CHRONIC BABESIOSIS

CAUSED BY *BABESIA ODOCOILEI*

PATHOPHYSIOLOGY, DIAGNOSIS AND TREATMENT

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Disclosures

I have no relevant financial or non-financial relationships to disclose.

I will disclose all references to the off-label or non-FDA approved usage of medications

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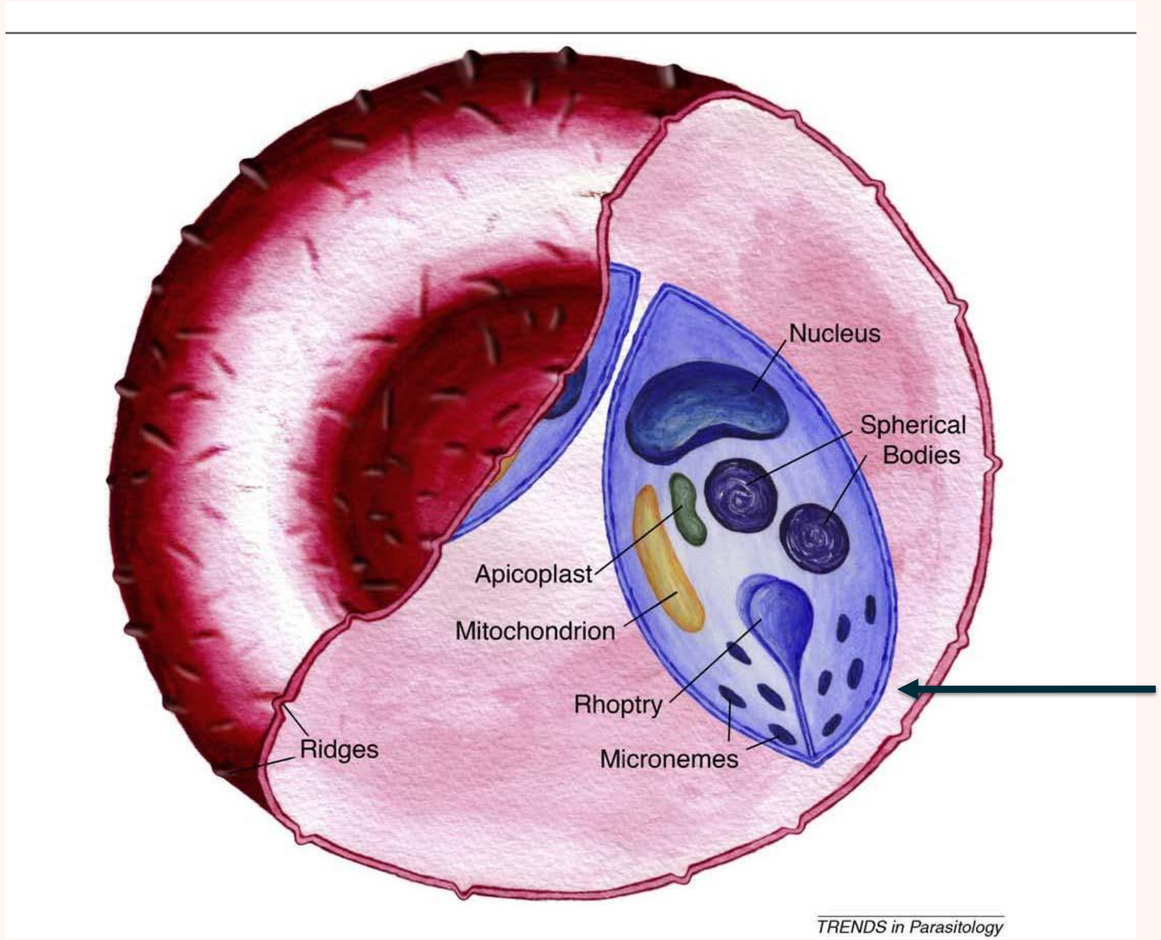
BABESIA: PROTOZOA RELATED TO MALARIA



Merozoite

Apical complex for invading erythrocytes

Gohil S et al. Recent insights into alteration of red blood cells by *Babesia bovis*: moovin' forward. *Trends Parasitol*. 2010;26(12):591-9. PMID: 20598944

BABESIA SPECIES (US/CANADA)

Intraerythrocytic parasite, sensitive to antimalarials

Apicoplast: incorporated cyanobacterium, sensitive to many antibiotics (→herxing)

***Babesia microti*: In <3% of *Ixodes scapularis* (deer) ticks, acute babesiosis only**

***Babesia duncani*: US West Coast, not deer ticks, BUT: *B. duncani* antibodies prevalent in humans across US and Canada (3x >*B. microti*!)**

Conclusion: Immunoassay cross-reaction with another babesia species

What species?

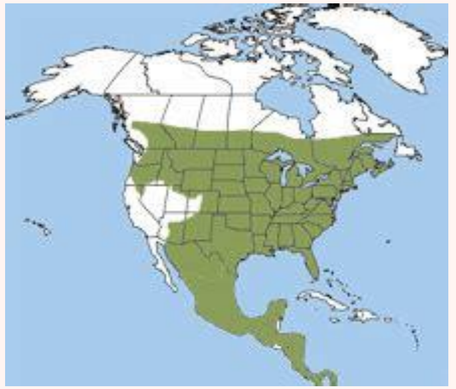
Schnittger L et al. Babesia: a world emerging. *Infect Genet Evol*. 2012;12(8):1788-809. PMID: 22871652

Swei A et al. Evidence for transmission of the zoonotic apicomplexan parasite *Babesia duncani* by the tick *Dermacentor albipictus*. *Int J Parasitol*. 2019 Feb;49(2):95-103. PMID: 30367862

Scott JD et al. Human Babesiosis Caused by *Babesia duncani* Has Widespread Distribution across Canada. *Healthcare (Basel)*. 2018;6(2):49. PMID: 29772759

Horowitz RI et al. Precision medicine: retrospective chart review and data analysis of 200 patients on dapsone combination th erapy for chronic Lyme…*Int J Gen Med*. 2019;12:101-119. PMID: 30863136

BABESIA ODOCOILEI



White-tailed deer range
http://www.nhptv.org

Babesia sensu stricto (s.s.) species—highly adapted parasite

Infects 10-30% of deer ticks in US and Canada (c/w Lyme@30%)

Host: White-tailed deer (*Odocoileus virginianus*), population doubled since 1950!

2021: Detected in 2 persons with chronic babesiosis*, Many more by TLab's FISH test

Why was it not discovered in humans until now?

Livengood J et al. Detection of *Babesia, Borrelia, Anaplasma*, and *Rickettsia* spp. in Adult Black-Legged Ticks from Pennsylvania…*Vector Borne Zoonotic Dis*. 2020;20(6):406-411. PMID: 31976829
Scott JD et al. Detection of *Babesia odocoilei* in *Ixodes scapularis* Ticks Collected in Southern Ontario, Canada. *Pathogens*. 2021;10(3):327. PMID: 33802071
Milnes EL et al. *Babesia odocoilei* and zoonotic pathogens identified from Ixodes scapularis ticks in southern Ontario, Canada. *Ticks Tick Borne Dis*. 2019;10(3):670-676. PMID: 30833200
*Scott JD et al, Detection of *Babesia odocoilei* in Humans with Babesiosis Symptoms. *Diagnostics (Basel)*. 2021;11(6):947. PMID: 34070625

BABESIA SENSU STRICTO SPECIES

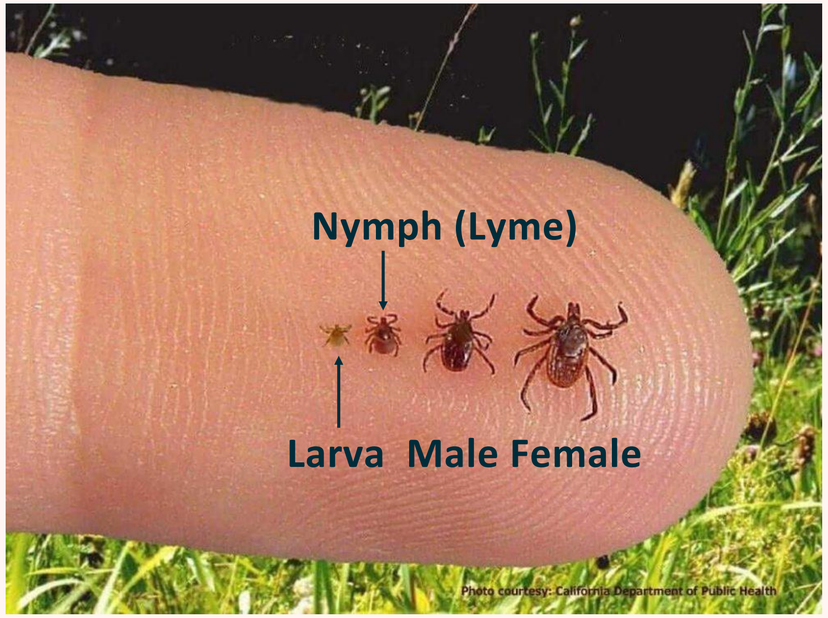
7.5x larger genome than Lyme-*Borrelia sp.*

Evades and suppresses host immune system

Cytoadherence and sequestration

Age-related immune response; Life-long infestation

Uniquely specialized for tick transmission



Transovarial transmission: Tick larvae born infected/infective; @1000 per female

Chauvin A et al. Babesia and its hosts: adaptation to long-lasting interactions as a way to achieve efficient transmission. *Vet Res*. 2009;40(2):37. PMID: 19379662

Allred DR. Antigenic variation in babesiosis: is there more than one 'why'? *Microbes Infect*. 2001;3(6):481-91. PMID: 11377210

Zintl A et al. Possible mechanisms underlying age-related resistance to bovine babesiosis. *Parasite Immunol*. 2005;27(4):115-20. PMID: 15910419

Howell JM et al. Transovarial transmission efficiency of *Babesia bovis* tick stages acquired by *Rhipicephalus microplus*…*J Clin Microbiol*. 2007 Feb;45(2):426-31. PMID: 17166964

TRICK: FIBRIN CYTOADHERENCE/SEQUESTRATION

B. odocoilei **infects red blood cells (iRBCs), alters surface to promote fibrin deposition**

Cytoadherence—iRBCs adhere to endothelium of capillaries and post-cap. venules

Rosetting—iRBCs adhere to uninfected RBCs (uRBCs)

Sequestration of iRBCs and uRBCs, Occlusion of capillaries and venules (NESTS)

Local proliferation in fibrin-bonded NESTS, avoiding circulation, spleen

Chronic infestation of all tissues and organs, including brain

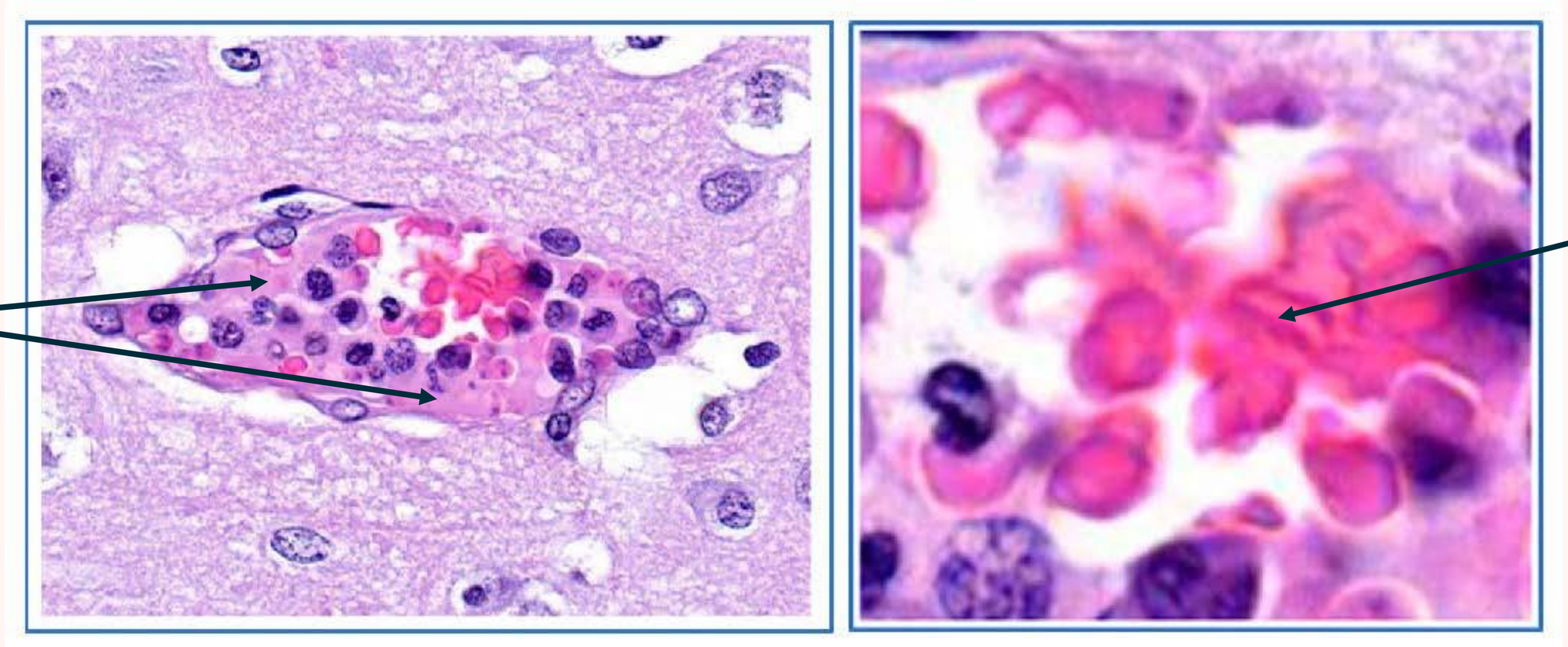
Schetters T. Mechanisms Involved in the Persistence of *Babesia canis* Infection in Dogs. *Pathogens*. 2019;8(3):94. PMID: 31261942

Allred DR et al, Antigenic variation and cytoadhesion in *Babesia bovis* and *Plasmodium falciparum*: different logics achieve the same goal. *Mol Biochem Parasitol*. 2004;134(1):27-35. PMID: 14747140

Allred DR. Babesiosis: persistence in the face of adversity. *Trends Parasitol*. 2003;19(2):51-5. PMID: 12586467

Wright IG. An electron microscopic study of intravascular agglutination in the cerebral cortex due to *Babesia argentina* infection. *Int J Parasitol*. 1972;2(2):209-15. PMID: 4652608

B. CANIS: FIBRIN-BONDED NEST



Dog's brain

Schetters T. Mechanisms Involved in the Persistence of *Babesia canis* Infection in Dogs. *Pathogens*. 2019;8(3):94. PMID: 31261942

MICROVASCULAR NESTS DISABLE THE HOST

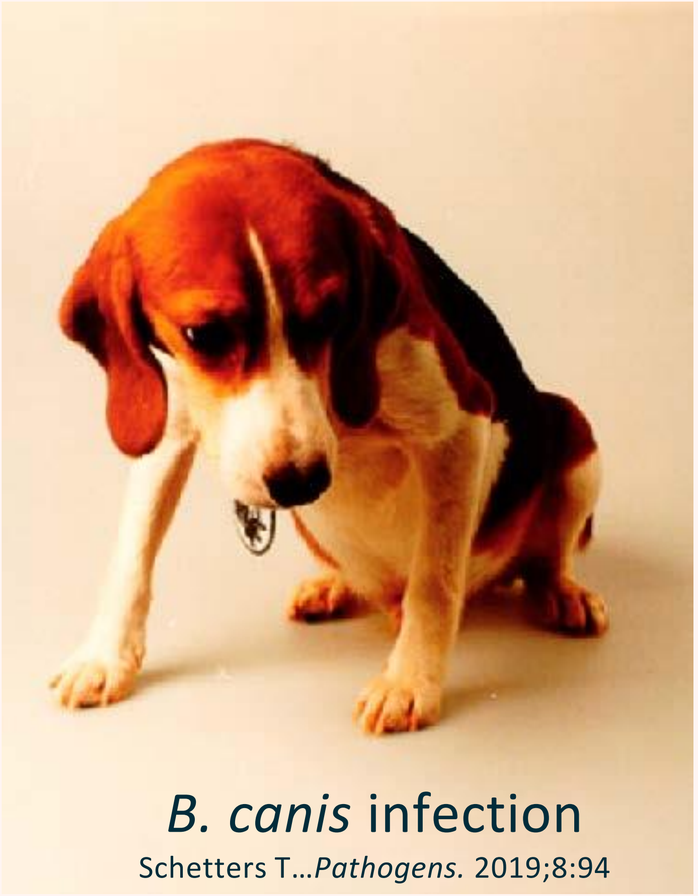
Localized ischemia and inflammation in all tissues/organs→ "multi-organ dysfunction syndrome"

Inflammation→↑nitric oxide (NO)→capillary leakage→edema and hypotension (POTS)

↑NO and cytokines cause mitochondrial dysfunction and ATP depletion→Fatigue, severe exertional intolerance

ATP reaccumulates during sleep; rapidly exhausted with activity
Pt. has energy in AM, then crashes and must rest

Severe exertional intolerance is babesiosis until proven otherwise



B. canis infection

Schetters T…*Pathogens.* 2019;8:94

Sanders, DA. Observations on (chronic) Canine Babesiosis (piroplasmosis). *J Am Vet Med Assoc*. 1937;90:27-40

Malherbe, W. The manifestations and diagnosis of *Babesia* infections. *Ann. N. Y. Acad. Sci.* 1956;64(2):128-146. 10.1111/j.1749-6632.1956.tb36609.x

Clark IA et al. The pathophysiology of falciparum malaria. *Pharmacol Ther*. 2003;99(2):221-60. PMID: 12888113

Clark IA et al. Do babesiosis and malaria share a common disease process? *Ann Trop Med Parasitol*. 1998;92(4):483-8. PMID: 9683899

NESTS CAUSE MULTI-ORGAN DYSFUNCTION

DIRECT EFFECTS (hypothyroid-like)

FATIGUE: Energy in AM only, then ATP depletion

Poor stamina/recovery—mental/physical

Slow/impaired cognition: memory/intellect intact

Gastrointestinal anergy—bloating, constipation

Hypotension/edema—POTS, heart racing

Appetite—reduced or excessive

Low body temp, cold intolerance

IMMUNE-MEDIATED (inflammation)

Systemic: Flu-like, night sweats, mast cell activation

Neurological: Numbness, headache, insomnia, etc.

Psychiatric: Anxiety, anhedonia, depression, etc.

Gastrointestinal: Irrit. bowel synd., diarrhea, nausea

Cardiopulmonary: palpitations, cough, air hunger

Rheumatologic: Muscle/joint pain, stiffness, etc.

Cause of many "idiopathic" disorders and diseases

Immune-mediated symptoms may appear only with treatment (herxing)

Greenberg R. Infections and Childhood Psychiatric Disorders: Tick-Borne Illness and Bipolar Disorder in Youth. *Bipolar Disord.* 2017; 3: 113. doi: 10.4172/2472-1077.1000113

Malherbe, WD The Manifestations and Diagnosis of *Babesia* Infections, 1956; 64(2) 128-146. https://doi.org/10.1111/j.1749-6632.1956.tb36609.x

Sanders DA, Observations on canine babesiasis (piroplasmosis), *J Am Vet Med Assoc*. 1937;90:27-40

Fonde, GH., Fonde, EC. Chronic Malaria: A Clinical consideration. *Arch Intern Med (Chic)*. 1939; 64(6):1156-1169. doi: 10.1001/archinte.1939.00190060025002

BABESIOSIS: A TALE OF TWO DISEASES

Acute Babesiosis: known to CDC/IDSA

Rare: Usually asplenic, immuncompromised

Easy to diagnose: Fever, hemolysis, parasitemia→pos. venous blood smear

Easy to treat: Just reduce parasitemia with 10 days atovaquone and azithromycin

Self-limited: Elimination (*B. microti, B. divergens*) or chronic infection (*B. odocoilei, B. duncani?*)

Chronic Babesiosis: unknown to CDC/IDSA

Common: Immunocompetent persons (everyone), transmitted by larvae

HARD to diagnose: No fever, Neg. venous blood smears, FISH, PCR; No *B. odocoilei* ab test

HARD to treat: Sequestered in Nests

Chronic: Severity depends upon *Babesia* load, host immune reaction

Need new Infectious Disease paradigm for lifelong parasitic infestations

TESTING FOR *B. ODOCOILEI*

CBC, CMP, ESR, CRP usually normal, often have ↓CD57 (NK cells), ↑C4a

IGeneX: FISH (active infection), *B. duncani* abs, new *Babesia* immunoblot: Genus IgG/IGM only = *B. odocoilei*

TLab: Research-only *B.odocoilei* 18s rRNA FISH, venous blood, sensitivity fair

Thomford JW et al. Isolation and in vitro cultivation of *Babesia* parasites from free-ranging desert bighorn sheep and mule deer in California. *J Parasitol.* 1993;79(1):77-84. PMID: 8437062
Bock R et al. Babesiosis of cattle. *Parasitology*. 2004;129 Suppl:S247-69. PMID: 15938514

DIAGNOSIS OF CHRONIC BABESIOSIS

Clinical judgment: Best Theory to explain History, Symptoms, and Tests

Exam: hypotension, edema, splenomegaly (with treatment)

Historical Clues:

- **Deer tick bite or exposure (everyone!)**
- **Initial flu-like syndrome – rare**
- **Improvement or worsening with hormones, medications, herbs, supplements, antibiotics, activities etc. (i.e., affects the immune system *or* the parasites).**
- **Interminable herxing with Rx for Lyme, Bartonella**
- ***Intolerance of antimalarials*!**

Ultimate Criterion: Diagnostic trial of atovaquone and/or other antimalarials

TREATMENT OF CHRONIC BABESIOSIS

1000x more resistant to antimalarials than malaria, and SEQUESTERED

Need Synergy: Atovaquone or Malarone, add tafenoquine, artesunate, and azithromycin (Start with antimalarials to confirm *Babesia*)

Ramp up: GO low and slow as tolerated, gradually increase to full doses of all

Then Erode Nests: Lumbrokinase, then add Nattokinase (synergy)

Increase/continue regimen until patient is well, does not herx with stopping/starting

Curable? May only need load reduction followed by Maintenance

*Abraham A et al. …*in vitro* culture of *Babesia duncani* in human erythrocytes reveals unusually high tolerance to recommended therapies. *J Biol Chem*. 2018;293(52):19974-19981. PMID: 30463941

See ILADS Babesia Webinar

SEQUESTRATION→PROLONGED HERXING

Billions of immune-evading parasites, most isolated in nests

"Shock Effect": Temporary improvement with adding/increasing antibabesials; then

Jarisch-Herxheimer: Immune response to die-off—exposed parasite antigens

Mental/physical activity causes Herxing: ↑'d blood flow, nest disruption

Herxing Severity: 1. *Babesia* load, 2. RX potency, 3. Pts.' immune reactivity

Butler T. The Jarisch-Herxheimer Reaction After Antibiotic Treatment of Spirochetal Infections… *Am J Trop Med Hyg*. 2017;96(1):46-52. PMID: 28077740
Parthasarathy G, Gadila SKG. Neuropathogenicity of non-viable *Borrelia burgdorferi* ex vivo. *Sci Rep*. 2022 Jan 13;12(1):688. PMID: 35027599

HERXING EVERYWHERE

Inflammation in all tissues/organs

Usual symptoms worsen; Others appear for first time

Physical: Flu-like, brain fog, achiness, dysgeusia, petechiae, acneiform eruptions, headaches, transient neurological symptoms, cough, gastrointestinal disturbances, etc.

Psychiatric: anger, irritability, anxiety, violent/suicidal ideation, hallucinations, etc.

Herxes are not "side effects"! Different agents cause same signs/symptoms

Labs: ↑'d LFTs, pancreatic enzymes NOT drug toxicity; due to inflammation from die-off

Dead organisms are more immunogenic than live ones

Parthasarathy G, Gadila SKG. Neuropathogenicity of non-viable *Borrelia burgdorferi* ex vivo. *Sci Rep*. 2022 Jan 13;12(1):688. PMID: 35027599

ATOVAQUONE (MEPRON®)

Inhibits protozoal, not human mitochondrial function; Patients can take CoQ10

"Mepron blues", "Mepron psychosis", rashes, ↑ LFTs, pancreatic enzymes are ALL HERXING!

Reduce dose if necessary but continue RX!

Dose: Start with ¼ tsp daily if very ill, ↑gradually to 1 tsp bid

FDA-approved only for the prevention and treatment of *Pneumocystis jirovecii* pneumonia at 1500mgs/day

Nixon GL et al. Antimalarial pharmacology and therapeutics of atovaquone. *J Antimicrob Chemother*. 2013;68(5):977-85. PMID: 23292347
Srivastava IK et al. Resistance mutations reveal the atovaquone-binding domain of cytochrome b in malaria parasites. *Mol Microbiol*. 1999;33(4):704-11. PMID: 10447880
Fiorillo M et al. Repurposing atovaquone: targeting mitochondrial complex III and OXPHOS to eradicate cancer stem cells. *Oncotarget*. 2016;7(23):34084-99. PMID: 27136895

TAFENOQUINE (KRINTAFEL®)

Most potent antibabesial agent*; like primaquine but more effective

R/O G6PD deficiency to avoid tafenoquine-induced hemolysis

Dose-dependent methemoglobinemia—lowers SpO2, asymptomatic at usual doses

Once weekly dose: 2 week half-life, accumulates for 3 mos

Usually not covered by ins.: $40 for 300mgs @GoodRx.com

Dose: Start 150mgs/wk, ↑gradually to 450mgs to 600mgs/wk (per SpO2)

FDA-approved for prevention of malaria, treatment of *Plasmodium vivax* malaria in patients 16 years and older receiving chloroquine therapy

Mordue DG, Wormser GP. Could the Drug Tafenoquine Revolutionize Treatment of *Babesia microti* Infection? *J Infect Dis*. 2019;220(3):442-447. PMID: 31099380

Walsh DS et al. Randomized trial of 3-dose regimens of tafenoquine (WR238605)…for preventing *Plasmodium vivax* malaria relapse. *Clin Infect Dis*. 2004;39(8):1095-103. PMID: 15486831

Youngster I et al. Medications and glucose-6-phosphate dehydrogenase deficiency: an evidence-based review. *Drug Saf.* 2010;33(9):713-26. PMID: 20701405

ARTESUNATE/ARTEMISININ

Highly Potent: Reacts with iron to produce carbon-centered iron radicals

Rapid babesiocidal action—1 to 4 hrs after dose

Artesunate caps: Start at 1 cap bid, ↑ as needed/tolerated to 2 caps bid

Toxicity: Dose-dependent neutropenia

Artemisinin cheaper, much weaker; may start with it—need 500mgs tid

FDA-approved for severe malaria by intravenous injection

Karunajeewa HA. Artemisinins: Artemisinin, Dihydroartemisinin, Artemether and Artesunate. *Milestones in Drug Therapy*. 2012;41:157-190 doi: 10.1007/978-3-0346-0480-2_9
Carvalho LJM et al. Activities of artesunate-based combinations and tafenoquine against *Babesia bovis* in vitro and *Babesia microti* in vivo. *Parasit Vectors*. 2020;13(1):362. PMID: 32690081

AZITHROMYCIN (ZITHROMAX®)

Babesiostatic: Antibiotics disable the babesial apicoplast

Side effects: Prolonged Q-T interval, tinnitus, possible hypersensitivity hepatitis

Little effect on Bartonella

Kills gut bacteria: Advise high-dose probiotic mix and *Saccharomyces boulardii*

Dose: 250mgs/day, increase to 500 mgs daily short-term if needed

FDA-approved only for 1-to-5 day courses for infections caused by susceptible bacteria

Peters DH et al. Azithromycin. A review of its antimicrobial activity, pharmacokinetic properties and clinical efficacy. *Drugs*. 1992;44(5):750-99. PMID: 1280567

Goodman CD et al. The effects of anti-bacterials on the malaria parasite *Plasmodium falciparum*. *Mol Biochem Parasitol*. 2007;152(2):181-91. PMID: 17289168

Vanoverschelde A et al. Macrolide-associated ototoxicity:…association of macrolide use with tinnitus and hearing loss. *J Antimicrob Chemother*. 2021:dkab232. PMID: 34312676

RIFABUTIN

Stronger than azithromycin, long term Rx experience with mycobacteria (TB, MAC)

Extensive tissue, intracellular penetration, less effect on gut bacteria

CYP3A4 inducer: ↓'s corticosteroid, atovaquone levels, but 50% less than rifampin

Highly effective against Bartonella coinfection→Bart herxing

Dose: 150mg capsule daily, ↑ as tolerated to 300mgs daily, Max. dose 600mgs/day

FDA-approved prevention of disseminated Mycobacterium avium complex (MAC) disease in patients with advanced HIV infection

Blaschke TF, Skinner MH. The clinical pharmacokinetics of rifabutin. *Clin Infect Dis*. 1996;22 Suppl 1:S15-21; discussion S21-2. PMID: 8785251

Brogden RN, Fitton A. Rifabutin. A review of its antimicrobial activity, pharmacokinetic properties and therapeutic efficacy. *Drugs*. 1994;47(6):983-1009. PMID: 7521834

Goodman CD et al. The effects of anti-bacterials on the malaria parasite *Plasmodium falciparum*. *Mol Biochem Parasitol*. 2007;152(2):181-91. PMID: 17289168

Phillips MC et al. Pharmacology, Dosing, and Side Effects of Rifabutin as a Possible Therapy for Antibiotic-Resistant *Acinetobacter* Infections. *Open Forum Infect Dis*. 2020;7(11):ofaa460. PMID: 33204754

METHYLENE BLUE

Safe & Effective against *Babesia* and *Bartonella,* esp. *Bartonella* biofilm persisters

Anti-oxidant: Electron donor, consumed with herxing like Vitamin C→colorless

Reduces tafenoquine-induced methemoglobinemia, allowing higher taf. dosing.

Dose: 50 to 300mgs once/day in G6PD-sufficient persons; Safe for long-term Rx.

Turns urine blue if not oxidized, High doses cause reversible urethritis/proctitis

FDA-approved for intravenous treatment of methemoglobinemia

Carvalho LJM et al. Activities of artesunate-based combinations and tafenoquine against *Babesia bovis* in vitro and *Babesia microti* in vivo. *Parasit Vectors*. 2020 Jul 20;13(1):362. PMID: 32690081

Zheng X et al. Effect of different drugs and drug combinations on killing stationary phase and biofilms recovered cells of *Bartonella henselae* in vitro. *BMC Microbiol*. 2020 Apr 10;20(1):87. PMID: 32276590

Kessler MR et al. Spurious pulse oximeter desaturation with methylene blue injection. *Anesthesiology*. 1986 Oct;65(4):435-6. PMID: 3767045

Kayabasi Y, Erbas O. Methylene blue and its importance in medicine, *D J Med Sci* 2020;6(3):136-145. doi: 10.5606/fng.btd.2020.25035

Lu G et al. Efficacy and safety of methylene blue in the treatment of malaria: a systematic review. *BMC Med*. 2018 Apr 25;16(1):59. PMID: 29690878

LUMBROKINASE AND NATTOKINASE

Enzymes lyse fibrin, Natto also an anticoagulant

Lumbro safe with anticoagulants, antiplatelets; Natto may ↑bleeding risk

Expensive: Boluoke® 20mg >$1/cap, ARG Nattokinase 100mg=75c/cap. Try cheap brands first

Lumbrokinase : 1 cap po tid, ↑ to 2 caps tid. Nattokinase: 100mg tid, ↑ to 2 caps tid

Synergy: Combination is much more effective

No FDA-approved form—over-the-counter supplements

Tjandrawinata RR et al. The Safety and Tolerability of Lumbrokinase DLBS1033 in Healthy Adult Subjects. *Drug Res (Stuttg)*. 2016 Jun;66(6):293-9. PMID: 27011386

Verma MK et al. Lumbrokinase – A Potent and Stable Fibrin–Specific Plasminogen Activator. *IJBSBT*. 2011;3(2):57-70. https://www.researchgate.net/publication/236264109

Jiang G et al. [Effect of lumbrokinase on patients with acute and moderate risk pulmonary thromboembolism]. *Zhong Nan Da Xue Xue Bao Yi Xue Ban*. 2017 Oct 28;42(10):1156-1162. PMID: 29093246

Chen H et al. Nattokinase: A Promising Alternative in Prevention and Treatment of Cardiovascular Diseases. *Biomark Insights*. 2018 Jul 5;13:1177271918785130. PMID: 30013308

HEMOLYSIS WITH TREATMENT

Death of *Babesia*→lysis of iRBCs→hemolysis including lysis of many uRBCs

Usually mild/minimal except immunocompromised pts. with high *Babesia* load

Monitor hemolysis with urine strips: hemoglobinuria and proteinuria (nests)

For severe hemolysis: Stop lumbro/natto, lower/stop antibabesials if necessary

No kidney injury with hydration, antioxidants, alkalinization (Alka Seltzer Gold)

Jakeman GN et al. Anaemia of acute malaria infections in non-immune patients primarily results from destruction of uninfected erythrocytes. *Parasitology*. 1999 Aug;119 (Pt 2):127-33. PMID: 10466119

Rother RP et al. The clinical sequelae of intravascular hemolysis and extracellular plasma hemoglobin: a novel mechanism of h uman disease. *JAMA*. 2005;293(13):1653-62. PMID: 15811985

Zager RA. Rhabdomyolysis and myohemoglobinuric acute renal failure. *Kidney Int*. 1996;49(2):314-26. PMID: 8821813

HEMOGLOBINURIA

-Pigment, -Protein

PIGMENTURIA

More pigmenturia with lumbrokinase

Red color suggests iron residues

2+Heme, 1+Protein

GREEN-BLACK PIGMENTURIA

High-load patient, longer time on lumbrokinase
Older nests?

Rancid odor—old blood, alkaline pH

4+Heme, 2+Protein

CAUTION IN IMMUNOSUPPRESSED AND AUTOIMMUNE PTS

Immunosuppression by *Bartonella* and/or corticosteroids → ↑Babesia load → ↑illness, ↑inflammation, ↑hemolysis with Rx

Large die-off → acute babesiosis, severe inflammation, hemophagocytic syndrome

Herxing may worsen *Babesia*- or *Bartonella*-related autoimmunity

IF Hx of "MS"—Herx may reignite acute disseminated encephalomyelitis (ADEM)

Go LOW and SLOW if possible!

Pappalardo BL et al. Immunopathology of *Bartonella vinsonii (berkhoffii)* in experimentally infected dogs. *Vet Immunol Immunopathol*. 2001 Dec;83(3-4):125-47. PMID: 11730925

Harms A, Dehio C. Intruders below the radar: molecular pathogenesis of *Bartonella* spp. *Clin Microbiol Rev*. 2012 Jan;25(1):42-78. PMID: 22232371

Auerbach M et al. Systemic babesiosis. Another cause of the hemophagocytic syndrome. *Am J Med*. 1986;80(2):301-3. PMID: 3946448

Schwarz S et al. Acute disseminated encephalomyelitis: a follow-up study of 40 adult patients. *Neurology*. 2001;56(10):1313-8. PMID: 11376180

SUPPORTIVE MEASURES

Antioxidants to protect tissues, reduce inflammation: astaxanthin, ALA, etc.

High-dose Vitamin C + N-acetylcysteine to ↓inflammation, ↓methemoglobinemia

Alka-Seltzer Gold to correct acidosis, Burbur Pinella to reduce herxing

Hydrocortisone/prednisone if necessary for very ill and/or autoimmune patients:

- **Seek lowest dose necessary to reduce nausea, headaches, weakness, brain fog, etc**
- **Patient-controlled: Dose rises with die-offs, drops with load reduction by antimicrobials.**
- **Must include DHEA (sublingually): mitigates steroid harms, but causes ↑herxing**
- **Steroids do not prevent eradication: but must ↑antimicrobials to kill organisms***
- **Consider alendronate early if prednisone >10mgs/day. Stop when prednisone is <10mgs/day**

Padayatty SJ et al. Vitamin C as an antioxidant: evaluation of its role in disease prevention. *J Am Coll Nutr*. 2003;22(1):18-35. PMID: 12569111
*Mordue DG et al. Could the Drug Tafenoquine Revolutionize Treatment of *Babesia microti* Infection? *J Infect Dis*. 2019;220(3):442-447. PMID: 31099380

MONITORING TREATMENT

Regular Reports from patient

Patient monitors urine with multistix

Tafenoquine: Patient monitors methemoglobinemia with pulse Ox; Hold TAF if SpO2 <90%, If severe, add methylene blue @150 to 300 mgs po qd (kills *Bart* and *Bab*!)

Safety labs: CBC, CMP, others as indicated; expect mild ↑LFTs, pancreatic enzymes

Hemolysis labs: ↑LDH, ↓haptoglobin, ↑reticulocyte count. ↑Ferritin and AST from lysed RBCs. Brisk bone marrow response→↑WBCs, myelocytes, platelets, NRBCs

Barker SJ et al. Effects of methemoglobinemia on pulse oximetry and mixed venous oximetry. *Anesthesiology*. 1989 Jan;70(1):112-7. PMID: 2912291