

Lyme Disease/MSIDS: Multiple Systemic Infectious Disease Syndrome: Differential Diagnostic Map

1) Infections:

- a) **Bacterial:** Lyme disease (*B. sensu stricto*) and other borrelia sensu lato species (*B. afzelii*, *B. garinii*, *B. mayonii*...), Relapsing fever borrelia (soft ticks: *B. hermsii*, *B. parkerii*...hard ticks: *Borrelia miyamotoi*), Ehrlichiosis (multiple spp)/Anaplasmosis, Bartonella (multiple species), Mycoplasma (multiple species, esp. *M. fermentans*), Chlamydia, RMSF, Typhus, Q-Fever (*Coxiella burnetii*), Brucella, Tularemia; Tick paralysis secondary to neurotoxins secreted by *Dermatocenter andersoni* & *variabilis*), rarely Ixodes ticks
- b) **Parasites: Babesiosis and other piroplasms** (especially *B. microti* and *WA-1/duncani*), FL-1953 (*protomyxoa rheumatica*), toxoplasmosis, filariasis, GI: amebiasis, giardiasis, strongyloides, hookworm, pinworm, ? roundworm
- c) **Viruses:** EBV, HHV-6, HHV-8, CMV, W Nile, EEE, Powassan encephalitis and other viral encephalopathies, Heartland and Bourbon viruses, SFTS (Severe Fever & Thrombocytopenia Syndrome), South Bay v., BLTPV-1
- d) **Candida and other fungi**

2) Immune dysfunction

☐ Positive ANA, RF and other autoimmune markers, ↑ severity with genetic HLA markers (HLA DR2, 4), elevated pro-inflammatory cells, low immunoglobulin and subclasses (seen w/chronic inf's w/borrelia). Consider Plaquenil, SQIG/ IVIG

3) Inflammation

☐ **Classical:** increase in inflammatory cytokines: (IL-1, IL-6, TNF-alpha, interferon gamma, IL-17), chemokines, bradykinins, leukotrienes, etc. Consider use of immune modulators (such as Plaquenil), drugs w/anti-inflammatory effect (macrolides, tetracyclines), IVIG for decreased immunoglobulins & small fiber neuropathy

☐ **Integrative Therapies:** block NFKappa B (NAC, GSH [oral, IV], ALA) and focus on down-regulation of the inflammatory NO cycle: use diet/supplements that are Nrf2 activators (antioxidants like curcumin, broccoli seed extract [sulforaphane], resveratrol, green tea extract), CoQ10, B vitamins, Mag++, Zn++, omega 3 FA's, and consider decreasing activation of the NLRP3 inflammasome w/ melatonin

4) **Toxicity:** Multiple Chemical Sensitivity, Environmental Illness, Heavy Metals, Mold and Neurotoxins (external and internal biotoxins)

- ☐ **Testing:** VOC's, pesticides, etc. through LabCorp, Bioreference, PacTox, etc for chem's; for heavy metals, consider blood levels for Pb, Hg, As (off fish/shellfish one week before) + unprovoked urine and/or hair evaluation through Doctor's Data; For mold, consider Real Time Labs mold toxin assay : do GSH 1-2 grams up to 1 hour before a sauna, then collect urine. Use Genova (ION /Organix testing) & functional medicine labs (Great Plains) to evaluate detoxification pathways
- ☐ Detoxification is an important part of the treatment plan. NAC, ALA, IV and PO Glutathione has been shown to be effective in a subset of resistant Lyme patients. Mold toxicity requires PC/GSH, binding agents (clay, charcoal, CSM, etc) with N-butyrate, NAC, ALA...sauna therapy helpful for removal toxins
- ☐ Detox protocols would include using supplements like Mag++, multimineral w/Zinc, Cu... NAC, Glycine, α lipoic acid, DIM, sulforaphane glucosinolate, (broccoli seed extracts), diet w \uparrow protein/cruciferous vegetables, Phosphatidylcholine Exchange (IV/PO) with glutathione & binders (clay/charcoal)

5) **Allergies:** foods, drugs, environmental...

- ☐ **Testing:** IgE (immediate), and IgG (delayed) antibodies, as well as evaluation for Mast Cell Activation Disorder (check histamine levels [blood, urine], chromogranin A, tryptase levels, PGD2 [blood, urine]) and Alpha Gal allergy (Lone Star tick bite)
- ☐ **Classical treatment:** Avoidance, rotation diets, immunization therapies, cromolyn sodium, H1/H2 blockers...
- ☐ **Integrative treatment:** consider treating underlying Candida or leaky gut if present (check zonulin levels, CDSA); MCAD requires H1/H2 blockade, Cromolyn, Quercetin, Hist-DAO, PEA, NeuroProtek...

6) **Nutritional & Enzyme Deficiencies/Functional medicine abnormalities in biochemical pathways**

- ☐ **Testing:** serum minerals (Mag++, Zn, Cu, iodine...), RBC minerals (Mag++, Zn, Cu), amino acid & fatty acid analysis (? Kennedy/Kreiger), ION test/ Organix test (Genova labs) + Great Plains to test functional biochemical pathways, lipid peroxides to check free radical exposure (important in CNS disease, ALS...) sulfates, nitrates (Metametrix), while checking detoxification pathways
- ☐ **Treatment:** Replace vitamins, minerals, amino acids, EFA's (essential fatty acids), enzymes (plant or pancreatic w/amylase, lipase, proteases)
- ☐ ? Role of enzymes between meals for viral infectionw/ inflammation

7) **Mitochondrial dysfunction:** Testing: lipid peroxides, 8-OH dG, protein carbonyls to test for oxidative stress. Organix test (Genova/Metametrix) may

provide indirect evidence through nutritional deficiencies, free radical exposure. European labs (UK, Germany) can test for mtDNA damage and DNA adducts
□ Treatment: NT factors (glycosylated phospholipids like ATP 360), CoQ10, NADH, L-carnitine, ? D-ribose (if no evidence of increased glycosylation and diabetes)

8) **Psychological**: stress, PTSD, abuse, depression, anxiety, OCD...

□ Health care providers should ask about previous psychiatric history and refer for counseling/psychiatric help. Up to 1/3 of patients may have a hx of abuse, and interferes with treatment outcomes

□ Treatment: Medications (SSRI's, bupropion, Remeron, anxiolytics,), Stress reduction (yoga, meditation, Tai Chi), Herbs (5 HTP, St John's Wort, Valerian root, Kava Kava, L-theanine), CBT (PTSD), Neurofeedback, Biofeedback, Journey work (Brandon Bays), EMDR, ?EFT, Annie Hopper's Dynamic Neural Retraining (DNRS): retrainingthebrain.com

9) **Neurological dysfunction**: ? overlapping neurological presentations, i.e. MS, ALS, pain syndromes (mononeuropathy, mononeuritis multiplex, trigeminal neuralgia, polyneuropathy, CIDP...), atypical features of a psychiatric disorder, neurocognitive deficits, apart from cranial nerve deficits (Bell's palsy). Treat underlying etiologie(s)

10) **Endocrine abnormalities**: thyroid, growth hormone (GH), adrenal, sex hormones, anterior and post pituitary hormones, Vitamin D deficiency

□ Hypothalamic-pituitary axis may be affected → check FSH, LH, GH and IGF1, TSH, T3 & T4, FT3/FT4, reverse T3, DHEA/Cortisol (salivary, blood), sex hormones, pregnenolone, MSH, ADH, VIP... and treat underlying abnormalities. Adrenal fatigue is oftentimes a common underlying abnormality needing attn

11) **Sleep disorders**: Acute and Chronic

□ Causes: Obstructive Sleep apnea, Medications, Caffeine, Nocturia/BPH, Pain, Depression/Anxiety, Restless Leg Syndrome (RLS)..

□ Evaluation: Sleep Study if unresponsive to standard treatment regimens

□ Treatment: Activating Agents in the AM, Sleep promoting agents in the PM, especially those that encourage stage 3/stage 4 non-REM sleep (Lyrica, Trazadone, Gabitril, Seroquel, Doxepin, Remeron, Xyrem...), cyclobenzaprine

□ CAM: check neurotransmitter levels. Balance neurotransmitters with 5-HTP, GABA, ? SeriPhos if elevated cortisol levels at bedtime, Valerian root, L-theanine, melatonin may also be useful, ? Honokiol, Herbsom, Cerenity PM...

12) Autonomic Nervous System (ANS) Dysfunction/POTS (Postural Orthostatic Tachycardia Syndrome)

□ Certain Chronic Lyme disease patients will complain of fatigue, dizziness w/standing, & concentration problems despite classical therapies. BP will be low on exam (< 90-100/60), with associated increases in heart rate (tachycardia, > 100 BPM) at rest.

□ Testing: Tilt table test, blood pressure log with home readings, sitting and standing BP and pulse at time zero, 3, 6 and 9-10 minutes in the doctor's office

□ Treatment: salt (minimum 3-4 grams/day, ? salt tab's), increase fluids (3 liters +), consider Florinef, Midodrine, Northera, Cortef (if low adrenals), and/or B blockers, occasionally clonidine and SSRI's like sertraline(Zoloft) if inadequate response

13) Gastrointestinal: Leaky Gut, food allergies, SIBO, Candida, dysbiosis, parasites, celiac disease/gluten sensitivity, colitis, cancer...

□ Celiac disease: one of several malabsorption syndromes, due to gluten sensitivity. Look for laboratory evidence of malabsorption: ↓ albumin as well as lowered cholesterol, Ca⁺⁺, Mag⁺⁺, B12, w/ macrocytic anemia, ↓ Fe, K⁺

□ Testing: Antigliadin AB, TTG, ? Cyrex panel, avoid gluten as therapeutic trial. Individuals may be gluten sensitive without having true celiac disease

□ Other GI: Crohns, Ulcerative Colitis (UC), parasites, Candida/Leaky gut/dysbiosis, other malabsorption syndromes

14) Elevated Liver Function Tests (LFT's): ? antibiotics, ETOH, Hepatitis, Hemochromatosis (iron overload), Wilsons disease (copper overload), α-1AT deficiency, chemicals (carbontetrachloride, drugs)...

□ Testing: ANA, AMA, Hepatitis A, B, C screen, Fe-TIBC/ferritin, ceruloplasmin levels, α-antitrypsin levels, tick-borne panel, lipid levels (high TG)...

□ Treatment: Treat symptomatically if above etiologies ruled out. CAM: Milk thistle (silymarin), Hepa #2 (TCM), NAC, alpha lipoic acid, glutathione..

15) Pain/Addiction: Consider LDN, Nrf2 activators (curcumin, sulforaphane, resveratrol, green tea extract), liposomal Glutathione capsules 6-8 qd/? Q 3days, NAC, ALA, drainage remedies [Pekana (Itires)] for lymphatic drainage, BLT/Greenwood Herbals Herx formula, IVIG?

16) Deconditioning: Need for physical therapy (PT)/exercise programs.

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