**Chronic Inflammatory Response Syndrome (CIRS) Treatment Protocol**

I have had the honor and privilege of learning from Dr Ritchie Shoemaker since 2014 when I started learning with him one on one to help heal my son. Dr Shoemaker’s protocol was life saving for my only child with tick borne infections and poor recovery from those inspite of years of treatment. I realized the incredible role that biotoxins and CIRS play in patients with tick borne infections and with Dr Shoemakers guidance was able to help my son and myself recover well. We saw amazing cognitive and physical gains in both of us once the inflammation was brought under control, the biotoxins removed and functional physiological parameters reestablished; quite a life altering experience.

Dr Shoemaker has always encouraged me to help other patients with the immense knowledge gained by mentoring with him and not just limit it to my family. I took that to heart, have continued my learning with Dr Shoemaker, and have helped over a hundred patients of all ages with CIRS. The biggest challenge and the best learning experiences have been with children on the spectrum with underlying CIRS. I am happy to report that 100% of the children responded well to Dr Shoemaker’s protocol and have made significant cognitive, behavioral and social gains.

Every patient I see receives a complete neurological, neuro-sensory and physical exam along with a detailed documentation of clinical history and symptoms. The patients I see are usually comorbid with tick borne infections and it is very important to follow Dr Shoemaker’s diagnostic criteria for CIRS and establish a careful clinical differential diagnosis. CIRS manifests itself in numerous organ systems and the complex pathophysiology of CIRS requires a meticulous, evidence based, step by step approach as highlighted by Dr Shoemaker with strict variable control to be able to quantify and monitor progress objectively.

- Clinical history to look for the CIRS symptom cluster
- CIRS related Labwork popularly known as “The Shoemaker Panel”
- Visual Contrast Sensitivity (VCS) test
- Real Time Labs mycotoxin panel – some patients insist on this one for some reason.
- Mycometrics labs ERMI or HERTSMI panels for home, work, car, school as needed
- MARCoNS : Deep nasal swab culture obtained through microbiology labs
- DNA PCR testing for tick borne infections – most patients request a retest.
Adults

The mainstay of history is Dr. Shoemaker’s standard 37 question symptom survey. In addition, the following are considered as standard practice when evaluating a CIRS patient:

• Presentation
• VCS
• In depth clinical history
• Physical Exam
• Labs
• Initial Treatment
• Follow Up

Adult Clinical Exam

• Pallor
• Marfanoid Body Habitus
• Red Sclerae
• Tremors
• Hyper flexibility
• Shoulder Weakness
• Rashes- Mold facies

Adult care labs

• Ten CIRS Biomarkers
• Genetics: HLA (DRB1, DQ, hi-res DRB3, B4, and B5)
• Anti-Inflammatory Cytokines- VIP, MSH
• Hypothalamic-pituitary-end organ function: ADH/osmolality, ACTH/cortisol
• **Innate Pro-Inflammatory Cytokines**: TGF-B1, MMP-9, C4a (and C3a)

• **Auto Antibodies**: ACLA, AGA

• **Abnormal MM Defenses**: MARCoNS

• **Other CIRS Related Labs**
  
  • Leptin
  
  • VEGF/Erythropoietin
  
  • vWF profile
  
  • CD4+, CD25+ and CD4+CD25+
  
  • ESR
  
  • CRP
  
  • CBC
  
  • Imaging
  
  • MR Spectroscopy
  
  • NeuroQuant
  
  • CPET
  
  • VO2 Max

**Pediatric Approach**

The backbone still remains as Dr Shoemakers 37 question symptom checklist. Additionally, different age groups will require differing amounts of symptoms to reach a threshold of significance. For children,

• < 8 years old
  
  • Threshold= x5 “Yes” Answers
• > 8 years old but <13 years old
• Threshold= x8 “Yes” Answers
• Teens and Adults
• Threshold= x13 “Yes” Answers

Pediatric Labs:

The standard Shoemaker labs drawn on adult patients requires a lot of volume, 22-32 vials. However, small children have smaller blood volume (~80 ml/kg). So, what I’ve learned is its helpful to start with:

• ADH/osmolality
• HLA DRB1, DQ and B3, B4 and B5 (hi res)
• ACTH/ Cortisol
• If 0 tests are abnormal do not pursue
• Is 1 test abnormal use clinical judgement
• If 2-3 tests abnormal do full CIRS work up.

Pediatric treatment points to consider

• Principles of treatment same but dosing of meds is different
• Some medicines used in adults not used in children

Meds not used in pediatric patients:

• Actos (pioglitazone)
• Procrit (erythropoietin)
• VIP nasal spray
The Biotoxin Pathway is a brilliantly conceived tool by Dr Shoemaker and has been invaluable in my practice both for patient education and practitioner training since many of my patients are physicians themselves.

The Six Stages of Biotoxin Illness

CIRS is often looked upon in stages in order to understand it better. The figure below has been designed to understand these 6 stages at a glance.
Dr Shoemaker’s 12 step protocol

Once a diagnosis of CIRS has been established we work with the collaborating physicians to get the patient started on this very complex 12 step protocol. Each patient needs to be closely monitored and progress from one step to the next needs to be objective, quantifiable and the outcome variables carefully assessed. Labwork is rerun at regular intervals to assess progress to monitor progress and to ascertain the next step.
Step 1 Removal from exposure

This is paramount. Most of my patients have been exposed to water damaged building (WDB) at home and / or at work. Many children have been exposed in school, on school buses, at tutoring centers, in therapy, at scout meeting etc. Remediation, 504 plans in school, teaching employers about the difference between a mold allergy and a genetic susceptibility to mycotoxins has been an important part of what we do. The afflicted become “sicker quicker” if re exposed as has been my personal experience as well, due to the fact that their immune system has already been “primed”.

The ERMI stands for the Environmental Relative Moldiness Index and is a quantitative PCR analysis that looks at spore equivalents of 36 species of mold. Dr. Shoemaker’s database of thousands of patients gives us the information that the cutoff for safety is an ERMI score of 2 if the MSH is < 35 and C4a is less than 20,000 and 0 if the C4a is greater than 20,000. He has also developed a derivative of the ERMI score looking at the top 5 virulent species, which he calls HERTSMI-2. This test is also done at Mycometrics and the cutoff for safety is a HERTSMI-2 of 10 for someone previously sickened by a water damaged building.

One huge challenge has been explaining to patients that sampling the air for spores is not an acceptable substitute for many reasons. One of the main limitations is that over 99% of the particles that carry the inflammmagens from water damaged buildings are smaller than 3 microns. Spore traps can only detect particles that are larger than 3 microns and therefore, miss over 99% of the inflammmagens.

Step 2 Cholestyramine (CSM) or Welchol

The intention here is to interrupt enterohepatic recirculation of biotoxins using a bile acid sequestrant either cholestyramine or Welchol for at least a month. The dose of cholestyramine is 4 grams ½ hour before eating 4 times a day. Some patients are unable to tolerate CSM. For them a lesser effective alternative is Welchol 2 tablets three times a day with food. Additonal for those people sensitive to the fillers in cholestyramine ,compounded cholestyramine without fillers is a good alternative. If there is no improvement, the most common cause is persistent exposure to a water damaged building. The success of this step can be monitored by seeing improvements in the VCS (Visual Contrast Sensitivity) Test.
Some patients ask me if calcium bentonite clay, charcoal, chlorella etc have some biotoxin binding activity, however Dr Shoemaker has seen any meaningful effect to reverse lab values in the same way that cholestyramine or Welchol have been observed to.

**Step 3 Eradicating MARCoNS**

One of the first tests we do right in the office at a new evaluation is the **nasal swab test** to look for **MARCoNS**. The figure below explains the mechanism of action of these organisms and the toxins they produce.

A compounded antibiotic spray is used BEG (Bactroban, EDTA, Gentamicin. The EDTA helps break down the biofilm and the two antibiotics eradicate the infection. Dosage is two sprays to each nostril three times each day for one month or more depending on the patient before we retest.

**Step 4 Correct antigliadins**

A strict adherence to a gluten free diet is very important for at least 3-4 months is required. Even after that I find that if reintroduction is requested by the patient hen
organic non GMO version of breads etc is the best approach. Many patients may need to adopt a gluten free lifestyle longterm.

**Step 5 Correct Androgens**

Clinically many patients have low androgen levels due to upregulation of the aromatase enzyme activity. Some patients respond well with HCG shots. Patients are advised to avoid direct testosterone supplementation as in creams etc. DHEA is also important to address and correct with supplementation as needed. Some children have responded well to small doses of HGH (Saizen) when they experience a delay in pubertal growth spurts due to advanced CIRS.

**Step 6 Correct ADH/osmolality**

Patients with CIRS will have out of proportion ADH (antidiuretic hormone) and osmolality levels with the most common pattern being a relative or absolute deficiency of ADH. Physiologically ADH causes the kidney to retain free water and when levels are relatively low, patients experience polydipsia and polyuria. In severe cases, people experience frequent static shocks.

The treatment is to use desmopressin 0.2 mg every other night. A nasal spray version is used for pediatric administration or where smaller increments of dosage is required. Sodium levels must be checked in 5 days then again in 10 days as hyponatremia can sometimes occur which can in turn cause patients to experience poor appetite and nausea.

**Step 7 MMP9 (Matrix Metallo Proteinase -9)**

If MMP 9 is over 332 ng/mL, its treated with a low amylose diet and high dose fish oil (2.4 g of EPA, 1.8 g of DHA). MMP 9 breaks down soft tissue and patients often experience multiple aches, pains, muscle soreness and stiffness. Actos can be used in some patients as well.
Step 8 Correct VEGF (Vascular Endothelial Growth Factor)

VEGF stimulates the growth of new blood vessels in response to Hypoxia Inducible Factor (HIF). In many people with CIRS, VEGF is suppressed to less than 31 pg/mL. The treatment is similar to the previous step.

Step 9 Correct Complement C3a

The levels if high are said to be in response to Borrelia still being a concern and that needs to be treated accordingly. Statins may be used in some patients with persistently high C3a.

Step 10 Correct Complement C4a

Its important that this lab be run at National Jewish Hospital in Denver. The current treatment plan is VIP nasal spray with dosage being 1 spray 4x/day.

Step 11 Correct TGF-B (Human Transforming Growth Factor Beta -1).

If elevated (over 2380 pg/mL), the treatment is losartan up to 25 mg bid. Recently Labcorp reference ranges have changed in a few states and this needs to be noted accordingly.

Step 12 VIP (Vasoactive Intestinal Polypeptide)

After all of the steps and treatments above if the patient is still symptomatic, VIP can be used but only after specific labwork has been completed to verify if VIP is appropriate to use at that time or not. Draw for Lipase and TGF Beta-1, then administer one nasal spritz of VIP. Wait for 15 minutes and then draw blood again for TGF Beta 1. If the levels rise, there is a hidden exposure to mold ongoing.

VIP is dosed at 50 mcg/mL, 1 spray 4 times a day. According to Dr. Shoemaker’s paper published in 2013, administration of VIP will correct C4a, TGF beta, VEGF, MMP-9,
estradiol, testosterone, vitamin D3, and MASP. The patient must have no continued exposure to mold, have a normal VCS and be clear of MARCoNs to ensure that VIP will be effective.

The above protocol has been life altering for patients of all ages in my practice that had been chronically inflamed and ill for many years inspite of being aggressively treated for tick borne infections, PANDAS/PANS and/or Autism spectrum Disorders. Dr. Shoemakers work has given thousands of patients and their families a new lease on life. His contribution to medical care of chronically ill patients shall go down in history as pioneering and groundbreaking research conducted singlehandedly by one visionary physician that has helped alter the lives of thousands for the better.

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