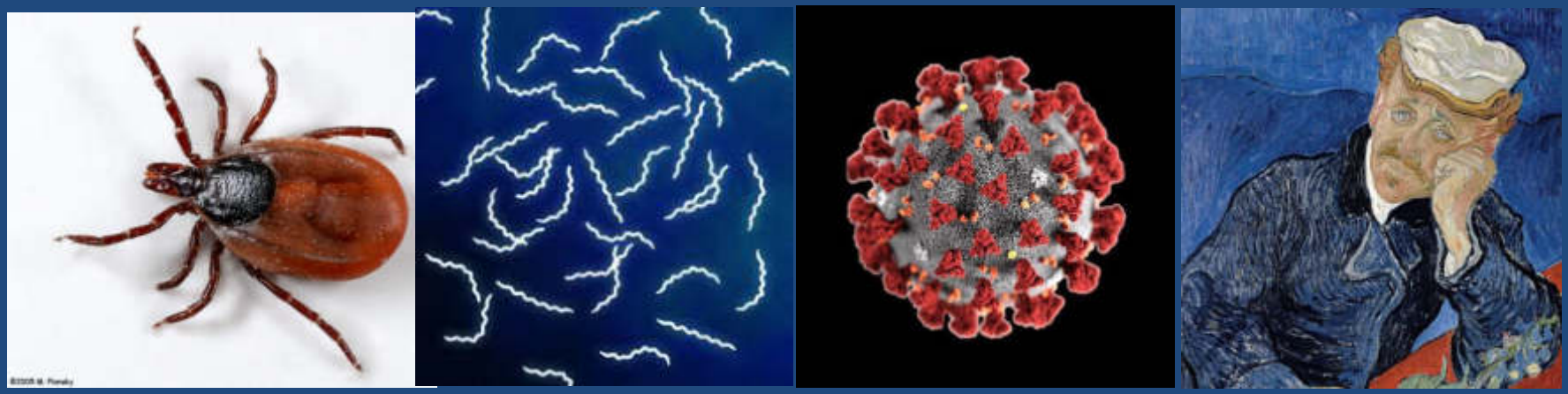
Chronic Lyme Disease & Chronic COVID-19



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The Three Great Imitators

- Syphilis imitates many diseases and has been called The Great Imitator.
- Lyme has been called The Second Great Imitator.
- The multiple chronic symptoms from COVID-19 are making it The Third Great Imitator.

How Effectively Have We Approached Emerging Diseases?

- Lyme Disease
- Chronic Fatigue/Myalgic Encephalitis, Autism, Fibromyalgia, AIDS, Gulf War Syndrome, Morgellons, PANDAS/PANS, Bartonellosis, Mycoplasma infections, Multiple Chemical Sensitivity, Mold Sensitivity, etc.
- Medical bureaucracies have consistently failed with complex, chronic, costly diseases.

Identifying Chronic Symptoms

- How can we identify, understand and treat chronic symptoms in patients with Lyme/tick-borne disease, patients with COVID-19 and patient with both Lyme/tick-borne disease and COVID-19?
- First let's identify what we are talking about.

Defining Chronic Disease

- A chronic disease is one lasting 3 months or more, by the definition of the U.S. National Center for Health Statistics. Chronic diseases generally cannot be prevented by vaccines or cured by medication, nor do they just disappear.

MedicineNet. Definition of Chronic Disease. (2016).
Available from: http://www.medicinenet.com/script/main/art.asp?articlekey=33490

Long-Haulers Defined

- Someone who travels long distances*
- *Especially* **:** a truck driver who transports loads over long distances (often traveling 100,000 miles per year, with an average daily run of 500 miles.*
- A person who suffers from symptoms of COVID-19 for longer than two weeks, and generally for several months. The experience of such persistent symptoms of COVID-19 are sometimes referred to as **long** COVID.
- Why use a trucker's term to define a medical condition?

*Merriam-Webster Dictionary

What Is a Better Term?

- Post-acute
- Chronic or persistent
  - Chronic infection or just chronic symptoms?
  - Chronic active or latent infection?
- Late stage
- Post treatment
- Syndrome
- Post infection: is it possible to prove the infection is actually gone?

Do Antimicrobial Treatments Help "Post Treatment Lyme Disease"?

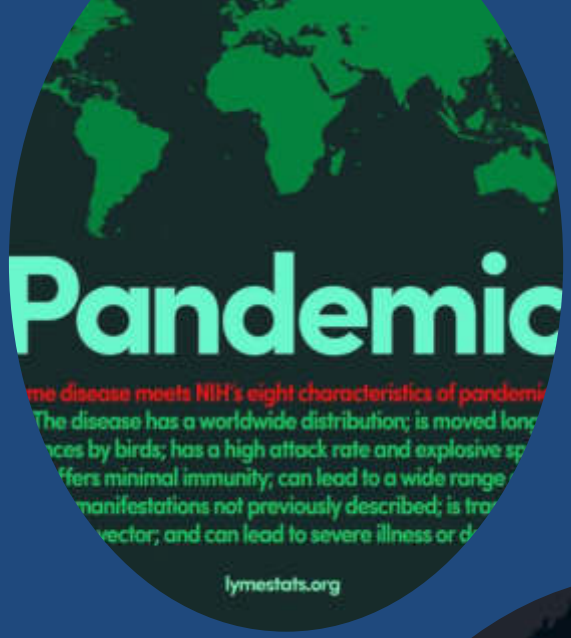
- Some propose there is no such thing as chronic Lyme.
- Why is *Borrelia burgdorferi* found in autopsies?
- Why do Lyme/TBD patients improve in response to disulfiram and other antimicrobial treatments?

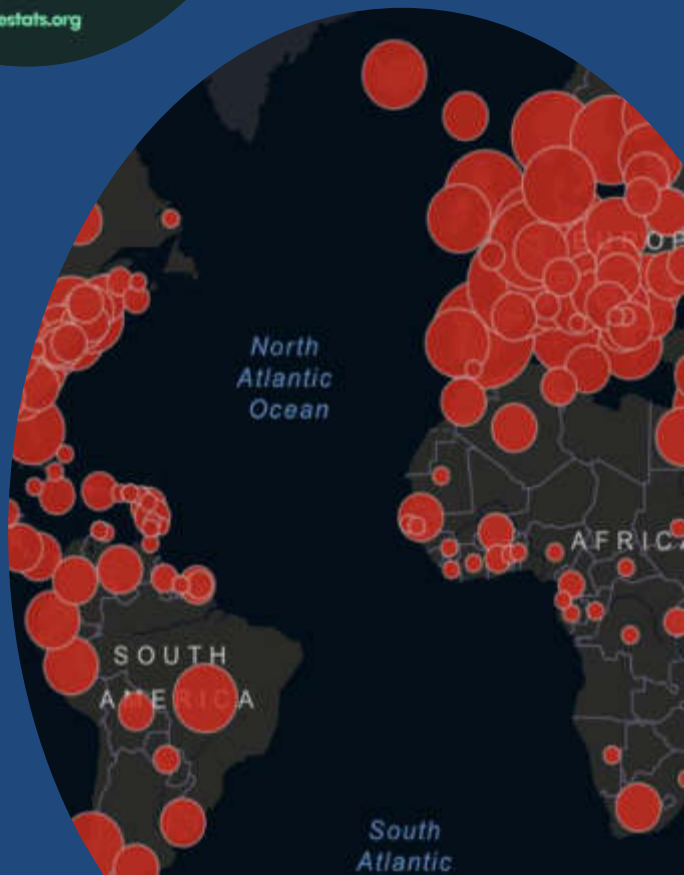
Does COVID-19 &/or Lyme Cause Chronic Symptoms?

- Both COVID-19 &/or Lyme may cause:
  - No acute symptoms in some
  - No chronic symptoms in some
  - Mild choric symptoms in others
  - Severe chronic symptoms in others
  - Relapsing, remitting &/or progressively increasing and expanding symptoms in some
- What about the combination of both?

Lyme & COVID-19 Comorbidity

- How does COVID-19 effect Lyme disease?
- How does Lyme effect COVID-19?





Lyme Disease in the Era of COVID-19: A Delayed Diagnosis and Risk for Complications

- We describe a patient with fever and myalgia who did not have COVID-19 but instead had Lyme disease. We propose that the co-occurrence of COVID-19 and Lyme disease resulted in a delayed diagnosis of Lyme disease due to COVID-19 pandemic-related changes in healthcare workflow and diagnostic reasoning.
- We present the use of telemedicine to aid in the diagnosis of Lyme disease and to provide prompt access to diagnosis and care during the ongoing COVID-19 pandemic and in the future.

Novak CB et al. case Reports in Infectious Disease. 2021

Both Lyme & COVID-19 Have Post-Acute, Chronic Symptoms

- We propose that once an acute COVID-19 infection has been overcome, a subgroup of remitted patients are likely to experience long-term adverse effects resembling CFS/ME symptomatology such as persistent fatigue, diffuse myalgia, depressive symptoms, and non-restorative sleep.

Perrin R, Riste L, Hann M, Walther A, Mukherjee A, Heald A. Into the looking glass: Post-viral syndrome post COVID-19. *Med Hypotheses*. 2020;144:110055. doi:10.1016/j.mehy.2020.110055

How Are Chronic COVID Symptom Different from Chronic Lyme Symptoms?

- COVID-19 has more:
  - Pulmonary symptoms
  - Myocarditis
  - Severe post-exertional fatigue
  - Similarities to CFS/ME
  - Clots and vascular symptoms
- Lyme/TBD more:
  - Cranial nerve symptoms
  - Arthritic symptoms
  - Neuropathy, radiculopathy

Does COVID-19 Trigger a Complex Interactive Infection?

- Does it activate and interact with other infections that may have been either active or latent?
- We see this occur with Lyme and EBV and with Lyme, Babesia, Bartonella, Anaplasma, opportunistic viruses, etc.
- Does COVID-19 sometimes activate a previously latent case of Lyme/TBD disease?

Lyme & COVID-19: Preliminary Hypothesis

- 1. If someone has a latent or active case of Lyme/TBD and is not in treatment and they acquire COVID-19, there may be an initial exacerbation of Lyme/TBD symptoms in addition to the COVID-19 symptoms, however some who have fever report a later improvement in Lyme/TBD symptoms, possibly from immune activation.
- 2. If someone is in treatment for Lyme/TBD and they acquire COVID-19, it is a milder infection and adaptive immunity to COVID-19 may be acquired. However some Lyme/TBD treatments my be more effective than others.

fatigue

SARS-CoV-2 RNA reverse-transcribed & integrated into the human genome

- Prolonged SARS-CoV-2 RNA shedding and recurrence of PCR-positive tests have been widely reported in patients after recovery, yet these patients most commonly are non-infectious.
- Human endogenous LINE-1 expression was induced upon SARS-CoV-2 infection or by cytokine exposure in cultured cells, suggesting a molecular mechanism for SARS-CoV-2 retro-integration in patients. This novel feature of SARS-CoV-2 infection may explain why patients can continue to produce viral RNA after recovery and suggests a new aspect of RNA virus replication.

Zhanng L et al.

NIH study uncovers blood vessel damage and inflammation in COVID-19 patients' brains but no infection

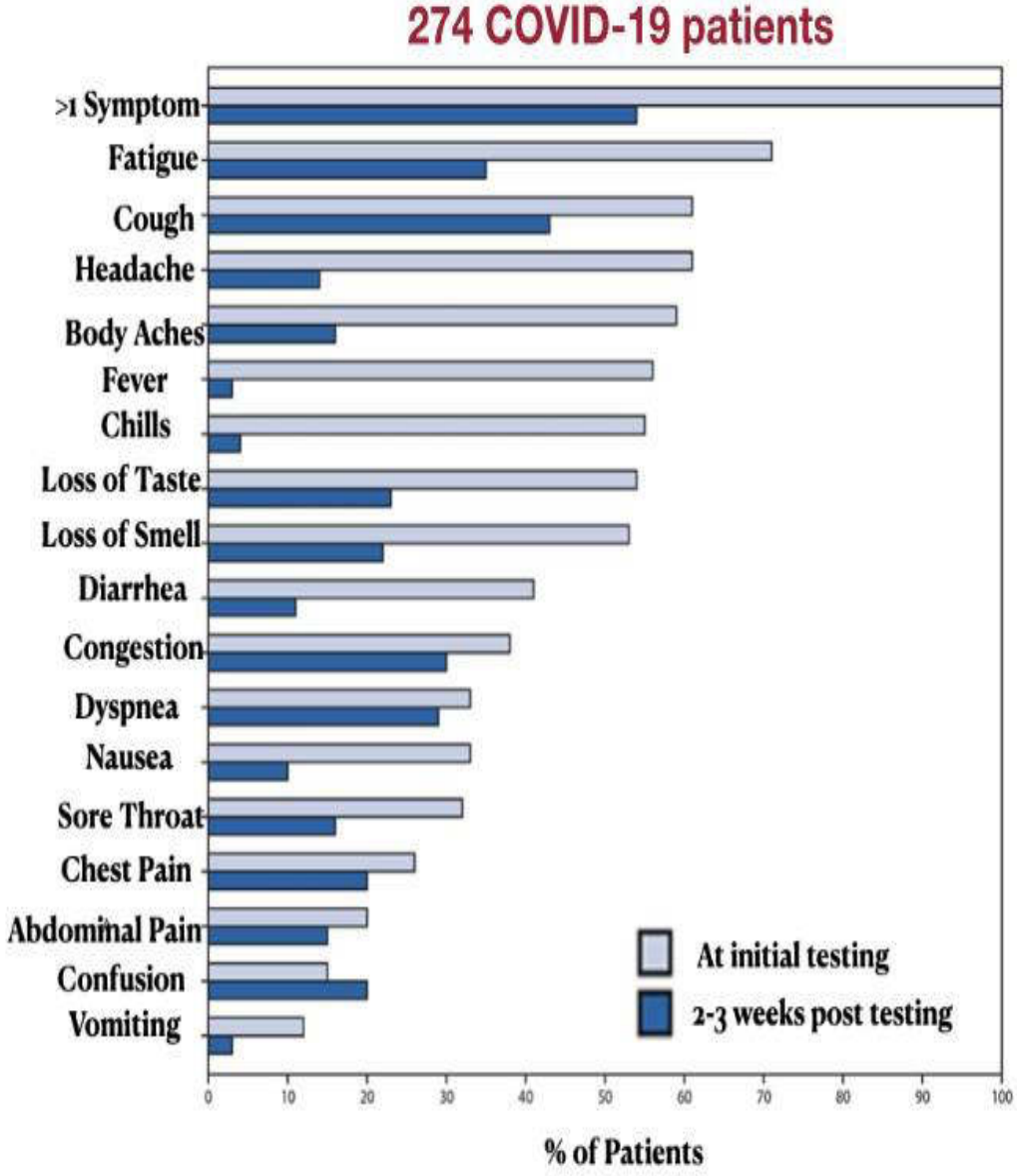
- In an in-depth study of how COVID-19 affects a patient's brain, NIH researchers consistently spotted hallmarks of damage caused by thinning and leaky brain blood vessels in tissue samples from patients who died shortly after contracting the disease. In addition, they saw no signs of SARS-CoV-2 in the tissue samples, suggesting the damage was not caused by a direct viral attack on the brain.
- Although COVID-19 is primarily a respiratory disease, patients often experience neurological problems including headaches, delirium, cognitive dysfunction, dizziness, fatigue, and loss of the sense of smell. The disease may also cause patients to suffer strokes and other neuropathologies.

Lee MH et al. Microvascular Injury in the Brains of Patients with Covid-19. N Engl J Med. 2021 Feb 4;384(5):481-483. doi: 10.1056/NEJMc2033369.

CDC Study: Post COVID Symptoms

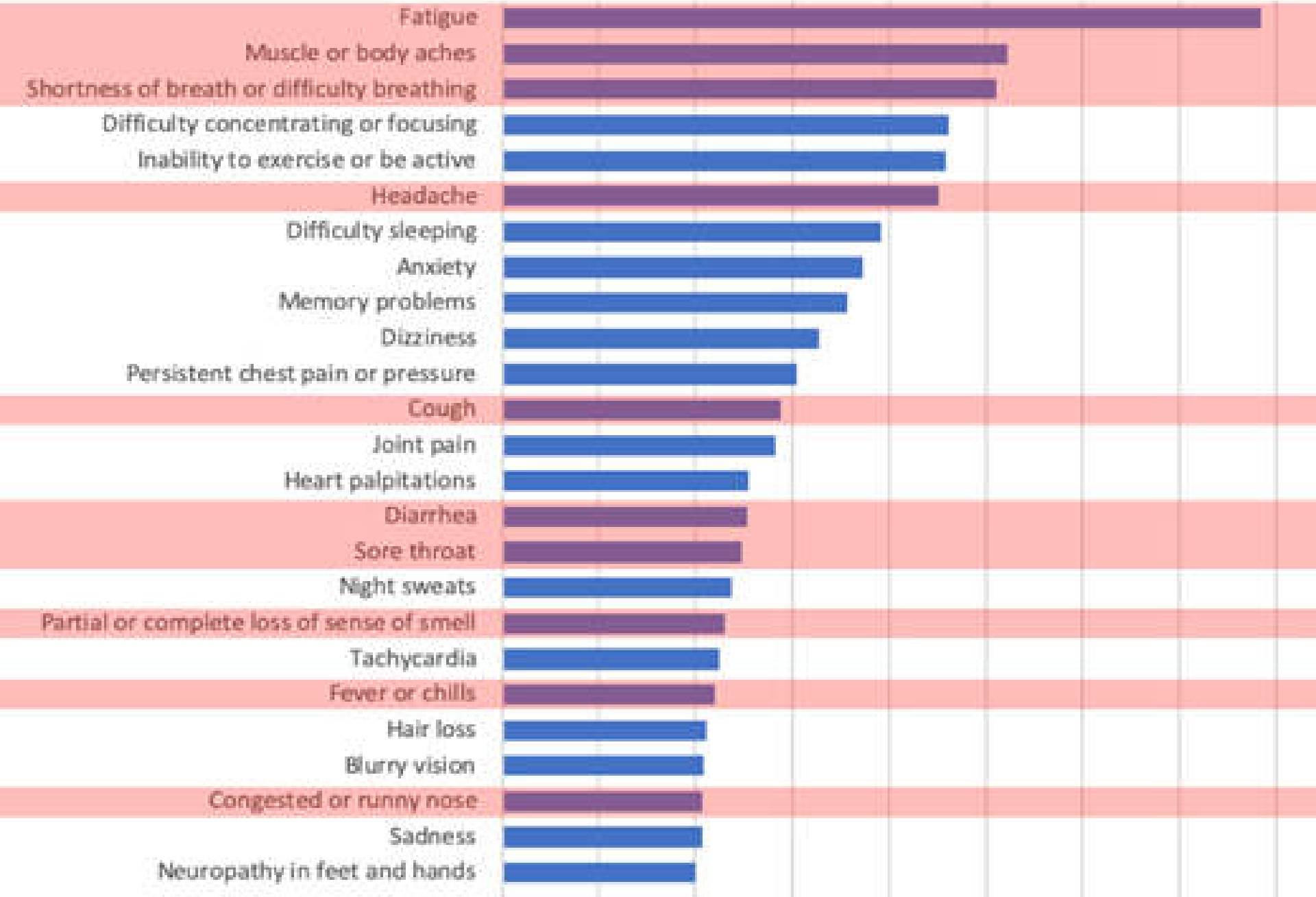
At 2-3 weeks post initial PCR:

- 35% did not return to their usual state of health
- Among young adults, 18–34 years with no chronic medical conditions, ~ 1/5 had not returned to their usual state of health
- Persistent neurological symptoms
  - **Fatigue, headache, loss of smell/taste, confusion**



Adapted from Tenforde, et al, Morbidity and Mortality Weekly Report, CDC, July 31, 2020 / 69(30);993-998

CDC (shaded) vs. Long Hauler Reported COVID-19 Symptoms



Significant Neuropsychiatric Symptoms

The 50 Most Common Long Hauler Symptoms

. Painful Symptoms

Painful vs. Painless

Six-month Neurological and Psychiatric Outcomes in 236,379 Survivors of COVID-19 (UK)

- 33.6% of the coronavirus survivors received a neurological or psychiatric diagnosis including stroke, intracranial hemorrhage, dementia, psychotic disorders, terrifying hallucinations, coordination issues, & memory lapses
- Patients who've been hospitalized are especially susceptible to psychiatric complications.

Taquet M et al. In review

Mental Health Symptoms during COVID-19: A Comparison of the United Kingdom and Austria

- In total, 3.2% of the Austrian sample and 12.1% of the UK sample had severe depressive symptoms, 6.0% in Austria vs. 18.9% in the UK had severe anxiety symptoms, & 2.2% in Austria & 7.3% in the UK had severe insomnia.
- The prevalence of severe depressive, anxiety or insomnia symptoms was around three times higher in the UK than in Austria.

Budimir S, Pieh C, Dale R, Probst T. Severe *Healthcare*. 2021; 9(2):191.

Bidirectional associations between COVID-19 and psychiatric disorder: retrospective cohort studies of 62 354 COVID-19 cases in the USA

- In patients with no previous psychiatric history, a diagnosis of COVID-19 was associated with increased incidence of a first psychiatric diagnosis in the following 14 to 90 days compared with six other health events. The HR was greatest for anxiety disorders, insomnia, and dementia. We observed similar findings, although with smaller HRs, when relapses and new diagnoses were measured. The incidence of any psychiatric diagnosis in the 14 to 90 days after COVID-19 diagnosis was 18·1%, including 5·8% that were a first diagnosis. The incidence of a first diagnosis of dementia in the 14 to 90 days after COVID-19 diagnosis was 1·6% in people older than 65 years.
- Survivors of COVID-19 appear to be at increased risk of psychiatric sequelae, and a psychiatric diagnosis might be an independent risk factor for COVID-19.

Taquet M et al. Lancet. VOLUME 8, ISSUE 2, P130-140, FEBRUARY 01, 2021

Characterizing Long COVID in an International Cohort: 7 Months of Symptoms and Their Impact

- Participants 3,762 respondents from 56 countries completed the survey. 96% reported symptoms beyond 90 days. Prevalence of 205 symptoms in 10 organ systems was estimated. Respondents experienced symptoms in an average of 9.08 organ systems. The most frequent symptoms reported after month 6 were: fatigue (77.7%), post-exertional malaise (72.2%), and cognitive dysfunction (55.4%). Respondents with symptoms over 6 months experienced relapses, with exercise, physical or mental activity, and stress as the main triggers. 86.7% of unrecovered respondents were experiencing fatigue at the time of survey reported requiring a reduced work schedule compared to pre-illness and 22.3% were not working at the time of survey due to their health conditions. Conclusions Patients with Long COVID report prolonged multisystem involvement and significant disability. Most had not returned to previous levels of work by 6 months. Many patients are not recovered by 7 months, and continue to experience significant symptom burden.

Davis et al. Prepint

Systematic Review & Meta-analysis

- 80% had chronic symptoms, >50 different symptoms
- 5 most common manifestations were fatigue (58%, 95% CI 42-73), headache (44%, 95% CI 13-78), attention disorder (27% 95% CI 19-36), hair loss (25%, 95%CI 17-34), dyspnea (24%, 95% CI 14-36) An abnormal chest X-Ray/CT in 34% (95% CI 27-42).
- Symptoms related to lung disease (cough, chest discomfort, reduced pulmonary diffusing capacity, sleep apnea, & pulmonary fibrosis), cardiovascular (arrhythmias, palpitations, myocarditis), neurological (dementia, depression, anxiety, attention disorder, OCD, confusion, vertigo, dizziness, tinnitus), and night sweat, sudden loss of body weight, ear pain, eye problems, sneezing, cold nose, burning feeling in the trachea & lungs, pain between the shoulder blades, Sicca syndrome, body aches

Lopez-Leon et al. BMJ Yale. In reveiw

Coronavirus ‘altered the brain’ of NYC ER doc who killed herself, sister says

NY Post

COVID GENERATION ‘Explosion’ of stressed Brit kids diagnosed with tics in COVID lockdown with fears they’ve ‘been sacrificed for the old’

- Dr Alasdair Parker, president of the British Paediatric Neurology Association, said: “The most severe tics disorders I have seen over the last 20 years have all presented in the last five months to my practise.”
- One mum told how her 13-year-old daughter had been a star pupil before the pandemic but has now developed a severe tic: “She shouts, she swears, she hits, she throws things, she drops to her knees, her legs kick out, her arms fly out, she head-butts things and smacks herself in the face.

Grealish S. **The Sun.** 14 Feb 2021

How Are Lyme & COVID-19 Similar?

- Zoonotic, global diseases
- Both are emerging infectious diseases
- Multiple genetic variants & coinfections
- No symptoms or spectrum of symptoms
- Immune reactions, cytokine storm cause multisystem disease
- Chronic symptoms in some
- Reinfection vs reactivation?
- Some of the same off-label treatments
- Similar conflicts of interest

Common Chronic COVID vs. Lyme

COVID-19 (Lambert)

- Fatigue
- Muscle or body aches
- Shortness of breath or difficulty breathing
- Difficulty concentrating
- Inability to exercise or be active
- Headache
- Difficulty sleeping
- Anxiety
- Memory problems
- Dizziness
- Persistent chest pain or pressure
- Cough
- Joint pain
- Heart palpitations
- Diarrhea

Lyme Disease (Bransfield et al)

- Sustained attention 84%
- Brain fog 84%
- Unfocused concentration 81%
- Joint symptoms 81%
- Low frustration tolerance 80%
- Distracted by frustration 79%
- Depression 79%
- Working memory 78%
- Recent memory 77%
- Fatigue 76%
- Non-restorative sleep 76%
- Multitasking 74%
- Sudden mood swings 74%
- Hypersomnia (daytime) 73%
- Insomnia 72%
- Apathy 72%
- Tingling 71%
- Word retrieval 70%
- Headache 68%

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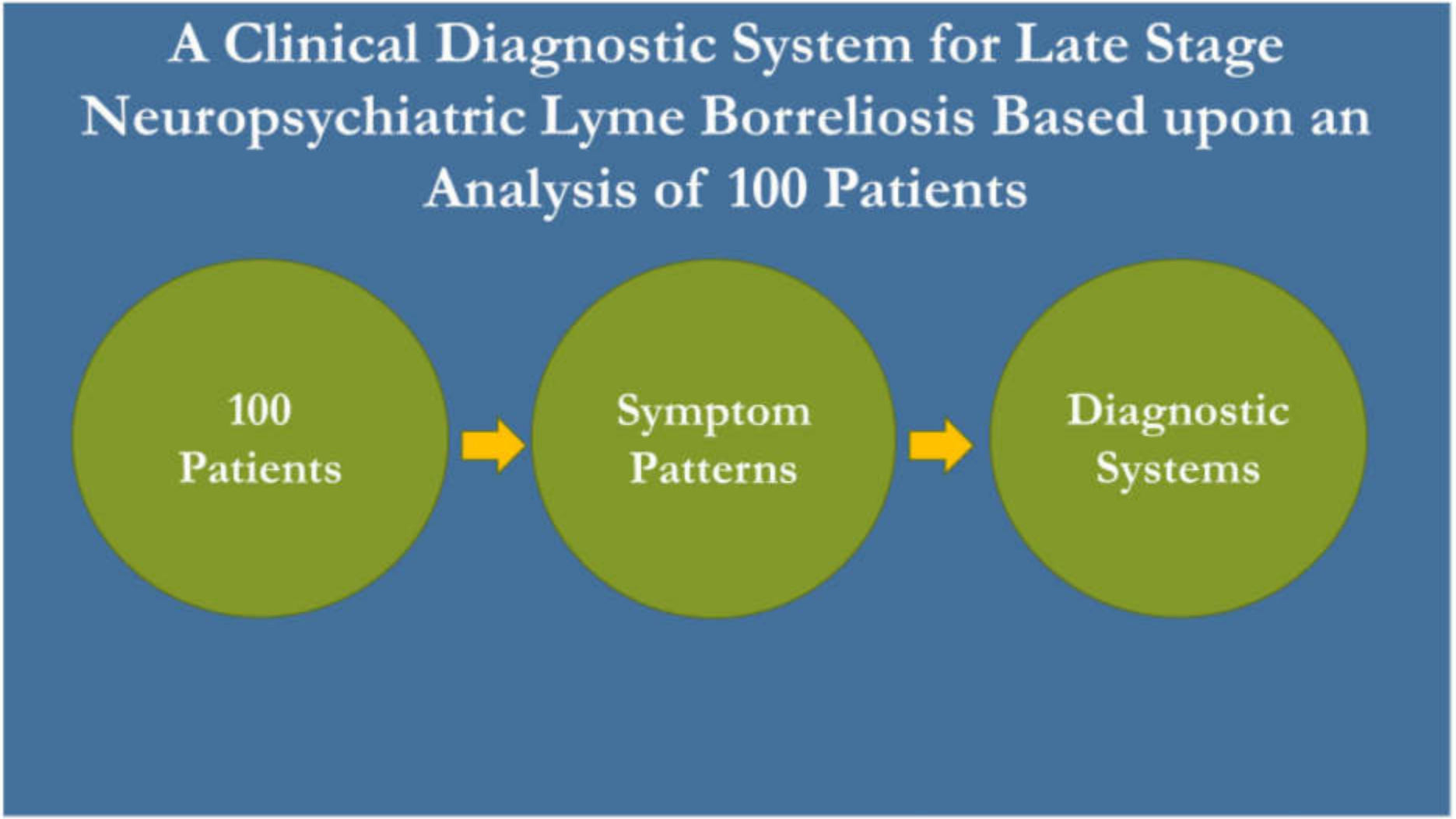
- 2. If someone is in treatment for Lyme/TBD and they acquire COVID-19, it is a milder infection and adaptive immunity to COVID-19 may be acquired. However some Lyme/TBD treatments my be more effective than others.

Assessment

- Like other illnesses, Lyme Borreliosis is diagnosed by a screening assessment followed by a thorough history, comprehensive psychiatric clinical exam, review of systems, mental status exam, neurological exam and physical exam relevant to the patient's complaints and findings with clinical judgment, pattern recognition and knowledgeable interpretation of laboratory findings facilitates diagnosis.

Bransfield RC. Neuropsychiatric Lyme Borreliosis: An Overview with a Focus on a Specialty Psychiatrist's Clinical Practice. Healthcare (Basel). 2018 Aug 25;6(3).

Method


A Clinical Diagnostic System for Late Stage Neuropsychiatric Lyme Borreliosis Based upon an Analysis of 100 Patients
100 Patients
Symptom Patterns
Diagnostic Systems

Screening & 3 Assessment Forms

- Screening questions
- 24-item patient self-assessment
- 61-item assessment (more common symptoms)
- 283-item assessment with 810 data points (full assessment)
- Coinfection Screen

Bransfield RC. Neuropsychiatric Lyme Borreliosis: An Overview with a Focus on a Specialty Psychiatrist's Clinical Practice. Healthcare (Basel). 2018 Aug 25;6(3).

Screening questions

- Do you live, vacation, or engage in occupational or other activities in areas that may expose you to ticks?
- Have family members, neighbors, or the family dog been infected?
- Is there a history of a tick bite, possibly with a flu-like illness and/or a bull's eye or other rash?
- Is there a point at which your health declined, followed by a fluctuating progression and development of multi-systemic symptoms, including cognitive, psychiatric, neurological, and somatic symptoms adversely impacting school, social life, family life?
- Have you ever been treated for Lyme disease, suspected you had Lyme disease but was told it was ruled out?
- Have antibiotics ever caused a sudden worsening followed by an improvement of symptoms?"

Reduced set of 24 highly significant impairments. Suitable for pre-evaluation by patients

- Concentration impairment
- Short term memory problems
- Word finding difficulty
- Name recall difficulty
- Fluency of speech difficulties
- Brain fog
- Sudden mood swings
- Decreased social functioning
- Decreased job/school performance
- Depression
- Fatigue
- Insomnia
- Night sweats
- Low body temperature
- Headache
- Blurred vision
- Floaters
- Tinnitus (ringing in the ears)
- Sensitive to sound
- Dizziness
- Numbness
- Tingling
- Joint pain, swelling
- Fluctuation of symptoms
- Stress increases symptoms

Most Common Symptoms

Common symptoms in which ≥50% or more have the clinical finding I

- **Attention span**
- Sustained attention
- Distracted by frustration
- Allocation of attention
- Hypersensitivity to sound
- Hypersensitivity to light
- **Memory**
- Working memory
- Recent memory
- Remote memory
- **Memory retrieval**
- Words
- Names
- Numbers
- **Processing**
- Fluency of speech
- Reading comprehension
- Spelling errors
- Word substitution errors
- Optic ataxia
- Calculation
- **Executive functioning**
- Brain fog
- Unfocused concentration
- Prioritizing multiple tasks
- Multitasking
- Mental apathy
- **Emotional**
- Decreased frustration tolerance
- Sudden mood swings

Common symptoms in which ≥50% or more have the clinical finding II

- **Behavioral**
- Decreased job/school performance
- Decreased social functioning
- Dropping objects
- **Psychiatric syndromes**
- Depression
- Generalized anxiety disorder
- Posttraumatic stress disorder
- **Energy**
- Fatigue
- **Sleep**
- Non-restorative sleep
- **Insomnia**
- Hypersomnia
- Insomnia, mid
- Insomnia, initial
- Insomnia, late
- **Sexual functioning**
- Decreased libido
- **Temperature control**
- Intolerance to cold
- Body temperature fluctuations
- Night sweats
- Chills
- Intolerance to heat
- Decreased body temperature

Common symptoms in which ≥50% or more have the clinical finding III

- **Neurological**
- Headache (neurological & other)
- Tension headache
- **Cranial nerves**
- II Optic/ophthalmologic
- Photophobia to bright light
- Floaters
- Dizziness
- VIII Tinnitus
- Blurred vision
- **Other neurological**
- Tingling
- Paresis
- Numbness
- Twitching
- Muscle tightness
- **Musculoskeletal**
- Joint pain, swelling, tightness, and crepitation (specify joints)
- Myalgia
- **Gastrointestinal**
- Irritable bowel
- **Symptom patterns**
- Progression of symptoms
- Fluctuation of symptoms
- Stress increased symptoms
- Herxheimer reaction
- Antibiotic reduce symptoms

Pre-infection prevalence of mental disorders in the patients studied compared to the prevalence of the same disorders in the 12 month National Comorbidity Replication Survey

Psychiatric Syndromes	Pre-Infection	95% CI	National Comorbidity Survey
Depression	9.0%	(3–15%)	8.2%
Rapid cycling bipolar	3.0%	(0–6%)	2.6%
Panic disorder	2.0%	(0–5%)	2.7%
Obsessive compulsive disorder	2.0%	(0–5%)	1.0%
Social anxiety disorder	7.0%	(2–12%)	6.8%
Generalized anxiety disorder	3.0%	(0–6%)	3.1%
Posttraumatic stress disorder	6.0%	(1–11%)	3.5%
Explosive anger	3.0%	(0–6%)	2.6%

Attention Span

Clinical Impairment	Pre-Infection	95% CI	Post-Infection	95% CI
Attention span				
Sustained attention	7%	(2–12%)	84%	(77–91%)
Distracted by frustration	7%	(2–2%)	79%	(71–87%)
Allocation of attention	6%	(1–11%)	66%	(57–75%)
Hypersensitivity to sound	3%	(0–6%)	66%	(57–75%)
Hypersensitivity to light	2%	(0–5%)	63%	(54–72%)
Hypersensitivity to touch	2%	(0–5%)	41%	(31–51%)
Hypersensitivity to smell	5%	(1–9%)	36%	(27–45%)
Sensory overload	No data			

Memory				
Working memory	3%	(0–6%)	78%	(70–86%)
Recent memory	5%	(1–9%)	77%	(69–85%)
Working spatial memory	1%	(0–3%)	46%	(36–56%)
Remote memory	4%	(0–8%)	35%	(26–44%)
Memory retrieval				
Words	3%	(0–6%)	70%	(61–79%)
Names	6%	(1–11%)	68%	(59–77%)
Numbers	3%	(0–6%)	52%	(42–62%)
Geographical/spatial	1%	(0–3%)	49%	(39–59%)
Faces	1%	(0–3%)	23%	(15–31%)
Motor memory	1%	(0–3%)	10%	(4–16%)