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Identifying & Testing for Chronic Inflammatory Response Syndrome (CIRS) Case Identification

- Does the patient have known biotoxin exposure?
  (tick borne infection, exposure to water damaged building/WDB, spike protein toxicity)
- Has patient failed Visual Contrast Sensitivity *(VCS)* Test, *www.vcstest.com*
- Does patient has 8+/13 positive clusters in Shoemaker ROS protocol

Testing Protocol For CIRS

Lab Test	Purpose/Relevance for CIRS	Typical Lab Values
HLA (Human Leukocyte Antigen)	Genetic susceptibility	
VIP (Vasoactive Intestinal Peptide)	Neuroregulatory & immune function	VIP, 23-63 pg/mL
MSH (Melanocyte Stimulating Hormone)	Neurohormone involved in inflammation	MSH, 35-81 pg/mL
VEGF (Vascular Endothelial Growth Factor)	Blood vessel growth & inflammation	VEGF, 31-86 pg/mL
MMP9 (Matrix Metallopeptidase 9)	Inflammatory processes	MMP-9, <332 ng/mL
TGFB1 (Transforming Growth Factor Beta 1)	Immune system regulation	Plasma TGFβ1, <2380 pg/mL
C3a	Complement system component	C3a 55-486 ng/mL
C4a	Complement system component	C4a <2830 ng/mL
Leptin	Energy regulation & weight	Males: 0.5-13.8ng/mL; Females: 1.1-27.5 ng/mL
ADH (Antidiuretic Hormone)	Water regulation	1-13.3 pg/mL
Osmolality	Fluid balance	280-300mOsm/L
ACTH (Adrenocorticotropic Hormone)	Adrenal gland function	8-77pg/mL
Cortisol	Stress response	4.3-22.4mcg/dL *(morning)*

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HLA DR/DQ Testing *(Human Leukocyte Antigen) $465*

HLA is set of genes on chromosome 6. This test determines if a patient is genetically susceptible to develop CIRS when exposed to specific biotoxins. In a normally functioning immune system, the innate system is first to respond to a toxin. This is a suboptimal response, but it becomes effective when the innate response hands the problem off to the more specialized adaptive immune system. People with CIRS susceptible genetic patterns are unable to pass the baton from the innate to adaptive immune system, leaving the innate response in a chronically upregulated state. This is dysfunctional response results in the over production of inflammatory cytokines and inflammation. This maladaptive response is what ultimately leads to the multi-system, multi-symptom illness known as CIRS.

Vasoactive Intestinal Peptide *(VIP, 23-63 pg/mL) $110*

VIP is a neuroregulatory peptide with anti-inflammatory, vasodilatory, and bronchodilatory effects. In CIRS, VIP levels can be disrupted, contributing to airway hyperreactivity, pulmonary hypertension, and abnormal blood flow. Treatment with VIP has been shown to improve symptoms and normalize other biomarkers in CIRS.

Melanocyte Stimulating Hormone *(MSH, 35-81 pg/mL) $280*

MSH is also a neuroregulatory hormone with powerful anti-inflammatory properties. MSH regulates several functions in the body, including inflammation, hormone production, and protection of mucous membranes. Low levels of MSH are common in CIRS and are associated with increased susceptibility to chronic pain, fatigue, sleep disturbances, temperature instability, muscle pain, gluten intolerance, ADH/osmolality imbalance, leptin resistant weight gain, and cognitive issues.

Vascular Endothelial Growth Factor *(VEGF, 31-86 pg/mL) $200*

VEGF is involved in the formation of new blood vessels (angiogenesis). In CIRS, dysregulation of VEGF can lead to inadequate blood flow and oxygen delivery to tissues, contributing to symptoms like fatigue and cognitive dysfunction. Normalizing VEGF levels is essential for restoring proper blood flow and tissue oxygenation. Low VEGF may be an indicator of capillary hypoperfusion leading to fatigue, brain fog, exercise intolerance. Treatment is necessary for levels <31. CIRS patients can also have extremely high levels of VEGF indicating upregulation of the innate immune system as the body compensates for poor oxygen delivery.

Matrix Metalloproteinase-9 (MMP-9, <332 ng/mL) $245

MMP-9 is an enzyme that breaks down extracellular matrix components, playing a role in inflammation and tissue remodeling. High levels of MMP-9 can lead to increased vascular permeability, including the blood brain barrier. Patients with high MMP9 may have more cognitive symptoms, brain fog, and sensitivity to treatment with binders. High dose omega-3 helps to lower MMP, low amylose diet.

Complement Components C3a and C4a *(C3a 55-486 ng/mL; C4a <2830 ng/mL) $330*
C3a and C4a are part of the complement system, which helps clear pathogens and damaged cells. Elevated levels of C3a and C4a in CIRS suggest an ongoing inflammatory response to biotoxins. Monitoring and managing these levels can help assess the inflammatory status of the patient and the effectiveness of treatment. In CIRS patients, high levels of C4a is more suggestive of mold/endotoxin related illness and high levels of C3a more suggestive of Lyme/tick borne infection related illness.

Leptin *(males: 0.5-13.8ng/mL; females: 1.1-27.5 ng/mL) $35*
Leptin is both a hormone and cytokine produced by adipocytes (fat cells). The elevated levels of CIRS related cytokines block hypothalamic receptors creating leptin resistance. Leptin resistance decreases the body's ability to use fat stores as energy which can lead to dramatic weight gain/inability to lose weight despite caloric restriction/regular physical exercise.

Antidiuretic Hormone (ADH) *(1-13.3 pg/mL) $175*
ADH regulates water retention in the body, affecting hydration and electrolyte balance. CIRS can disrupt ADH function, leading to frequent urination, excessive thirst, and issues with sodium and water balance. Optimal ADH levels are closely tied to osmolality (the concentration of solutes in the blood), and both should be in balance to maintain proper hydration and electrolyte homeostasis.

Osmolality *(280-300mOsm/L) $25*
Patients with CIRS often demonstrate abnormal patterns of ADH/vasopressin and osmolality which underlie the common symptoms seen in POTS (postural orthostatic tachycardia syndrome) or dysautonomia. Relative ADH deficiency is most commonly seen in the setting of mid/high normal osmolality. ADH causes kidneys to retain water, therefore when levels are low, patients will report frequent urination, excessive thirst, and orthostatic lightheadedness. Treatment involves the short term use of desmopressin as outlined above.

High osmo/high ADH is normal. Low osmo/low ADH is normal.

High osmo/low ADH is abnormal. Consider treatment with desmopressin.

Absolute and relative dysregulations may be seen:
-absolute high: ADH > 13 or osmo >300
-absolute low: ADH < 5 or osmo < 275
-relative: ADH < 2.2 with osmo 292-300
-relative: ADH > 4 with osmo 275-278

Adrenocorticotropic Hormone (ACTH) & Cortisol *(ACTH: 8-77pg/mL; AM Cortisol 4.3-22.4mcg/dL)* $55

ACTH stimulates the adrenal glands to release cortisol, a stress hormone that plays a vital role in the body's response to stress, metabolism, and immune response regulation. In CIRS, the ACTH and cortisol levels are important for assessing the functionality of the hypothalamic-pituitary-adrenal *(HPA)* axis. Dysregulation in this axis can contribute to fatigue, poor stress tolerance, and other CIRS symptoms. Optimal ranges for these hormones are typically within standard laboratory reference values, but specific levels should be interpreted in the context of clinical symptoms and other test results.

High: ACTH >45 or Cortisol >21
Low: ACTH < 5 or Cortisol < 4
Relative High: ACTH > 15 with Cortisol > 16
Relative Low: ACTH < 10 with Cortisol < 7

Lipase $15

Testing lipase levels for CIRS *(Chronic Inflammatory Response Syndrome)* may be considered to assess potential involvement of the pancreas in the syndrome. While the primary focus of CIRS diagnosis and management is typically on identifying and addressing biotoxin exposure, systemic inflammation can affect various organs, including the pancreas. Elevated lipase levels could indicate pancreatic involvement, suggesting additional avenues for treatment or management strategies to address organ-specific inflammation and improve overall patient outcomes. Therefore, testing lipase levels can provide valuable information for comprehensive evaluation and personalized management of individuals with CIRS.

Human Transforming Growth Factor Beta 1 *(TGF-β1)* $140

In the diagnosis of Chronic Inflammatory Response Syndrome (CIRS), testing Human Transforming Growth Factor Beta 1 (TGF-β1) levels holds significance due to its pivotal role in immune dysregulation and chronic inflammation. CIRS is characterized by an abnormal immune response to biotoxins, triggering persistent inflammation and diverse systemic symptoms. Elevated TGF-β1 levels have been associated with CIRS, as this cytokine is believed to be centrally involved in the syndrome's pathophysiology. Biotoxin exposure, such as mold, can stimulate an immune cascade leading to heightened TGF-β1 production, perpetuating chronic inflammation and symptomatology. Therefore, assessing TGF-β1 levels aids in diagnostic confirmation, offering insights into the underlying immunological processes driving CIRS. Monitoring TGF-β1 levels over time further facilitates treatment evaluation and personalized management strategies aimed at modulating immune responses and mitigating inflammation in individuals affected by CIRS.

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Cardiolipin Antibodies $45
In the evaluation of Chronic Inflammatory Response Syndrome *(CIRS)*, testing for cardiolipin antibodies can be integral due to their association with autoimmune phenomena often observed in the condition. CIRS is characterized by an aberrant immune response to biotoxins, leading to chronic inflammation and systemic symptoms. Cardiolipin antibodies, particularly IgG and IgM isotypes, are autoantibodies that target cardiolipin, a phospholipid found in cell membranes. Elevated levels of cardiolipin antibodies may indicate an autoimmune component contributing to the pathogenesis of CIRS, potentially exacerbating inflammation and symptom severity. Therefore, testing for cardiolipin antibodies aids in identifying autoimmune involvement in CIRS, guiding appropriate treatment strategies to modulate the immune response and alleviate symptoms for affected individuals.

The Gliadin (Deamidated) Antibody (IgG, IgA) $80
This test is a blood test used to detect antibodies against deamidated gliadin peptides (DGP) in the body. Deamidated gliadin peptides are fragments of gluten, a protein found in wheat and related grains. Elevated levels of these antibodies, particularly IgG and IgA, indicate an immune response to gluten exposure.

A provider may order this test in the context of diagnosing Chronic Inflammatory Response Syndrome (CIRS), which is a condition characterized by an exaggerated immune response to environmental toxins, such as mold. Some individuals with CIRS may have gluten sensitivity or intolerance as part of their overall immune dysregulation. Therefore, testing for gliadin antibodies can help identify gluten sensitivity as a contributing factor to the patient's symptoms and overall health issues.

Additionally, gluten sensitivity can exacerbate inflammation and immune dysregulation in individuals with CIRS, leading to worsened symptoms and delayed recovery. By identifying and addressing gluten sensitivity through testing, healthcare providers can implement dietary interventions and lifestyle modifications to support the patient's overall health and improve treatment outcomes for CIRS.

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CIRS Check List Highlights

- ☐ Known exposure to biotoxin and history consistent with CIRS
- ☐ Initial failed VCS
- ☐ Initial labs through Quest
- ☐ Test for/eliminate exposure
- ☐ Testing the home/work environment if needed *(Envirobiomics.com)*
- ☐ Testing for chronic infections if needed *(Vibrant tick panel 2.0)*
- ☐ Testing for urine mycotoxins if indicated *(Mosaic urine mycotoxins)*
- ☐ Spike dilution testing *(LabCorp)*
- ☐ Consider Neuroquant*, Genie**, EKG, PFTs, Echo
- ☐ Start lipid replacement *(PC, omegas, SPM, +/- wheat germ oil)*
- ☐ Start Synapsin/BPC nasal spray
- ☐ Treat/bind biotoxin
- ☐ Doxy x 30d for Lyme/tick borne infection
- ☐ Treat spike protein illness if indicated
- ☐ Start Welchol on all
- ☐ Test for MARCoNs *(nasal swab)*
- ☐ Treat MARCoNs if present *(EDTA nasal spray)*
- ☐ Monthly VCS testing, continue Welchol until pass VCS
- ☐ Monthly visits *(alternate RX with provider)*
- ☐ Correct hormonal & lab abnormalities
- ☐ Recheck abnormal labs to assess for progress/backtracking
- ☐ Final step is correction of abnormal gene expression with the use of VIP nasal spray

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Chronic Inflammatory Response Syndrome (CIRS)

Understanding & Managing

What is Chronic Inflammatory Response Syndrome (CIRS)?

Chronic Inflammatory Response Syndrome (CIRS) is a complex, multi-system, multi-symptom illness that results from exposure to a biotoxin in genetically susceptible individuals. These biotoxins trigger an abnormal and unregulated inflammatory response driven by overexpression of cytokines produced by the innate immune system. High levels of these circulating biomarkers lead to dysregulation of multiple downstream neuropeptides and hormones resulting in the complicated clinical presentation seen in patients with CIRS.

Key Characteristics

- **Triggered by Biotoxins**
  - Commonly from mold exposure, but also other sources like bacteria, algae, and certain types of fish.
- **Chronic Inflammation**
  - Persistent and excessive innate immune response activation leading to inflammation.
- **Multiple System Impact**
  - Affects various systems including neurological, respiratory, gastrointestinal, and musculoskeletal.

Symptoms of CIRS

Symptoms can vary widely from person to person, but often include:

Fatigue
Weakness
Aches/Muscle cramps
Sharp pain
Headache
Light sensitivity
Red eyes
Blurred vision
Tearing
Sinus problems
Cough
Shortness of breath
Joint pain
Morning stiffness
Memory issues
Difficulty with focus/concentration
Word finding difficulties
Decreased assimilation of new knowledge
Confusion
Disorientation
Skin sensitivity
Mood swings
Sweats (especially night sweats)
Temperature regulation or dysregulation problems
Excessive thirst despite frequent water intake
Static shocks
Numbness
Tingling
Vertigo/Dizziness
Metallic taste
Abdominal pain
Diarrhea
Tremors
Unusual pain
Migraine/facial pain
Appetite swings
Increased urination/nocturia

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Shoemaker Protocol

The Biotoxin Pathway