ENCEPHALITIS CAUSED BY CHRONIC BARTONELLOSIS AND BABESIOSIS

HENRY H. LINDNER, MD

ILADS 2022

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Associated Diseases Society™

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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VALERIE: ENCEPHALITIS X 2

Inconsolable infant: Frustrated, needed to see/do, bouncing to sleep, not cuddly, never crawled, slow to walk.

Tick bites@10yrs: No rash or fever, no antibiotic prophylaxis

@14 yrs: Depressed, fatigued, angry, suicidal, eventually disabled

Finally considered tick-borne encephalitis @ age 25: “All emotions hurt”

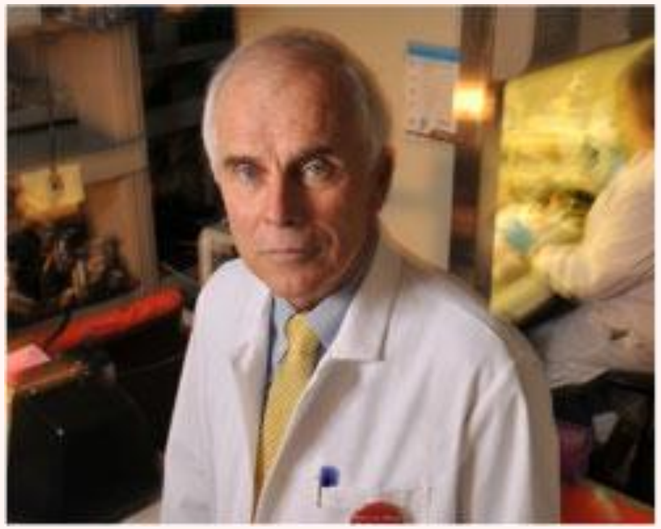
Initial testing @LabCorp and IGeneX Negative for “Lyme and coinfections”

Empiric antimicrobial treatment caused Herxing*

*Named after Jarisch-Herxheimer reaction—Illness that occurs when immune evading parasites are killed, and thereby exposed to the immune system.

VALERIE: GALAXY FINDS BART ANTIBODIES

Target	Sample	Collection	Type	Result	Titer	Reference
B. henselae	GH18-3406-1-S	10/29/2018	Serum	Reactive	1:128	Non-reactive
B. quintana	GH18-3406-1-S	10/29/2018	Serum	Reactive	1:64	Non-reactive



Ed Breitschwerdt, DVM, DACVIM
NC State University

Galaxy Diagnostics, 6 Davis Drive, Suite 201, Research Triangle Park, NC 27709, https://www.galaxydx.com/

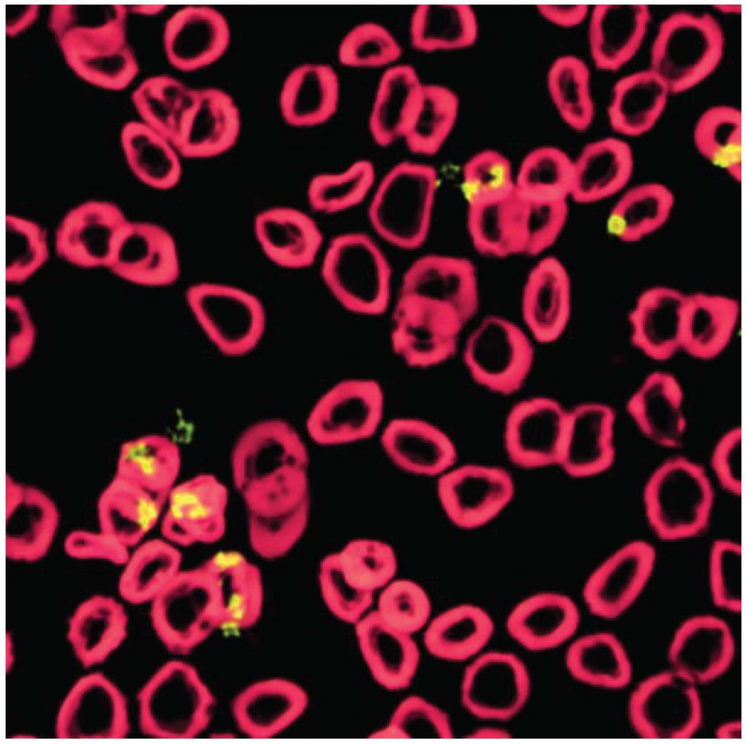
TLAB FINDS BART IN HER BLOOD

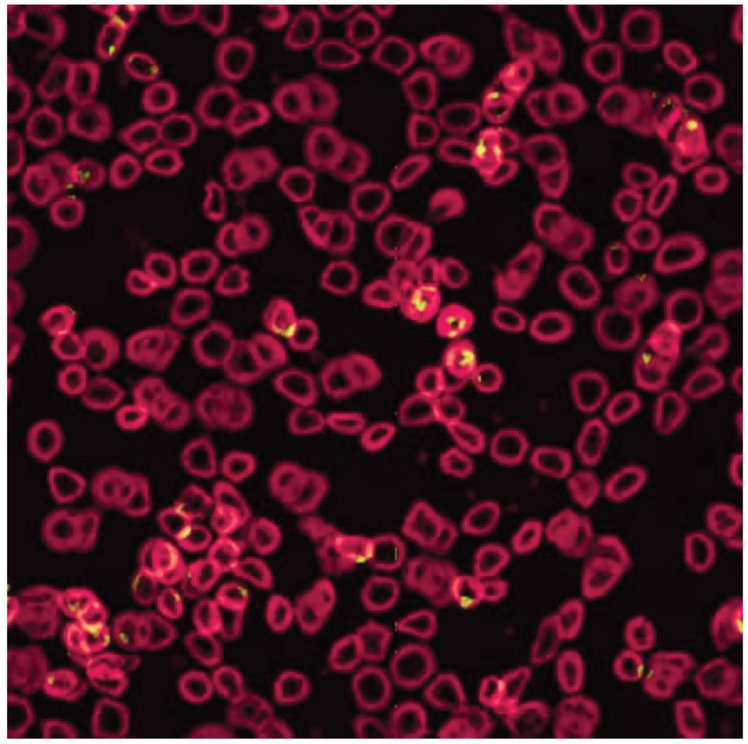
Robert Mozayeni, MD

TEST RESULT		
Target	**Method**	**Result**
B. henselae 23s rRNA* **	***in situ* hybridization and Confocal Laser Microscopy**	Your result is: **Positive** (Research Use Only) (Reference value is “negative”)

Indicates ongoing Infection

REPRESENTATIVE IMAGES

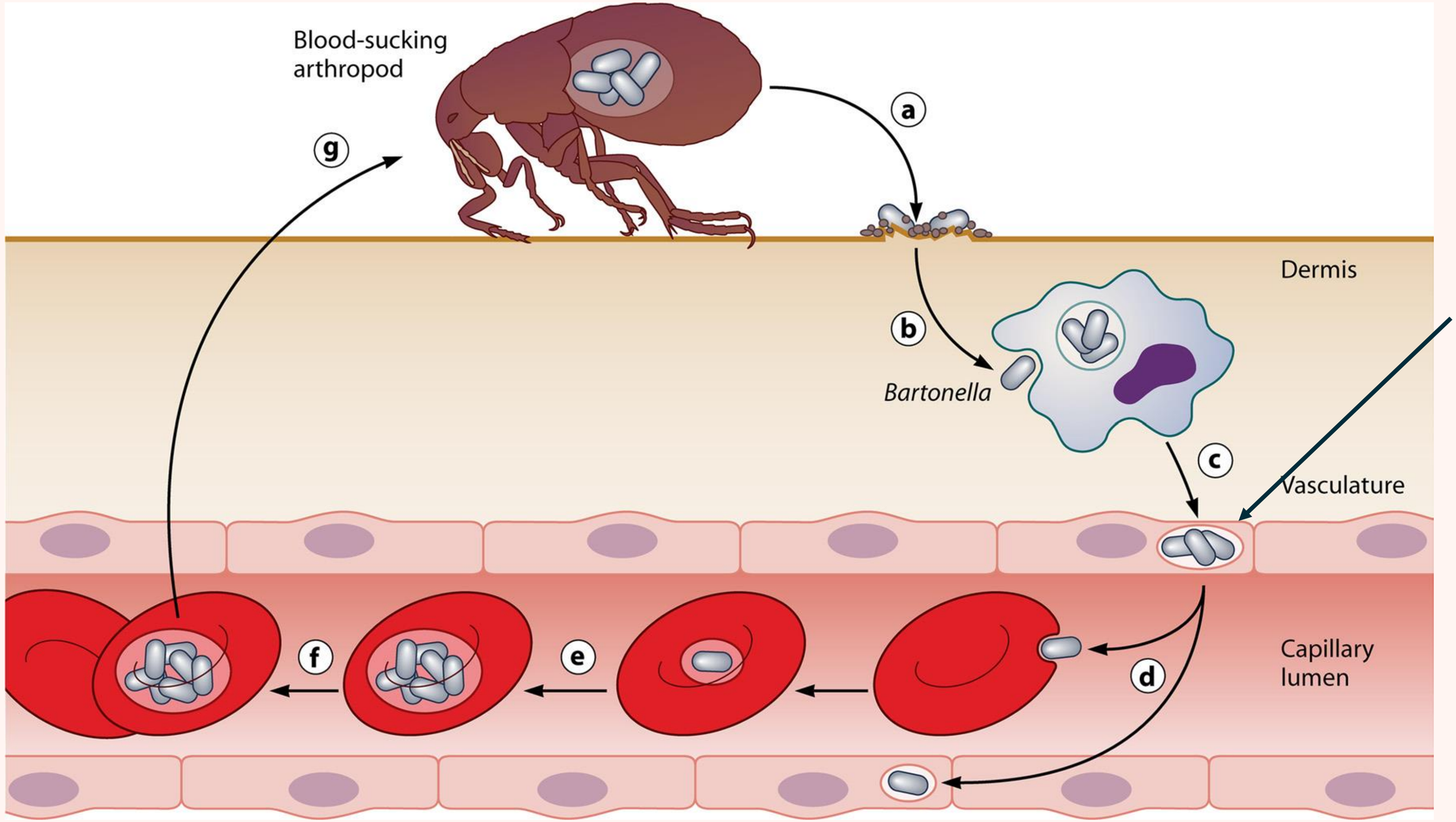




TLab Inc., 910 Clopper Road, Suite 220S, Gaithersburg, MD 20878, BR Mozayeni,, director. https://www.tlabdx.com/

BARTONELLA: INTRACELLULAR/VASCULAR PARASITE

Proliferates in extracellular matrix surrounding endothelial cells



Inhabits Endothelial cells, RBCs

Common, many arthropod, animal vectors

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

Chiaraviglio L et al. An immunocompromised murine model of chronic *Bartonella* infection. *Am J Pathol*. 2010 Jun;176(6):2753-63. PMID: 20395436

SINCE 2008: *BARTONELLA* SPECIES ROUTINELY CULTURED FROM PATIENTS' BLOOD

JOURNAL OF CLINICAL MICROBIOLOGY, Sept. 2008, p. 2856–2861 Vol. 46, No. 9
0095-1137/08/$08.00+0 doi:10.1128/JCM.00832-08

Bartonella sp. Bacteremia in Patients with Neurological and Neurocognitive Dysfunction▽

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Received 1 May 2008/Returned for modification 16 June 2008/Accepted 10 July 2008

We detected infection with a *Bartonella* species (*B. henselae* or *B. vinsonii* subsp. *berkhoffii*) in blood samples from six immunocompetent patients who presented with a chronic neurological or neurocognitive syndrome including seizures, ataxia, memory loss, and/or tremors. Each of these patients had substantial animal contact or recent arthropod exposure as a potential risk factor for *Bartonella* infection. Additional studies should be performed to clarify the potential role of *Bartonella* spp. as a cause of chronic neurological and neurocognitive dysfunction.

Breitschwerdt EB et al. *Bartonella* sp. bacteremia in patients with neurological and neurocognitive dysfunction. *J Clin Microbiol*. 2008 Sep;46(9):2856-61. PMID: 18632903
Maggi RG et al. *Bartonella* spp. bacteremia and rheumatic symptoms in patients from Lyme disease-endemic region. *Emerg Infect Dis*. 2012 May;18(5):783-91. PMID: 22516098
Breitschwerdt EB et al. *Bartonella* Associated Cutaneous Lesions (BACL) in People with Neuropsychiatric Symptoms. *Pathogens*. 2020 Dec 4;9(12):1023. PMID: 33291688
Maggi RG et al. Bartonella spp. bacteremia in high-risk immunocompetent patients. *Diagn Microbiol Infect Dis.* 2011 Dec;71(4):430-7. PMID: 21996096

BARTONELLA: MULTI-ORGAN DYSFUNCTION

Systemic: Flu-like sxs, fever, fatigue, mast cell activation

Neurological: Numbness, headache, insomnia, brain fog, balance, tremors, uveitis

Psychiatric: Rage, anxiety, depression, OCD, PANS

Gastrointestinal: Irrit. bowel synd., diarrhea, nausea

Pulmonary: Shortness of breath, cough

Rheumatologic: Muscle/joint pain, stiffness, part. Lower extremity pain.

Dermatologic: rashes, atypical striae

Cardiac: tachycardia, pericarditis, endocarditis

Breitschwerdt EB et al. *Bartonella* sp. bacteremia in patients with neurological and neurocognitive dysfunction. *J Clin Microbiol*. 2008 Sep;46(9):2856-61. PMID: 18632903
Maggi RG et al. *Bartonella* spp. bacteremia and rheumatic symptoms in patients from Lyme disease-endemic region. *Emerg Infect Dis*. 2012 May;18(5):783-91. PMID: 22516098
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Maggi RG et al. *Bartonella* spp. bacteremia in high-risk immunocompetent patients. *Diagn Microbiol Infect Dis*. 2011 Dec;71(4):430-7. PMID: 21996096

BARTONELLOSIS: A TALE OF TWO DISEASES

Acute Bartonellosis: known to CDC/IDSA

Easy to diagnose: Fever, lymphadenopathy, complications

Self-limited: Resolves without Rx. Parasites “cleared” (NOT)

Chronic Bartonellosis: unknown to CDC/IDSA

Common: Large percentage of humans→neuropsychiatric, rheumatologic, dermatologic morbidity

Hard to diagnose: Galaxy Diagnostics for antibodies/blood culture, TLab’s *B. henselae* FISH

Hard to treat: Intracellular or in collagen, persisters

Chronic: “Asymptomatic” to very ill according to *Bartonella* load, host immune reaction

Vayssier-Taussat M et al. Identification of Novel Zoonotic Activity of *Bartonella* spp., France. *Emerg Infect Dis*. 2016 Mar;22(3):457-62. PMID: 26885624

Arvand M, Schäd SG. Isolation of *Bartonella henselae* DNA from the peripheral blood of a patient with CSD up to 4 months after the cat scratch injury. *J Clin Microbiol*. 2006 Jun;44(6):2288-90. PMID: 16757642

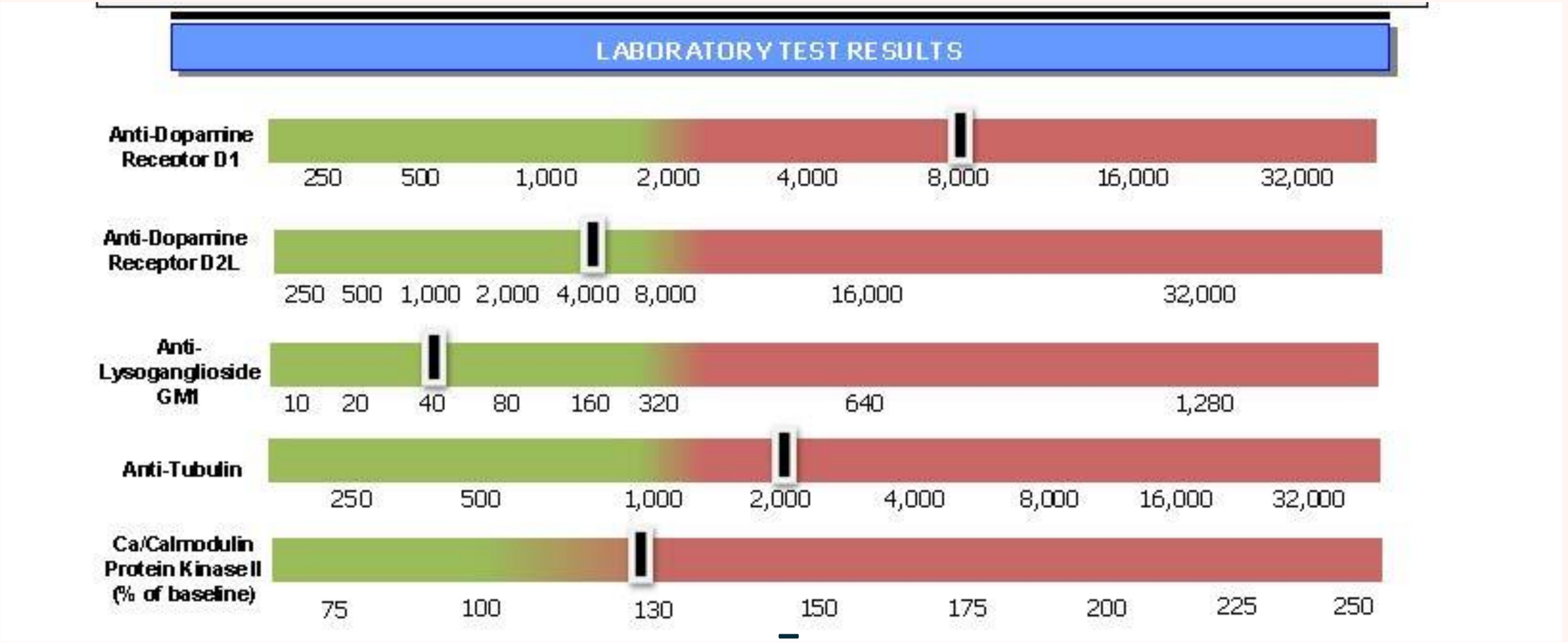
Breitschwerdt EB et al. *Bartonella* species in blood of immuno-competent persons with animal and arthropod contact. *Emerg Infect Dis*. 2007 Jun;13(6):938-41. PMID: 17553243

Breitschwerdt EB et al. *Bartonella* sp. bacteremia in patients with neurological and neurocognitive dysfunction. *J Clin Microbiol*. 2008 Sep;46(9):2856-61. PMID: 18632903

Breitschwerdt EB et al. *Bartonella* Associated Cutaneous Lesions (BACL) in People with Neuropsychiatric Symptoms. *Pathogens*. 2020 Dec 4;9(12):1023. PMID: 33291688

VAL'S CUNNINGHAM PANEL

Herxed for 9 mos with anti-Bartonella therapy, no improvements



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No benefit from corticosteroids, IVIG

Moleculara Labs, 755 Research Parkway, Suite 410, Oklahoma City, OK 73104 https://www.moleculeralabs.com/

VALERIE: REPEAT IGENEX TEST FINDS *BABESIA*

Nick Harris, PhD

BABESIOSIS

B. microti IFA - IgM	Serum	<20	< 20 : Negative = 20 : May or may not indicate active infection >=40 : Indicates active infection	Titer
B. microti IFA - IgG	Serum	<40	< 40 : Negative < 160 : May or may not suggest active infection >=160 : Indicates active infection	Titer
Babesia FISH	W blood	**Pos**		

Remained Lyme-Negative

Ongoing infection with a *Babesia* species

Jyotsna Shah, PhD

TEST	SPECIMEN	RESULT	REFERENCE RANGE	UNITS
Babesia PCR				
B. microti	W blood	Neg		
B. duncani	W blood	Neg		
B. duncani IFA - IgM	Serum	**80**	< 20 : Negative = 20 : May or may not indicate active infection >=40 : Indicates active infection	Titer
B. duncani IFA - IgG	Serum	<40	< 40 : Negative < 160 : May or may not suggest active infection >=160 : Indicates active infection	Titer

***Babesia duncani* antibodies**

Mepron caused rage, achiness, fatigue:

Could not continue!

CAN'T TREAT HER INFECTIONS!
TRY LOW DOSE IMMUNOTHERAPY

BABESIA ANTIGEN FLARING

Flu-like symptoms: Severe fatigue, chills, aches

↑↑Corticosteroid requirement

Cognitive dysfunction, delirium

Anxiety, depression, tearfulness

↑Hunger, abdominal bloating, nausea

Hypotension/Edema: POTS, heart racing

BARTONELLA ANTIGEN FLARING

↑Anhedonia

Rage: suicidal/homicidal ideation

Intrusive negative thoughts/images

Agitation: Forced to do things

Violent urges: hitting, throwing things

Mental pain: Only opioids helped

Different Encephalitic Effects

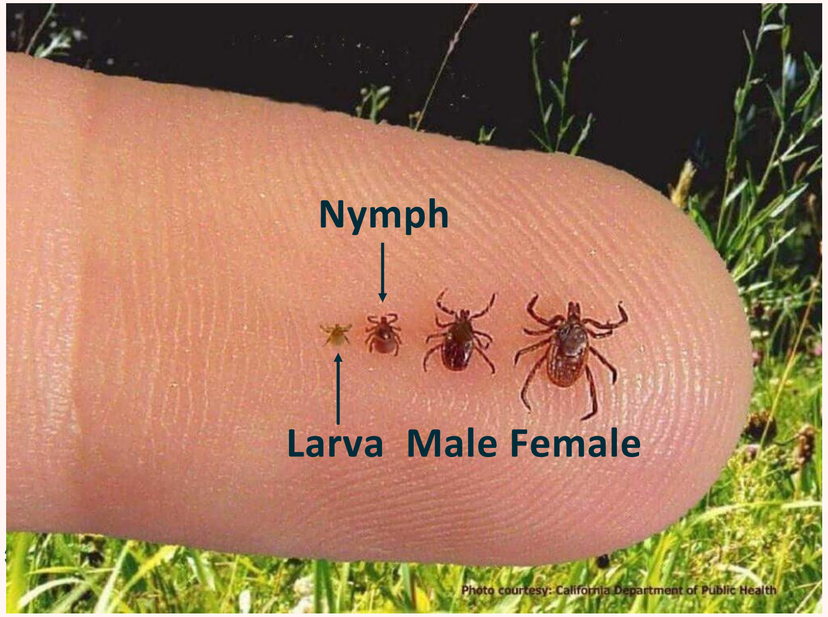
Bystander effect: Flaring to one antigen caused partial flaring to the other

LDI flares permanently increased her immune reaction to the infections; left her in a much worse state.

BABESIA SPECIES IN US/CANADA

***Babesia microti*: <3% of deer ticks, acute babesiosis only**

***Babesia duncani*: US West Coast only, not in deer ticks,**
***B. duncani* ab tests are cross-reactions with abs to:**



***Babesia odocoilei*: 10-30% of deer ticks (Lyme@30%)**

- **Host: White-tailed deer (*Odocoileus virginianus*)**
- **Sensu stricto *Babesia* sp., Highly evolved parasite**
- **Proven in two patients with chronic symptomatic babesiosis**
- **Life-long Infestation: "asymptomatic" to severe mental/physical exertional intolerance**
- **Transovarial transmission: 1000 invisible infected larvae per female – not with Lyme, *B. microti***

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
Zembsch TE et al. Evidence for Vertical Transmission of *Babesia odocoilei* in *Ixodes scapularis* (*Acari: Ixodidae*). *J Med Entomol*. 2021 Nov 9;58(6):2484-2487. PMID: 33939830
***Scott JD et al, Detection of *Babesia odocoilei* in Humans with Babesiosis Symptoms. *Diagnostics (Basel)*. 2021;11(6):947. PMID: 34070625**

TRICK: FIBRIN CYTOADHERENCE/SEQUESTRATION

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

Cytoadherence—iRBCs adhere to endothelium

Rosetting—iRBCs adhere to uninfected RBCs (uRBCs)

Sequestration of iRBCs and uRBCs in capillaries and venules (NESTS)

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

Chronic infestation of all tissues and organs, including brain

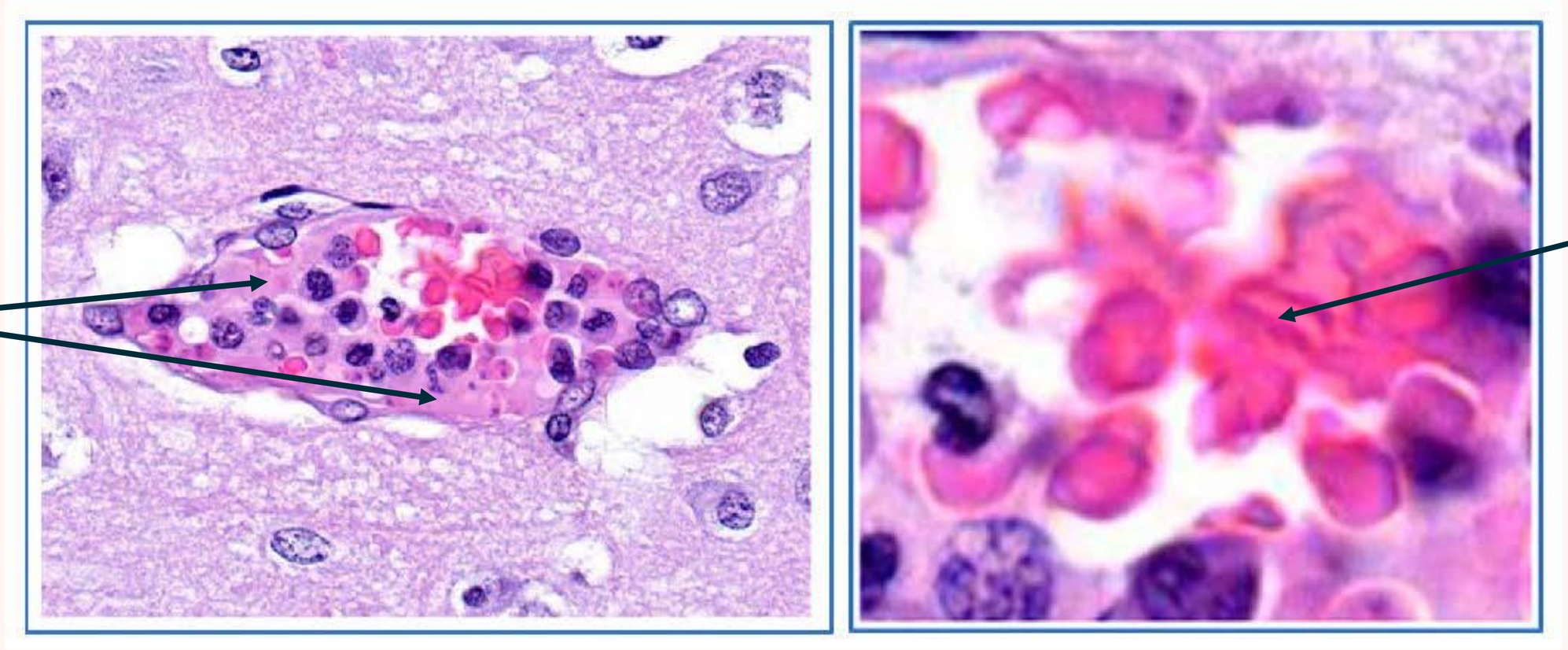
Schetters T. Mechanisms Involved in the Persistence of *Babesia canis* Infection in Dogs. *Pathogens*. 2019;8(3):94. PMID: 31261942

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

BABESIA 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)

Mitochondrial dysfunction and ATP depletion→Fatigue, exertional intolerance

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

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

BABESIA 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

BRAIN NESTS→ENCEPHALITIS

Brain favored site for sequestration→ischemia, inflammation and ATP depletion

White matter most affected→"disconnect syndrome", slowed/distorted cognition

Rupture of blood-brain barrier (BBB) at infected/inflammed capillaries

Inflammation distorts neurotransmission: ↑NO, cytokines, quinolinic acid

Result: Low brain energy, slow cognition, neuropsychiatric disorders

Clark IA et al. Proposed link between cytokines, nitric oxide and human cerebral malaria. *Parasitol Today*. 1991;7(8):205-7. PMID: 15463497

Nonaka H et al. The microvasculature of the cerebral white matter: arteries of the subcortical white matter. *J Neuropathol Exp Neurol*. 2003;62(2):154-61. PMID: 12578225

Lin J et al. Multiple Factors Involved in the Pathogenesis of White Matter Lesions. *Biomed Res Int*. 2017;2017:9372050. PMID: 28316994

Felger JC, Miller AH. Cytokine effects on the basal ganglia and dopamine function: the subcortical source of inflammatory malaise. *Front Neuroendocrinol*. 2012 Aug;33(3):315-27. PMID: 23000204

BABESIOSIS: ALSO 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

New Infectious Disease paradigm required for lifelong parasitic infestations

TREATMENT OF CHRONIC BABESIOSIS

1000x more resistant to antimalarials than malaria, and SEQUESTERED

Need Synergy: Atovaquone or Malarone, then add tafenoquine, artesunate or artemisinin, 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 with 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→HERXING UNTIL ERADICATION

Billions of immune-evading parasites, most isolated in nests

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

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

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

BARTONELLA-BABESIA COINFECTION

Intravascular Parasites: BOTH in ALL TISSUES including brain; life-long infestations

Coinfecting most vertebrates; Coevolving for hundreds of millions of years

BOTH vertically transmitted—from mother to fetus (yes, humans too)

***Bartonella* is immunosuppressive→*Babesia* proliferation→↑Babesia load**

***Babesia* is immune-evading, *but* highly immunostimulatory if killed/exposed.**

***Bartonella* persists in *Babesia* nests; preventing eradication with antimicrobials**

Breitschwerdt EB et al. Molecular evidence of perinatal transmission of *Bartonella vinsonii* subsp. *berkhoffii* and *Bartonella henselae* to a child. *J Clin Microbiol*. 2010 Jun;48(6):2289-93. PMID: 20392912

Velho PE et al. *Bartonella henselae* as a putative cause of congenital cholestasis. *Rev Inst Med Trop Sao Paulo*. 2016 Jul 11;58:56. PMID: 27410916

Rojas-Pirela M et al. Congenital Transmission of Apicomplexan Parasites: A Review. *Front Microbiol*. 2021 Sep 29;12:751648. PMID: 34659187

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

Capo C et al. *Bartonella quintana* bacteremia and overproduction of interleukin-10: model of bacterial persistence in homeless people. *J Infect Dis*. 2003 Mar 1;187(5):837-44. PMID: 12599058

COMBINED *BARTONELLA-BABESIA* ENCEPHALITIS

Dual infestation of brain's vasculature → ↑'d encephalitis of various kinds/degrees

***Babesia* nests reduce blood flow, cause inflammation, disrupt BBB**

***Bartonella* inhabits endothelial cells, crosses leaky BBB, infects microglia → ↑'d inflammation, disrupted neuronal function**

Bystander Effect*: Babesia* nests → ↑'d *Bartonella* brain inflammation and vice versa

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

Muñana KR et al. Infection of fetal feline brain cells in culture with *Bartonella henselae*. *Infect Immun*. 2001 Jan;69(1):564-9. PMID: 11119554

Felger JC, Miller AH. Cytokine effects on the basal ganglia and dopamine function: the subcortical source of inflammatory malaise. *Front Neuroendocrinol*. 2012 Aug;33(3):315-27. PMID: 23000204

BASAL GANGLIA MOST AFFECTED

BG critical to emotions and initiating/sustaining mental and physical actions

Most sensitive to cytokines (inflammation)→Disrupted dopamine signaling

BG injury/inflammation→central fatigue, psychic malaise, anhedonia, anger, anxiety

Caudate nucleus inflammation→hypermetabolism→obsessive-complusive disorder

Capuron L et al. Basal ganglia hypermetabolism and symptoms of fatigue during interferon-alpha therapy. *Neuropsychopharmacology*. 2007 Nov;32(11):2384-92. PMID: 17327884

Chaudhuri A, Behan PO. Fatigue and basal ganglia. *J Neurol Sci.* 2000 Oct 1;179(S 1-2):34-42. PMID: 11054483

Felger JC, Miller AH. Cytokine effects on the basal ganglia and dopamine function: the subcortical source of inflammatory malaise. *Front Neuroendocrinol*. 2012 Aug;33(3):315-27. PMID: 23000204

Hansen ES et al. The caudate nucleus in obsessive-compulsive disorder. Reduced metabolism following treatment with paroxetine: a PET study. *Int J Neuropsychopharmacol*. 2002 Mar;5(1):1-10. PMID: 12057027

BGE: "PANS" VS. PARASITIC INFLAMMATION

"Pediatric acute neuropsychiatric syndrome"—misnomer—also adult, chronic

Proper name: "Autoimmune basal ganglia encephalitis" (ABGE) = systemic autoantibodies to BG dopamine receptors, other neuronal proteins

ABGE responds to IVIG, steroids; Infectious BGE responds partially, temporarily

***Bart* and *Bab* are in the BG→↑↑Inflammation, no need to posit autoimmunity**

PROBLEM: PANS Rx (immunosuppression)→↑'d parasite load, worse encephalitis

EITHER WAY: MUST reduce/eliminate the parasites

Chang K et al. PANS Collaborative Consortium. Clinical evaluation of youth with pediatric acute-onset neuropsychiatric syndrome (PANS). *J Child Adolesc Psychopharmacol*. 2015 Feb;25(1):3-13. PMID: 25325534
Swedo SE et al. Overview of Treatment of Pediatric Acute-Onset Neuropsychiatric Syndrome. *J Child Adolesc Psychopharmacol*. 2017 Sep;27(7):562-565. PMID: 28722464

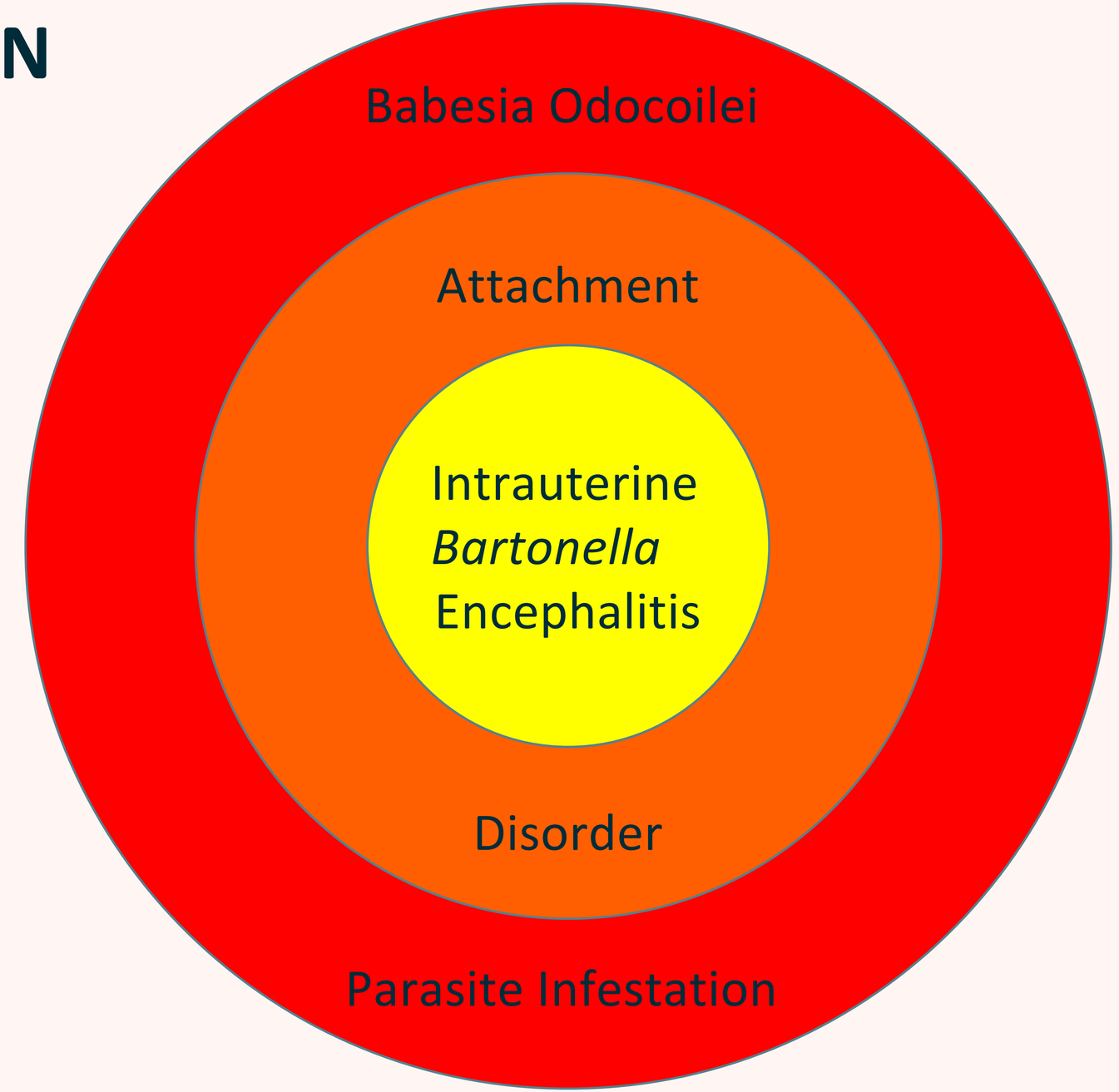
VALERIE: COMBINED *BART*/*BAB* ENCEPHALITIS

In utero: *Bartonella* sp.→Mental suffering from birth, needed distraction; Anhedonia→poor bonding to parents

Atypical attachment disorder – Need to attach to another to feel human

@age 10: *B. odocoilei*→Worsened *Bart* encephalitis, ↓'d brain energy/function, unable to distract→↑'d unhappiness, suicidal ideation, escape into romantic fantasies

VAL'S ONION


Babesia Odocoilei
Attachment
Intrauterine
Bartonella
Encephalitis
Disorder
Parasite Infestation

VALERIE'S ANTIMICROBIAL HX

@age 27: Needing 400mgs predisone daily to control encephalitis

Started Aggressive *Babesia* Rx (AAAT)→Hemolysis, improved stamina, but confusion

@ 6 mos: Lumbrokinase→Herxing/hemolysis followed by new levels of improvement

Repeated Lumbrokinase cycles: Herxing/Hemolysis, more improvements

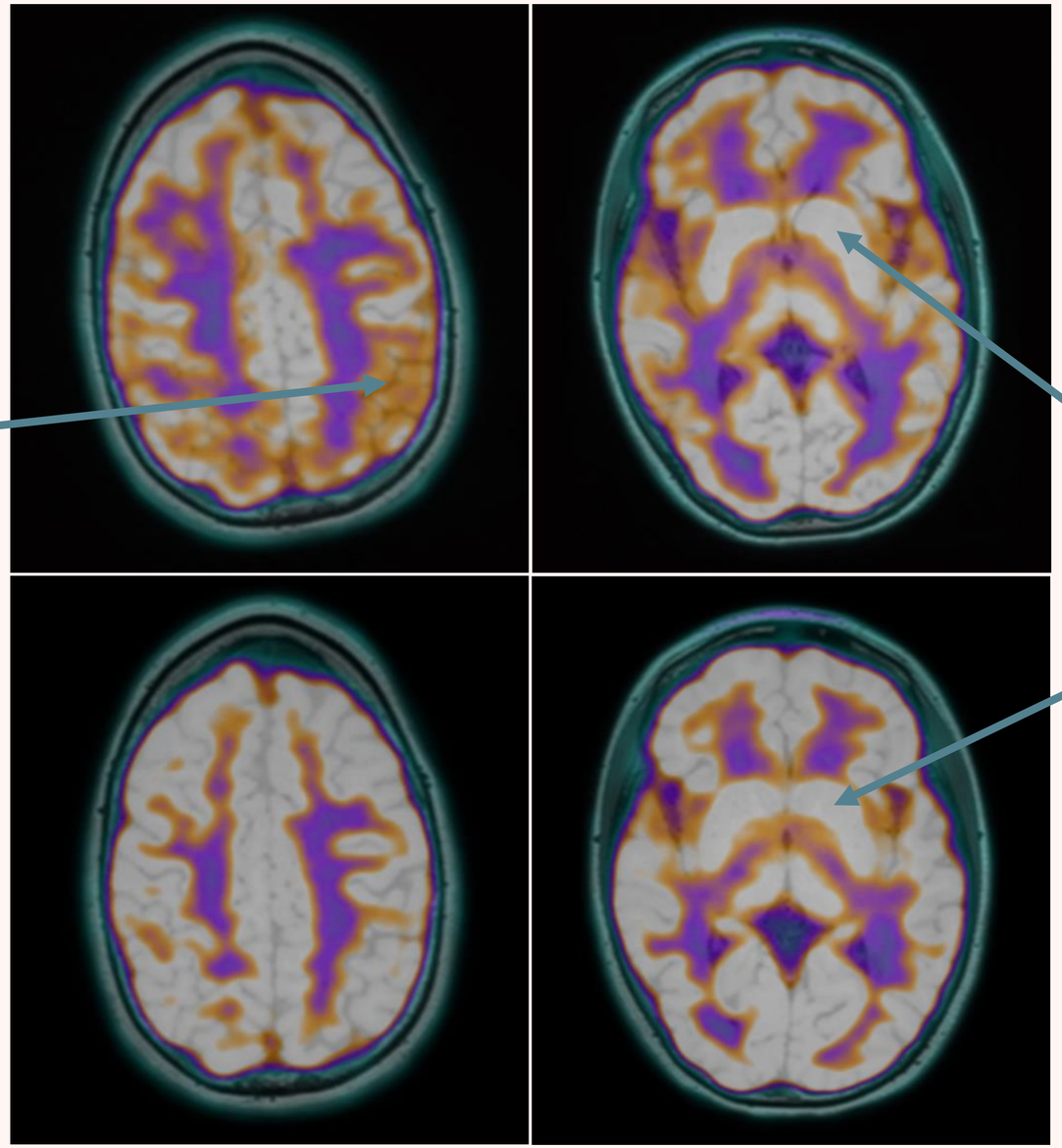
@ 1yr: Rifabutin substuted for Zithro for *Bart*→Mental pain, rage

AAAT=Atovaquone, artesunate, azithromycin. and tafenoquine

None are FDA-approved for babesiosis

VALERIE—*BART*/*BAB* ENCEPHALITIS ON PET/MRI

Before
Antibabesial Treatment
Darker areas=hypometabolism



After
18 months of Antibabesial Treatment

Improved cortical metabolism, but persisting

Basal ganglia encephalitis (hypermetabolism)
(anhedonia, mental pain, anger, etc.)

BART/BAB REGIMEN@20 MONTHS (JULY 2022)

Tafenoquine 600mgs/wk
Artesunate 50mgs tid
Atovaquone 750mgs bid

→ **Anti-*Babesia***

Rifabutin 600mgs/day
Methylene blue 300mgs/day
Allitridi 50 mgs tid (Allicin)

→ **Anti-*Babesia* and Anti-*Bartonella***

Houttuyfonatis 135mgs tid (from *Houttuynia cordata*)— Anti-*Bartonella*

Lumbrokinase (Boluoke®) 4 caps tid — *Babesia* nest dissolution

Methylene Blue effective against *Bartonella* and *Babesia*: also antioxidant, reduces tafenoquine-induced methemoglobinemia

Atovaquone: FDA-approved only for the prevention and treatment of *Pneumocystis jirovecii* pneumonia at 1500mgs/day
Tafenoquine: FDA-approved for prevention of malaria, treatment of *Plasmodium vivax* malaria in patients 16 years and older receiving chloroquine therapy
Artesunate: FDA-approved for severe malaria by intravenous injection
Rifabutin: FDA-approved prevention of disseminated *Mycobacterium avium* complex (MAC) disease in patients with advanced HIV infection
Methylene blue: FDA approved for intravenous treatment of methemoglobinemia

@20 MOS: 10-WK HERX FROM DRAWING/NATTO/ACTIVITY

Drawing/Fantasizing x 3 days→↑'d blood flow to brain→herxing

Added Nattokinase (ARG) 100mg tid for 2 days, 200mg tid for 2 days→

Severe mental Herx: Unbearable without high prednisone doses

To kill *Babesia*: ↑'d Tafenoquine, artesunate, atovaquone, and meth. blue doses

@Grad school: ↑'d activity→↑'d herxing, steroid need, proteinuria

@10 weeks prednisone dose plummeted→pred withdrawal, MORE Improvements!

Sumi H et al. Enhancement of the fibrinolytic activity in plasma by oral administration of nattokinase. *Acta Haematol*. 1990;84(3):139-43. PMID: 2123064
Weng Y et al. Nattokinase: An Oral Antithrombotic Agent for the Prevention of Cardiovascular Disease. *Int J Mol Sci*. 2017 Feb 28;18(3):523. PMID: 28264497

16 YO ♀: “OBSESSIVE-COMPULSIVE DISORDER”

@age 14: Anxiety, derealization, screaming, crying, TMJ pain

Mental discomfort relieved by destroying clothes, pulling out eyebrows

Exposed: Rural home, inside/outside pets, cat scratches/bites, adopted dog with fleas

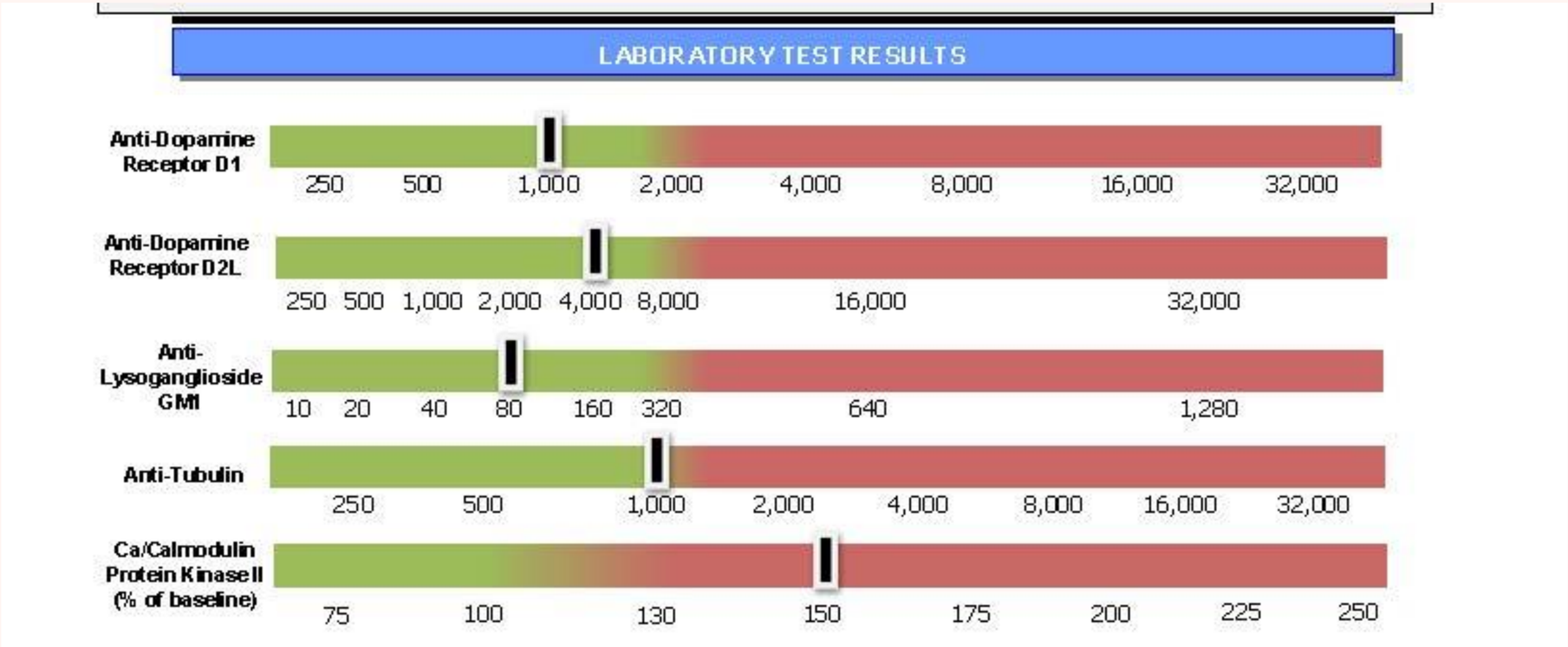
Lyme testing Negative, including cerebrospinal fluid

Neurologist: Intravenous immunoglobulin (IVIG) for “seronegative autoimmune encephalitis”→minimal temporary improvement

16 YO ♀: “OBSESSIVE-COMPULSIVE DISORDER”

Cunningham Panel Negative for D1/D2 abs. Pos. for CaMKII activity

Partial improvement with removal of tonsils*, Augmentin→No improvement



***Observation: Remove any source of immune activation and infested patients will improve. Anything that increases immune activation makes *Babesia* patients worse (→ “Long COVID”).**

IGENEX TESTING

TEST	SPECIMEN	RESULT	REFERENCE RANGE	UNITS
Babesia FISH	W blood	Negative		
B. duncani IFA - IgM	Serum	<20	< 20 : Negative = 20 : May or may not indicate active infection >=40 : Indicates active infection	Titer
B. duncani IFA - IgG	Serum	40	< 40 : Negative < 160 : May or may not suggest active infection >=160 : Indicates active infection	Titer

BARTONELLOSIS

BARTONELLA IMMUNOBLOT IGG			
Bartonella genus	Serum	**Positive**	Positive: Detected 2 or more Bartonella genus or species-specific antibody. Indeterminate: Detected only 1 Bartonella genus or species- specific antibody. Negative: No Bartonella specific antibody detected.
B. elizabethae	Serum	Negative	
B. vinsonii	Serum	Negative	
B. henselae	Serum	Negative	
B. quintana	Serum	**Positive**	

BORRELIOSIS- Relapsing Fever Borrelia

TEST	SPECIMEN	RESULT	REFERENCE RANGE	UNITS
TBRF Borrelia ImmunoBlot IgG				
TBRF Borrelia genus ImmunoBlot IgG	Serum	**Pos(TBRF)**	Positive: Detected 2 or more TBRF Borrelia	

GALAXY DIAGNOSTICS

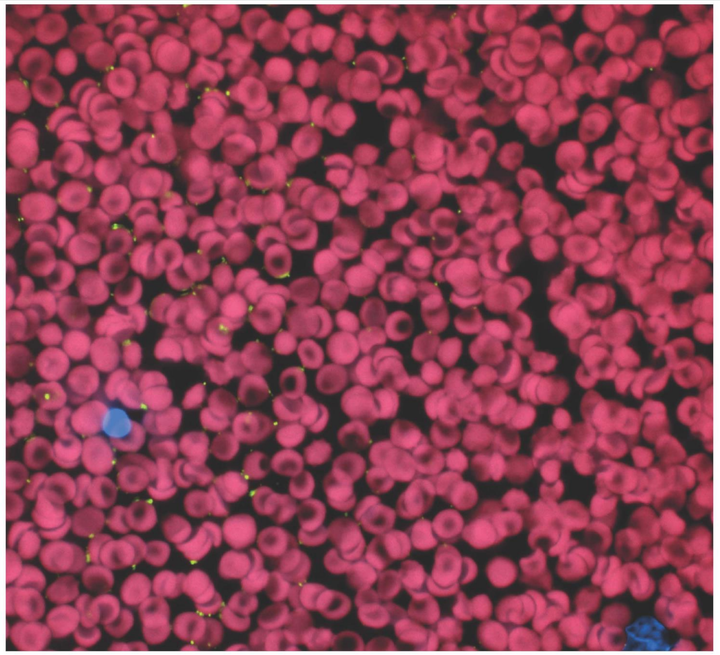
BARTONELLA IFA (IgG) RESULTS

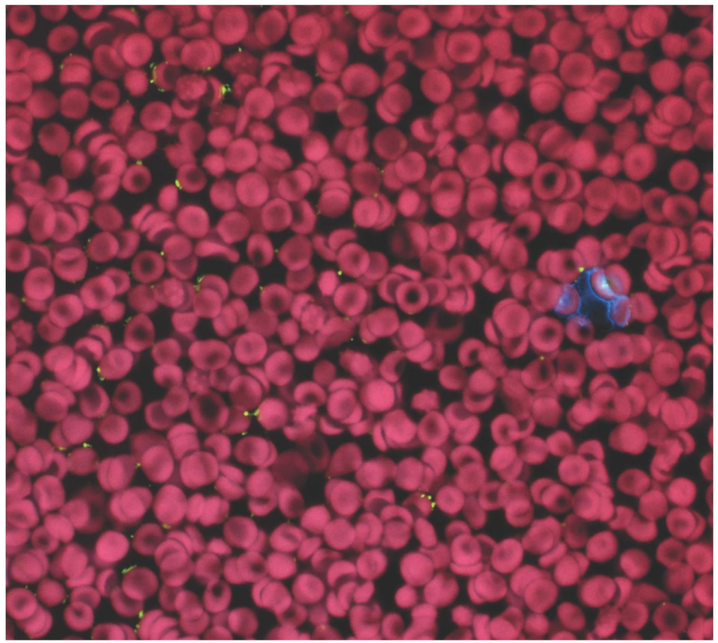
TARGET	COLLECTION	SAMPLE	TYPE	RESULT	TITER	REFERENCE
Bartonella henselae	2022-02-01	S-1	Serum	Reactive	1:256	Non-Reactive
Bartonella quintana	2022-02-01	S-1	Serum	Reactive	1:256	Non-Reactive
Bartonella vinsonii berkhoffi	2022-02-01	S-1	Serum	Reactive	1:256	Non-Reactive
Bartonella koehlerae	2022-02-01	S-1	Serum	Reactive	1:128	Non-Reactive

TLAB: POSITIVE *BARTONELLA HENSELAE* FISH

TEST RESULT		
Target	**Method**	**Result**
Bartonella henselae* H1 23s rRNA*	***in situ* hybridization and Confocal Laser Microscopy**	Your result is: **Positive - probe signal detected significantly above background level** (Research Use Only) (Reference value is “negative”)

REPRESENTATIVE IMAGES

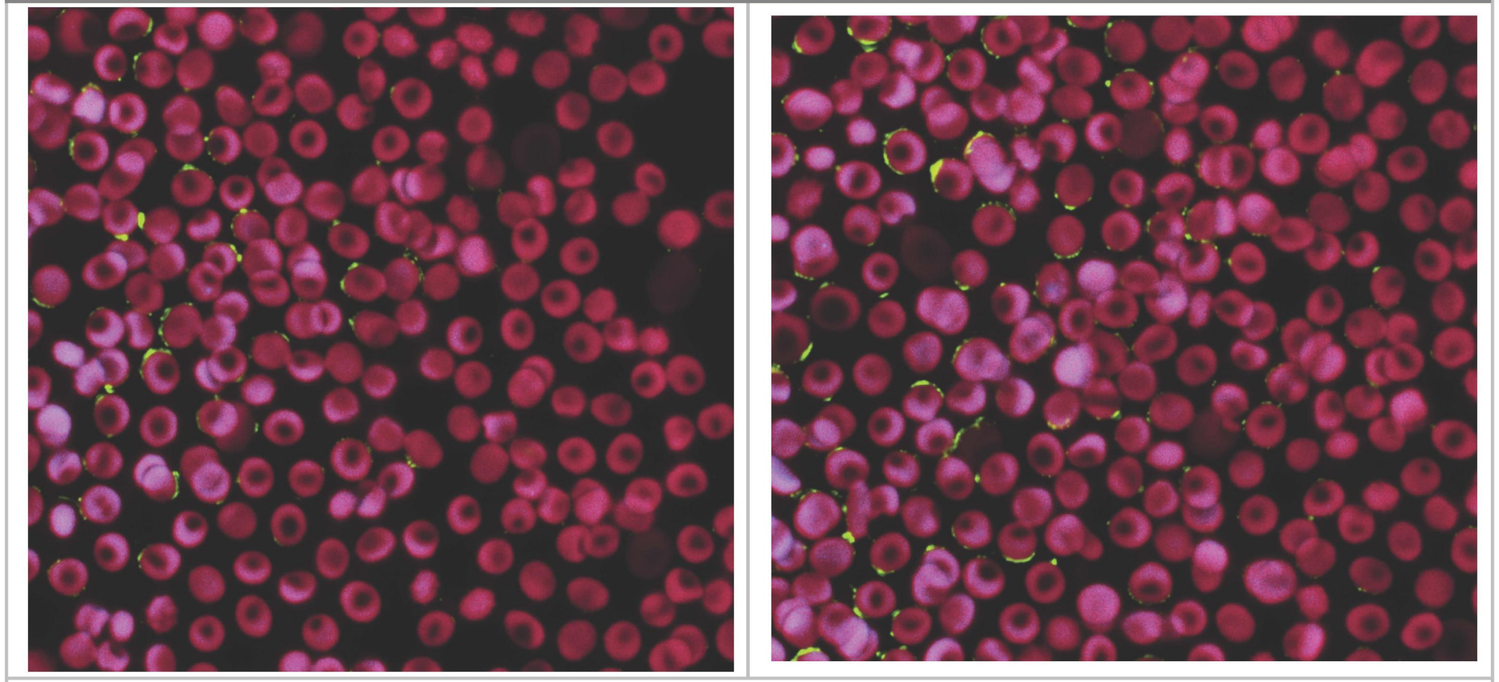




TLAB: POSITIVE *BABESIA ODOCOILEI* FISH

TEST RESULT		
Target	**Method**	**Result**
Babesia odocoilei* 18s rRNA*	***in situ* hybridization and Confocal Laser Microscopy**	Your result is: **Positive - probe signal detected significantly above background level** (Research Use Only) (Reference value is “negative”)

REPRESENTATIVE IMAGES



16 YO ♀: TREATMENT OF *BART/BAB* ENCEPHALITIS

Antibabesials→Mental herxing, “head on fire”, body aches, ruined more clothes

AntiBart: Rifabutin (600mgs) and meth. blue (300mgs)→mental herxing, improvements

@3 mos: Reduced intrusive thoughts, able to keep clothes, developed *Bart* striae

@4 mos: Stopped Rifabutin, Lumbro—Symptoms returned

Houttuyfonatis→severe mental herxing (*Bartonella*)

@8 mos: Improved over baseline, continues to improve

ENCEPHALITIS: ALSO A TALE OF TWO DISEASES

Acute/Severe Encephalitis: known to neurologists

- Rare: May never see a case
- Easy to diagnose: Altered consciousness, psychosis, seizures, movement disorders, etc.
- Many Causes: Infectious, autoimmune, toxic, metabolic, etc.

Chronic/Mild Encephalitis: unknown to neurologists and psychiatrists

- Common: Large percentage of humans have *Bart*, *Bab*, *Toxoplasma*, and non-infectious causes
- Hard to diagnose: "Subjective" complaints, normal neuro exam, subtle EEG/PET/SPECT changes
- Hard to treat: Especially *Bart* and *Bab*, worsens before improving
- Chronic: Minimal to severe according to parasite load, host immune reaction

Unthinking Modern Medicine: Attends only to the obvious, objective, and quantifiable
Fails to believe patient, think about the cause, use clinical judgment, use diagnostic trials

ENLIGHTENED NEUROPSYCHIATRY

Bartonella **and/or** ***Babesia*** **infect large portion of population→encephalitis in many**

Transmitted transplacentally→infant/child neurological, psychiatric, behavioral disorders, attachment disorders

DON'T STOP AT LABELS (depression, schizophrenia, OCD, anxiety d/o, bipolar, etc.)

LOOK FOR THE CAUSE including parasite-related encephalitis: (PET/SPECT scans, Cunningham Panel, Best microbiology tests at Best labs, trials of antimicrobials, brain biopsy, etc.)

Amen DG, Easton M. A New Way Forward: How Brain SPECT Imaging Can Improve Outcomes and Transform Mental Health Care Into Brain Health Care. *Front Psychiatry*. 2021 Dec 10;12:715315. PMID: 34955905

Müller N. Inflammation in Schizophrenia: Pathogenetic Aspects and Therapeutic Considerations. *Schizophr Bull*. 2018 Aug 20;44(5):973-982. PMID: 29648618

Nicolson GL, Haier J. Role of Chronic Bacterial and Viral Infections in Neurodegenerative, Neurobehavioral, Psychiatric, Autoimmune and Fatiguing Illnesses: Part 1. *BJMP* 2009:2(4) 20-28

Nicolson GL, Haier J. Role of Chronic Bacterial and Viral Infections in Neurodegenerative, Neurobehavioral, Psychiatric, Autoimmune and Fatiguing Illnesses: Part 2. *BJMP* 2010;3(1):301