

# Chronic Inflammatory Response Syndrome (CIRS)

CORE TREATMENT	
<b>Stage 1: Remove biotoxin exposure</b>	
<b>Test for presence of mould in home, work, school and remove exposure</b>	
Use Environmental Relative Mouldiness Index (ERMI)	
<b>Bind biotoxins</b>	
Therapeutic ingredient options*: zeolite, charcoal, bentonite clay, modified citrus pectin, chitosan <i>*not available through Metagenics</i>	NA
<b>Eradicate MARCoNS and biofilms if present</b>	
<b>Metagenics Specialised Gut Detox Program</b> AND <i>Antimicrobial Sinus Spray</i>	Refer to Detoxification protocol 2 sprays in each nostril, twice daily
<b>Correct sex hormones</b>	
<i>Tribulus Reproductive Support</i> OR <i>Soy, Methylating Nutrients &amp; BCM-95™ Turmeric to Clear Oestrogen</i>	2 tablets twice daily 1 tablet twice daily
<b>Remove gluten exposure if positive anti-gliadin antibody titer</b>	
<b>Gluten free diet</b>	Minimum of 3 months
<b>Stage 2&amp;3: Address the inflammation and immune dysregulation involved in CIRS pathology</b>	
<b>Reduce Matrix metalloproteinase (MMP-9)</b>	
<i>BCM-95™ Turmeric &amp; Devil's Claw to Treat Chronic Inflammation</i>  <i>Mental and Physical Energy Powder</i>  <b>If MMP-9 &gt;332 ng/mL</b> <i>Low amylose diet - Shake It Practitioner Weight Management Program</i>  <i>High Purity, Low Reflux, Concentrated Fish Oil liquid or capsules</i>	3 capsules twice daily 2 level scoops in water twice daily    6mL daily OR 3 capsules twice daily
<b>Normalise VEGF</b>	
<i>High Purity, Low Reflux, Concentrated Fish Oil liquid or capsules</i>	6mL daily OR 3 capsules twice daily
<b>Reduce TGF-β1 levels</b>	
<i>Alpha Lipoic Acid for Antioxidant Support</i>  <i>Liquid Vitamin D3/Vitamin D3</i>	1 tablet daily 4 capsules or 1mL daily
<b>Increase Vasoactive Intestinal Peptide (VIP)</b>	
<i>Mental and Physical Energy Powder</i>  Fasting and daily exercise – start low and go slow	1 serve twice daily

ADDITIONAL TREATMENT OPTIONS	
<b>Reduce pain and muscle tension</b>	
<i>Meta Mag-Magnesium Bisglycinate, Corydalis and California Poppy for Pain</i>	1 serve twice daily
<b>Improve T-regulatory cells function</b>	
<i>Lactobacillus paracasei LP-33® and Lactobacillus rhamnosus (LGG®) for Immune Control</i>	1 capsule daily
<i>Liquid Vitamin D3/Vitamin D3</i>	1-4 capsules (1000IU-4000IU) daily
<i>High Bioavailability Zinc with Vitamin C</i>	1 serve (1/2 tsp) daily
<i>BCM-95™ Turmeric &amp; Devil's Claw to Treat Chronic Inflammation</i>	3 capsules twice daily
<i>T-Helper Cell Regulation</i>	1 tablet 3 times daily
<b>Improve gut epithelial health and reduce intestinal permeability</b>	
<i>Probiotics for Gut Microbiota Restoration and Support</i> <b>AND</b> <i>Glutamine &amp; Boswellia (BosPure® Boswellia) for Intestinal Integrity</i>	1 capsule twice daily  1 serve twice daily
<b>Address dietary and lifestyle factors</b>	
<p><i>If overweight or obese:</i>  <b>Shake It Practitioner Weight Management Program</b></p> <p><i>If Stress and/or depressed:</i>  <b>See Stress Less Program</b></p>	

Alphabetical Reference of Nutritional Support	
Formula Catch Phrase	Key Benefits
<i>Alpha Lipoic Acid for Antioxidant Support</i>	Alpha-lipoic acid (ALA) is an important intracellular antioxidant for the management and prevention of diabetes and diabetic complications, such as neuropathy, nephropathy and cardiovascular disease. ALA regenerates glutathione and supports mitochondrial energy production, whilst improving insulin sensitivity and heavy metal clearance.
<i>Antimicrobial Sinus Spray</i>	Direct nasal delivery of saline and essential oils helps to provide rapid anti-inflammatory and antimicrobial relief.
<i>BCM-95™ Turmeric &amp; Devil's Claw to Treat Chronic Inflammation</i>	A combination of herbs to provide powerful long-term synergistic anti-inflammatory and analgesic effects by inhibiting RAGE, COX-2 expression, TNF-α and NFκB.
<i>Glutamine &amp; Boswellia (BosPure® Boswellia) for Intestinal Integrity</i>	Glutamine, Boswellia and nutrients blend to manage the unique impact of gut micro-organisms (biofilm) on inflamed intestinal mucosa with prebiotic, antimicrobial and anti-inflammatory activity, all of which help improve gut health, reduce gut permeability.
<i>High Bioavailability Zinc with Vitamin C</i>	A therapeutic level of zinc bisglycinate to support several aspects of immunological function, including the development, function and mediation of immune cells, such as neutrophils, monocytes and natural killer cells. Zinc also affects the development of acquired immunity and T-lymphocyte function.
<i>High Purity, Low Reflux, Concentrated Fish Oil Liquid or Capsules</i>	Omega 3 essential fatty acids are shown to offer systemic protection from inflammation. These are safe in the long term, making them suitable for managing the inflammation of chronic infection.
<i>Lactobacillus paracasei LP-33® and Lactobacillus rhamnosus (LGG®) for Immune Control</i>	Two probiotic strains which help restore immune control and moderate over-active immune responses. These strains assist immune regulation by supporting T-reg cell function and increasing anti-inflammatory cytokines such as IL-10.
<i>Liquid Vitamin D3/Vitamin D3</i>	Vitamin D is essential for T-reg stimulation to regulate the immune response.
<i>Mental and Physical Energy Powder</i>	Magnesium is essential for a healthy brain, supporting brain plasticity, normal vasodilation and healthy cerebral blood flow. It also supports neurotransmitter synthesis, mitochondrial function and energy production system-wide. Animal studies suggest that glycine promotes the “master hormone” vasoactive intestinal peptide (VIP) ALC is neuroprotective, enhancing neuronal metabolism in the mitochondria and counteracting glutamate-mediated neurotoxicity and hypothalamic–pituitary–adrenocortical axis hyperactivity.
<i>Meta Mag-Magnesium Bisglycinate, Corydalis and California Poppy for Pain</i>	A magnesium and herbal formula for acute or chronic pain management. Magnesium has been shown to block glutamate via inhibition of the NMDA receptor, thereby reducing excitatory neurotransmission. Corydalis is an effective analgesic in both inflammatory and neuropathic pain.
<i>Probiotics for gut microbiota restoration and support</i>	Highly researched probiotic strains, <i>Lactobacillus rhamnosus</i> (LGG®), <i>Saccharomyces cerevisiae</i> (boulardii), <i>Bifidobacterium animalis ssp lactis</i> (BB-12®) have demonstrated the ability to disrupt pathogenic bacteria, protect commensal groups and encourage restoration in the event of disruption, enhance gastrointestinal mucosal integrity, and have a beneficial impact on gastrointestinal function.
<i>Soy, Methylating Nutrients &amp; BCM-95™ Turmeric to Clear Oestrogen</i>	A comprehensive herbal nutritional blend to modulate all aspects of oestrogen production, signalling, metabolism and detoxification, to support clearance of excess oestrogen activity in the body, associated with conditions such as fibrocystic breast disease and PMS.
<i>T-Helper Cell Regulation</i>	Astragalus stimulates the activity, and enhances the cytotoxicity, of Natural Killer cells and can promote IL-2 production. It supports immunity by enhancing T-helper activity, thereby moderating immune responses, reducing inflammation, and increasing resistance to infection.
<i>Tribulus Reproductive Support</i>	A herbal combination including tribulus and damiana to support testosterone, dehydroepiandrosterone (DHEA), and dihydrotestosterone for masculine support. Combined with zinc this formula supports reproductive function, including sperm health and libido.

Supportive Lifestyle Programs	
<i>Wellness and Healthy Ageing Program</i>	This program recommends a low glycaemic load diet with lifestyle recommendations for exercise, relaxation, intellectual stimulation and effective stress management – all factors associated with creating a low antigenic and anti-inflammatory environment – a healthy terrain for efficient immunity.
<i>Shake It Practitioner Weight Management Program</i>	There is growing evidence that obesity is a disorder of energy homeostasis, and that the metabolic set-point for overweight individuals is set to a higher level. <b>The Shake It Practitioner Weight Management Program</b> is a novel 3 phase program structure designed to prevent metabolic adaptation, reset the patient's metabolic set point, and provide regular psychological breaks from active dieting to achieve sustained weight loss. The program provides supportive materials in order to implement behavioural change techniques and two diet options: Ketogenic (low carbohydrate, high fat), or Low fat (low fat, liberal carbohydrate). Further information and resources can be found online at <a href="http://www.metagenics.com.au">www.metagenics.com.au</a> or <a href="http://www.metagenics.co.nz">www.metagenics.co.nz</a> and <a href="http://www.shake-it.com.au">www.shake-it.com.au</a>
<i>Stress Less Program</i>	This holistic program systematically addresses the drivers associated with imbalanced mood and stress responses, shown to predispose to neurological dysfunction. <b>The Stress Less Program</b> incorporates dietary and lifestyle advice alongside tailored prescriptions of herbal and nutritional recommendations to restore balance to patients' neurobiology (brain chemistry) to support emotional wellbeing and mental health, and completes a holistic prescription for stress management.

## Definition

Chronic inflammatory response syndrome (CIRS) is a progressive, multisystem, multi-symptom illness caused by an aberrant immune response to certain biotoxins including those produced by some cyanobacteria, dinoflagellates, tick-borne microbes and fungi. The most common source of biotoxin exposure are moulds from water damaged buildings, which is particularly concerning when an estimated 40% of Australian residential buildings constructed in the last 15 years are affected by condensation, leading to mould growth. Further, the 'leaky homes crisis' in New Zealand has affected tens of thousands of buildings constructed between 1993 to 2005 and continues to pose significant health risks as moulds and spores develop in damp, decaying timber framing. The following criteria warrant a CIRS diagnosis:

- History, signs, and symptoms consistent with biotoxin exposure see table 1 below
- A genetic predisposition to biotoxin-related illness based on identification of an HLA susceptible haplotype.
- Abnormalities documented by Visual Contrast Sensitivity (VCS) testing.
- Biomarkers consistent with the neuroimmune, vascular, and endocrine abnormalities that characterise CIRS.

**Table 1 Multi-system presentation of CIRS.<sup>1</sup>**

Organ System	Symptom	% of CIRS Patients Impacted	Organ System	Symptom	% of CIRS Patients Impacted
<b>General</b>	Fatigue	92	<b>GIT</b>	Abdominal pain	31
	Weakness	58		Diarrhoea	31
<b>Multi-factorial; unique</b>	Headache	73	<b>Hypo-thalamic</b>	Night sweats	69
	Skin sensitivity	8		Mood swings	73
				Poor temperature regulation	54
				Appetite swings	69
<b>Musculoskeletal</b>	Aches	92	<b>CNS</b>	Poor memory	85
	Cramps	46		Poor focus/concentration	85
	Unusual pain	54		Confusion	62
	Ice pick pain	65		Decreased assimilation of new knowledge	69
	Lightning bolt pain	19		Decreased word finding ability	65
	Joint pain	77		Disorientation	19
	Morning stiffness	42			
<b>Antidiuretic hormone</b>	Excessive thirst	69	<b>Sinus</b>	Sinus	85
	Frequent urination	62		Cough	69
	Static shocks	50		Shortness of breath	77
<b>Neurologic</b>	Numbness	54	<b>Eye</b>	Light sensitivity	77
	Tingling	62		Red eyes	58
	Metallic taste	38		Blurred vision	54
	Vertigo	46		Tearing	50

#### **Diet and Lifestyle**

- Reduce pro-inflammatory foods in the diet including saturated fats, refined foods, and sugar.
- Promote well-cooked warm foods to facilitate easy digestion, avoid raw foods and cold drinks.
- Emphasise foods high in essential fatty acids such as oily fish and nuts/seeds.
- Eat a minimally processed diet rich in antioxidants, phytonutrients and bioflavonoids.
- Drink plenty of water - a dehydrated body functions less efficiently.
- Counselling may assist the patient in restoring mental clarity, problem solving, and coping with life stresses.
- Acupuncture is effective in reducing the symptoms of fatigue.
- Yoga, Tai Chi or other relaxing activities may also be useful.

Pathology Tests and Point-of-Care Screenings	
TEST	INTERPRETATION GUIDELINES
<b>CIRS &amp; Biotoxins Questionnaire</b>	<ul style="list-style-type: none"> <li>A score of 8 or more of the 13 clusters is considered diagnostic (98.4% sensitivity in adults).</li> <li>A score of 3 out of 3 of in section 2 treatment is recommended (73.3% specificity, 97.7% positive predictive value).</li> </ul>
<b>VCS Visual contrast sensitivity test</b>	Positive or Negative Screens for nerve damage and capillary hypoperfusion, which are associated with CIRS
<b>HLA DR/DQ gene testing</b>	Positive in CIRS - HLA Haplotype Determines Susceptibility to Specific Biotoxin
<b>Secondary testing</b>	
<b>Leptin ng/mL</b>	Male 0.5-138 Female 1.1-27.5
<b>TGF-β1 pg/mL</b>	<2380 pg/mL Increased in CIRS
<b>Vasoactive intestinal polypeptide (VIP) pg/mL</b>	23-63 pg/mL
<b>Melanocyte stimulating hormone (MSH) pg/mL</b>	35-81 pg/mL
<b>Anti-diuretic hormone (ADH) pg/mL</b>	1-13.3 pg/mL
<b>Osmolality mOsmol</b>	280-300 Increased in CIRS
<b>Environmental Relative Mouldiness Index (ERMI)</b>	

Other Considerations	
<b>Anti-gliadin antibodies (AGA)</b>	0-19
<b>MARCoNS swab</b>	N/A Positive in CIRS
<b>VEGF pg/mL</b>	31-86 Decreased in CIRS
<b>ACTH pg/mL</b>	8-37
<b>Cortisol µg/dL</b>	am 4.3-22.4 pm 3.1-16.7
<b>MMP-9 ng/mL</b>	9.5-80.2 Increased in CIRS
<b>C4a ng/mL</b>	20-2830 Increased in CIRS
<b>C3a ng/mL</b>	20-940 Increased in CIRS

<sup>1</sup> Shoemaker RC, House DE. Sick building syndrome (SBS) and exposure to water-damaged buildings: time series study, clinical trial and mechanisms. Neurotoxicol Teratol. 2006 Sep-Oct;28(5):573-88.