A person with their arms raised in a field of tall grass under a blue sky. The person is wearing a light-colored top and dark pants. The background is a bright, sunny outdoor setting with a clear blue sky and a field of tall, golden-brown grass. The overall mood is one of joy and freedom.

SOLVING THE PUZZLE OF POST TREATMENT LYME DISEASE SYNDROME

**Gary Kaplan D.O. DABFM, DABPM, FAAMA
Medical Director**

**The Kaplan Center of Integrative Medicine
Associate Professor-Georgetown University
School of Medicine**

THE KAPLAN CENTER FOR INTEGRATIVE MEDICINE



**First Integrative Medicine Center in
the Washington D.C. region
(established 1985)**

6829 ELM STREET SUITE 300 MCLEAN, VA 22101

THE KAPLAN CENTER FOR INTEGRATIVE MEDICINE

- Physicians Boarded in Family Medicine, Pain Medicine, PM&R and Acupuncture
- Functional Medicine
- Physical Therapists
- Acupuncturist
- Psychotherapist
- Nutritionist
- Meditation/Yoga Instructor
- IV Therapy

OUTLINE: PTLDS

1. Definition, Diagnosis and Testing
2. Antibiotic Treatment
3. Detoxification and Management of Jarisch-Herxheimer Reactions
4. Gut Protection and Repair
5. Immune Response
6. The Missing Piece



FIRST PIECE OF THE PUZZLE

DEFINITION, TESTING, DIAGNOSIS

DEFINITION: LYME DISEASE

- The most common vector-borne infection in North America
- Caused by *Borrelia Burgdorferi sensu stricto*, found in *Ixodes scapularis*
- *Ixodes pacificus* is the main vector in Western United States and Western Canada
- Recently *Borrelia mayonii* was identified and may be responsible for a proportion of cases, however no diagnostic tools are available yet
- In Europe, *Borrelia afzelii*, *B. garinii*, *B. burgdorferi*, *B. spielmanii*, *B. bissettii* cause Lyme disease with wider variety of symptoms than reported in the North America

CO-INFECTIONS

Ixodes scapularis

Anaplasmosis

Babesiosis

Borrelia mayonii

Borrelia miyamotoi

Powassan Disease

Lone star tick

Ehrlichiosis

Heartland virus

STARI

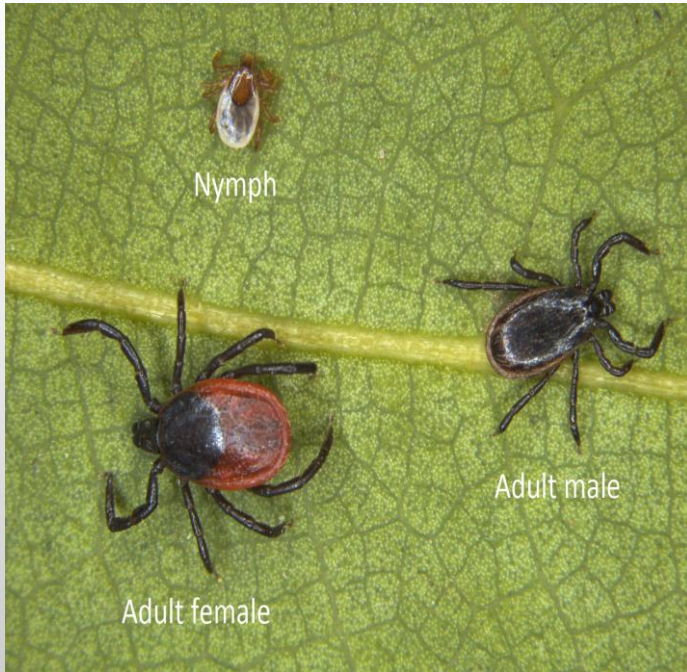
Tularemia

BARTONELLA

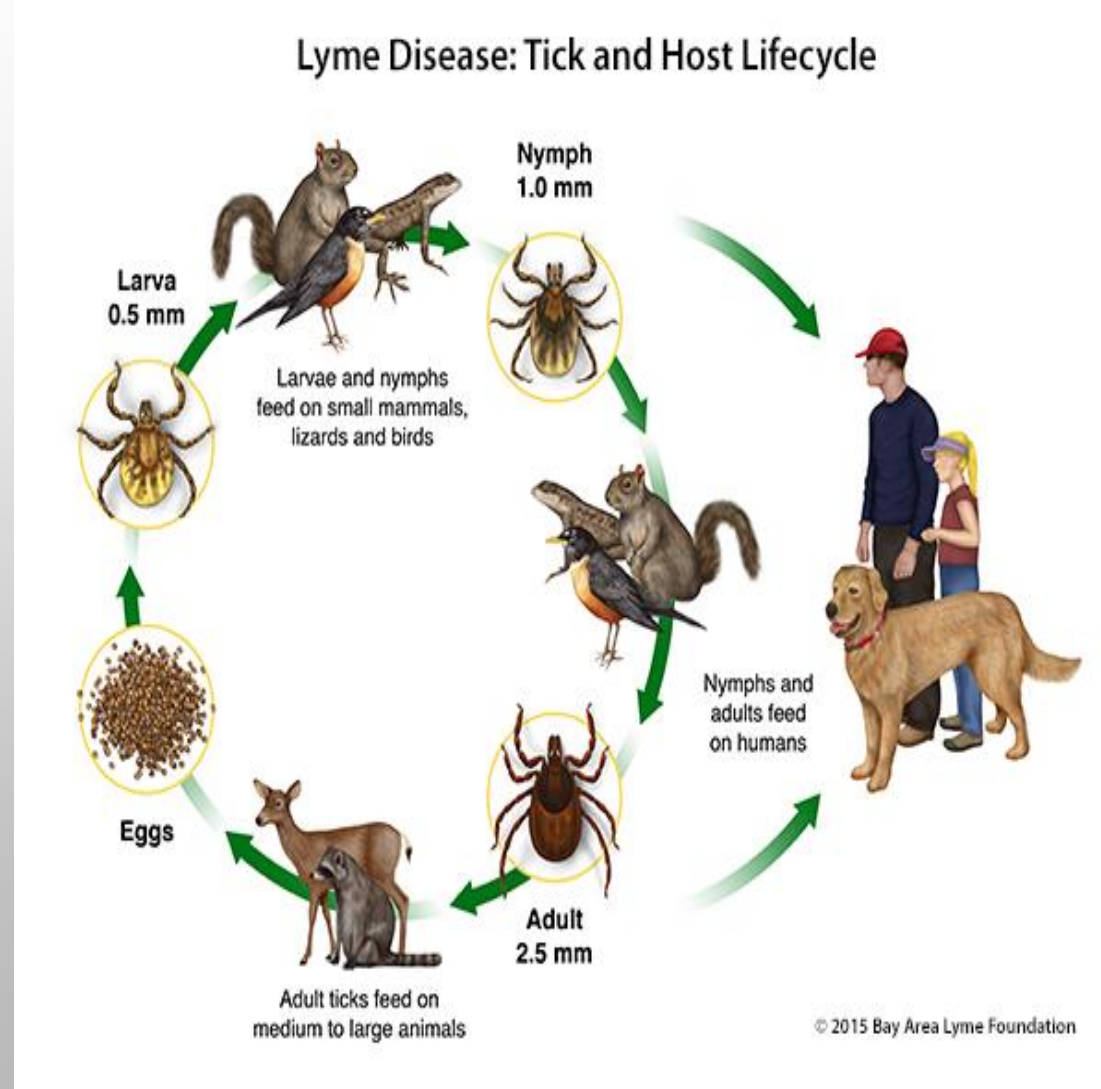
- A disease caused by several bartonella species transmitted either by a flea, tick, mosquito, cat scratch or lice
- *B. henselae* is often transmitted along with other tick-borne microbes
- Common symptoms of Bartonellosis:
 - Low grade fever
 - Headache
 - Sore throat
 - Swollen lymph nodes
 - Conjunctivitis



DEFINITION: LYME DISEASE



Ixodes scapularis



Ixodes pacificus

EPIDEMIOLOGY

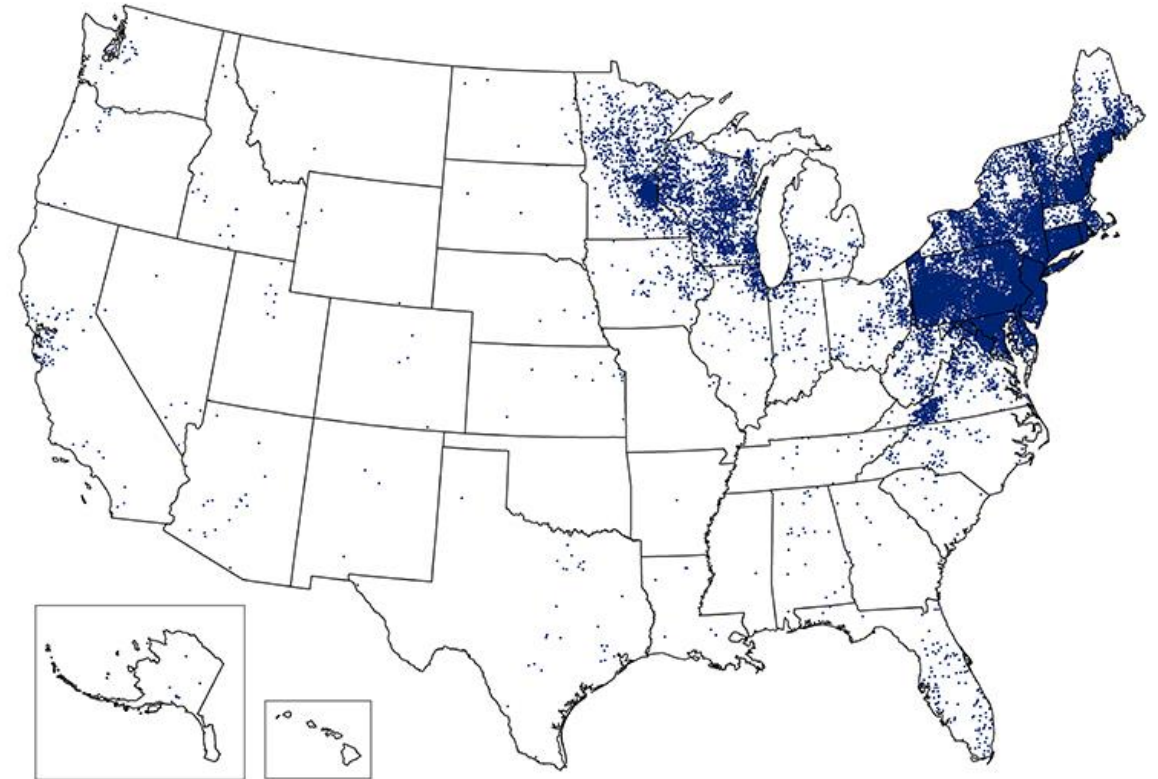
- 300,000 diagnosed annually in U.S.
- Lyme Disease and its sequelae are responsible for significant numbers of school and work absences, estimated to cost more than \$1 billion per year for healthcare in the US
- Due to insensitivity in the diagnostic tests, incidence estimates based solely on these tests are likely to significantly undercount the numbers of infected people

CDC REPORT: CASES OF LYME DISEASE



1 dot placed randomly within county of residence for each reported case

2001



2017

DEFINITION OF POST TREATMENT LYME DISEASE SYNDROME (PTLDS)

- Also called Lyme Disease Complex, Chronic Lyme Disease
- PTLDS is characterized by incapacitating fatigue, pain and neurocognitive dysfunction that persists for more than 6 months after an acute Lyme disease diagnosis
- Symptoms can be intermittent or constant, and are often subjective and varied in nature
- Single case definition for PTLDS, and its diagnosis is often made based on exclusion of other conditions, such as tick-borne co-infections

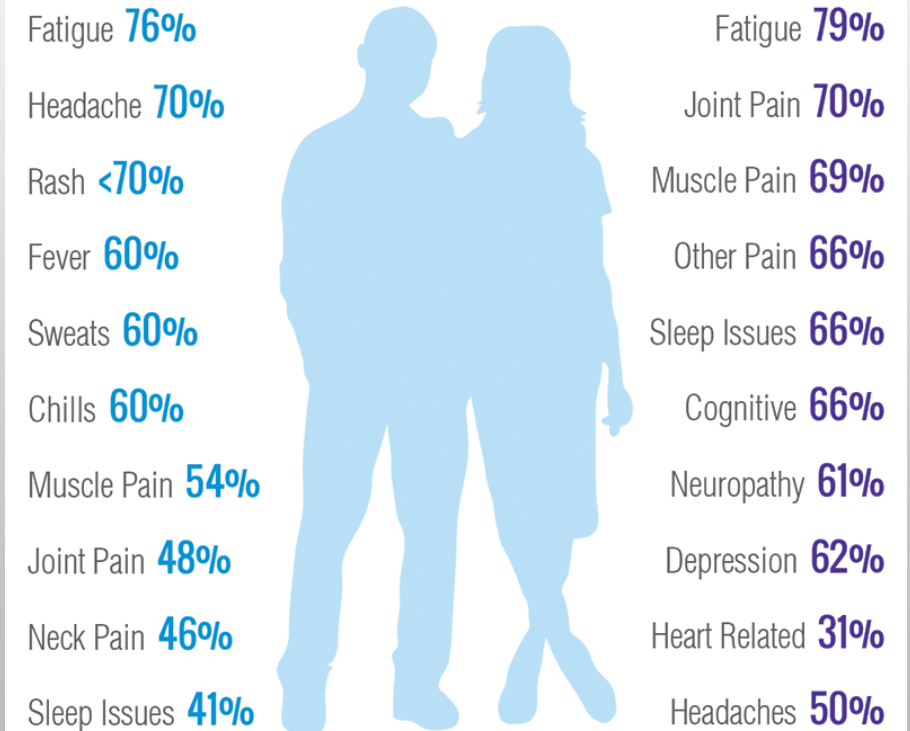
SYMPTOMS OF PTLDS

Most common symptoms:

- Migratory joint and muscle pain
- Cardiac symptoms
- Neurologic symptoms (Parkinson's?, Alzheimer's?)
- Neuropsychiatric issues: mood and behavioral disorders
- Dysautonomia
- Peripheral Neuropathy

LYME DISEASE SYMPTOMS

EARLY LYME* -vs- CHRONIC LYME**



* (Aucott 2013) ** (Johnson 2014. Moderate to very severe symptoms)
Estimates of rash rates range from 25-80% <http://tinyurl.com/kfvu8yt>

EPIDEMIOLOGY OF PTLDS

- PTLDS prevalence estimates for 2016 ranged from 69,011 persons to 1,523,869
- Prevalence in 2020 predicted to be as high as 1,944,189 cases



TESTING

Indirect tests

Measure an antibody's response to the infection, not the infection itself

- Western Blot (LabCorp, Quest)
- ELISA
- C-6 peptide test
- ImmunoBlot

Direct tests

Detects the DNA or RNA of the Lyme bacteria in the host

- PCR (polymerase chain reaction)
- FISH (RNA)
- Nanotrap

CHALLENGE WITH TESTING

The **immunoBlot** test for Lyme disease has a sensitivity and specificity greater than 93%, whereas the **ELISA** and **Western Blot** two-tier testing protocol recommended by the CDC has a sensitivity of only 57.6%

CHALLENGE WITH TESTING AND DIAGNOSIS

1. Low sensitivity and specificity of the available tests
2. The issue of false negative tests
3. A large number of people are subsequently diagnosed with LD but don't remember the tick bite
4. 25% of LD patients never developed the erythema migrans (EM) rash or Bulls' eye Rash
5. Gradual progress of symptoms
6. The right tests are not necessarily done at the right time



CLEARANCE OF NEW LYME TESTING BY THE FOOD AND DRUG ADMINISTRATION (FDA)

- The new diagnostic tool uses a new testing paradigm where two tests called enzyme immunoassays (EIA) are run concurrently or sequentially
- It is a modified two-tier testing that doesn't use the Western blot as its second step after and the initial EIA (ELISA) step
- FDA indicated that these new tests will aid in the diagnosis of Lyme Disease

OUR APPROACH

1. History and physical exam

2. Testing:

- Horowitz health questionnaire
- ImmunoBlot (IGeneX labs)
- Western Blot (LabCorp/Quest)
- Galaxy Labs for certain tick borne infections (Bartonella)
- Ceres Nanotrap (antigen testing)

Article

Precision Medicine: The Role of the MSIDS Model in Defining, Diagnosing, and Treating Chronic Lyme Disease/Post Treatment Lyme Disease Syndrome and Other Chronic Illness: Part 2

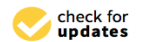
Richard I. Horowitz ^{1,2,*} and Phyllis R. Freeman ²

¹ HHS Tickborne Disease Working Group, Washington, DC 20201, USA

² Hudson Valley Healing Arts Center, New York, NY 12538, USA; freemanp63@gmail.com

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Received: 6 August 2018; Accepted: 31 October 2018; Published: 5 November 2018



Empirical validation of the Horowitz Multiple Systemic Infectious Disease Syndrome Questionnaire for suspected Lyme disease

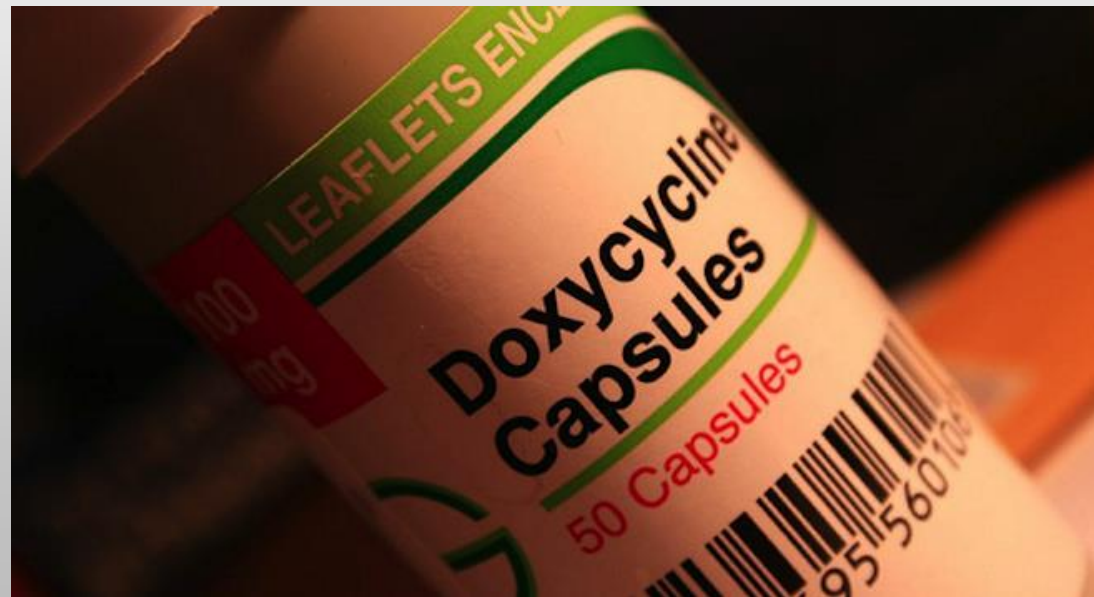
Maryalice Citera¹
Phyllis R Freeman²
Richard I Horowitz²

Purpose: Lyme disease is spreading worldwide, with multiple *Borrelia* species causing a broad range of clinical symptoms that mimic other illnesses. A validated Lyme disease screening questionnaire would be clinically useful for both providers and patients. Three studies evaluated

SECOND PIECE OF THE PUZZLE



IT'S MORE THAN JUST DOXY!!



ANTIBIOTIC TREATMENT

INTRACELLULAR

- Cephalosporin
- Zithromax
- Penicillin
- Rocephin

EXTRACELLULAR

- Doxycycline
- Rifampin

L-FORM/ CYSTIC

- Flagyl
- Tindamax

PERSISTERS

- Disulfiram
- Dapsone

SPIROCHETE
FORM



borrelia burgdorferi



lyme disease

CYST FORM



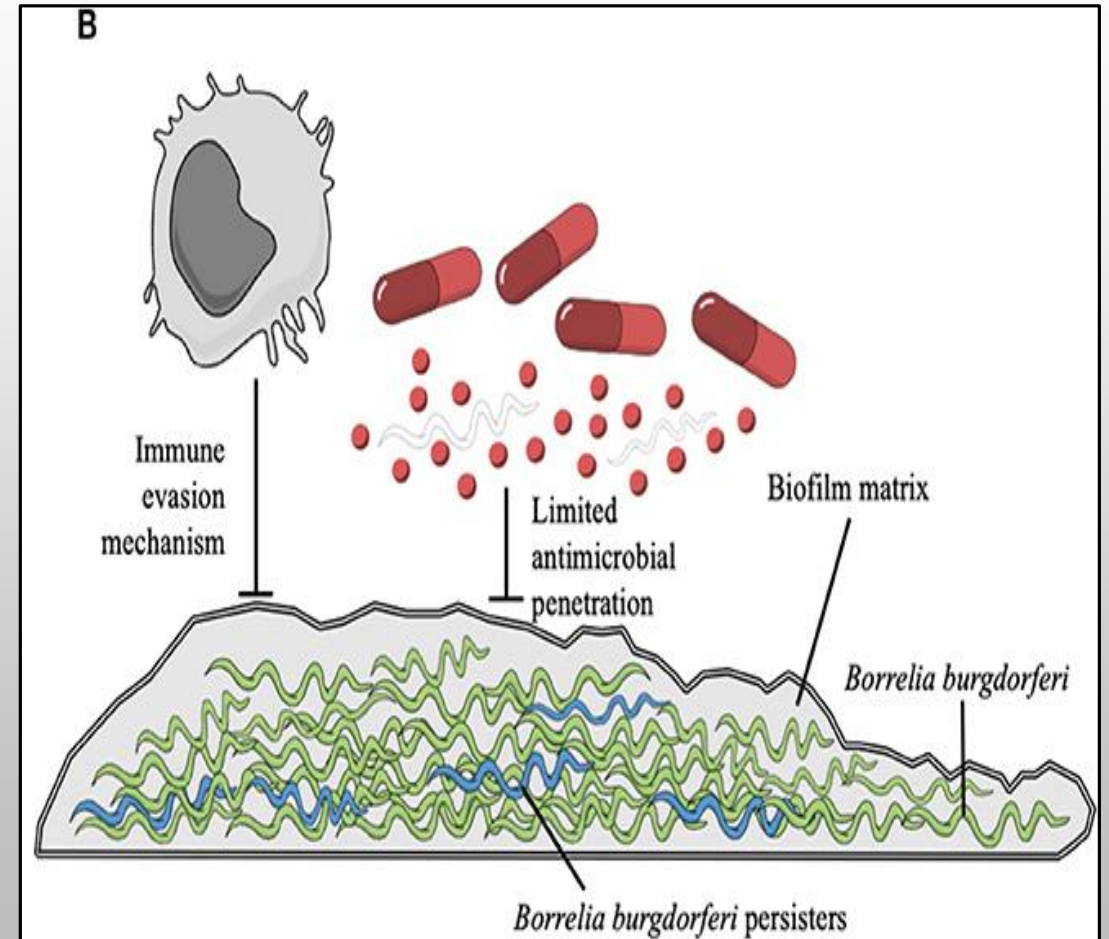
BIOFILM



LYME DISEASE PERSISTERS

3 mechanisms via which the infection persists:

1. Immune evasion mechanisms
2. Limited antimicrobial penetration
3. Biofilm matrix



NEW TREATMENTS

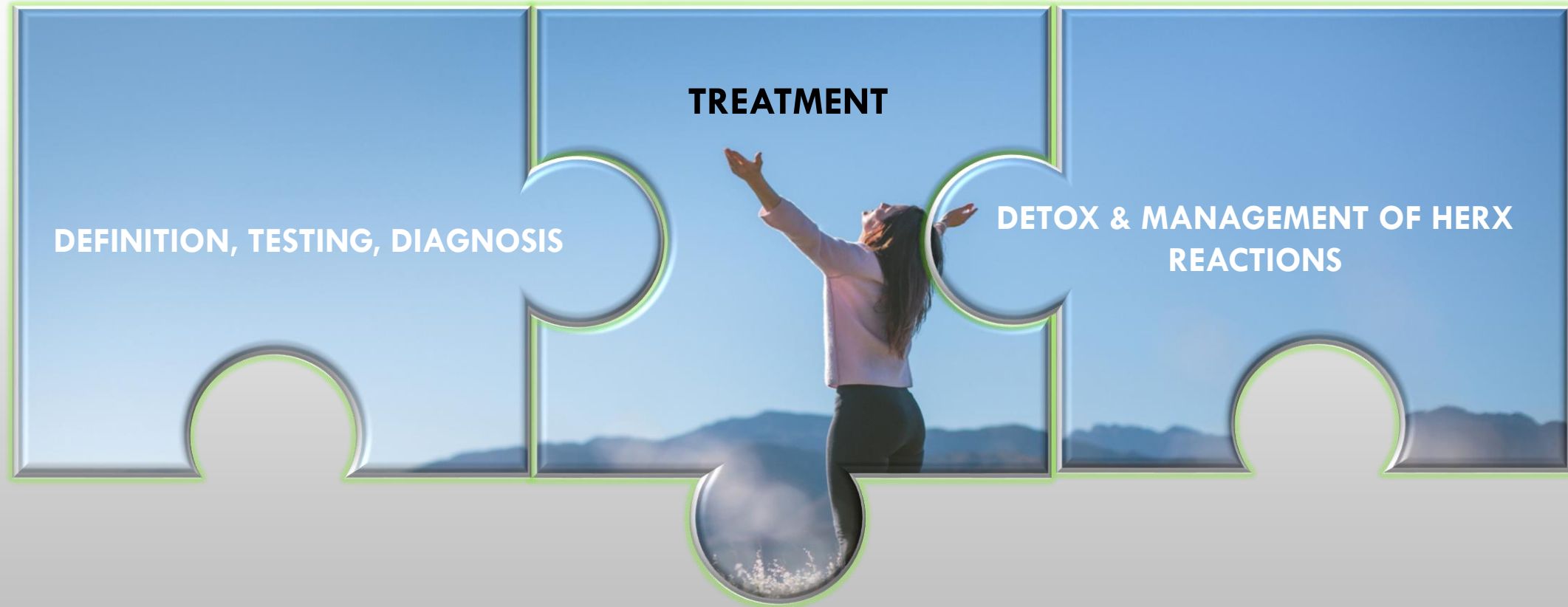
DAPSONE

- Effective treatment against slow growing, intracellular persister bacteria like leprosy
- Anti-parasitic properties (Babesia)
- Patients report significant improvements in Lyme and Babesia related symptoms
- Has anti-inflammatory effects in autoimmune conditions

DISULFIRAM

- Novel potential treatment for chronic Lyme Borreliosis
- Has anti-mycobacterial properties
- Anti-parasitic properties (Babesia)
- Has been recognized to have anti-cancer agents, and reduces plaque-burden in a mouse model of Alzheimer's disease

THIRD PIECE OF PUZZLE



DETOXIFICATION: PREPARING YOUR BODY TO HEAL

- Glutathione
- N-acetylcysteine
- Methylated B complex (MTHFR)
- IV Vitamins
- Epsom Salt Baths
- Infrared Sauna
- Dry Brushing
- Lymphatic Drainage
- Gentle Exercise
- Acupuncture
- Magnesium citrate/taurate/glycinate
- Activated Charcoal
- Ultra Binder/ GI Detox
- Hypoallergenic Diet/Detox food plan

DEFINITION & MANAGEMENT OF JARISCH-HERXHEIMER REACTIONS

*“temporary worsening of the symptoms of Lyme disease that occurs when the Lyme spirochete is being killed off by antibiotics, creating inflammation...These Herx reactions produce cytokines, which then create **inflammatory** symptoms, including increased **fever, muscle and joint pain, headaches, cognitive impairment,** and a general worsening of the underlying symptomology.”*

Dr. Richard Horowitz



MANAGEMENT OF HERXHEIMER REACTIONS

- N-acetylcysteine
- IV vitamins W/ Glutathione
- Resveratrol
- Curcumin
- Alka-seltzer Gold
- Alpha Lipoic Acid
- Lemon Juice
- Epsom salt baths
- Infrared Sauna
- Acupuncture
- Magnesium
- Burbur/Pinella

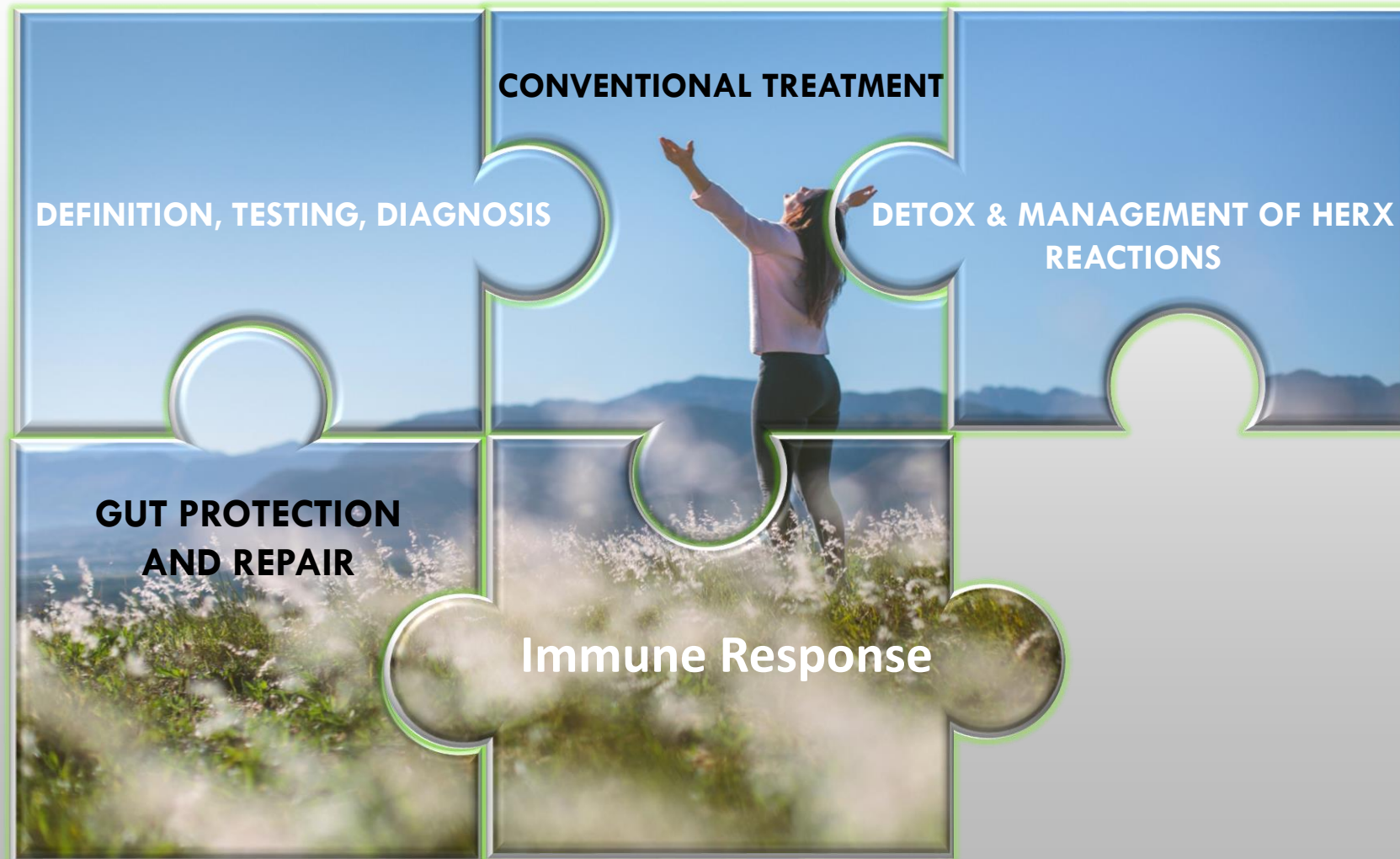
FOURTH PIECE OF PUZZLE



GUT PROTECTION AND REPAIR

MICROBIOME BALANCE	FUNGAL INFECTIONS	INTESTINAL PERMEABILITY	NUTRITIONAL DEFICIENCIES
<ul style="list-style-type: none">• PROBIOTICS• PREBIOTICS• YEAST-TYPE PROBIOTICS• SPORE-FORMING PROBIOTICS	<ul style="list-style-type: none">• DIFLUCAN/NYSTATIN• OIL OF OREGANO• CAPRYLIC ACID• CAT'S CLAW• BLACK WALNUT• BERBERINE• UVA URSI• NEEM• SWEET WORMWOOD	<ul style="list-style-type: none">• DEGLYCYRRHIZED LICORICE• SLIPPERY ELM• ALOE VERA• MARSHMALLOW ROOT• PEPPERMINT• GINGER TEA	<ul style="list-style-type: none">• GLUTAMINE• ZINC• CoQ10• B VITAMINS

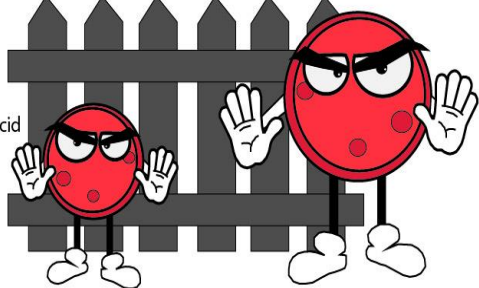
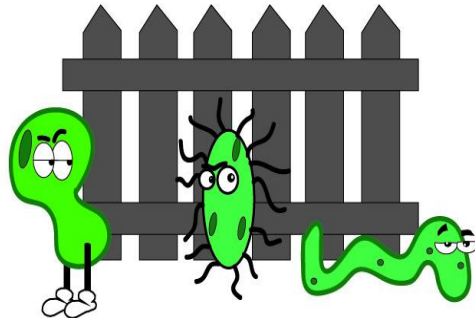

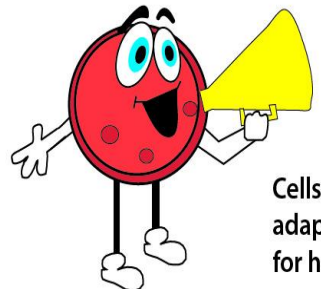
FIFTH PIECE OF PUZZLE



INNATE IMMUNE SYSTEM

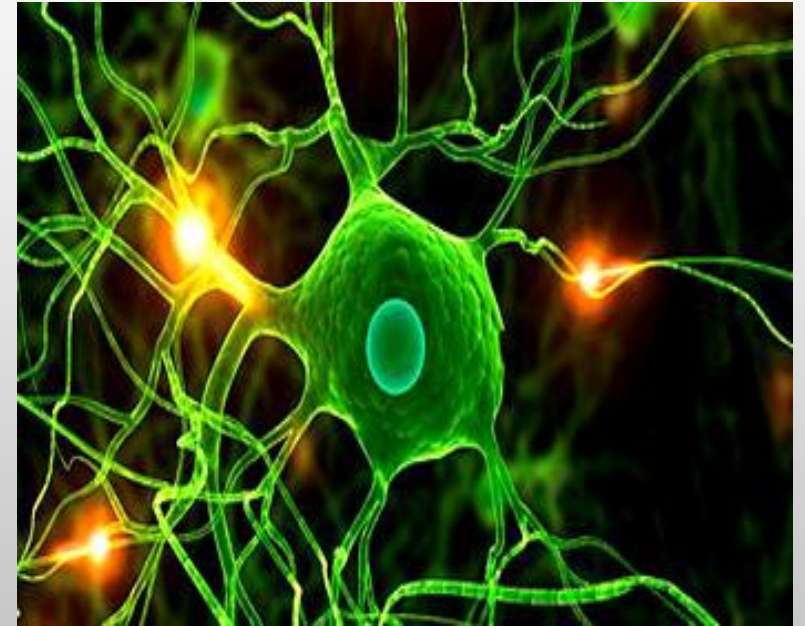
- Our first responders
- In the brain:
 - Microglia
 - Mast Cells

The Innate Immune System: The first line of defense
Physical and chemical barriers that try to keep foreign invaders from getting into the body.

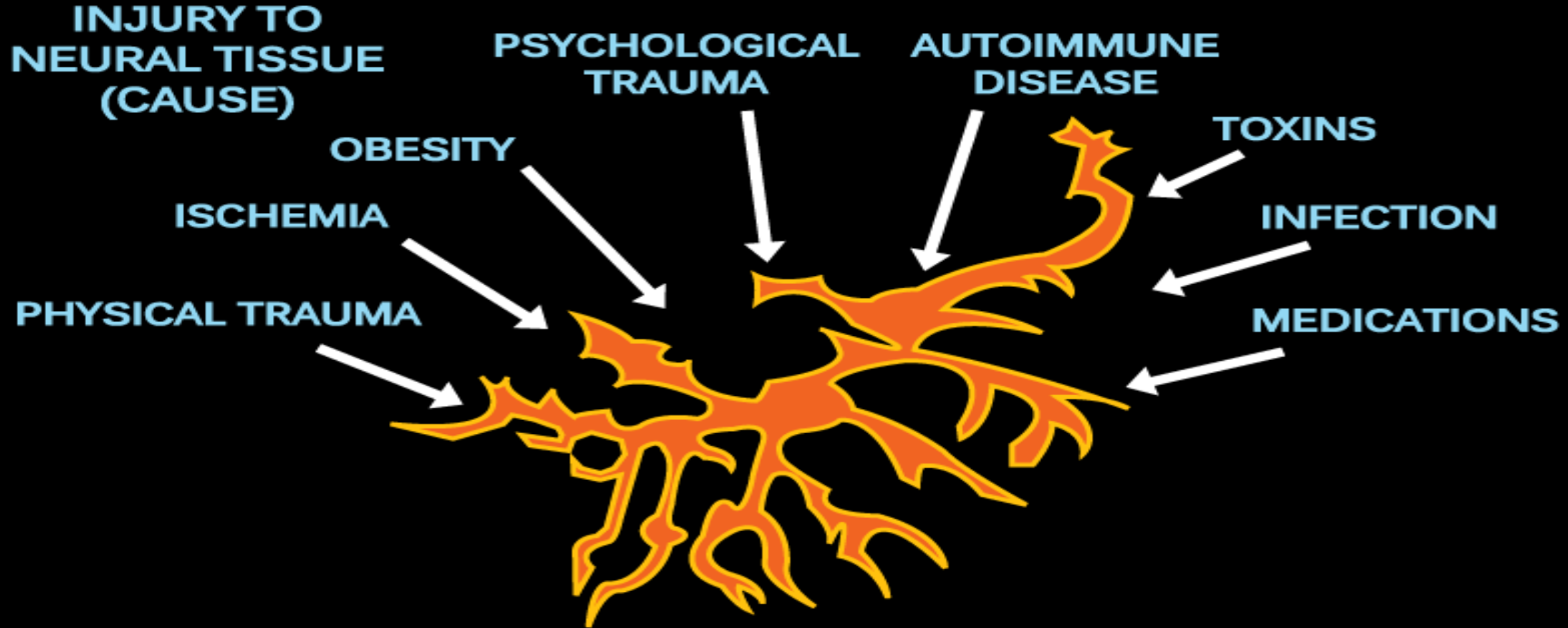
<p>Physical barriers like ...</p> <ul style="list-style-type: none">- Skin- Tears- Earwax- Mucus- Urine- Stomach acid  <p>Bacteria, viruses and fungi are constantly invading.</p>	 <p>Sometimes some get around the barriers</p>
<p>Innate immune cells try to do what they can.</p>  <p>They are like the garbage man and target anything foreign.</p>	<p>Sometimes backup is needed.</p>  <p>Cells signal to the adaptive immune system for help!</p>

INNATE IMMUNE SYSTEM MAJOR PLAYERS: **MICROGLIA**

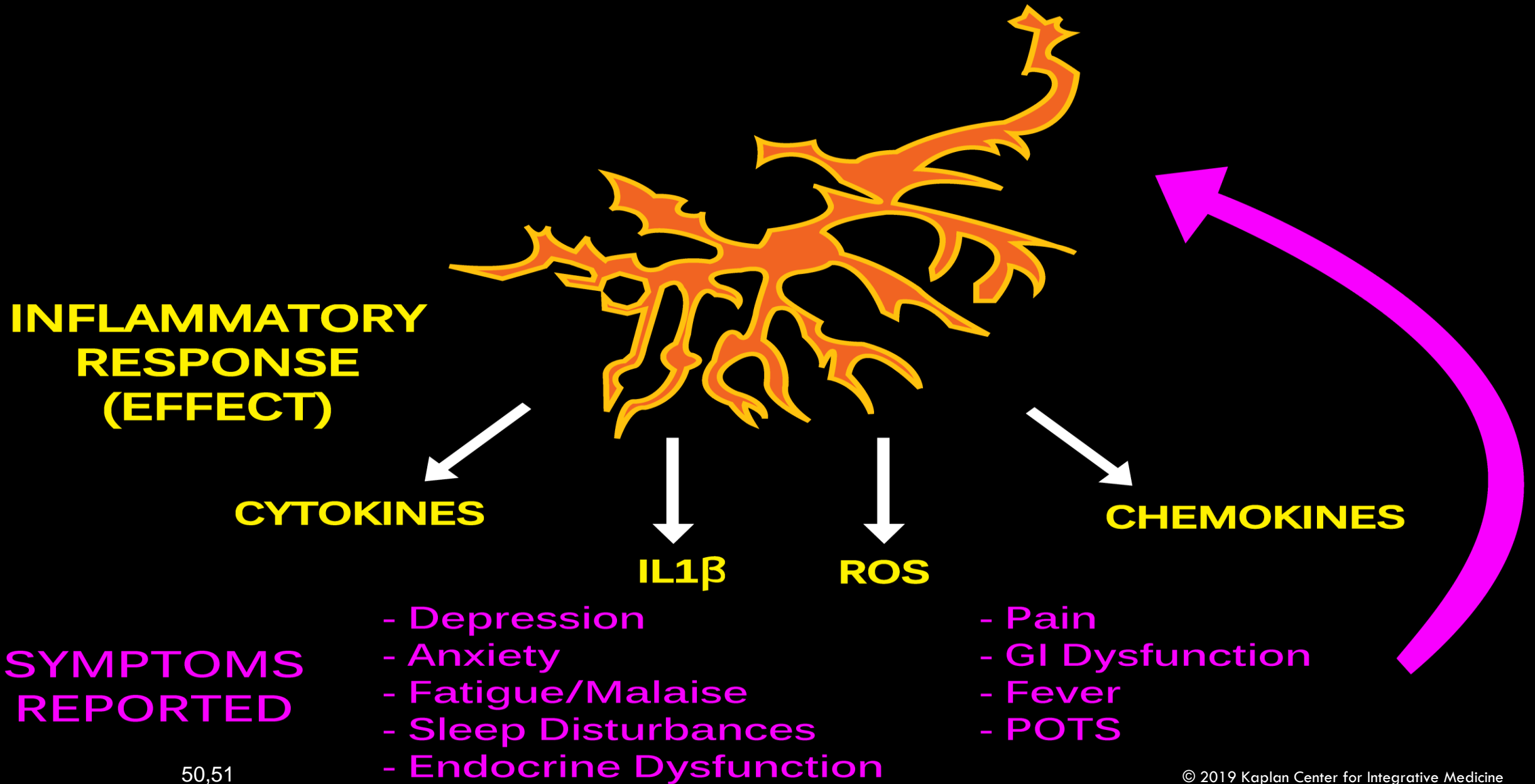
- Microglia are resident cells of the brain involved in regulatory processes critical for development, maintenance of the neuronal environment, injury and repair”
- “Electricians” of the Central Nervous System (CNS)
- Innate immune cells of the CNS



NEUROIMMUNE INTERFACE



NEUROIMMUNE INTERFACE



"I highly recommend this book to anyone who has suffered without relief or wants a deeper insight into how our bodies work."

—MARK HYMAN, MD, author of the #1 *New York Times* bestseller
The Blood Sugar Solution, and chairman, Institute for Functional Medicine

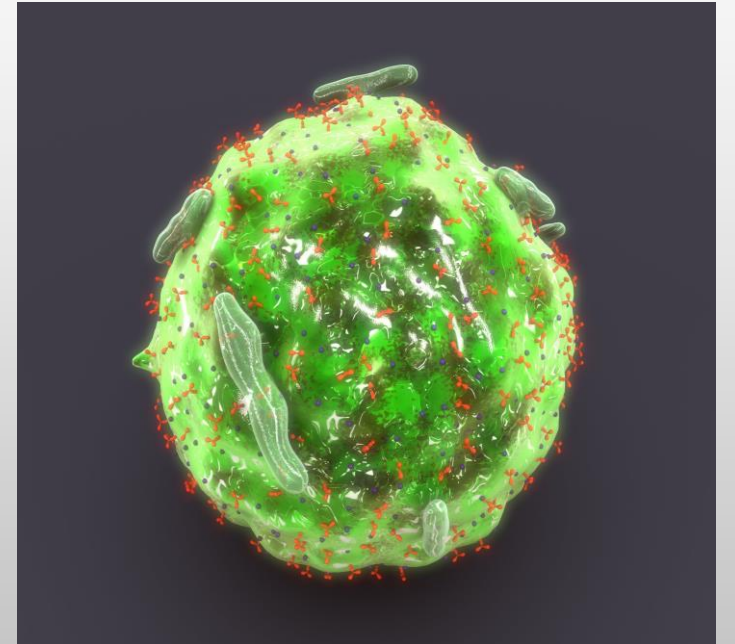
**A REVOLUTIONARY NEW APPROACH
TO BREAKING THE CYCLE OF
PAIN AND DEPRESSION**

TOTAL RECOVERY

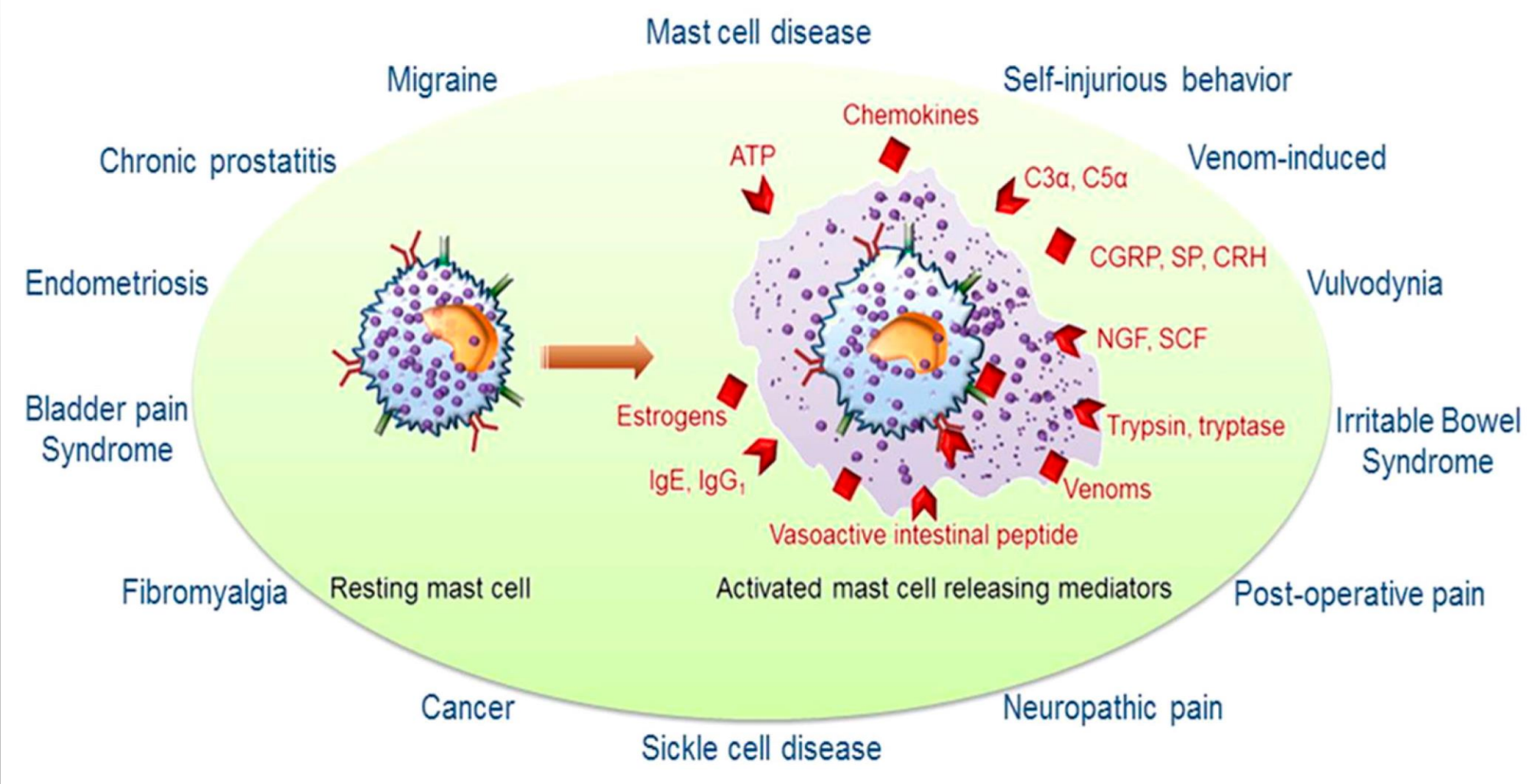
DR. GARY KAPLAN, DO
with DONNA BEECH

INNATE IMMUNE SYSTEM MAJOR PLAYERS: **MAST CELLS**

- Type of white blood cells: Granulocyte
- Part of the immune and neuroimmune systems
- Common in areas of close contact to external environment: skin, GI, airways
- Distributed in all organs and vascular tissue
- Can move across the blood brain barrier in inflamed and non-inflammatory conditions



INNATE IMMUNE SYSTEM MAJOR PLAYERS: MAST CELLS



ADAPTIVE IMMUNE SYSTEM

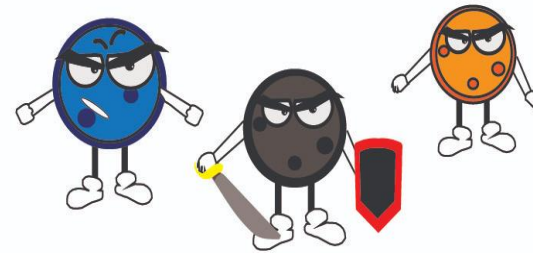
- The “smart” immune system
- Develops specialized cells (antibodies) to defend against specific infections such as the flu
- Creates immune memory

The Adaptive Immune Response:

Cells that are called in to fight the infection. This response is specific to the type of invader.

Meet the team:

The Special Defense Unit: T cells and B cells



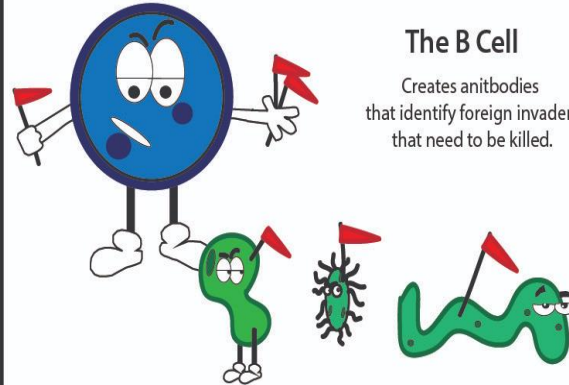
The Helper

Uses chemical signals to call on the B cells and other T cells to help fight the invader.



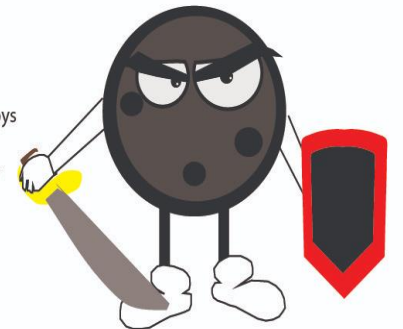
The B Cell

Creates antibodies that identify foreign invaders that need to be killed.



The Killer

Identifies infected host cells and employs chemical signals to cause them to die and be eliminated from the body.



Adaptive immunity: When things go wrong

- Autoimmunity is a condition where the adaptive immune system is attacking its own healthy cells and tissues
- Autoimmune Disease is the result of the aberrant immune response
- About 5% of the population suffers from an autoimmune disease
- Examples of Autoimmune Disease:
 - Multiple Sclerosis
 - Rheumatoid Arthritis
 - Systemic Lupus Erythematosus
 - Sjögren's
 - Hashimoto's Thyroiditis



GEORGETOWN UNIVERSITY
Georgetown University Medical Center



FOUNDATION *for*
TOTAL RECOVERY
Finding A Cure For Neuroinflammatory Diseases

Autoimmune Encephalopathy of Infectious Etiology

Gary Kaplan D.O, DABFM, DABPM, FAAMA
Medical Director, The Kaplan Center for Integrative Medicine
Clinical Associate Professor, Georgetown University School of Medicine

6829 Elm Street, suite 300
McLean, VA 22101
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www.kaplanclinic.com

June 15-16, 2019

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AUTOIMMUNE ENCEPHALOPATHY OF INFECTIOUS ETIOLOGY

CLINICAL PRESENTATIONS

- **Neuropsychiatric symptoms**
- **Chronic headaches**
- **Sensory or motor complaints**
- **Seizures**
- **Dyssomnia**
- **Chronic Fatigue**
- **Fibromyalgia**
- **Dysautonomia**


INFECTIOUS ETIOLOGIES

- **Streptococcus**
- **Mycoplasma pneumoniae**
- **Bartonella**
- **Toxoplasmosis**
- **Influenza**
- **Babesia**
- **Borrelia**
- **Epstein Barr Virus**

TESTING



Sample Date	Parameter	Cut off	Units/ml
11.03.2019	Anti AT1R Antibodies	<10.0 U/ml: negative 10.0-17.0 U/ml: at risk > 17.0 U/ml: positive	13.4 (at risk)
11.03.2019	Anti ETAR Antibodies	<10.0 U/ml: negative 10.0-17.0 U/ml: at risk > 17.0 U/ml: positive	12.8 (at risk)
11.03.2019	<i>Anti α-1-adrenergic Antibodies</i>	<7.0 U/ml: negative >7.0 U/ml: positive	16.9 (positive)
11.03.2019	<i>Anti α-2-adrenergic Antibodies</i>	<15.0 U/ml: negative >15.0 U/ml: positive	15.9 (positive)
11.03.2019	<i>Anti β-1-adrenergic Antibodies</i>	<15.0 U/ml: negative >15.0 U/ml: positive	22.7 (positive)
11.03.2019	<i>Anti β-2-Adrenergic Antibodies</i>	<8.0 U/ml: negative 8.0-14.0 U/ml: at risk >14.0 U/ml: positive	9.5 (at risk)



Patient DOB: 10/15/1981 Patient
ID Number: C010-832-WL Date of
Test Report: 11/27/2018

moleculera labs
Cunningham Panel™ Testing Results

PATIENT REPORT

Submitting Prescriber: Gary Kaplan, DO
Date of Collection: 11/13/2018
Date of Receipt: 11/15/2018

LABORATORY TEST RESULTS COMPARED TO NORMAL RANGES

	Anti-Dopamine Receptor D1 (titer)	Anti-Dopamine Receptor D2L (titer)	Anti-Lysoganglioside GM1 (titer)	Anti-Tubulin (titer)	CaM Kinase II ² (% of baseline)
Patient Result	1:4,000	1:8,000	1:320	1:4,000	126
Normal Ranges	500 to 2,000	2,000 to 8,000	80 to 320	250 to 1,000	53 to 130
Normal Mean	1,056	6,000	147	609	95
INTERPRETATION*	ELEVATED	BORDERLINE	BORDERLINE	ELEVATED	BORDERLINE

ADDRESSING THE IMMUNE SYSTEM MANIFESTATIONS

INNATE

- Low Dose Naltrexone
- Celebrex
- Minocycline
- Cytoquel
- Acupuncture

MAST CELLS

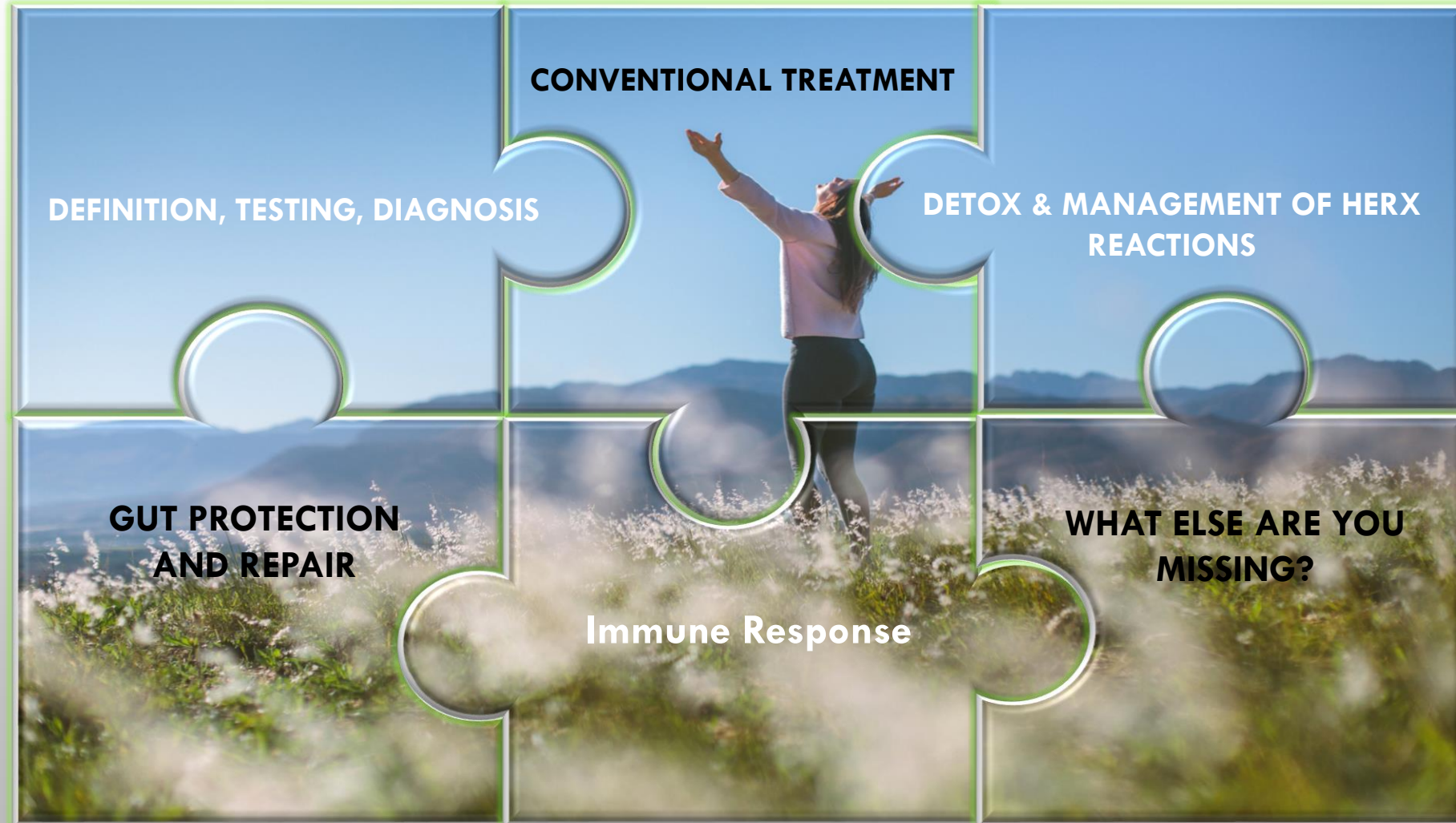
- IV therapies
- Ketotifen
- H1 Blockers
- H2 Blockers
- Leukotriene
- Cromolyn Sodium

ADAPTIVE

- Metformin (mTOR)
- IVIg
- Plasmapheresis
- Rituximab
- ?Human Cells and Tissue-based Products (stem cell)

NUTRITIONAL SUPPLEMENTS

SIXTH PIECE OF PUZZLE



DIAGNOSIS, DIAGNOSIS, DIAGNOSIS...

- Co-infections
- Mold Toxins
- Viral Infections: EBV, CMV, HPV
- Mycoplasma Pneumoniae
- Celiac Disease
- Toxoplasmosis
- Heavy Metals: lead, mercury
- Hypermobility (EDS)
- POTS
- Sleep Apnea, Narcolepsy
- Thyroid, Hormone Imbalance
- Parasites

SOLVING THE PUZZLE





**I kindly thank you for your
attention.**

Dr. Gary Kaplan, D.O. DABFM, DABPM, FAAMA

Medical Director, Kaplan Center for Integrative Medicine
Clinical Associate Professor, Georgetown University School of Medicine
Author, Total Recovery: Breaking the Cycle of Chronic Pain and Depression