Lyme, Tick Borne Diseases & Mental Symptoms, Autism and Morgellons: Lyme Disease in the Family

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Disclosure Statement
Robert Bransfield, MD, DLFAPA, PC

- Patients pay me money in return for trying to help them.
- Most of my income is paid directly from patients.
- I have no contract with any insurance company or other payer that might restrict or alter patient care in return for referring patients or providing other benefits.
- No Lyme disease financial interests.
- Speakers Bureau (currently): Astra Zeneca, Avanir, Cephalon, Dey, Forest, Merck, Novartis, Somaxon, Suvonion.
Outline

• Introduction
• Pathophysiology
• Lyme disease and psychiatric illness
• Lyme, tick-borne infections and autism spectrum disorders
• Morgellon’s disease
• Assessment
• Treatment
• Lyme disease controversies
Introduction
Lyme Disease: History

- **1883**: First described in European by Buchwald, subsequently called many names.
- **1975**: Critical attention to an epidemic in Lyme CT by Polly Murray.
- **1975-**: Multiple errors explaining the disease.
- **1982**: *Borrelia burgdorferi*, the bacterium that causes Lyme disease, was first isolated in 1982 by Willy Burgdorfer, Ph.D.
- **1997**: Genomic sequencing of first strain by Fraser
- **1883-**: Constantly expanding disease definition.
The Problem

• A large and growing number of patients have unexplained chronic illnesses.
• There is increasing recognition that Lyme disease and associated co-infections contribute to a broad spectrum of symptoms and syndromes which leads to chronic illnesses. Although chronic Lyme and other tick-borne diseases and seronegative Lyme disease is controversial, its existence is scientifically proven, widely spread and often overlooked. Improving diagnosis and treatment improves effectiveness in helping our patients.
Can Microbes & Immune Reactions Contribute to...

- Chronic illnesses?
- Mental illness?
- Personality change?
- Violent & criminal behavior?
- Cognitive decline?
- Degenerative neurological disease?
- Changes in sexual functioning?
- Obesity?
- Developmental disabilities?
- Improved human functioning?
The History of Mental Illness

• You’re possessed by demons & need punishment...
• Your mother caused it & you need psychoanalysis...
• Your serotonin is low & you need Prozac...
• Your genes are bad, you can’t change them...
• Your immune system & chronic infections contribute & you need antibiotics & immune treatments...
• Regardless patients with “medically unexplained symptoms” & doctors who treat them are possessed by demons & need punishment...
Mentally Ill Until Proven Otherwise

• Complex, poorly understood diseases are often considered to predominately have a psychological basis until proven otherwise. Tuberculosis, hypertension, and stomach ulcers were once considered to be psychosomatic.

• A failure to make a diagnosis based upon various so-called “objective tests” is not a basis for a psychiatric diagnosis.

• Many patients are given a psychiatric diagnosis as a result of an inadequate medical exam.

• Mental illness is always caused by something.
Pathophysiology
With Emerging Diseases
Think Outside the Box
Categories of disease causation

- genetic (inherited alleles)
- parasitic
- noninfectious environmental (diet, lifestyle, chemicals, radiation)

Paul W. Ewald
CDC: Emerging Infectious Determinants of Chronic Diseases

• Non-communicable chronic diseases can stem from infectious agents.

• Identifying the relationships can affect health across populations, creating opportunities to reduce the impact of chronic disease by preventing or treating infection.

• Infectious agents likely determine more cancers, immune-mediated syndromes, neurodevelopmental disorders, and other chronic conditions than currently appreciated.

• To capitalize on these opportunities, clinicians, public health practitioners, and policymakers must recognize that many chronic diseases may indeed have infectious origins.

NIH Human Microbiome Project

- A study researching all of the various microbes that live in people. The project has already established that the bacteria in the human microbiome collectively possess at least 100 times as many genes as the 20,000 or so in the human genome.
- Bacterial cells outnumber human cells by 10 to 1.
- Humans depend on their microbiome for essential functions, including digestion, leading microbiologists to conclude that a person should really be considered a superorganism.

http://nihroadmap.nih.gov/hmp
The Decade of the Microbe

- ILADS announces a global health initiative
- Many diseases, syndromes and symptoms unexplained by a narrow and fragmented approach can be explained in a broader and more comprehensive manner that recognizes the role of chronic, persistent infections in explaining the cause of many symptoms, signs, syndromes and diseases.
- We encourage research, education and cooperative effort on this subject.
Disease Models

Most current disease models

Acute infection  
Acute toxic exposure  
Genetic defect  
Trauma  
Cancer  
Degenerative disease

Fairly well understood pathophysiology

Well-defined diagnostic signs and symptoms

Model for complex disease with multiple variables

Complex and multiple contributors: genetic and environmental (e.g., infections, toxins and deficiencies)

Complex and multiple pathophysiological processes

Complex and multiple clinical presentation with multiple signs and symptoms

Always move forward

• Medicine is undergoing a paradigm shift.
• High level researchers and some community physicians recognize the importance of infections and immune reactions to them towards causing many previously unexplained chronic diseases.
• Just as mathematics shifted from Newton to Einstein, we need to make a similar shift in medicine to use more complex models to understand complex disease.
Broad Disease Definition

• Time
  – Evolutionary concepts
  – The patient: disease progression over years and decades

• Space
  – A systems approach that considers multi-systemic contributors and deterrents to disease
What Causes Chronic Illness (Time)?

• From an evolutionary perspective:
  – Genetic vulnerabilities from the unique path of evolution
  – Design compromises
  – Competing organisms (always consider parasites)

• From the perspective of the organism:
  – Interaction of vulnerabilities & environment
  – Trauma causing adaptive mechanisms to go awry
Time

- Predisposing & precipitating factors
- Infections
- immune & other reactions
- Pathophysiological processes
- Dysfunction
- Symptoms & Syndromes
- Ineffective Treatment
- Disease Progression
What Provokes & Weakens the Immune System?

- Infections
- Cancer
- Allergens
- Stress
- Sleep deprivation
- Vaccinations
- Trauma
- Toxins
- Degenerative changes
- Foehn, barometric pressure drops
- Molecular mimicry
- Low glutathione levels
- Increased oxidative stress
- Metal toxicity
- Elevated leptin levels
Direct or Immune Effects Causing Pathophysiology?

- Infection or Complex Interactive Infections
- Immune Effects Th1 & Th2
- Pathophysiology Causing Symptoms
Cousins: Lyme Disease & Syphilis

**Lyme disease**
- Chromosome + 21 plasmids
- 132 genes
  - More genetic material
  - 90% genes unrelated to any other known bacteria
  - Perhaps the most complex bacteria known

**Syphilis**
- Only 22 genes

Syphilis is the dumb cousin

Jemsek J
Latent Spirochete Infections

• There are cases of Lyme disease where people contracted it years before coming down with the disease. In animals, you have chronic disease with spirochete in the brain tissue that is viable months later... I am convinced the same thing is true with humans" ---Dr. Willy Burgdorfer
Infections Present in Tick-Borne Disease Patients

- **Bacteria**: Lyme disease, Ehrlichiosis, Bartonella, Mycoplasma, Chlamydia, RMSF, Typhus, Tularemia, Q-Fever,
- **Parasites**: Babesiosis and other piroplasms, filariasis, amebiasis, giardiasis...
- **Viruses**: EBV, HHV-6, HHV-8, CMV, St Louis Encephalitis, W Nile, Powassan encephalitis and other viral encephalopathies
- **Candida** and other fungi
Defining Chronic Lyme Disease: MCIDS: Differential Diagnosis

1. Infections: a) Bacterial: Lyme disease, Ehrlichiosis, Bartonella, Mycoplasma, Chlamydia, RMSF, Typhus, Tularemia, Q-Fever, Tick paralysis  
   b) Parasites: Babesiosis and other piroplasms, filariasis, amebiasis, giardiasis...  
   c) Viruses: EBV, HHV-6, HHV-8, CMV, St Louis Encephalitis, W Nile, Powassan encephalitis and other viral encephalopathies, ?XMRV virus  
   d) Candida and other fungi

2. Immune dysfunction: ANA+, RF+ ↑ HLA DR-4

3. Inflammation: ↑ IL-1, IL-6, TNF-α→ “Sickness syndrome”

4. Toxicity: Multiple Chemical Sensitivity, Environmental Illness, Heavy Metals, Mold, and Neurotoxins

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

6. Nutritional & Enzyme Deficiencies/ functional medicine abnormalities in biochemical pathways

7. Mitochondrial dysfunction

8. Psychological

9. Endocrine d/o

10. Sleep disorders  
11. ANS dys (f)  
12. G.I.  
13. Elevated LFT’s

14. Drug Use/Addiction  
15. Deconditioning: Need for PT

Horowitz R.
PubMed Citations

- Tick borne diseases: 20,000
- Lyme disease: 9,600
- Borrelia burgdorferi: 6,250
- Mycoplasma: 18,000
- Babesia: 2,900
- Bartonella: 1,900
- Ehrlichia: 1,900
- Anaplasma: 1,500
- Masters Disease or Stari: 700
Lyme Disease and Psychiatric Illness
As a psychiatrist I see the failures of our healthcare system

• If a patient’s symptoms are “medically unexplained” by current beliefs, the patient is considered to need a psychiatrist.
• Many patients are frustrated with the current system and need psychiatric assistance.
• In regard to Lyme disease, the late stage symptoms are mostly neuropsychiatric.
• I have seen thousands of patients with a broad spectrum of neurological, cognitive and psychiatric symptoms, including cases of suicide, violence, homicide, autism, developmental disabilities and dementia.
Basic Hypothesis

• Infectious diseases and the immune reactions to them contribute to causing psychiatric symptoms and illness.

• Acute stress & inflammatory reactions are adaptive to short term environmental stress, but chronic stress & inflammatory reactions are pathogenic.

• Identifying & treating infections and other causes of immune dysfunction improve the treatment effectiveness of mental illness.
Psychiatric Syndromes & Infections

- The same syndrome may be caused by different infections in different individuals
- The same infection can cause different syndromes in different individuals
- Lyme/tick-borne disease can cause any psychiatric syndrome in the DSM-IV
Research & Clinical Observation: Microbes Cause Mental Illness

• Thousands of peer-reviewed journal articles demonstrate the causal association between infections and mental illness.
• 250 peer reviewed scientific articles demonstrate the causal association between Lyme/tick-borne disease and mental illness.
• Clinical observation by front line physicians also supports this view.
How Do Microbes Cause Disease?

- Infection that is no longer present ("hit & run")
- Persistent infections
- Direct effect of the microbe upon the organism
- Immune reactions impacting the organism
Go round up the usual suspects...
Some microbes associated with mental symptoms & mental illness

- **Spirochetes** • *Borrelia afzelii* (Lyme disease in the UK and the rest of Europe) • *Borrelia burgdorferi sensu stricto* (Lyme disease in the USA, UK and rest of Europe) • *Borrelia garinii* (Lyme disease in the USA, UK and rest of Europe) • *Borrelia hermsii* (relapsing fever) • *Borrelia turicatae* (relapsing fever) • *Leptospira* (Leptospirosis) • *Treponema pallidum pallidum* (syphilis) *Bacteria* • *Anaplasmas phagocytophilum* (human granulocytic ehrlichiosis) • *Bartonella henselae* (cat scratch fever) • *Bartonella quintana* (trench fever) • *Bartonella rochalimae* (bartonellosis) • *Chlamydia pneumoniae* (chlamydia) • *Chlamydia psittaci* (chlamydia) • *Coxiella burnetti* (Q-fever and post-Q fever fatigue syndrome) • *Ehrlichia chaffeensis* (human monocytic ehrlichiosis) • *Francisella tularensis* (rabbit fever or tularemia) • *Haemophilus influenzae* (haemophilus) • *Listeria* • *Meningococcus* (meningococcal meningitis) • *Mycoplasma fermentans* • *Mycoplasma pneumoniae* • *Mycobacterium tuberculosis* (tuberculosis) • *Rickettsia akari* (rickettsialpox) • *Rickettsia rickettsii* (rocky mountain spotted fever) • *Rickettsia species* (eastern tick-borne rickettsiosis) • *Shigella* (shigellosis) • *Streptococcus pneumoniae* or pneumococcus (pneumonia) • *Streptococcus* (pediatric autoimmune diseases associated with *Streptococcus*, Sydenham’s chorea and St Vitus dance) • *Yeasts* • *Candida albicans* (candidiasis) • *Candida dubliniensis* Prion • Variant Creutzfeldt–Jakob • *Borna virus* • *Coltivirus* (Colorado tick fever) • *Coxsackievirus* • *Cytomegalovirus* • *Enterovirus* • *Flaviviridae* virus (Japanese B encephalitis) • *Hepatitis C virus* • *Herpes virus family* • *Human endogenous retroviruses* • *Human herpesvirus* 4 or Epstein–Barr virus • *HIV* • *Influenza A virus* subtype H3N2 (Hong Kong flu) • *Influenza virus* • *Pandemic influenza of 1918* • *Papovavirus* • *Paramyxovirus* (measles virus) • *Parvo B19* • *Poliavirus* • *Rabies virus* • *Rubella* • *Toga virus* • *Varicella zoster virus* (chicken pox) • *Viral meningitis* • *West Nile virus* • *Protozoa* • *Plasmodium* (malaria) • *Babesia microti* (babesiosis) • *Babesia duncani* (babesiosis) • Other *Babesia species* (babesiosis) • *Toxoplasma gondii* (toxoplasmosis) • *Parasites* • *Blastocystis* (blastocystosis) • *Taenia solium* (neurocysticercosis or cysticercosis) • *Fungal* • *Cryptocococcus* • *Coccidiomycosis* • *Histomycosis*
Pediatric Autoimmune Diseases Associated with Strep (PANDAS)

- Strep infections in a genetically susceptible individual at a young age can result in OCD, tics and sometimes attention span difficulties.
- Symptom flares follow a strep infection and correlate with increased antibody production.
- ASO titers are elevated.
- Antibiotics are effective in treating and preventing these symptoms.
- Plasmapheresis can also be effective.
Cytokine Activation Causes Psychiatric Symptoms

• Interleukin-6 Is Elevated in the Cerebrospinal Fluid of Suicide Attempters and Related to Symptom Severity (1)
• Interluken-1Beta & Self-Inflicted Aggressive Behavior (2)
• IL-1Beta Causes Fatigue (3)

Hepatitis C & Interferon Treatment

• A good model for inflammation mediated mental symptoms

• Symptoms include depression, anxiety, mania, irritability, impulsiveness, hostility, relapse of substance abuse & lassitude.[1]

• Cognitive impairments

[1] Henry, Castera, Demotes-Mainard
Effects of Immune Activation Resemble Depressive Symptoms

- Cytokines Induce Sickness Behavior
  - Anhedonia
  - Malaise
  - Hypersomnia
  - Anorexia
  - Social Withdrawal
  - Poor Concentration
  - Weakness

The Blood Brain “Barrier”

- Partial barrier to infection and treatment
- Penetration early in infection
- Penetration through cranial nerves
- Pathogens can cross the blood–brain barrier transcellularly, paracellularly and/or in infected phagocytes (Trojan-horse mechanism). Consequently, pathogens can cause blood–brain barrier dysfunction, including increased permeability, pleocytosis and encephalopathy*
- Neurotoxins and cytokines penetrate
- No barrier to HERV or other parasite sequences incorporated in DNA
- Infections in the body can effects in the brain by cytokine penetration & neurotoxin effects

Different immune reactions directly influence neuronal proliferation, differentiation, migration, and apoptosis. Microglia become activated after stress, trauma, or infection. They react with tissue repair or induction of immune responses: phagocytosis, secretion of cytokines, neuronal growth factors, and antigen presentation. Microglial activation may sustain chronic brain inflammation.\textsuperscript{2} NK, natural killer.
Some Lyme Pathophysiology is a Failure to Shift from Th1 to Th2

- Persisting immune activation causes the cytokine storm in chronic Lyme.
- In these patients, the innate immune system is not turned off by a series of specific immune peptides.
- Specific genetic types are more prone to this phenomenon.
- (Compare this to PTSD.)

Newall K.
Inflammation and central nervous system Lyme disease

- Lyme disease, caused by the bacterium Borrelia burgdorferi, can cause multi-systemic signs and symptoms, including peripheral and central nervous system disease. This review examines the evidence for and mechanisms of inflammation in neurologic Lyme disease, with a specific focus on the central nervous system, drawing upon human studies and controlled research with experimentally infected rhesus monkeys. Directions for future human research are suggested that may help to clarify the role of inflammation as a mediator of the chronic persistent symptoms experienced by some patients despite antibiotic treatment for neurologic Lyme disease.

Lyme and Increased Proinflammatory Cytokines

• Increased levels of the proinflammatory cytokines IL-6, IL-8, IL-12, IL-18 and interferon γ and of the chemokines CXCL12 and CXCL13 have been reported in the CSF of patients with neurologic Lyme disease (Weller et al., 1991; Grusell et al., 2002; Widhe et al., 2002, 2005). The magnitude of IL-6 in human serum and CSF has been shown to correlate with disease activity in neurologic Lyme disease (Weller et al., 1991).

• Elevated levels of IL-6 can cause symptoms of fatigue and malaise, common to many infectious conditions as well as Lyme disease (Pachner et al., 1997).

**Delta Sleep and Lyme Disease**

- Chronic fatigue & sleep disturbances are prevalent in Lyme disease. (1)
- Sleep restriction increases IL-6 and pain-related symptoms in healthy volunteers (2)
- Impaired Sleep Correlates with Impaired Immune Functioning (3)
- Growth hormone is dependent upon delta sleep & modulates immune response (4)
- Increasing delta sleep is therapeutic

(1) Greenberg HE; Ney G; Scharf SM; Ravdin L; Hilton E. Sleep, 18(10):912-6 1995
(2) M. Haack, E. Sanchez, J. Broussard, M. Regan, J. Mullington J Pain; April 2004, Supplement 1 • Volume 5 • Number 3
Bidirectional Communication between the Brain and the Immune System: Implications for Physiological Sleep and Disorders with Disrupted Sleep

• Cytokines produced by cells of the immune and nervous systems regulate sleep.

• Particularly interleukin-1beta and tumor necrosis factor-alpha, signal neuroendocrine, autonomic, limbic and cortical areas of the CNS to affect neural activity and modify behaviors (including sleep), hormone release and autonomic function.

• Sleep disorders are commonly associated with chronic inflammatory diseases and chronic age- or stress-related disorders. The best studied are rheumatoid arthritis, fibromyalgia and chronic fatigue syndromes.

Circadian Rhythms

Healthy

Alertness

Deep Sleep

Chronic Stress

Alertness

Deep Sleep

AM

AM
Variability in Sleep Patterns in a Normal Adult vs a Patient With Major Depression

Adapted with permission from Winokur A, Reynolds CF III. *Primary Psychiatry*. Nov/Dec 1994:22-27.

Please see important safety information on accompanying slides and full prescribing information.
Disease Progression

Non-Restorative Sleep

- Fatigue
- Cognitive Impairments
- Emotional Impairments
- Pain Sensitivity
- Immune Dysfunction
Chronic Infections and Stress

• Chronic infections cause chronic stress

• Chronic stress reactions and non-restorative sleep contribute to perpetuating the disease process & are associated with:
  – Decreased regenerative functioning
  – Compromised immunity
  – Oxidative stress
  – Decreased resistance to infectious disease
Progressive Infection & Inflammation is Associated with Increasing Encephalopathy & Increasing Mental Symptoms

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<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
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<td>Executive dysfunction</td>
<td>Increasing cognitive deficits</td>
<td>Dementia</td>
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<tr>
<td>Reduced frustration tolerance, irritability, dysthymia</td>
<td>Anxiety disorders, depression, impulsivity, personality disorders</td>
<td>Major psychiatric disorders, psychosis, suicide, homicide</td>
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Increasing Neurological, Multisystemic Symptoms & Fatigue
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<tr>
<th>Persistent Infections &amp; Lyme/Tick-borne Disease Cause...</th>
<th>Chronic Somatic Illnesses</th>
<th>Chronic Mental Illness</th>
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<tr>
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<td>Epidemiology</td>
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Inflammation, Psychosis, and the Brain

• Hundreds of studies of schizophrenic illness in adults have documented immunological abnormalities in these patients
• First-episode psychosis in children is associated with evidence of increased inflammation
• Increasing evidence now suggests that the glia, cerebral vasculature, and the BBB may be involved.
• Our results support the inflammatory theory of schizophrenia that was formulated over a 100 years ago and perhaps offer hope that prevention of chronicity can occur if the first episode of psychosis is rapidly and effectively controlled.

Systemic infections and inflammation affect chronic neurodegeneration

• In chronic neurodegenerative diseases such as Alzheimer's disease, with an ongoing innate immune response in the brain, systemic infections and inflammation can cause acute exacerbations of symptoms and drive the progression of neurodegeneration.

Perry et. Al. Nature Reviews Immunology 7, 161-167 (February 2007)
LYME NEUROBORRELIOsis 
& AGGRESSION

• The link between Lyme neuroborreliosis (LN) and aggression is reviewed from multiple perspectives. Cases are presented and discussed. It appears Lyme disease (LD) and other related tick-borne diseases contribute towards causing human aggression and violence. Greater attention to this area has the potential of reducing crime and saving lives.

Bransfield R. 14th International Scientific Conference on Lyme Disease and Other Tick-Borne Disorder. 2001
Lyme, Tick-borne Infections and Autism Spectrum Disorders
Chronic Infections, Lyme/Tick-Borne Disease & Autism Spectrum Disorder

A Model for Infections Contributing to Autism Spectrum Disorder

Infections and/or other immune provocations in genetically susceptible individual

Aberrant immune reactions causing inflammation, oxidative stress, mitochondrial dysfunction and excitotoxicity resulting in impaired neural development and dysfunction

Autism spectrum disorders

Genetic Heritability and Shared Environmental Factors Among Twin Pairs With Autism

- Among 192 twin pairs for ASD, susceptibility to ASD has moderate genetic heritability and a substantial shared twin environmental component.
- Only about 60 to 70 percent of the identical twins had dual autism diagnoses and 20 to 30 percent of the fraternal twins had dual diagnoses.
- A mathematical equation determined only about 38 percent of autism risk could be tied to genetics.

# Top 15 States for Autism & Lyme Disease vs. Obesity (Control)

**Autism**
- 1. Minnesota
- 2. Oregon
- 3. Indiana
- 4. Maine
- 5. Massachusetts
- 6. Michigan
- 7. California
- 8. Maryland
- 9. Connecticut
- 10. Wisconsin
- 11. Rhode Island
- 12. New Jersey
- 13. Pennsylvania
- 14. Hawaii
- 15. Virginia

**Lyme**
- 1. Delaware
- 2. Connecticut
- 3. New Jersey
- 4. Massachusetts
- 5. Pennsylvania
- 6. New York
- 7. Wisconsin
- 8. Maryland
- 9. New Hampshire
- 10. Maine
- 11. Minnesota
- 12. Vermont
- 13. Rhode Island
- 14. Virginia
- 15. West Virginia

**Obesity**
- 1. Mississippi
- 2. Alabama
- 3. West Virginia
- 4. Louisiana
- 5. Kentucky
- 6. Tennessee
- 7. Arkansas
- 8. Indiana (tie for 8th)
- 9. South Carolina
- 10. Texas
- 11. Michigan
- 12. Georgia
- 13. Oklahoma
- 14. Missouri
- 15. Alaska
Autism prevalence and precipitation rates in California, Oregon, and Washington counties

• These results are consistent with an environmental trigger for autism among genetically vulnerable children that is positively associated with precipitation.

# Infections associated with autism spectrum disorders

- **Babesia**
- **Bartonella**
- **Blastocystis**
- **Borna (animal model)**
- **Borrelia burgdorferi** and other tick-borne diseases
- **Chlamydia pneunomiae**
- **Cytomegalovirus**
- **Ehrlichia**
- **Herpes simplex**
- **Human Herpesvirus-6**
- **Herpes virus family**
- **Mycoplasma fermentans**
- **Mycoplasma genitalium**
- **Mycoplasma hominis**
- **Mycoplasma pneumoniae**
- **Plasmodium** (malaria)
- **Rubella**
- **Rubeola**
- **Shigella**
- **Taenia solium** (Neurocysticercosis)
- **Toxoplasma gondii** (Toxoplasmosis)
- **Treponema pallidum pallidum** (Syphilis)
- **Varicella**
- **Unknown viral and other infectious**
- **XMRV** (unpublished)

Chronic infections associated with autism spectrum disorder

- Babesia
- Bartonella
- Blastocystis
- Borrelia burgdorferi
- Chlamydia pneumoniae
- Cytomegalovirus
- Ehrlichia
- Herpes simplex
- Herpes virus family
- Human heprevirus-6
- Mycoplasma fermentans
- Mycoplasma genitalium
- Mycoplasma hominis
- Mycoplasma pneumoniae
- Plasmodium
- Taenia solium
- Toxoplasma gondii
- Treponema pallidum pallidum
- XMRV (unpublished)
Critical periods of vulnerability for the developing nervous system: evidence from humans and animal models

- Brain developmental processes (i.e. cell proliferation, migration, differentiation, synaptogenesis, myelination, and apoptosis) occur at vulnerable periods during the development of the nervous system and are sensitive to environmental insults that can contribute to autism.

Stereotypies and hyperactivity in rhesus monkeys exposed to IgG from mothers of children with autism

• Rhesus monkeys gestationally exposed to IgG class antibodies from mothers of children with ASD consistently demonstrated increased whole-body stereotypies across multiple testing paradigms. These monkeys were also hyperactive compared to controls.

Here we show that the cytokine interleukin-6 (IL-6) is critical for mediating the behavioral and transcriptional changes in the offspring. A single maternal injection of IL-6 on day 12.5 of mouse pregnancy causes prepulse inhibition (PPI) and latent inhibition (LI) deficits in the adult offspring. Moreover, coadministration of an anti-IL-6 antibody in the poly(I:C) model of MIA prevents the PPI, LI, and exploratory and social deficits caused by poly(I:C) and normalizes the associated changes in gene expression in the brains of adult offspring. Finally, MIA in IL-6 knock-out mice does not result in several of the behavioral changes seen in the offspring of wild-type mice after MIA. The identification of IL-6 as a key intermediary should aid in the molecular dissection of the pathways whereby MIA alters fetal brain development, which can shed new light on the pathophysiological mechanisms that predispose to schizophrenia and autism.
Gestational LYD/TBD & ASD

- Jones et al. performed a comprehensive case history review on the charts of 102 gestational LYD/TBD cases.
- 9% had been diagnosed with autism and 56% with attention deficit disorder. Psychiatric symptoms included irritability or mood swings (54%), anger or rage (23%), anxiety (21%), depression (13%), emotional (13%), OCD (11%) and suicidal thoughts (7%). Neurological symptoms included headache (50%), vertigo (30%), developmental delays (18%), tic disorders (14%), seizure disorders (11%), involuntary athetoid movements (9%) and hypotonia (7%). Sensory sensitivity symptoms included photophobia (43%), hyperacuity (36%), motion sickness (9%) and other (tactile, taste or smell) (23%). Cognitive symptoms included poor memory (39%), cognitive impairments (27%), speech delays (21%), reading/writing (19%), articulation (17%), auditory/visual processing (13%), word selectivity (12%), and dyslexia (18%). GI symptoms were common and included GERD (27%), abdominal pain (29%), diarrhea or constipation (32%), and nausea (23%).
- As a control, 66 mothers with Lyme disease who were treated with antibiotics prior to conception and during the entire pregnancy; all gave birth to normal healthy infants.

Testing ASD Patients for Lyme/TBD

Controlled Trials:
- Vojdani 22% of (12/54) LYD tested positive for IgG and IgM by CDC criteria.
- LIAF 26% positive for LYD of ASD children were compared to 0 controls.
- Nicolson 20–30% positive for LYD.

58% were positive for Mycoplasma species while 5% of 45 age matched controls were positive for Mycoplasma (Odds ratio = 13.8) with 35% M. fermentans vs. 0% control, 33% M. pneumoniae vs. 5% control, 10% M. homonis vs. 0% control, 2% M. penetrans vs. 0% control and 25% were M. fermentans and other species.

8% were positive for C. pneumoniae vs. 2% of controls (Odds ratio = 5.6) 29% were positive for Human Herpes Virus-6 (HHV-6) vs. 8% of controls. 6.5% of healthy family members were positive for Mycoplasma and 8% were positive for HHV-6 (P < 0.001) [18].

LYD WB positive patients had a 68% coinfection rate with Mycoplasma (M. Fermentans was 70%), Bartonella, Ehrlichia, and Babesia.

Case Series:
- Levin 100% (9/9) LYD positive of ASD children in Connecticut with WB by IGeneX Laboratory criteria.
Immune reactions, chronic infections & autism spectrum disorders

- Immune reactivity in the mother, fetus and child appear to adversely affect developing neural tissue and contribute to the pathophysiology associated with autism spectrum disorders. This reactivity can be evoked by a number of causes including both acute and persistent infections such as Anaplasma, Babesia, Bartonella, Borrelia burgdorferi, Chlamydia pneumoniae, Ehrlichia, Human heprevirus-6, Mycoplasma (in particular Mycoplasma fermentans) and XMRV. Possible pathophysiological mechanisms include both inflammatory processes as well as autoantibodies to developing neural tissue.

Bransfield RC. Pediatric Health
Is ASD partially autoimmune?

- Based upon three different studies, antibodies that react to the 36, 37, 39, 61 and/or 73 kDa bands on Western Blot testing are associated with provoking an immune reaction and contribute to causing autism. Reactivity to these bands is also associated with *Borrelia burgdorferi* and to a lesser degree to *Bartonella henselae, Bartonella quintana, Mycoplasma, Chlamydia pneumoniae and Streptococcus pneumoniae*.

Percentage of GWI Patients with Mycoplasmal Infections

- M. fermentans
- M. pneumoniae
- M. genitalium
- M. hominis
- M. penetrans

All Single + Multiple Infections
All Multiple Infections 21% of Total Infections

Prof. G. L. Nicolson
Institute for Molecular Medicine
% of GWI CSF-Family with Mycoplasmal Infections

$M. \text{ fermentans}$

$M. \text{ pneumoniae}$

$M. \text{ genitalium}$

$M. \text{ hominis}$

$M. \text{ penetrans}$

$M. \text{ fermentans} + M. \text{ pneumoniae}$

$M. \text{ fermentans} + M. \text{ hominis}$

$M. \text{ fermentans} + M. \text{ genitalium}$

All Single + Multiple Infections

All Multiple Infections

18% of Total Infections

Prof. G. L. Nicolson
Institute for Molecular Medicine
% of GWI Children/Autism with Mycoplasmal Infections

M. fermentans

M. pneumoniae

M. genitalium

M. hominis

M. penetrans

M. fermentans + M. pneumoniae

M. fermentans + M. hominis

M. fermentans + M. genitalium

All Single + Multiple Infections

All Multiple Infections 18% of Total Infections

Prof. G. L. Nicolson
Institute for Molecular Medicine
Brain SPECT: Mother with Lyme Disease & 3 ASD Children

• SPECT scans of a mother with LYD/TBD and her three children with ASD.
• 4 generations of Lyme disease and multiple coinfections.
Mother, 48: There is an extensive hypoperfusion pattern, prominently in the cerebral cortices and much of the frontal lobes, with a lesser degree in the temporal lobes and a small degree hypoperfusion in the cerebellum. The hypoperfusion is moderately extensive and is likely associated with toxic, inflammatory and infectious processes. There is hyperperfusion of the Basal Ganglia, which is associated with anxiety and mood dysregulation. The diagnosis is chronic fatigue syndrome, multiple sclerosis, depression and possible congenital Lyme disease. **Lab testing was positive for Borrelia burgdorferi, Babesia duncani, Bartonella henselae, Mycoplasma fermentans, HHV-6, EBV, high anti-streptolysin o titre and gamma Strep in stool.**
Son, 26: Some motion artifacts, however significant hypoperfusion pattern is both focal as well as generalized. The focal pattern is throughout the cerebral cortex bilaterally and the cerebellar hemispheres (which demonstrate atrophy on MRI). There is mild hyperperfusion of the basal ganglia and a focally intense hypeperfusion area in the deep white matter of the temporal lobe. There is a hyperperfusion pattern involving the temporal lobes and cerebellar hemispheres. The focal decrease is more suggestive of etiologies that would include hypoxic, neuroimmune, traumatic factors, infectious and inflammatory. There is a hyperperfusion pattern of the basal ganglia which may be associated with element of anxiety, whereas the focal intense areas can be associated with present interictal seizure focus and is clinically significant as the present dose of anticonvulsant is not controlling this area. The patient is low functioning with autism spectrum disorder since two years, grand mal seizures, movement disorder, ataxia, hypotonia, megacolon, possible mitochondrial disorder, mild hypergammaglobulenia and syncope.

Lab testing was positive for *Borrelia burgdorferi*, *Babesia duncani*, *Bartonella henselae*, *Mycoplasma fermentans*, HHV-6, EBV and high strep titers; stool positive for *Citrobacter fundii*, *Klebsiella p.* and gamma Strep in stool.
Daughter, 23: There is an extensive hyperperfusion pattern in the cerebral cortices, temporal lobes and cerebellum and hypoperfusion of the frontal lobes and is likely associated with toxic, inflammatory and infectious processes. The diagnosis is Asperger’s, obsessive compulsive disorder, generalized anxiety, social anxiety disorder, depression, posttraumatic stress disorder from an auto accident, possible narcolepsy, tremors, cardiac disease, myocardial infarction, osteopenia, arthritis and pseudo rheumatoid nodules since 5 years of age. Lab testing was positive for *Borrelia burgdorferi*, *Anaplasma phagocytophilum*, *Mycoplasma fermentans*, *Homopholis*, *HHV-6*, *EBV*, elevated Strep titres; stool was positive for *Toxoplasmosis*, *Cornybacteria* and *gamma Strep*. 
Daughter, 20: there is extensive hypoperfusion in the frontal lobes, temporal lobes and to a lesser degree to the occipital lobes and slightly to the cerebellum. There is hyperperfusion in the right cerebellar hemisphere. The hypoperfusion is likely associated with neuroinflammatory, neuroimmunological, infectious and toxic substance exposure. There is a seizure focus with hyperperfusion in the right cerebellar hemisphere. The diagnosis is autism spectrum disorder since 14 months, petit mal seizure disorder, hypotonia, perceptual impairments, and anxiety. Lab testing was positive for *Borrelia burgdorferi*, *Bartonella henselae*, *Mycoplasma fermentans*, HHV-6; stool positive for Parvo/B-19, *Klebsiella*, *p.*, *Citrobacter f.*, and *gamma Strep*. 

• The weighted current ASD point-prevalence was 11 per 1000. We estimate that 673,000 US children have ASD.[1]

• According to background information in the study, the life-time healthcare costs for a person with autism are estimated to be more than $16 million.[1]

• Chronic infections may be a contributor in well over 50% which would be trillions of dollars.