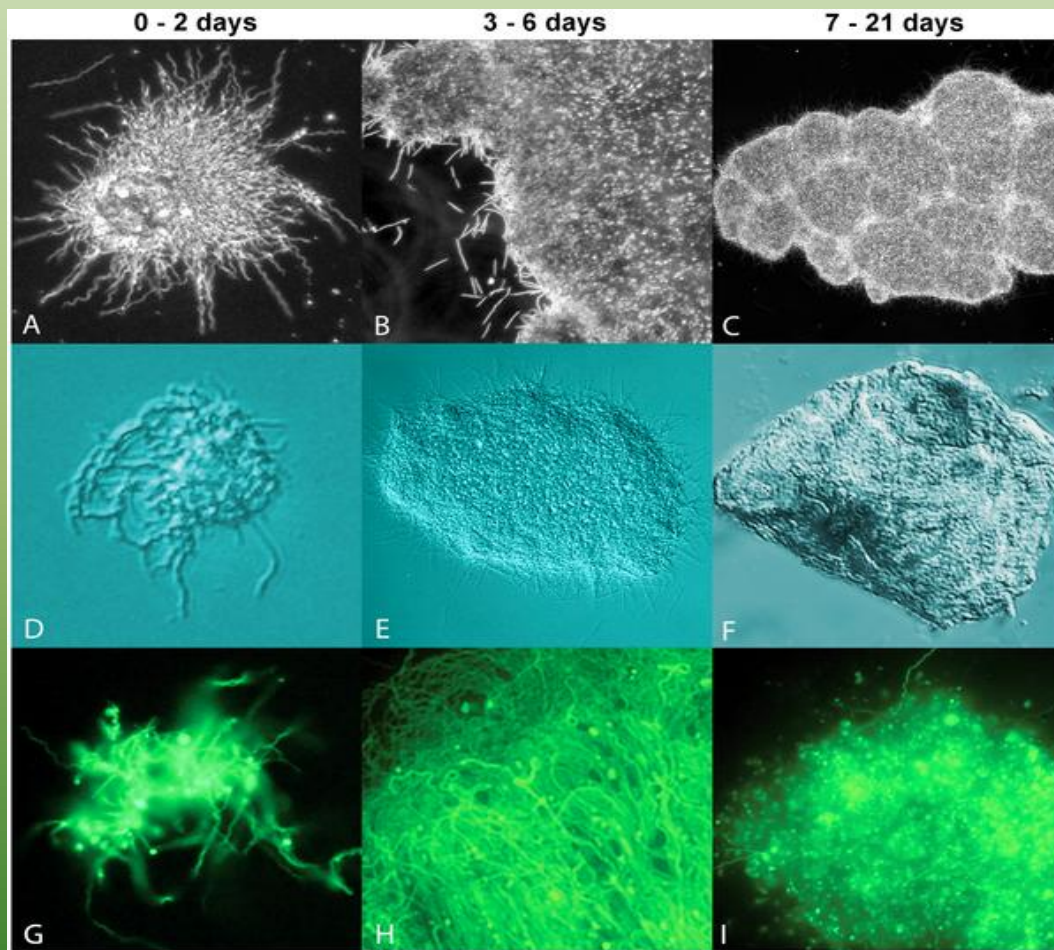
Sapi E, Bastian SL, Mpoy CM, Scott S, et al. (2012) Characterization of Biofilm Formation by *Borrelia burgdorferi* In Vitro. PLoS ONE 7(10): e48277. doi:10.1371/journal.pone.0048277
<http://www.plosone.org/article/info:doi/10.1371/journal.pone.0048277>

Figure 8. *Borrelia burgdorferi* B31 aggregates surrounded by individual spirochetes (marked with white arrows) stained with the DDAO [7-hydroxy-9H-(1, 3-dichloro-9, 9 dimethylacridin-2-one DNA binding fluorescent dye.

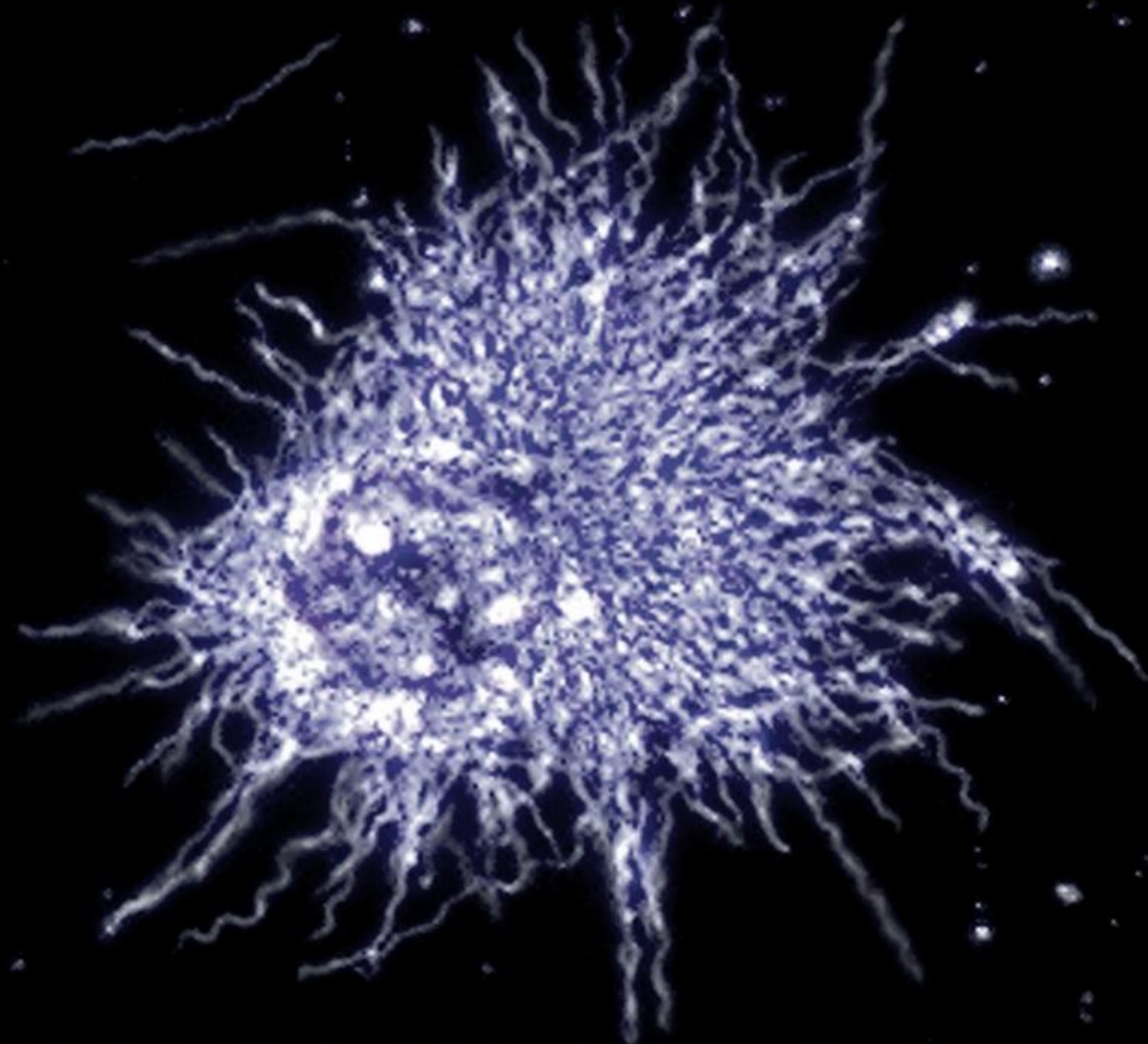


Sapi E, Bastian SL, Mpoy CM, Scott S, et al. (2012) Characterization of Biofilm Formation by *Borrelia burgdorferi* In Vitro. PLoS ONE 7(10): e48277. doi:10.1371/journal.pone.0048277
<http://www.plosone.org/article/info:doi/10.1371/journal.pone.0048277>

Figure 1. Representative images of *Borrelia burgdorferi* B31 strain aggregates in the early (1st column, 0 to 2 day), middle (2nd column, 3 to 6 days) and late (3rd column, 7 to 21 days) stages of development, observed with dark field (A, B, C – 400× magnification); differential interference contrast (D, E, F - 400× magnification); and FITC-band epifluorescence (G, H, I – 400× magnification).



Sapi E, Bastian SL, Mpoy CM, Scott S, et al. (2012) Characterization of Biofilm Formation by *Borrelia burgdorferi* In Vitro. PLoS ONE 7(10): e48277. doi:10.1371/journal.pone.0048277
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B. burgdorferi early development of biofilm-like structure

dark field 40X

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Treatment of an early stage of Lyme disease (LD)

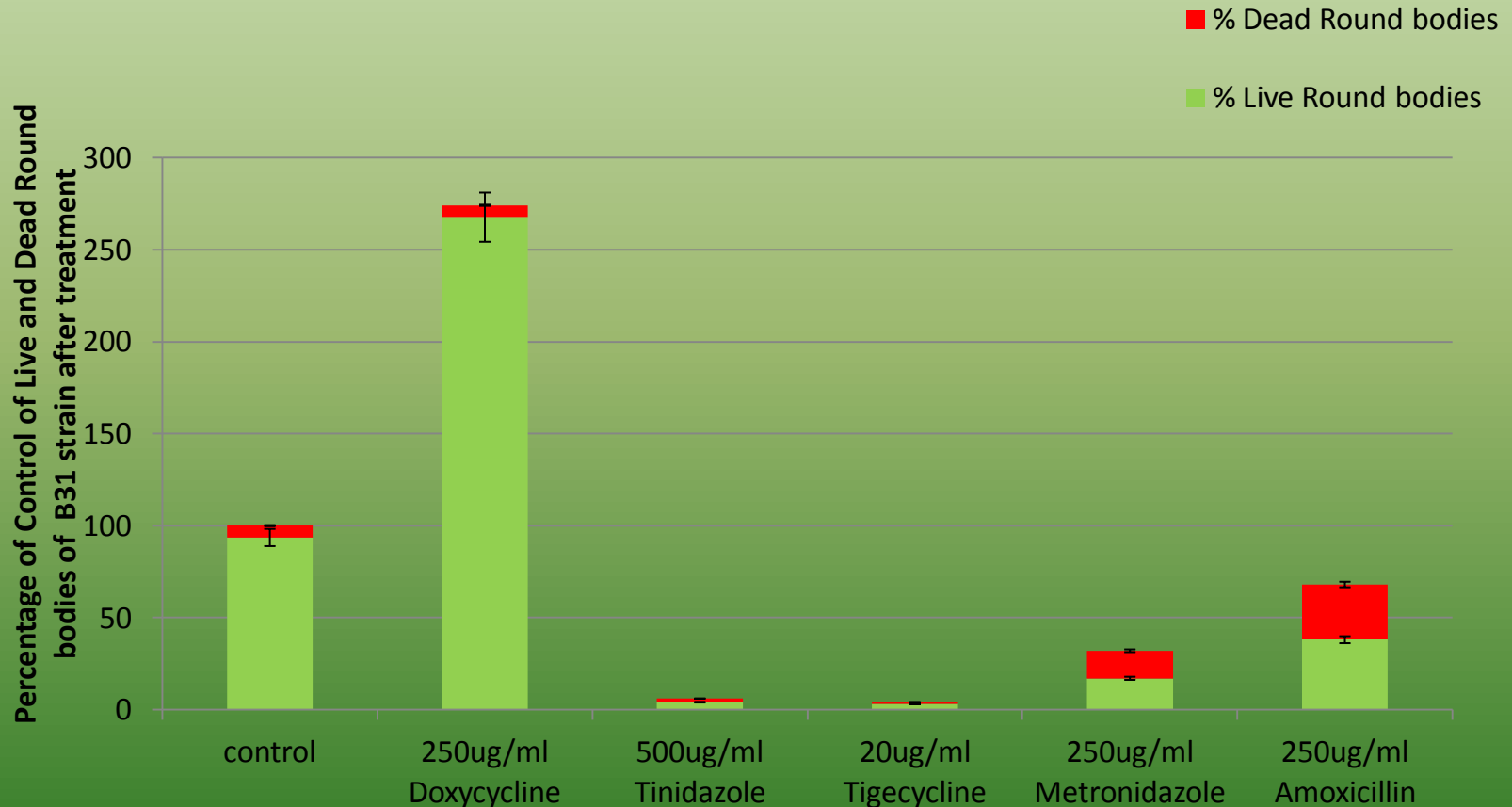
- **Amoxicillin** 3 x 1000 mg for 30 days (especially for pregnant women, for children according to weight)
- **Clarithromycin** 2 x 500 mg (starting with half the dose over a period of 4 days) for 30 days for adults, weight adapted for children (7,5 mg/kg body weight bid).
- **Minocyclin** with 2 x 100 mg for patients of 50 -70 kg bodyweight (always start with only 50 mg/day and then increase slowly 50mg more every 3 days to prevent the possible sideeffects headaches and vertigo)

Treatment of a late stage of Lyme disease

- **Azithromycin** 500 mg-600 mg /day for 4 days, then 3 days off because of the intracellular accumulation of the drug
- **Doxycyclin/Minocyclin** should always be given in **combination** with **Hydroxychloroquine** (Quensyl[®]) , **Tinidazol** (Fasigyn[®]) or **Rifampicin** (Rimactane[®], Rimpacin[®]) to prevent the formation of round bodies and biofilms. Only with this combination the viability of *Borrelia* s.l. can be reduced enough to prevent the clinical relapses.

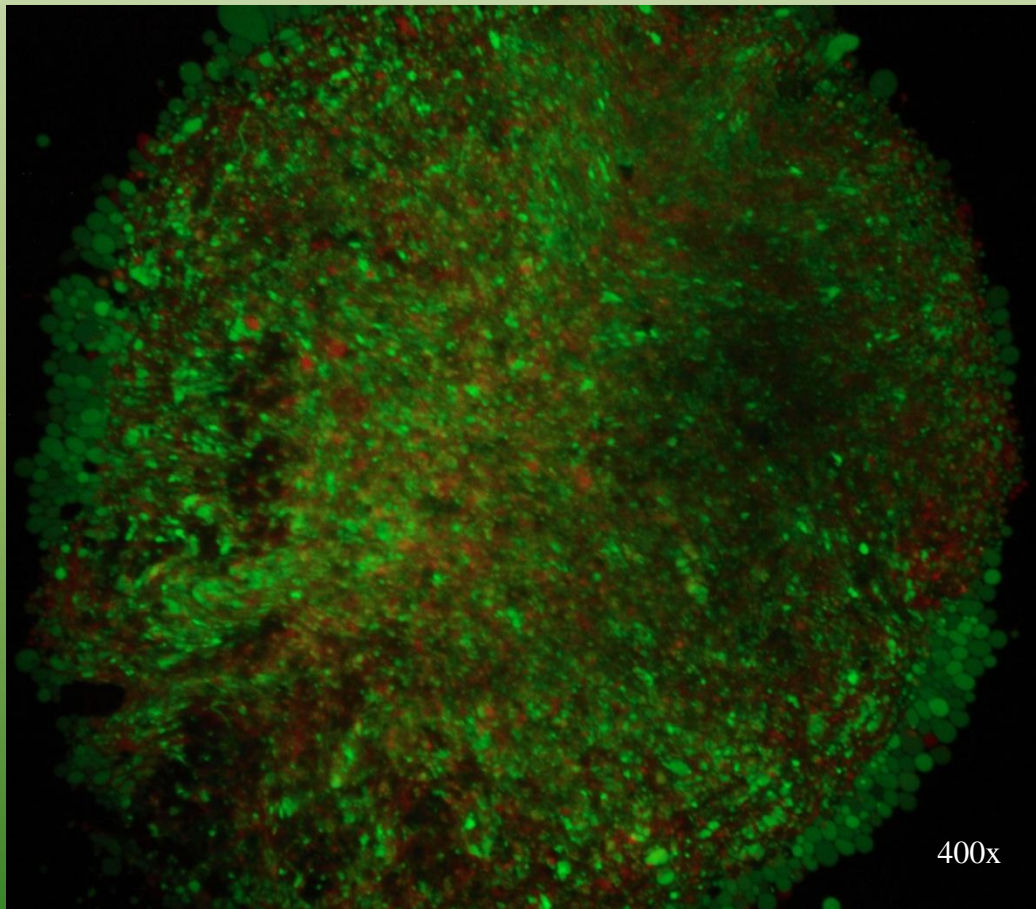
Very recent study results of Eva Sapi, Ph.D., show which drugs are the most effective against different life forms of *Borrelia* (see references)

Evaluation of live/dead spirochete and round body forms of *B. burgdorferi* following various antibiotics treatment

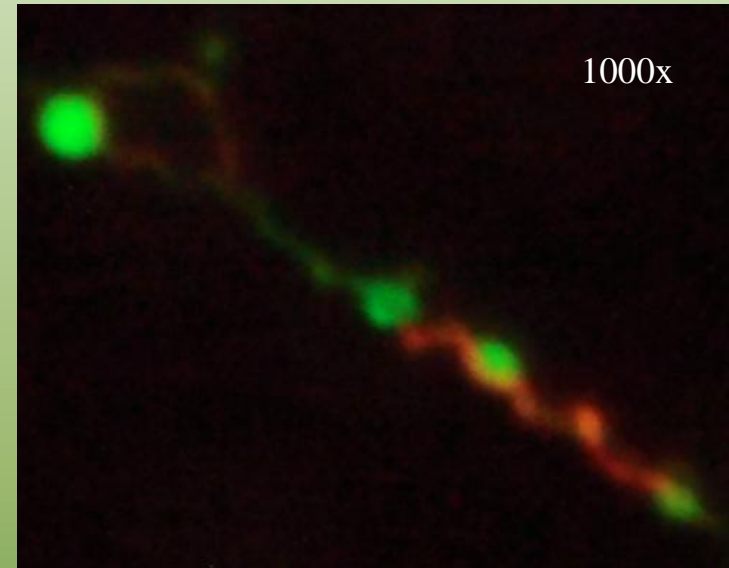


©Sapi E et al 2011

Doxycycline treated biofilm and spirochete

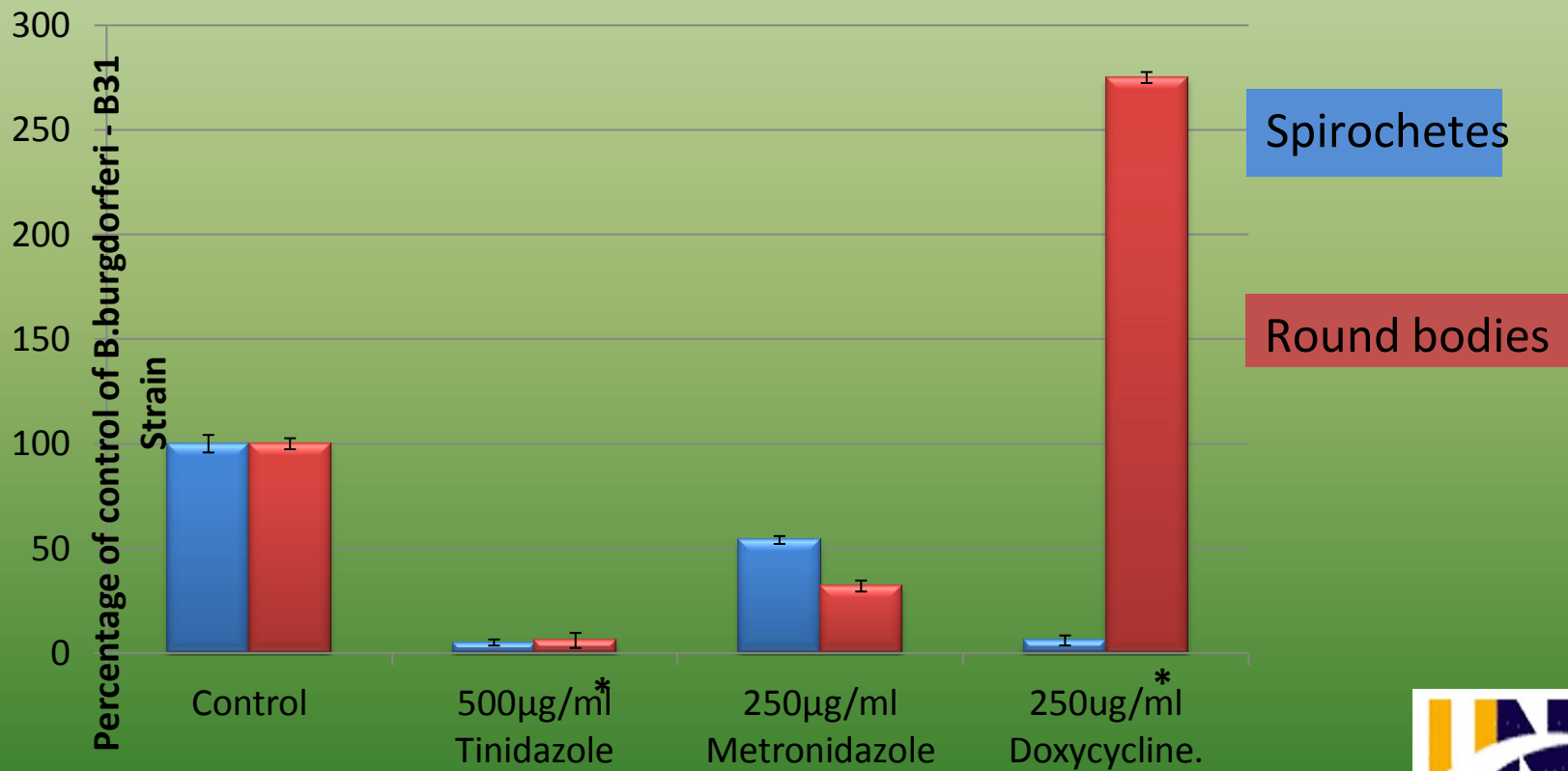


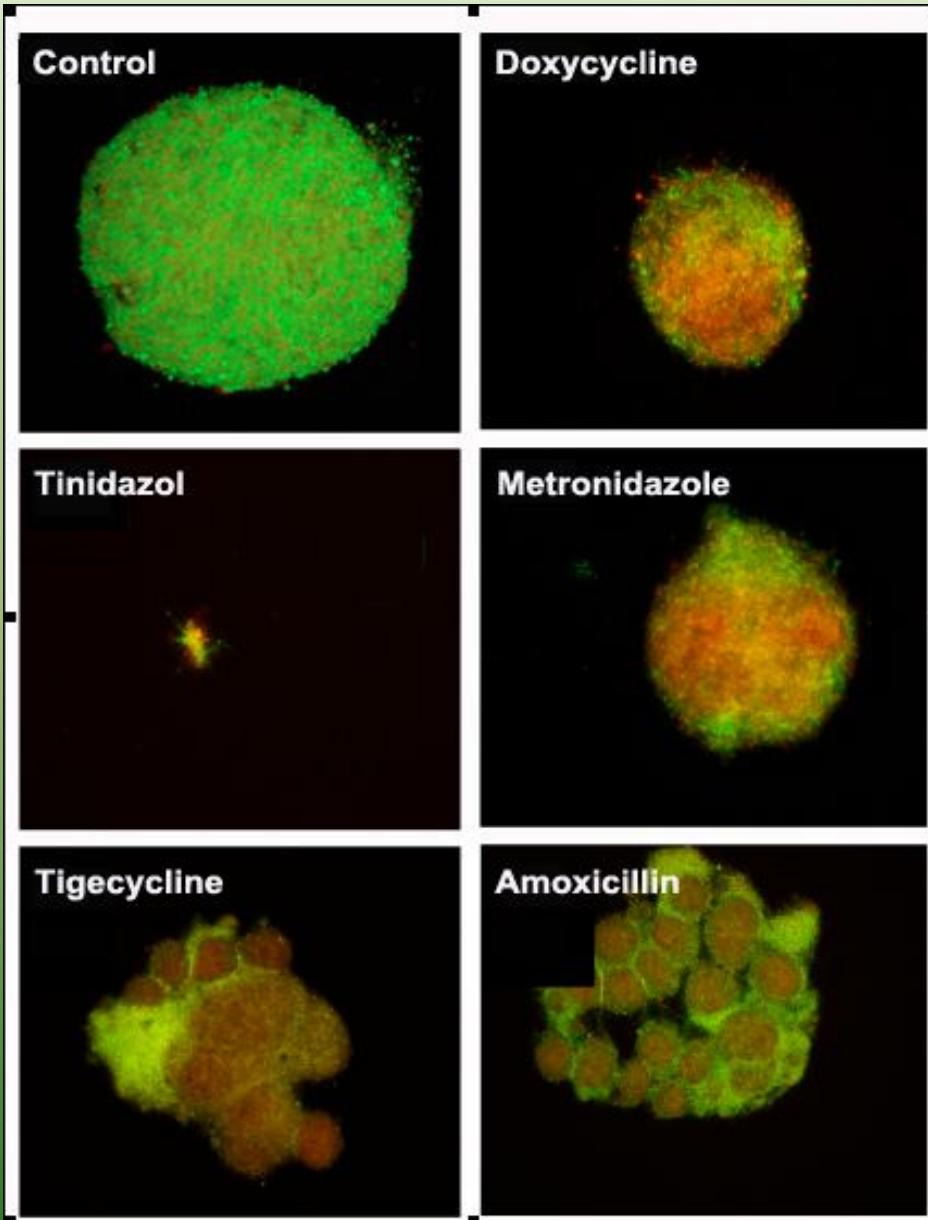
D. Luecke, Kaur N and E Sapi unpublished data 2010



Red stain: Dead
Green stain: Viable

Effect of Different Antibiotics of the Spirochete and Round Body formation of *Borrelia burgdorferi* -3 weeks

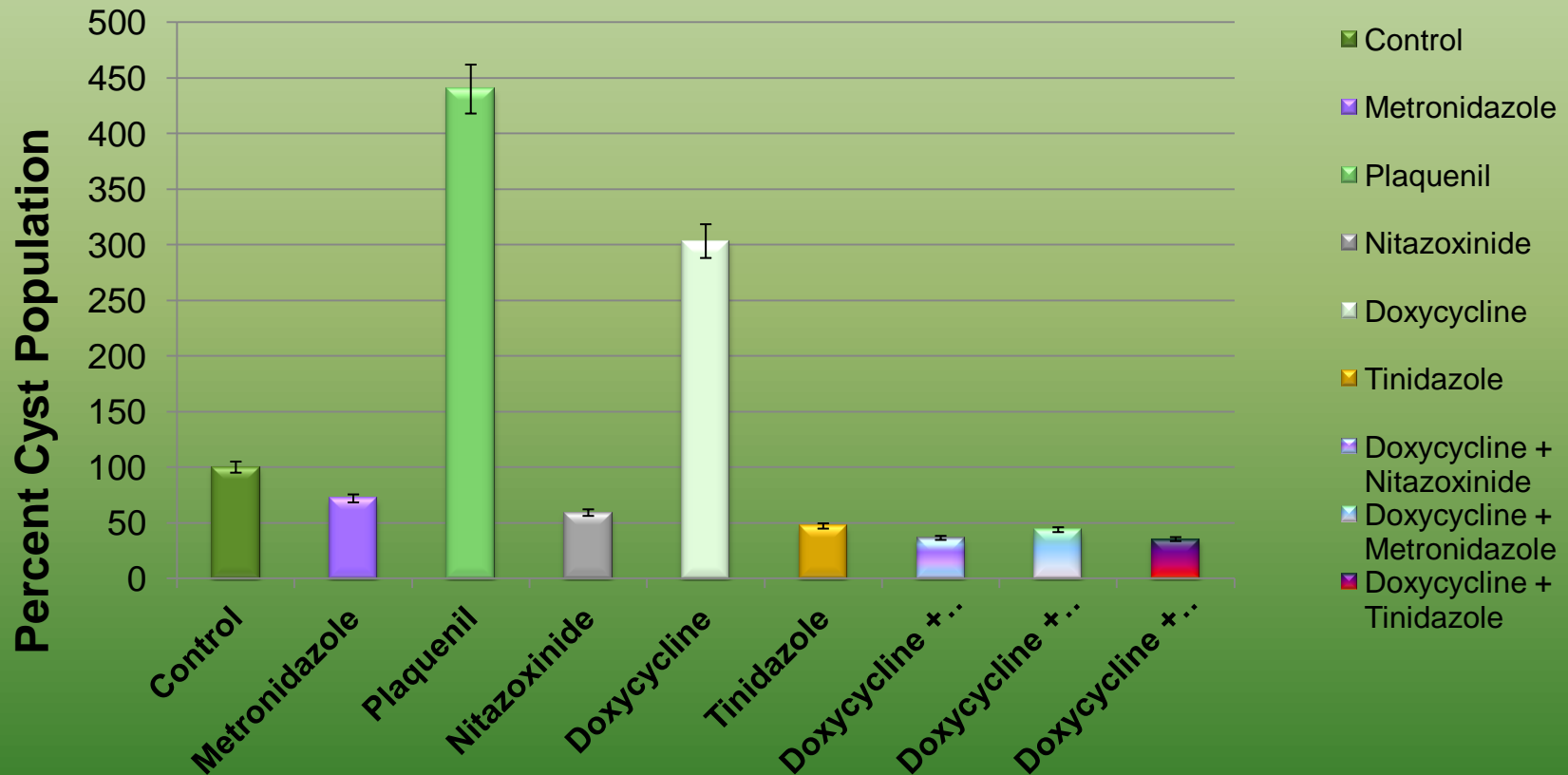




Red stain: Dead
Green stain: Viable

Effect of antibiotics on the biofilm-like colonies of *Borrelia* measured BacLight staining

Effect of Quensyl, Doxycyclin and combined treatment on cysts



© Prof. Sapi



Effective Antimicrobials for the Different Forms of *Borrelia burgdorferi*

Priyanka, A.S., Theophilus, M.S., Divya Burugu, B.S., Akhila Pourers, B.S., Daniel S. Phillips, B.S., David F. Luecke, B.S. Eva Sapi Ph.D¹
Lyme Disease Research Group, Department of Biology and Environmental Sciences,
University of New Haven, CT, 06516

Our data show that the combination treatment including doxycycline and HCQ, doxycycline and rifampicin, resulted in a significant reduction in the numbers of spirochetal form by 75%-58% and round body forms by 91%-73%. Doxycycline reduced the spirochetal forms by 65% but showed a marked increase in the round body form at higher concentration. The treatment with minocycline also show similar trends but less effective than doxycycline. HCQ at high concentration (20 µg/ml) reduced the spirochete forms by 40% and the round bodies by 82%. Rifampicin reduced the spirochete form by 73% and round body form by 82% which also show considerable effect in reducing the spirochetal and the round body forms. When quantitative effects on biofilm were evaluated, the four antibiotics reduced the formation of colonies by 29-37%. The Doxycycline + HCQ combination treatment reduced the colony formation by 37%. In terms of qualitative effects, only doxycycline and the combination treatment involving doxycycline and HCQ reduced viable organisms by 30%. Following treatment with other antibiotics, viable organisms were detected in 70-80% of the biofilm.



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Conclusions:

As our previous report demonstrated¹, antibiotics show varying effects on the different morphological forms of *Borrelia*. Persistence of the round body forms and biofilm may explain the reason for relapse when antibiotic treatment is discontinued.

Therefore in conclusion the **combination treatment involving doxycycline and HCQ show significant reduction in all the three forms of *Borrelia***, and hence they **might provide better clinical responses for Lyme disease patients.**

HCQ = Hydroxychloroquine (Quensyl®, Plaquenyl®)

General recommendations for treating chronic - persistent Borreliosis/LD

- The earlier given recommendations of treatment for LD for **14 -21 days only** with 200 mg **Doxycyclin** alone or **2g Ceftriaxon** (Rocephin[®], Monocef[®]) alone should be revised as it could be demonstrated in vitro that these drugs, if given alone, will even form round bodies and biofilms. These forms most probably **lead to chronic LD with relapses.**
- **Combinations** of antibiotics are much more effective than single drugs given against *Borrelia* s.l.
- Antibiotics should always be effective **intracellular** when treating chronic LD

References:

Sapi, Eva: www.evasapi.net

Sapi, Eva: Killing Borr. burgd.- is it possible? (PP-Vortrag 3/12 Saarbrücken)

Sapi, E. and Mac Donald, A.: Biofilms of Borr. burgd. in chronic cutaneous borreliosis in: Am.J.Clin.Pathol. 129, 2008, 988-989

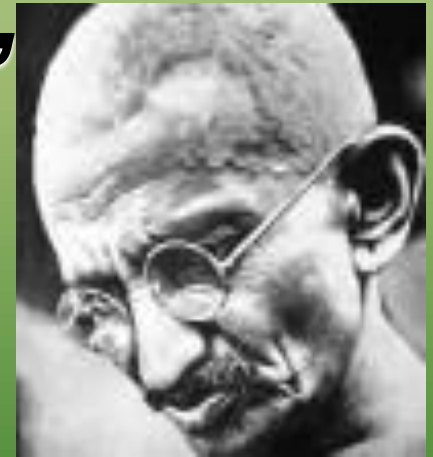
Priyanka A.S., E.Sapi et al: Effective antimicrobials for different forms of Borrelia burgdorferi, Poster presentation of the Univ.of New Haven 2012

Sapi,E., Bastian, SL., Mpoy CM, Scott S, Rattelle A, et al (2012)
Characterization of Biofilm Formation by Borrelia burgdorferi in Vitro.
PLoS ONE 7 (10), 1-11:e48277.doi:10.1371/journal.pone.0048277

Brorson, O. et al: An in vitro study of the susceptibility of mobile and cystic form fo Borr. burgd. to Tinidazol
in: Int. Microbiol. 7(2):139-140

Dear Dr. Shroff,
this applies equally to you and your wonderful work to make the „incurable“
ailments of mankind treatable....don`t give in !

***First they ignore you,
then they laugh at you,
then they fight you
and then
you win!!***



***Mahatma Gandhi
(1869-1948)***

More information you may find
online: www.dr-hopf-seidel.de or in my book



ISBN 3426873923

Thank you for your attention