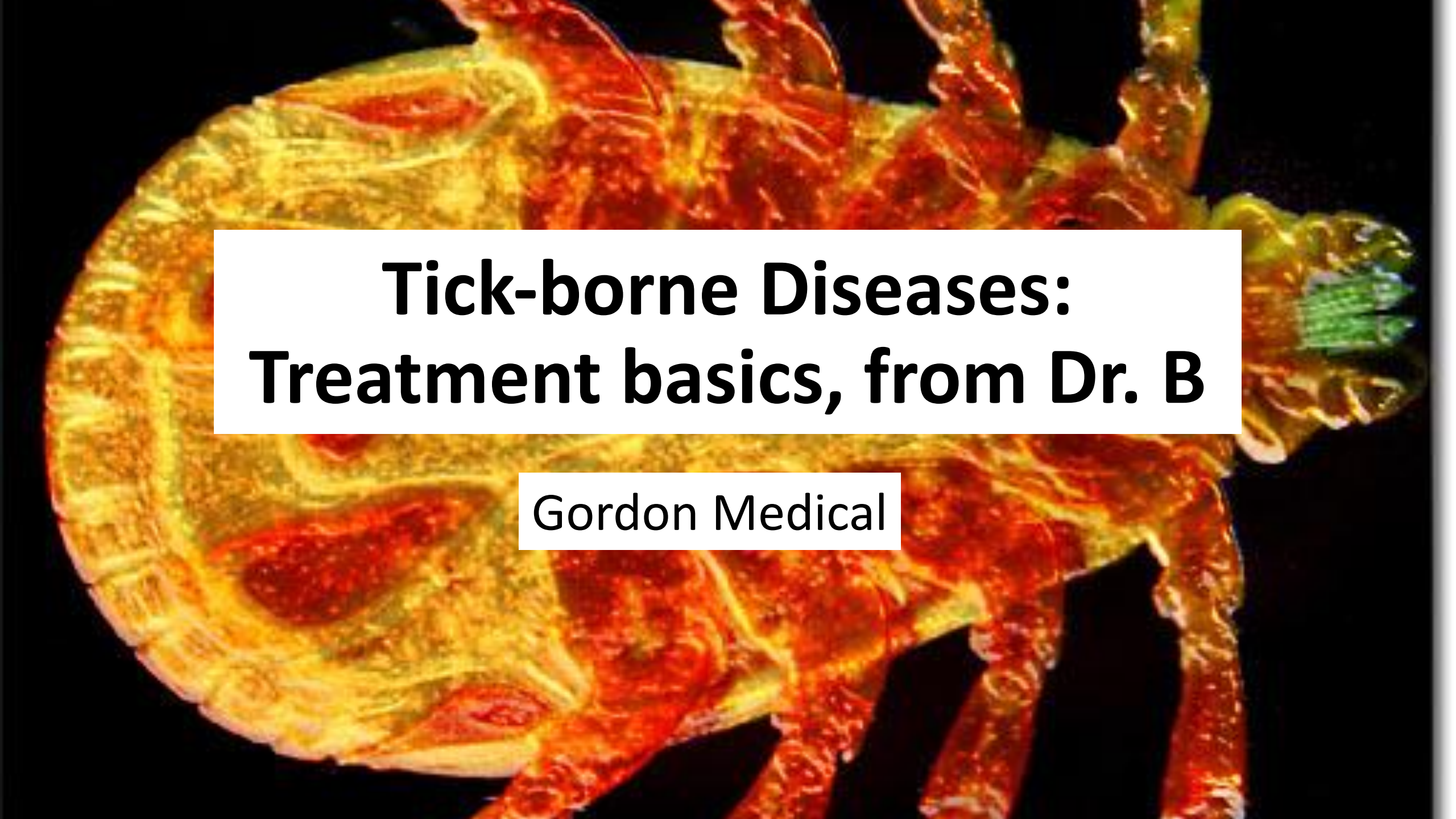

Tick-borne Diseases: Treatment basics, from Dr. B

Gordon Medical

Rapid transmission of pathogens

- Lyme disease: W. Burgdorfer: “5-10% of ticks that are carrying Lyme Disease have a systemic infection and have the microbes in their saliva and can transmit it as soon as they bite.”
- Relapsing fevers can be transmitted in as little as one minute or less (soft-bodied ticks)
- Bartonella is found in tick saliva so rapid transmission is likely
- Rickettsias (Ehrlichia, Anaplasma, RMSF) and arboviruses are also present in tick saliva
- Babesia- “Invasion of the salivary gland by B. microti occurs before feeding of the nymph begins, and development of the parasite is further stimulated by feeding.”

Early dissemination of Lyme: (P. Coyle, SUNY Stony Brook, International Lyme Congress, 3/26/2000)

- “B. burgdorferi can be found in the CNS within hours of exposure”
- “Have seen CNS Lyme even before the appearance of Erythema Migrans.”
- “CSF in late Lyme:
  - Immune complexes in 30%
  - Elevated protein in 7%
  - Intrathecal antibody production in 7%
  - Monoclonal and oligoclonal bands in 3%

Treating acute Lyme

- To understand what is needed, must understand the biology of the pathogens
- Lyme Borrelia have a four-week cyclic pattern of growth, and can only be killed during their growth phase
- Therefore, any effective treatment must fully bracket this four-week cycle. So for confirmed, active early Lyme, 4 weeks is minimum and six weeks is recommended
- Note that doxycycline is only bacteriostatic, so even six weeks of this may NOT prevent chronic Lyme. This argues against use of doxy for early Lyme but favors amoxicillin or cefuroxime

Treating acute Lyme

- Clearly, single dose doxycycline is totally insufficient and must never be used
- What about co-infections? Cell wall drugs are ineffective against the Rickettsias, which can rapidly progress to a fatal disease

My solution: a hybrid regimen:

- Begin with two weeks of doxycycline to cover the Rickettsias. This may not kill all Borrelia, but will keep them in check
- After doxy ends, switch to cefuroxime for another four weeks. This then covers the Borrelia
- In early disease, this hybrid regimen seems to also prevent Bartonella and possibly Babesia too

Time-killing curves of antibiotics in Lyme

Cell wall drugs (penicillins, cephalosporins, vancomycin, carbapenems, etc.)

- Need SUSTAINED bactericidal levels for 24-36 hours
- Favors multiple daily doses and meds with a long half-life

Tetracyclines- doxycycline, minocycline

- Low doses are bacteriostatic; high doses can be bactericidal
- Need a large spike of dose to be effective
- Favors single large daily dose; favors IV administration

Lyme: Predictors of need for longer duration of therapy

- Multiple bites (at once or serially)
- Active synovitis with high sedimentation rate
- Murmurs
- Hormonally active females

Lyme: Indicators for IV therapy

- Illness for more than one year
- Reactive spinal fluid (↑WBC, ↑Protein)
- Synovitis with high ESR
- Major Cognitive Dysfunction
- Age over 60
- Documented immune deficiency
- Prior use of steroids or other immune suppressants
- Acute carditis
- Acute disseminated illness in first trimester
- Failure or intolerance of oral therapy

Pulse therapy for Lyme

Takes advantage of long time-killing curve for Borrelia, and its slow recovery after antibiotic exposure

- Treat for 2-3 days in a row each week
- No treatments on the other days
- Allows for higher doses
- Better tolerated
- Best way to administer IV meds for Lyme
  - Simple heparin lock
  - Radically decreased treatment side effects

Treatment plateaus

- Reassess diagnosis- any missed co-infections, mold or other toxins, endocrine abnormalities, etc.
- Confirm drug levels
- Change meds
- Change route of administration- oral to IV
- Better targeting of persisters
- Consider “cycle therapy”

Cycle therapy for Lyme treatment plateaus

- To break a plateau after having already been treated for several months
- Once Borrelia are exposed to therapeutic doses of meds, those that are not killed remain dormant (persisters, cysts) for several weeks, then they revert to planktonic growth
- Generally follows a four-week cycle
- So treat until a plateau, then hold meds completely until symptoms begin to increase (generally 3 weeks). This is a sign that the Borrelia have begun to grow
- Then resume full dose treatment to kill the growing Borrelia. Continue for 4-6 weeks then hold meds until symptoms again begin to increase.
- Repeat- usually takes four full cycles to work

Babesiosis

- Just as with Lyme, need to optimize drug levels- atovaquone especially
- Atovaquone is poorly absorbed. Liquid is better than tablets
- Atovaquone efficacy may be inhibited by adding Co Q-10 so avoid giving this
- Doxycycline LOWERS atovaquone levels so avoid co-administration
- Duration for established infection- 4 months minimum

Babesiosis

- Babesia meds all seem to work, at least in part, via oxidative damage to Babesia organelles
- Therefore avoid strong antioxidants and consider adding oxidative therapies
- Because chronic Babesiosis often involves organisms embedded in biofilms and fibrin nests, consider carefully adding Boluoke plus nattokinase- some patients experience a flare of symptoms as trapped organisms are released
- Currently favored regimens consist of a combination of tafenoquine, atovaquone and artemesinins

Bartonella

- Stealth pathogen- not well recognized nor controlled by the immune system
- Lives in all three body spaces- blood, tissues and within cells
- Treatments must achieve bactericidal levels in all three compartments
- Treatment is challenging! No one drug is ideal
- Combinations of antibiotics are needed
- Combinations of botanicals should be added too

Bartonella antibiotics

Fluoroquinolones are the most effective, but risky!

- Effective in all three compartments
- Can try to mitigate FQ side effects by ensuring generous magnesium levels (IM supplementation is often needed) and by adding high doses of vitamin C
- Still, can get severe side effects on tendons (weakness, rupture) and the CNS (stimulatory- anxiety, insomnia)

Bartonella antibiotics

- Cephalosporins are very effective in the vascular space, less so in the tissues (IVs only) but not within cells
- Macrolides and azalides are good within cells and tissues, less so within vascular space
  - Genetically-based Bartonella drug resistance is common- is the main reason why these meds must be combined with another one or two
  - Host-based immune tolerance has been described
  - Immune tolerance may be reversed with arginine
- Tetracyclines are said to be totally ineffective when used alone, but may enhance efficacy of azalides and macrolides

Bartonella antibiotics

Rifampin and derivatives are not bactericidal so cannot be used alone

- However they do penetrate cells, tissues and the CNS well, therefore are often included in multidrug regimens
- Be aware of drug interactions because it is an inducer of hepatic cytochromes; may also lower adrenal corticosteroid levels

Gentamicin and analogs are the most effective of all

- But do not penetrate the CNS
- Can be toxic to ears and kidneys, especially if combined with macrolides/azalides (don’t combine these!!)
- Must be given IV or IM, but IM is painful!

Rickettsias

- Probably is more common than originally thought!
- Look for unexplained low WBC counts
- Acute infections usually can be cleared with two weeks of treatment
- Chronic infections may take many months of antibiotics- just like Q-fever. I suspect occult endocarditis
- Tetracyclines are the drugs of choice
- Many advocate adding hydroxychloroquine