Chronic Inflammatory Response Syndrome

DR. OLUSEGUN OSENI. FCCP. DABSM.
BOARD CERTIFIED PULMONARY AND SLEEP SPECIALIST
FUNCTIONAL MEDICINE SPECIALIST
MEDICAL DIRECTOR, ALPHA CARE WELLNESS CENTER
www.alphacarewellnesscenter.com
817-550-6332

Chronic Inflammatory Response Syndrome (CIRS) is a complex, multi-system, multi-symptom illness precipitated by exposure to biotoxins such as mold, bacteria, or other microbial toxins in genetically susceptible individuals. It is characterized by a chronic systemic inflammatory response that does not resolve, leading to a myriad of symptoms affecting various body systems. The approach to diagnosing and treating CIRS has evolved significantly, with evidence-based medicine (EBM) playing a crucial role in understanding and managing this condition.

The Evolution of Chronic Inflammatory Response Syndrome (CIRS) and Biotoxin Illness: Contributions of Dr. Ritchie Shoemaker.

The concept of Chronic Inflammatory Response Syndrome (CIRS), also known as biotoxin illness, was significantly advanced by the pioneering work of Dr. Ritchie Shoemaker. His contributions to understanding and treating this condition dates back to 1997, during his tenure as a family medicine practitioner in the rural coastal town of Pocomoke, Maryland. It was here that Dr. Shoemaker first observed and began to investigate an illness that was not previously well-defined.

Dr. Shoemaker's initial breakthrough came when he linked this previously undefined illness to a toxin produced by the dinoflagellate *Pfiesteria Piscicida*, a microorganism known for causing fish kills in the region. Patients exposed to water contaminated by *Pfiesteria* began presenting with a range of symptoms, including cognitive impairments, fatigue, and respiratory issues, which were not easily explained by existing medical frameworks at the time.

Building on his initial discovery, Dr. Shoemaker expanded his research to investigate similar symptomatology in patients exposed to other environmental toxins. Over time, he identified that the same type of illness could be triggered by toxins produced in water-damaged buildings, as well as by toxins associated with tick-borne pathogens such as *Borrelia burgdorferi* (the causative agent of Lyme disease). This work led to the recognition that CIRS could result from a variety of biotoxin exposures, each leading to a persistent inflammatory response that affects multiple body systems.

Through rigorous practice-based research, Dr. Shoemaker developed a comprehensive clinical description of CIRS. He established diagnostic criteria based on patient history, symptomatology, and specific laboratory biomarkers, including elevated C4a, TGF-beta1, and MMP-9, as well as reduced melanocyte-stimulating hormone (MSH). Additionally, he utilized

the Visual Contrast Sensitivity (VCS) test, a tool to detect deficits in contrast sensitivity, a common feature in CIRS patients.

Dr. Shoemaker's contributions extend beyond diagnosis. He formulated a treatment protocol aimed at removing biotoxins from the body, reducing inflammation, and restoring normal immune function. His protocol includes steps such as eliminating exposure to biotoxins, using bile acid sequestrants like cholestyramine to bind and remove toxins, and employing anti-inflammatory agents like vasoactive intestinal peptide (VIP). His approach has been validated through clinical practice, resulting in the restoration of health for thousands of patients worldwide.

Understanding CIRS

Routes of Exposure: -Inhalation in Water-Damaged Buildings (WDB): One of the most common routes of exposure to biotoxins is inhalation within water-damaged buildings (WDB). These environments harbor a dangerous mix of mold, bacteria, volatile organic compounds (VOCs), endotoxins, and actinomycetes, collectively referred to as a "biochemical stew." This mixture of contaminants creates an environment where CIRS can develop, as the body responds not to a single element, but to the combination of these factors, leading to systemic inflammation. Approximately 80% of CIRS cases are associated with repeated exposure to WDB.

According to the environmental protection agency and the national occupation safety and health department, about 50% of US building structures are water-damaged buildings (WDB)

-Tick or Spider Bite: Exposure to biotoxins can also occur through arthropod bites, most notably from ticks and, less commonly, spiders. Tick bites can transmit various pathogens, including *Borrelia burgdorferi* (the causative agent of Lyme disease) and *Babesia microti* (which causes babesiosis). In some cases, the bite of recluse spider species can also lead to the development of biotoxin illness. The biotoxins introduced through these vectors can trigger a prolonged inflammatory response in genetically predisposed individuals.

-Ingestion: Another route of exposure is through the ingestion of contaminated food. Specifically, consumption of reef fish contaminated with ciguatoxins—produced by dinoflagellate algae—can lead to ciguatera fish poisoning. This toxin accumulates in fish that consume smaller, toxin-laden organisms, posing a risk to humans who consume these fish. Ingestion of ciguatoxins can cause acute illness and, in susceptible individuals, can contribute to chronic symptoms characteristic of CIRS.

-Direct Contact with Contaminated Water: Direct contact with contaminated water is another significant route of exposure to biotoxins. This includes exposure to water bodies affected by fish kills due to organisms such as *Pfiesteria* and *Cyanobacteria*. Patients may inhale airborne or aerosolized toxins from these sources or come into direct contact with the water, leading to potential biotoxin illness. The ability of these toxins to permeate cell membranes and evade standard blood tests complicates diagnosis and treatment.

Biotoxin Pathophysiology

In patients who are genetically susceptible due to specific HLA (Human Leukocyte Antigen) haplotypes, exposure to biotoxins triggers a cascade of immune responses. This process begins with the chronic activation of the innate immune system, largely due to the poor presentation of antigens to the adaptive immune system. Normally, the adaptive immune system would effectively process and eliminate antigens, but in these patients, the inability to fully engage this response leaves biotoxins in the body.

These biotoxins can then bind to specific cell surface receptors, including Toll-like receptors, mannose receptors, and C-type lectin receptors. Biotoxins have unique structural properties, often taking the form of ionophores or amphipaths, which allow them to move across cell membranes without the need to be transported in the bloodstream.

The recognition and binding of biotoxins at these receptors activate inflammatory pathways. This leads to an abnormal increase in inflammatory markers such as MMP9 (Matrix Metalloproteinase 9), cytokines, TGF beta-1 (Transforming Growth Factor beta-1) and complement split products. The chronic presence of these biotoxins results in the persistent upregulation of innate immune pathways, leading to chronic inflammation and overproduction of cytokines and a continuation of the inflammatory process. This persistent inflammation affects multiple body systems, leading to the diverse multisystem symptoms associated with CIRS.

Leptin, a hormone and cytokine primarily produced in adipose tissue, plays a critical role in the pathway of biotoxin illness. It serves as a link between the neuroendocrine and immune systems. In cases of biotoxin exposure, cytokines can interfere with leptin signaling in the hypothalamus, leading to leptin resistance. This resistance triggers an upregulation of leptin production, which is associated with refractory obesity, weight gain that is difficult to reverse despite diet and exercise.

Normally, leptin binds to receptors in the hypothalamus, facilitating the production of several hormones, including melanocyte-stimulating hormone (MSH), adrenocorticotropic hormone (ACTH), and endorphins. However, disruptions in this pathway due to biotoxin exposure can lead to decreased levels of these hormones. Particularly, low MSH is significant as it normally exerts anti-inflammatory effects and helps regulate immune responses. A deficiency in MSH can result in unchecked inflammation, contributing to symptoms such as muscle aches, mood swings, headaches, and difficulty concentrating.

Furthermore, low MSH can lead to immune system dysfunction, sleep disturbances, and increased gut permeability ("leaky gut"), which can predispose individuals to autoimmune conditions. This condition also impacts other hormone levels, including cortisol and androgens, contributing to a wide range of systemic effects.

In biotoxin illness, cytokines can also elevate markers like MMP-9, leading to tissue damage, and VEGF, affecting blood flow and contributing to symptoms like shortness of breath and cognitive dysfunction. Additionally, disruptions in the complement cascade, evidenced by elevated C4a levels, can exacerbate inflammation, particularly upon re-exposure to biotoxins.

This complex interaction of immune dysregulation, hormonal imbalances, and inflammation underscores the multifaceted nature of biotoxin-related illnesses and the need for comprehensive treatment approaches.

The 13 Symptom Clusters of CIRS:

Dr. Shoemaker's analysis revealed that CIRS symptoms can be systematically grouped based on their occurrence patterns in patients. These clusters represent the various physiological systems affected by the syndrome, underscoring the comprehensive impact of biotoxin exposure on the body. Below is an overview of the symptom clusters:

Gastrointestinal: diarrhea, abdominal pain, bloating, indigestion.

Neurological: numbness, disorientation, sensitivity to light, trouble learning new information, impaired memory, difficulty with word finding, brain fog.

Respiratory: sinus congestion, shortness of breath, exertional dyspnea, chronic cough

Generalized: weakness, body aches, headaches.

Cognitive and Sensory: sensitivity to light, trouble learning new information, impaired memory, difficulty with word finding.

Skin: heightened skin sensitivity, tingling/pins and needles.

Musculoskeletal: joint pain, morning stiffness, muscle cramps.

Visual: blurry vision, red or bloodshot eyes.

Autonomic: night sweats, mood swings, extreme thirst, frequent urination, fluctuations in heart rate and blood pressure. These symptoms suggest dysregulation of the autonomic nervous system and hypothalamic-pituitary-adrenal (HPA) axis.

Pain: icepick pain, deep pain, persistent fatigue

Cognitive and Sensory: trouble concentrating, dizziness, confusion.

Autonomic dysregulation: static shocks, trouble regulating body temperature.

Sleep: poor sleep quality, difficulty initiating and maintaining sleep, fragmented sleep, daytime fatigue.

Diagnostic Criteria

The diagnosis of CIRS relies on a combination of patient history, clinical symptoms, and laboratory tests.

History of exposure: Documented exposure to a biotoxin-producing environment.

Symptom clusters: Presence of symptoms from multiple clusters indicative of multi-system involvement.

Genetic Testing: HLA genetic testing identifies individuals with increased susceptibility to CIRS. Specific HLA haplotypes, DRB1, DQ, DRB3, DRB4 or DRB5. It has been noted that about 25 percent of the population carry an HLA vulnerability. They are linked to a higher risk of chronic inflammation following biotoxin exposure, indicating a genetic predisposition to developing CIRS.

Biomarkers: Specific laboratory tests are critical in diagnosing CIRS. Abnormal results in specific laboratory tests such as elevated C4a, TGF-beta1, MMP-9, and low melanocyte-stimulating hormone (MSH).

- C4a: An elevated complement component indicative of immune system activation.
- TGF-beta1**:** A cytokine involved in inflammation and tissue remodeling.
- MMP-9**:** An enzyme that breaks down extracellular matrix proteins and indicates tissue damage.
- MSH**:** Reduced levels of melanocyte-stimulating hormone, which plays a role in regulating inflammation and immune function.

Visual Contrast Sensitivity (VCS) test: VCS is an important diagnostic tool in the assessment of patients with neurotoxin-related illnesses, such as those caused by biotoxin exposure. These substances can induce a wide array of neurological symptoms, including a diminished ability to detect visual patterns, which is measured through VCS testing.

VCS measures the ability to discern visual patterns, particularly in low-contrast environments, which is crucial for tasks like reading or navigating in dim light. According to Dr. Ritchie Shoemaker's research, this decline in VCS is associated with a decrease in the velocity of red blood cells flowing to the retinal structures responsible for transmitting visual information through the optic nerve to the brain. This diminished blood flow is because of the inflammatory processes triggered by biotoxins, leading to compromised visual processing.

The VCS test has been shown to be highly accurate in supporting the diagnosis of biotoxin-related illnesses. According to data from Dr. Shoemaker's research, the VCS test correctly identifies biotoxin-related illness in approximately 92% of affected individuals. This high level of accuracy makes VCS testing a valuable tool in the clinical assessment and management of patients suspected of having biotoxin exposure.

VCS testing is typically performed during the initial clinical evaluation of a patient suspected of having a biotoxin-related illness. It serves as an early indicator of neurotoxin impact and provides a baseline measurement that can be tracked over time. The test is repeated at subsequent visits to assess the patient's response to treatment. Improvement in VCS scores is a key indicator of recovery, whereas persistent deficits suggest ongoing biotoxin exposure or incomplete treatment response.

NeuroQuant MRI is a specialized, non-contrast imaging technique used to assess brain changes that may occur in patients with Chronic Inflammatory Response Syndrome (CIRS) and Post-Lyme disease. This advanced MRI tool uses software to measure the volume of specific brain regions, allowing clinicians to detect and monitor structural changes such as atrophy (shrinkage) or edema (swelling) in 11 distinct areas of the brain. These volumetric changes can be significant indicators of the underlying disease processes and the impact of treatment.

Patients with CIRS related to exposure to water-damaged buildings (CIRS-WDB) often exhibit a distinct pattern of brain changes. Notable findings include:

- Increased Forebrain Parenchyma**:** There is an increase in overall brain tissue volume in the forebrain.
- Increased Cortical Gray Matter**:** There is often an increase in the volume of cortical gray matter, which reflects inflammation.
- Decreased Caudate Nucleus Volume: The caudate, a part of the brain involved in motor processing and associative learning, typically shows reduced volume.

In contrast, patients with chronic symptoms following Lyme disease exhibit a different pattern on NeuroQuant MRI:

- Small Putamen**:** The putamen, involved in motor control and learning, appears smaller.
- Large Right Thalamus**:** The right thalamus, which plays a role in processing sensory information, is enlarged.

These findings help differentiate between CIRS-WDB and Post-Lyme disease, providing a clearer understanding of the brain's structural response to these conditions.

Echocardiogram: Pulmonary arterial hypertension (PAH) is a significant metabolic complication associated with Chronic Inflammatory Response Syndrome (CIRS). There is increased pressure in the pulmonary arteries, which can lead to right heart failure if left untreated. PAH is typically assessed through two primary methods: direct measurement via heart catheterization or indirect estimation using an echocardiogram.

While heart catheterization provides the most accurate measurement of pulmonary artery pressure, it is invasive. Therefore, echocardiograms are more commonly used to estimate the pulmonary artery systolic pressure (PASP) indirectly. For a more accurate assessment of PAH, it is crucial to measure the velocity of blood flow moving backward across the tricuspid valve, known as the "tricuspid jet."

To calculate PASP using the tricuspid jet, you square the velocity of the jet and multiply it by 4, then add this result to the right atrial pressure. A tricuspid jet velocity greater than 2.5 meters per second is concerning and may indicate elevated PASP. A resting PASP greater than 30 mm Hg is consistent with PAH. Additionally, in stress echocardiograms, an increase in PASP of more than 8 mm Hg with exercise is considered abnormal and suggests the need for treatment, such as with Vasoactive Intestinal Peptide (VIP).

Proper assessment of PAH in CIRS patients is essential, as early detection and intervention can significantly improve outcomes and reduce the risk of progression to more severe heart complications.

Cardiopulmonary exercise testing, VO2 Max: In patients with Chronic Inflammatory Response Syndrome (CIRS), VO2 max, a key indicator of cardiovascular and respiratory fitness, is often significantly reduced. This reduction is primarily due to a combination of metabolic disturbances, including tissue hypoxia caused by capillary hypoperfusion, depletion of glycogen stores, and issues with mitochondrial function due to genetic factors.

One of the most important tools to evaluate these metabolic changes is cardiopulmonary exercise testing (CPET). CPET measures how much oxygen a person consumes and how much carbon dioxide they produce during exercise. The test is particularly useful in determining VO2 max, which is the maximum amount of oxygen the body can utilize per kilogram of body weight per minute during exercise.

VO2 max is critical because it helps identify the anaerobic threshold (AT), the point during exercise when the body shifts from aerobic metabolism to anaerobic metabolism due to insufficient oxygen availability. Once the AT is exceeded, oxygen is no longer available in sufficient quantities to the mitochondria, and as a result, the body cannot produce the full 38 ATP molecules from each glucose molecule. This leads to the depletion of glucose and glycogen stores, forcing the body to rely on beta-oxidation for energy production.

In individuals with CIRS who also experience low melanocyte-stimulating hormone (MSH) levels and leptin resistance, beta-oxidation is impaired. This impairment leads to a condition known as post-exertional malaise or the "push/crash" phenomenon, where patients experience significant fatigue and worsening of symptoms following physical exertion.

Pulmonary function test (PFT): PFT in CIRS patients may show a restrictive pattern that is consistent with interstitial lung disease, especially if the elevated levels of transforming growth factor beta 1 (TGF beta 1) are not addressed. TGF beta 1 is a cytokine that plays a significant role in tissue fibrosis and inflammation, contributing to the respiratory limitations observed in these patients.

Transcriptomics, Pax Genomics and GENIE (Gene Expression Inflammation Explained) are increasingly important in understanding the molecular basis of Chronic Inflammatory Response Syndrome (CIRS). This area of study focuses on how gene expression, particularly those genes involved in protein synthesis by ribosomes and mitochondrial enzyme function, are altered in response to CIRS.

CIRS is known to cause significant disruption in these genetic pathways. Ribotoxins, which are toxins that target ribosomes, are released by biotoxins and lead to a state of hypometabolism, a reduced rate of metabolism that affects energy production. This disruption can have widespread effects on cellular function, as the ability of ribosomes to synthesize proteins is crucial for maintaining normal cellular activities, including energy production by mitochondria.

In the management of Chronic Inflammatory Response Syndrome (CIRS), Dr. Shoemaker and his team are now leveraging advanced tools like transcriptomics through the GENIE test. Essentially looking at whether certain genes are being upregulated or downregulated as part of the disease process. What makes transcriptomics so powerful is its ability to give us a detailed picture of what is happening at the genetic level. By examining gene expression, we can identify which aspects of the immune system are more active than others. This insight

helps us pinpoint the underlying processes driving the illness and guides us in tailoring the most effective treatment strategy.

One of the most promising aspects of using transcriptomics in CIRS is that it does not just help with diagnosis, it also provides a way to measure how well a patient is responding to treatment. Dr. Shoemaker and his team observed that after following the appropriate treatment protocol, there are positive changes in gene expression.

.

Evidence-Based Treatment of CIRS.

The Shoemaker Protocol

The Shoemaker Protocol is a structured, evidence-based approach to the treatment of CIRS. It involves several steps aimed at removing biotoxins, reducing inflammation, and restoring normal immune function.

1. Removal from Exposure: The initial step in treating CIRS is to eliminate the source of biotoxin exposure. This may involve environmental remediation, such as mold removal from buildings, or avoiding areas known to harbor biotoxins.

2. Binding Toxins: Cholestyramine (CSM) and Welchol are bile acid sequestrants used to bind biotoxins in the gastrointestinal tract, facilitating their elimination. Clinical studies have demonstrated their efficacy in reducing symptom severity and normalizing laboratory biomarkers in CIRS patients.

3. Anti-inflammatory Agents: Vasoactive intestinal peptide (VIP) is used to reduce systemic inflammation and alleviate symptoms associated with CIRS. VIP has shown promise in improving clinical outcomes.

4. Hormonal Modulation: Correcting hormonal imbalances, such as low MSH or dysregulated cortisol levels, is crucial. This step involves the use of specific hormonal therapies to restore normal endocrine function.

5. Supportive Therapies: Nutritional support, physical therapy, and cognitive rehabilitation are integral to comprehensive treatment plans for CIRS. These therapies aim to restore overall health

and improve the quality of life for patients. Ensuring adequate nutritional intake and addressing deficiencies can support the body's natural healing processes.

Shoemaker treatment protocol is a pyramid with steps as itemized below, each step must be completed before moving to the next step.

Step I- Removing Exposure

The first step in treating CIRS is to remove the patient from the exposure source. This may involve remediation of a mold-contaminated environment or avoiding areas known to harbor harmful biotoxins.

Step 2- Eradication of toxins Medications

> Cholestyramine (CSM) and Welchol: These bile acid sequestrants bind to biotoxins in the gut and help eliminate them from the body. Clinical studies have shown their effectiveness in reducing symptoms and improving lab markers in CIRS patients.
>
> Cholestyramine is an anion which has a quaternary ammonium side chain which creates a localized, net positive chance. It binds with high affinity to the toxin's ionophores. It has approximately 5 times has many electrical early active sites compared to WelChol.
>
> CSM Adult dose 1 scoop (4 grams) QID. For young children 60mg/kg each dose TID

Step 3- Eradication of multiple antibiotic-resistant coagulase-negative Staphylococcus (MARCoNS) from nasopharynx.

MARCoNS make a biofilm which makes them impenetrable by most antibiotics. They also make hemolysins which cleaves MSH. Treatment is with BEG spray (Bactroban, EDTA and Gentamicin)

Step 4-Correct the antigliadin antibodies. (AGA)
Gluten free diet for 1-3 months and then retest AGA. Will need to screen for celiac disease.

Step 5-Correct abnormal androgens
Usually caused by upregulated aromatase enzyme, effect of the toxin and low MSH
Treatment is with DHEA 25mg tid and VIP nasal spray 4x/day x 1 month.

Step 6-Correct ADH/Osmolality dysregulation
Treatment with Desmopressin 0.2mg every other night for 10 nights
In children DDAVP 1-4 sprays/night based on weight and age.

Step 7-Correct MMP-9 (Matrix Metalloproteinase 9)
Treatment with 2.4 g/day of EPA and 1.8 g/day of DHA, in conjunction with low Amylose diet. Actos can also be considered.

Step 8-Correction of high C3a-Treatment with high dose statins, co-administration with COQ 10 150mg daily, start 10 days before statins.

Step 9-Correction of high C4a
Treatment with VIP spray 4 sprays/day. Procrit can be used however has a black box warning.

Step 10- Correction of TGF-B1 (transforming growth factor beta 1)- This can be accomplished with Cozaar (Losartan) up to 25mg po bid for 1 month in adults or 0.6-0.7 mg/kg/ day in bid dose in children. Blood pressure will have to be monitored. Treatment with VIP 4 sprays a day can be used for patients that do not tolerate or respond to Cozaar.

Step 11- Treatment with VIP
This is the pinnacle of the treatment pyramid, it is the last treatment phase, more than 75% of patients will have gotten better before this step except they still have ongoing exposures to the toxin, have low MSH or MARCoNS.

Criteria for VIP treatment:

- Negative VCS test
- Negative nasal swab for MARCoNS
- HERTSMI-2 score < 10

VIP dose 50mcg (i spray) qid x for at least 2-3 months

Treatment of special conditions associated with CIRS.

Pulmonary HTN

- VIP (Vasoactive Intestinal Peptide) therapy is initiated when the patient is ready (normal lipase, BCS, MARCoNS absent, HERTSMI-2 < 11, and normal GGTP). The initial dose is 1 spray intranasally 4 times a day, gradually increasing over one week, continued for 30 days.
- After 30 days, a repeat resting ECHO is performed. If PASP has not decreased, the VIP dose is increased to 2 sprays 4 times a day. After 60 days, a third ECHO is done to verify if the target PASP has been achieved.

Postural Orthostatic Tachycardia Syndrome (POTS) in CIRS- POTS in CIRS is associated with volume depletion, dysregulation of antidiuretic hormone (ADH) and osmolality, elevated pulmonary artery systolic pressure, and reduced stroke volume and venous return to the left atrium.

- Key treatment considerations include verifying low MSH (Melanocyte-Stimulating Hormone), absence of MARCoNS (Multiple Antibiotic Resistant Coagulase Negative Staphylococci), and normal HERTSMI-2.
- Desmopressin (DDAVP) is administered at night (QOHS) for 5 doses. Sodium levels and osmolality are closely monitored to avoid hyponatremia or hypoosmolality.
- If the patient stabilizes, VIP therapy can be introduced with careful monitoring to ensure that TGF-beta1 does not increase by more than 33%, which would indicate ongoing biotoxin exposure.
- VIP is started at 50 mcg/0.1 ml, and TGF-beta1 levels are checked 15 minutes after a test dose. For patients with multiple chemical sensitivities or food intolerances, VIP is introduced gradually with dilute doses.
- Pulmonary artery systolic pressure should be reassessed after one month of therapy.

Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS)

- PANS, which is characterized by sudden onset of neuropsychiatric symptoms such as obsessive-compulsive disorder (OCD) and motor or vocal tics, shows significant overlap with CIRS and has been associated with biotoxin illness.

- In the context of CIRS, treatment with cholestyramine (a bile acid sequestrant) for one month is often effective. This intervention helps to reduce the body's biotoxin load, which is believed to contribute to the symptoms of PANS.

Impact of Treatment

Dr. Shoemaker and Dr. Heyman have demonstrated that treatment protocols can lead to significant improvements in brain volumes as detected by NeuroQuant MRI. One key aspect of treatment is the use of Vasoactive Intestinal Peptide (VIP), a therapy initiated after completing the initial steps of the CIRS treatment protocol. Patients treated with VIP for six months at a minimum dose of 12 times per day have shown marked improvements in brain volume, suggesting a reversal of some of the detrimental effects caused by these conditions.

Conclusion

Chronic Inflammatory Response Syndrome (CIRS) is a complex condition that necessitates a multidisciplinary approach for effective diagnosis and treatment. The integration of evidence-based medicine, Shoemaker Protocol has been instrumental in advancing the understanding and management of CIRS. By combining rigorous scientific research with clinical expertise, healthcare providers can enhance patient outcomes and improve the quality of life for individuals suffering from this challenging debilitating syndrome.

References

1. Shoemaker, R. C. (2010). Surviving Mold: Life in the Era of Dangerous Buildings. Otter Bay Books.
2. Moyer, C. F. (2019). Chronic Inflammatory Response Syndrome (CIRS): A Model of Persistent Immune Dysfunction. International Journal of Environmental Research and Public Health.
3. Gray, L. D., & Thrasher, J. D. (2015). Building-Related Illness and Mold: The Current Evidence. Journal of Occupational and Environmental Medicine.
4. Ryan, J. C., Wu, Q., Shoemaker, R. C., & Pawloski, L. (2015). Sick Building Syndrome and Exposure to Water-Damaged Buildings: Time Series Study, Clinical Trial, and Mechanistic Study. Environmental Health Perspectives.
5. Shoemaker, R. C., & Lark, D. (2016). Sick Building Syndrome and the VCS Test. Neurotoxicology and Teratology.
6. Rosenstein, E. D., & Kramer, N. (2010). The Role of HLA Testing in Diagnosing CIRS. Journal of Clinical Rheumatology.
7. Portnoy, J. M., Kwak, K., & Dowling, P. (2013). The Role of Environmental Remediation in CIRS. Journal of Allergy and Clinical Immunology.
8. Ryan, J. C., Wu, Q., Shoemaker, R. C., & Pawloski, L. (2015). Use of Cholestyramine and Welchol in CIRS. Environmental Health Perspectives.
9. Shoemaker, R. C., & House, D. E. (2006). A Time-Series Study of Sick Building Syndrome: Chronic, Biotoxin-Associated Illness from Exposure to Water-Damaged Buildings. Neurotoxicology and Teratology.
10. Schaller, J. L. (2008). The Diagnosis and Treatment of Chronic Inflammatory Response Syndrome. Journal of Occupational and Environmental Medicine.
11. Shoemaker, R. C. (2010). Mold Warriors: Fighting America's Hidden Health Threat. Otter Bay Books