

SURVIVING MOLD DOWN UNDER

A Guide to Implementing Dr Shoemaker's
14 Step Mold Eradication Process in Australia

Dr Sandeep Gupta MBBS MA FRACGP FACNEM

The term Chronic Inflammatory Response Syndrome (CIRS) was coined by Dr Ritchie Shoemaker, a general practitioner in Maryland, USA, who describes a syndrome triggered by exposure to biotoxins, whether the source be mold from water damaged buildings, tick-borne infections such as *Borrelia* or *Babesia*, dinoflagellates such as *Pfiesteria* or *Ciguatera*, blue-green algae such as cyanobacteria and brown recluse spider bites. In susceptible hosts, exposure to biotoxins triggers a chain reaction of events that causes a predictable multisystem array symptoms and signs. The 14 step process for overcoming Chronic Inflammatory Response Syndrome (CIRS) is a precise and systematic methodology for overcoming the various disturbances to systemic physiology that occur in this condition.

In Australia, similarly to other parts of the world, chronic inflammatory illness is extremely common. This includes rheumatological conditions such as systemic lupus erythematosus and rheumatoid arthritis and collagen vascular diseases such as scleroderma, and Wegener's granulomatosis. Inflammatory bowel disease, which includes Crohn's disease and ulcerative colitis, is also on the rise. Many studies have also recognised that inflammation is an important player in chronic conditions such as cancer, ischaemic heart disease, obesity, depression and type 2 diabetes.

CIRS is a "new kid on the block" in terms of chronic inflammatory conditions. The condition is well established however in the medical literature. Notable are the similarities between the molecular mechanisms of CIRS and the condition known as Systemic Inflammatory Response Syndrome (SIRS), an acute syndrome associated with sepsis, pulmonary embolism and other life-threatening conditions. SIRS is a condition usually treated in a hospital Intensive Care Unit (ICU) setting.

Through Dr Shoemaker's work we can see that the evidence for an association between environmental exposure to biotoxins and inflammatory sequelae is well documented and predictable in individuals with certain genetic patterns whose physiology has been primed by a previous cytokine storm of some sort. This provides major hope for persons suffering from multisystem illness that does not fall into the major diagnostic categories of modern medicine.

For those practising the new science of functional medicine, complex multisystem disease is the rule rather than the exception. Searching for a common thread is a major aim in these patients. CIRS offers a new way of looking for an answer to these multisystem ill patients.

When a patient applies to visit the author's practice, they fill out an extensive questionnaire which includes a timeline of symptoms, past medical history, medications and supplements, family history and a questionnaire for symptoms of Chronic Inflammatory Response Syndrome, as well as a Visual Contrast Sensitivity (VCS) test online via www.survivingmold.com.

In CIRS, there are specific symptoms, which are often systemic. Generally the symptoms include at least 4-6 different bodily systems in a patient with Chronic Inflammatory Response Syndrome (CIRS).

When the patient reaches the author's practice room, the questionnaire is used as a basis for an even more comprehensive patient history. It finishes with a "Systems Review" which is a precise scan of other symptoms that may have been missed in the initial history. Use of questionnaires without medical history appears to be an unreliable form of data collection.

The process then leads to a thorough physical examination looking for disturbances of various bodily organ systems, such as the cardiovascular, gastrointestinal and respiratory systems of the body. As a physician trained in functional medicine, the author has learned that early stage problems may sometimes simply manifest in signs such as generalised mild abdominal tenderness, in dry skin and mucous membranes, in white spots or longitudinal ridges on the nails. These signs are recorded in the patient chart, in addition to their vital signs such as blood pressure, temperature, pulse, height and weight. These examination signs are followed in subsequent consultations to confirm improvement or lack thereof of the patient's disease entity.

Finally a differential diagnosis is formed and the major in-clinic testing is performed, which includes a urine dipstick and a handheld version of the Visual Contrast Sensitivity (VCS) test. Laboratory tests sent off to confirm or refute Chronic Inflammatory Response Syndrome (CIRS) or other possible differential diagnoses, and causative symptoms.

The accuracy of the VCS test deserves further discussion at this point. Overall the test appears to have a high sensitivity and specificity and a low cost; the key criteria for a useful diagnostic test. False negatives appear to occur in only around 8% of cases. The sensitivity is therefore 92%. False negatives (or “pass” results in those with CIRS) may be in those with extra keen vision, such as in artists or baseball players. False positives are relatively rare as well, with a false negative rate of around 21.5%. The peer reviewed literature tells us that exposure to solvents, hydrocarbons and petrochemicals may also produce a “Fail” result on the VCS test, in addition to biotoxins.

Pathology lab testing includes testing for the DQ/DR haplotypes. This is relatively easy to perform in Australia by requesting “Coeliac DQ/DR gene studies” through a Sonic Healthcare Group pathology laboratory. Other laboratories appear to report Coeliac Gene studies in a different format through which the exact haplotype cannot be so readily inferred.

It should be noted that roughly 24% of the population are susceptible to CIRS due to mold exposure, and 21% to Lyme inflammatory responses. “Dreaded” gene types such as 4-3-53 and 11-3-52B number only 3 to 3.5% of the population. The 11-3-52B (and 12-3-52B) haplotypes may be suggested in patients who are unusually tall and have hypermobile joints. A simple, but not diagnostic, test for this in the practice room is to ascertain whether the patient can flex their fingers past the proximal wrist crease.

It is notable that those with a “dreaded” or multi-susceptible haplotype often require more steps of the Surviving Mold protocol and find it more difficult to achieve remission than other haplotypes.

95% of patients with CIRS have a specific sensitive haplotype, however it should be noted that 5% of patients with this disorder may not have a known biotoxin sensitive haplotype. The outcome of these patients is likely to be more favourable in patients without a known genetic susceptibility.

Testing for the various markers of inflammation and hormonal disturbance in CIRS is performed. Currently this testing is not available under Medicare in Australia, although some individual tests (including ACTH, cortisol, DHEA, testosterone, antiigliadin antibodies and osmolality) are available under Medicare.

Currently the only available laboratory providing the remainder of tests is Nutripath in Melbourne. At the time of writing reproducibility issues in comparison to the Dr Shoemaker-approved testing methods are being addressed. It is hoped that favourable reproducibility will be achieved by mid September 2014. There is considerable expense associated with this testing, however it is a mandatory part of the 12 step protocol, including repeat testing after the respective steps are completed.

To differentiate as to whether mold exposure or Lyme disease may be the main contributory factor in multisusceptible patients, a NeuroQuant brain MRI should be performed and electronically uploaded to Cortechs Laboratory in California for processing. Currently Pacific Radiology in Maroochydore QLD is the only laboratory sending NeuroQuant MRIs to Cortechs Laboratory. St Vincent's Hospital in Sydney is also performing NeuroQuant, however at the time of writing, their interpretation was not being performed by Cortechs. Elevated C3a levels may also tend to favour the diagnosis of Lyme disease rather than CIRS.

Treatment is generally offered if a patient meets the case definition for CIRS. At this stage the patient is enrolled into the 12 step process for elimination of CIRS which will be the subject of the remainder of this essay.

The CIRS 12 Step Process

1. REMOVAL FROM EXPOSURE

This is a key step and clearly differs according to the cause of exposure. While avoiding further external exposure in the case of tick-borne disease or dinoflagellate poisoning may be relatively straightforward, in the case of water-damaged buildings, it may not be anywhere near as straightforward.

In the case of a patient suffering from CIRS, the water-damaged building they may be exposed to may be in the home, work or school environment. Each may need to be tested. The recommended laboratory is Mycometrics LLC in New Jersey, USA, and in the case of a home environment a dust sample from both the bedroom and living room is suggested. The full Environmental Relative Mold Index (ERMI) test costs around US\$285, while the HERSTMI-2 test (which tests for a smaller number of pathogenic mold) is approximately US\$150 and usually recommended for follow-up after remediation of a water-damaged building. Request forms (known as the

'Chain of Custody' form) can be downloaded from the "Downloads" section of www.mycometrics.com.

Details of any visible mold must be elicited. If there is visible mold, Dr Shoemaker recommends immediately seeking professional advice on options for remediation if the problem is structural or a result of water damage and removal of any mold-contaminated furnishings or belongings, checking ERMI scores only after remediation has been completed.

The ERMI score, as performed by Mycometrics and many other laboratories, is calculated as the sum of the logs of group I molds (known to be associated with water-damaged buildings in humans) from which the sum of the logs of group II molds (known to be not associated with water-damaged buildings in humans) is subtracted. The result varies from between -10 and +20. The closer it is to the +20, the more severe the mold infestation of that building.

If the home, school or work environment has an ERMI score towards the upper end of this scale, then continued exposure is incompatible with healing. Remediation work, although not cheap, may be the only alternative to moving. The distribution of various mold species on the ERMI test may be helpful in guiding remediation attempts. Killing mold spores alone is generally considered inadequate, as their toxins, fragments and spores must also be removed.

The Dr Shoemaker recommended remediation company in Australia is Mycotox in Newcastle which can be contacted via www.mycotox.com.au or on 1300 046 442.

2. REMOVAL OF BIOTOXINS

This is another key step of the biotoxin pathway and probably the most self-evident. The key to diagnosing and monitoring the presence of biotoxins in the system is the Visual Contrast Sensitivity (VCS test). The online version of this test is online at www.survivingmold.com and a handheld version is recommended and can be purchased at www.survivingmold.com/store1.php/vcs-aptitude-handheld-kit.

The key medication for this step is called cholestyramine (CSM). It is available under the PBS as Questran Lite, a formulation which includes aspartame. Many patients react adversely to aspartame, a compound which has been referred to as a brain "excitotoxin" by neurosurgeon Dr Russell Blaylock. A preparation free of aspartame, can be procured from a compounding pharmacy, such as Your Solution Compounding Pharmacy in Brisbane.

The pharmacological action of cholestyramine is due to its ability to bind cholesterol, bile acids and salts. The positively charged nature of its ammonia side-chains allow negatively charged biotoxins to bind to the cholestyramine molecule and safely exit the body via the faeces. This prevents the enterohepatic circulation of biotoxins which generally allows the amount of biotoxin to stay constant in the body following exposure in a sensitive individual.

The usual alternative to cholestyramine, Welchol, is not available commercially in Australia at this time. Natural compounds such as calcium bentonite, charcoal, chitosan, chlorella and the like possess some biotoxin binding activity, however Dr Shoemaker has not experienced them to meaningfully reverse lab values in the same way that cholestyramine or Welchol have been observed to. Use of these alternatives is not recommended unless cholestyramine is not tolerated at all. The usual dosage of compounded (or commercial) cholestyramine is 4g QID, however this can be reduced to 60mg/kg TID in those younger than 18 or weighing less than 60kg. Cholestyramine can cause undesirable side-effects such as gastro-esophageal reflux, constipation and/or bloating. The dosage may have to be lowered if these symptoms are debilitating.

Generally repeat VCS testing is recommended at the one month mark, then at monthly intervals. Improvement is generally heralded by an improvement of at least two extra marks becoming correct in at least one row.

In Lyme Disease patients, a special situation exists in that many of these patients experience an “intensification reaction” characterised by a worsening of symptoms apparently due to a worsening of inflammation due to an apparent increase in the passage of biotoxins in the blood, a drop in the VCS result and a simultaneous increase in MMP-9.

This intensification reaction can be prevented by pre-treating for five days with a low amylose diet along with omega 3 oil at a dosage of 2.4g EPA plus 1.8g DHA (which can be achieved via the Metagenics product OmegaCare for Kids at 3 tsp daily), or Actos at a dosage of 45mg daily. Either treatment needs to be accompanied by a no-amylose diet, which is a diet in which the polysaccharide amylose (a major component of starch) is excluded. Actos is available in Australia but Medicare subsidy is limited to type 2 diabetics in certain circumstances, so cost may be a limiting factor. A ten day run of high dose omega 3 or Actos is all that is needed (with CSM started on day 6 of 10). Actos should be avoided in those with risk factors for bladder cancer or with a low leptin. Omega 3 oil is the preferred agent in most patients.

3. ERADICATION OF MARCONS

MARCoNS is an acronym for Multi-Antibiotic Resistant Coagulase-Negative Staphylococci. These bacteria colonise the nasopharynx and sinuses and grow in biofilm, which are polysaccharide coatings which protect these bacteria from the immune system. They occur in 80% of MSH deficient patients, but <1% in patients with a normal MSH value. These bacteria are resistant to at least 2 classes of antibiotics. MARCoNS bacteria create hemolysins which elevate cytokine levels and exotoxins A & B which cleave MSH.

MARCoNS bacteria can be tested for with an API-Staph nasal swab. The test must be collected from the posterior nasopharynx. The swab must be inserted almost horizontally and 7.5 to 10cm deep and kept in place for 3-5 seconds. Twisting the swab stick around is recommended to obtain a sufficient sample. It is recommended to obtain the specific swab collection kits from Diagnostic Laboratory Medicine and send specimens to them via Express Post International at 14 Crosby Drive, Bedford MA 01730, United States. A request for a MARCoNS nasal swab can simply be provided to the laboratory on a practice letterhead.

If positive the treatment for MARCoNS colonisation is what is known as the BEG nasal spray, which contains Bactroban a strong-anti staph antibiotic, EDTA to overcome biofilm, and Gentamicin, an even stronger antibiotic.

Re-check nasal swab after one month of treatment to confirm eradication.

4. ELIMINATION OF ANTI-GLIADIN ANTIBODIES

Part of CIRS in many patients is a T cell dysregulation which occurs in response to a deficient MSH response. This T cell regulation can affect tight junctions in the gastrointestinal tract leading to increased intestinal permeability which has been colloquially referred to as "leaky gut syndrome". This can lead to IgG and IgA antibodies being produced to the gluten molecule, due to triggering of the already hypersensitive immune system by the gluten molecule.

If gliadin IgG and IgA antibodies are positive, the patient should be referred for transglutaminase antibodies. If these are also positive, they should be referred to a

gastroenterologist for an endoscopy and multiple duodenal biopsies to exclude Coeliac disease. Presence of this condition means lifelong exclusion of gluten. Note that the patient needs to continue consuming a significant amount (eg 4 slices of wheat bread per day for 4 weeks) of gluten immediately prior to this testing being performed for the test to have a sufficient sensitivity. Moreover multiple (3 or more) biopsies need to be collected.

If specific tests for Coeliac Disease (TTG antibodies and duodenal biopsies) are negative then the person needs to trial a gluten-free diet for three months, after which time the gliadin antibodies are rechecked. If negative, the patient can be re-trialled on gluten, however if gliadin antibodies reappear, or symptoms reappear, the patient will need to remain on a gluten-free diet indefinitely. It may be beneficial for such patients to join Coeliac Australia under the umbrella of “Non-coeliac gluten intolerance”. This society provides many resources for one to remain gluten free.

5. CORRECTION OF ANDROGENS

Another sequela of CIRS is low VIP, and as a result of low VIP, the aromatase enzyme which converts testosterone to estrogen can become elevated. As a result low levels of testosterone with high levels of estrone and estradiol can ensue. This syndrome has been termed “Estrogen Dominance” by the functional medicine community.

The androgen precursor DHEA can help to upregulate testosterone levels in the serum and DHEA levels should be checked in addition to estradiol and testosterone levels. 25mg TDS of DHEA is a reasonable dosage. DHEA can be sourced from compounding pharmacies in each major city, however is not available as a PBS-subsidised medication in Australia at this stage.

Estradiol levels should be monitored to ensure these are not rising. If so, VIP nasal spray may also be used to stabilise the aromatase enzyme induction that is occurring.

6. CORRECTION OF OSMOLALITY

ADH (also known as vasopressin) is a posterior pituitary hormone which is produced in response to stimulation by osmoreceptors in the hypothalamus in response to changes in serum osmolality. 60% of biotoxin patients appear to have dysregulated ADH/osmolality. After carrying out the first five steps of the biotoxin

pathway, many patients' ADH levels will normalise. However there are some patients with persistent abnormalities of ADH/osmolality.

A low ADH tends to result in a dehydration of the system due to a relative diuresis and reabsorption of sodium. This can result in thirst and regular urination. Some salt may also be released onto their skin, resulting in static electric shocks.

ADH levels should be checked via Nutripath and if low and the serum osmolality is high (serum sodium may also be relatively high), then Minirin (Desmopressin) should be utilised. Minirin 200mcg tablets are available in Australia under PBS authority for "Cranial Diabetes Insipidus" which some patients may meet criteria for.

200mcg of Minirin is administered every other night for a total of 10 days. Side-effects such as weight gain are monitored for. Sodium levels and osmolality should be monitored before the end of the 10 days. If symptoms still persist and labs are normal the 200mg Minirin may be used every day for 10 days. Minirin nasal spray has been successfully utilised by Dr Scott McMahon, the first Dr Shoemaker-certified physician, for paediatric patients.

7. CORRECTION OF ELEVATED MMP-9

MMP-9 is one of the first cytokines released in response to biotoxins in the white blood cells, which leads to certain inflammatory molecules entering the brain, nerves, muscles, lungs and joints. It may have a relationship with atherosclerosis, as it is hypothesised that its binding with PAI-1 to Lipoprotein A allows oxidised LDL cholesterol to enter the subintimal space.

Correction of elevated MMP-9 is similar to prevention of intensification reactions to CSM as detailed above. It involves administration of 2.4g EPA and 1.8g DHA in the form of omega 3 fish oil for 30 days in conjunction with a no amylose diet as detailed above. Blood tests for MMP-9 should be repeated after the 30 day period. Actos at 45mg daily may be used if the fish oil is not successful in reducing MMP-9 levels however it should be explained to patients that long-term usage is associated with higher levels of bladder cancer.

According to Dr Dietrich Klinghardt, MMP-9 levels should always be checked before supplementing with high-dose zinc. If MMP-9 is elevated, zinc supplementation can worsen this elevation.

8. CORRECTION OF LOW VEGF

Vascular Endothelial Growth Factor (VEGF) is a vital molecule which promotes angiogenesis and therefore blood flow in the body. VEGF levels are reduced in CIRS and often lead to capillary hypoperfusion, reducing oxygenation to the tissues.

VEGF levels also often correct with the above-mentioned combination therapy of a “no amylose diet” plus high dose fish oil. Again if this is not successful, through monitoring of repeat pathology testing, then Actos at 45mg daily for 30 days (also in combination with the low amylose diet) can be trialled.

9. CORRECTION OF ELEVATED C3A

C3a is often elevated in early Lyme Disease and is a product of split complement. It can lead to physiological effects including smooth muscle constriction, capillary hypoperfusion and increased vascular permeability. Dr Shoemaker recommends use of high-dose statin therapy to treat elevated c3a. High dose statins have been shown to markedly lower inflammation, including reduced T cell activation, macrophage infiltration and vascular wall inflammation.

Patients should be predosed with coQ10 at 150mg daily for 10 days then continued while the patient is on the statin, to prevent complications. Bioceuticals have a suitable product “CoQ10 Excel”. Lovastatin, the usual agent used by Dr Shoemaker, is not available commercially in Australia. Atorvastatin (Lipitor) 80mg daily or Rosuvastatin (Crestor) 40mg daily should therefore be used with monitoring of renal and hepatic function with regular pathology testing.

10. CORRECTION OF ELEVATED C4A

C4a is another split complement product and more commonly elevated than C3a in biotoxin illness. It causes capillary hypoperfusion and cellular hypoxia. An important sequela of raised C4a is defects in cognitive executive functioning, such as memory concentration, memory and word finding difficulties.

MRI brain spectroscopy in patients with elevated c4a levels will often show an elevated lactate in the frontal lobes and hippocampus and a reduced glutamate to glutamine ratio. These changes are pathognomonic of the cognitive impairment which occurs in CIRS.

Low dose synthetic erythropoietin (marketed as “Eprex” in Australia) can be used in an off-label manner if abnormal signs are seen on MRI brain spectroscopy. Patients must not have any of the contraindications which are noted in the MIMS product

information, which includes uncontrolled hypertension . Then are treated with Eprex 8,000units subcutaneously twice weekly for five doses. FBC and iron studies are checked before each dosage and c4a, D-dimer and blood pressure are also monitored. A consent form should ideally be signed before the patient is started on Eprex as it is a powerful agent.

After the five doses of erythropoietin, the MRI spectroscopy is checked for normalisation of the glutamine/glutamate ratio, lactate levels. Executive cognitive functions should have improved.

11. CORRECTION OF ELEVATED TGF BETA-1

TGF beta-1 is quite a destructive cytokine when in excess, as in many cases of CIRS. TGF beta-1 can contribute to gastrointestinal dysfunction. It has been shown to cause fibrosis of lung tissue in susceptible hosts. It also can contribute to severe neurological problems such as atypical seizures, tremor and Parkinson-like symptoms.

Another sequela of high TGF beta-1 levels is that CD4+ and CD25+ cells are plasticised to become more effective. This plasticisation results in release of pathogenic effector T cells, which then start a vicious cycle by producing even more TGF beta-1.

When CD4+CD25++ T regulatory cells are low as well as TGF beta-1 levels being high, there are two management options. The first is using the angiotension II blocker Losartan (marked at "Cozavan" in Australia) at 25mg daily and increase this to 25mg BD if tolerated well. In patients with low blood pressure, they may be started at very low dosages, such as a ¼ tablet daily. If they are not able to tolerate this, then VIP nasal spray will be their only option. However they must meet the criteria to use VIP, as documented below.

12. CORRECTION OF VIP

Correction of VIP is the top step of the ladder of the biotoxin pathway. Many patients will be much improved, if not totally improved by the time they reach this apex of the biotoxin pathway. VIP deficiency has a wide array of pathogenic effects, including upregulating pulmonary artery pressure, dysregulating vitamin D metabolism in the body, and upregulating the aromatase enzyme in the body.

Correcting VIP is dependent on the patient meeting these eligibility criteria, which if not met, is unlikely to result in a successful response to VIP administration:

- VCS must be normalised
- No exposure to buildings with ERMI > 2
- Recent negative MarCONS swab
- Normal lipase levels

If these criteria are met, VIP spray is started at 50mcg QID for 30 days. Pathology tests, including a serum lipase, should be done during and after completion of therapy. Elevated lipase is generally the only reason to date that patients have had to cease VIP nasal spray.

VIP nasal spray is currently not available in Australia and needs to be imported with a TGA exception form from Hopkinton Pharmacy, 52 Main Street Hopkinton, MA 01748, United States. It is hoped that compounding pharmacies in Australia may be able to offer this medication before long.

13. TREAT CAPILLARY HYPOPERFUSION

Capillary hypoperfusion is an important problem of its own in CIRS, and can be due to decreased VEGF levels, reduced VIP levels and the reduced anaerobic threshold that occurs as a result. Once VEGF and VIP levels have been normalised as per previous steps of the biotoxin pathway, a graduated exercise program can be introduced, which remains within the patient's anaerobic threshold.

The cardiopulmonary anaerobic threshold can be approximated through the VO₂max on a cardiopulmonary stress test. An exercise regime can be designed based on this read with the following elements:

- Start with cardio exercises for 5 min daily working up to 15 min daily
- Then add floor exercises 5 min daily working up to 15 min daily
- Then add free weights 5 min daily working up to 15 min daily
- After one month of this, go back to each exercise and increase intensity

14. FOLLOW-UP

Ideally following the preceding steps, the patient's VCS should have normalised, or near normal VCS. Pathology results should have returned to near normal. These should stay normal after all biotoxin medications have been ceased and the patient is in a safe building.

An annual VCS is a good follow-up measure to ensure reactivation or relapse of CIRS has not taken place.

The preceding steps are vigorous and the testing not without considerable cost, however this 14-step protocol for CIRS offers hope for a normal life in affected patients, whose life may be severely compromised due to the resultant health problems.