Dr. Shoemaker's 11 Step Treatment Protocol
2/22/2013

When an ill patient enters my office for the first time, my staff and I follow an extensive, systematic approach toward determining the cause of illness. Ideally, old records have been received and already reviewed. A Visual Contrast Sensitivity (VCS) test is performed. I sit with the patient and go through a 37 question standardized checklist of symptoms. This is not just a "yes or no" experience because patients and physicians often use different vocabulary. I learned long ago that what a new mom means by "difficulty breathing", "diarrhea" or "constipation" might be very different than the technical definitions I learned during training. Once I feel sure a patient does or does not have a symptom, I mark the appropriate "yes" or "no" space. I follow how the multiple symptoms fall into at least four systems (and usually six to nine systems in all but the youngest patients). Upon completing the inventory, the interview continues. I ask about sleep disturbances, menstrual problems as appropriate, bleeding history and any other symptoms the patient might be experiencing. A thorough past medical history is taken which includes other diseases previously diagnosed, medicines, herbals and supplements being taken, allergies, surgeries and major traumas, family history, review of systems and an extensive environmental history. A developmental history is also taken on younger children with queries into school performance for older kids. A work history is also reviewed. All during this process, a differential diagnosis is being compiled and refined. The underlying question in my mind is this: are all these symptoms, crossing all these systems, the result of a single illness or multiple maladies?

Next, a nine system head to toe physical exam looking for evidence of potentially confounding illness is performed. This also looks for findings found frequently in patients with Chronic Inflammatory Response Syndrome (CIRS). Common findings amongst CIRS patients include tremor, cool hands and/or feet, discolored hands and/or feet, pallor and unilateral weakness in the shoulder anti-gravity muscles. The latter is found in roughly 85% of my patients. Curiously, almost all right handed patients with weakness are weaker in the dominant arm whereas weaker lefties split between arms evenly. Also interesting is the fatigability factor. I usually press down on the hands or distal forearms of the extended arms, checking for strength. Then I have the patient squeeze my fingers (checking grip strength) and shrug their shoulders against resistance. Then I recheck the arms in the extended position and usually will find the weaker arm

even weaker than before. If I check a third time, I can usually push the weaker arm down with two fingers. Once the database is complete, a decision is made as to the most likely diagnosis using the differential diagnosis process. Labs are typically ordered which are intended to confirm or disprove the diagnosis of CIRS as well as possible confounding illnesses. The results of my findings are discussed at great length with the patient. A conference is arranged for roughly a month later to discuss the results of the labs.

When the combination of history, physical exam and VCS testing point overwhelmingly toward CIRS, treatment is offered immediately. In cases which are less clear, I will wait until the labs confirm the diagnosis of CIRS or point in another direction.

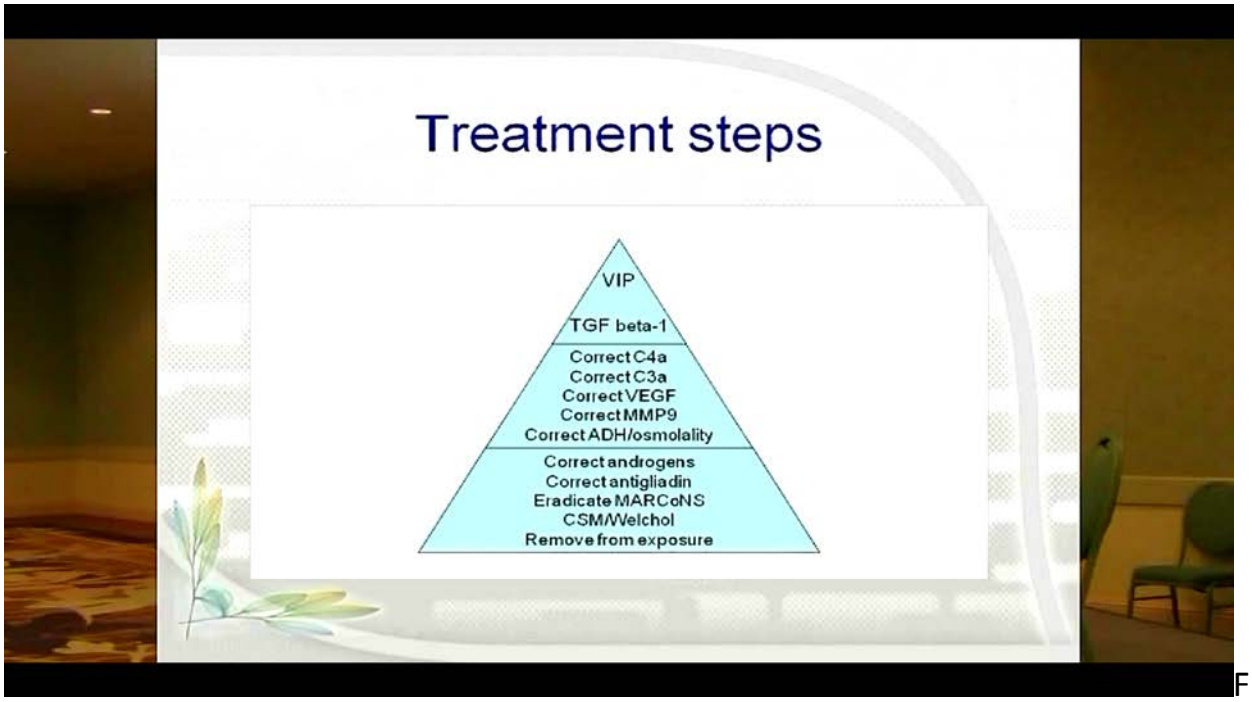

Figure 1

The treatment of choice for CIRS is Dr. Ritchie Shoemaker's 11 Step Biotoxin Removal Protocol (see figure 1). While there are many practitioners, each with their own "proprietary" treatment plan, caring for these patients, only Dr. Shoemaker has performed prospective trials and published his protocol in peer reviewed journals. He is THE pioneer in this field, he created the science AND the treatments. Most every breakthrough in our understanding of CIRS and the care of patients has come through him. Further, I have been to his office, seen how he collects data, seen how he makes clinical decisions and seen how he conducts his

research. He is methodical, meticulous, contemplative and systematic in his approach toward everything. Only one step at a time, one change at a time, then re-evaluate. Evidence Based Medicine defines his approach. Finally, my own data, collected since 2010, shows similar results to his.

The treatment protocol is simple to understand, yet strict adherence is required in the treatment sequence. Variations have been attempted and substitutions have been tried. It is critically important to follow the pathway to health in the order it is prescribed.

The first and most important step is removal from exposure. Effort via history must be made to determine the source of the toxin, be it from a Borrelia spirochete, from dinoflagellate food poisoning or from exposure to the interior of water-damaged buildings (WDB). My local patients almost exclusively suffer from the latter, whereas the disease of more distant patients could be triggered by any of these toxins or even in combination. Once identification of the source(s) of exposure is completed, every effort must be made to remove the potential of continued or future exposure.

Most CIRS patients count WDB as their source of exposure. Removal from exposure, for some, will mean remediating their home. For others, moving to a new home is a more realistic option. Some employers will alter the workspaces they offer, but often, ill workers will have to change job locations. Some school boards take this illness and remediation of their WDB seriously while others stick their heads in the sand and continue to expose teachers, staff and children. Some kids will need to relocate or even home school.

Toxin avoidance goes beyond merely addressing home, school and work. The Environmental Protection Agency and the National Institute for Occupational Safety and Health suggest that 50% of U.S. structures are WDB. Small, brief exposures may not trigger symptoms immediately, early in disease, but as one approaches the “sicker quicker” phenomenon, very brief exposures (measured in minutes) can lead to a profound worsening or re-activation of illness for days. Some patients are uniquely sensitive and can identify a WDB immediately. Some get headaches, others stomach problems and some “just don’t feel right”. Regardless of the symptoms, their bodies are telling them to avoid that building. I encourage my patients to listen to those warnings.

In lieu of some measure to minimize disease re-activation, avoidance of WDB is a lifelong strategy. Though I counsel every patient on this, I have seen many relapses in patients who had become asymptomatic (or symptoms = controls) because they failed to be diligent regarding re-exposures.

I offer to patients this crude analogy. I tell them that their body is like a bathtub with water in it. The water represents the toxins in their body. The goal is to drain the water from the tub (remove the toxins). We accomplish this in Step 2. However, failing to eliminate exposures to toxins would be similar to turning the faucet on while draining the tub. It is very hard, if not impossible, to drain a tub while water is still being added!

Some might argue that draining the tub of large amounts of the water will be effective enough if the refilling is small. After all, there is a relatively smaller amount of toxin present. This approach assumes a dose response relationship between toxin and physiologic problems. While this may be true of toxins/poisons that are ingested and have direct effects on tissues and organs, this is not true when the biological and physiologic responses are mediated through immune system cascades. Indeed, the immune system is designed in several ways for rapid response to foreign antigens with even their first presentation. Even more defenses are activated for immediate response with the second and subsequent exposures. There is no safe level of toxin exposure for those who are genetically predisposed and for those, without predisposition, who suffer from CIRS anyway.

The 2nd step in the pathway is focused on toxin elimination from the patient's body. Those genetically predisposed do not recognize the offending toxins as foreign. Without this recognition, the antigen presentation system is never activated against these particles. There becomes no effective way for the body to rid itself of the toxins. That is where the protocol steps in.

Cholestyramine (CSM) is an anion binding resin which has a quaternary ammonium side chain which creates a localized, net positive charge. The ammonium is of the right size and charge to bind with high affinity to the toxic ionophores which cause CIRS. It is the drug of choice to begin therapy since it contains roughly 5 times as many electrically active sites as does the second choice, Welchol (colesevelam). CSM is often difficult to use and is dosed 4 x a day but it works well to remove toxins from a body. Adults use 1 scoop (4 grams) QID, persons over 60 pounds but < 120 pounds use 1 scoop TID. Young children use 60 mg/kg for each dose TID. Treatment durations vary and are continued until VCS normalizes. Older and sicker patients often cannot tolerate 4 grams QID and are started more slowly. A ten day run in with Actos or Omega-3 fatty acids (described below) with a no amylose diet can ameliorate most detox/intensification reactions (start CSM on day #6 of 10). The therapy for older persons can take several months. Young children respond quickly and usually

take just a month. Compliance is key. Those who get better faster tend to be younger, less sick, have better genetics and are able to avoid toxic exposures.

Treatment which goes poorly or more slowly than expected is usually from one of three causes: 1) continued exposure, i.e., failure to complete the first step 2) poor compliance with CSM, i.e., failure to complete the second step and 3) failure to eradicate MARCoNS, i.e., failure to complete the third step.

In the eleven step process, the third is the eradication of multiply antibiotic resistant coagulase negative staphylococcus (MARCoNS) from the nasopharynx, if present. These bacteria form a biofilm making it hard for many antibiotics to penetrate, sheltering the bacteria. Further, as their name implies, they are resistant to at least two classes of antibiotics. MARCoNS rarely exist if a patient has a normal MSH (melanocyte stimulating hormone), but normal MSH is unusual in CIRS patients. MARCoNS make hemolysins which cleaves MSH rendering it ineffective. Inadequate treatment of MARCoNS will render CSM therapy impotent, perhaps because of the continued assault on MSH. To treat MARCoNS, a combination of therapies is used. Rifampin, a powerful but rarely used oral antibiotic is a mainstay. It is able to penetrate the biofilm and get to the "bugs". I use 300 mg, 2 tabs daily for 30 days for adults and 10-20 mg/kg/day for children. Also used, in combination with rifampin, is BEG spray, an acronym for Bactroban (mupirocin), EDTA and gentamicin. The EDTA dissolves the biofilm clearing the way for a direct attack by the topical antibiotics. Two sprays 2-3 times a day for 30 days usually do the trick. For children, I use 1 spray twice a day, alternating nares. Start the rifampin and BEG spray on the same day to discourage new resistance emergence.

The fourth step is correction of antigliadin antibodies. Many, but not most, patients will have a positive antigliadin antibody (AGA) in their initial lab work. In such cases, a tissue transglutaminase antibody test (TTG) should be performed. If this is positive, the patient has celiac disease and should be treated accordingly. However, in CIRS patients, TTG is usually negative. Treatment of TTG negative patients consists of a gluten free diet for one to three months followed by retesting. If the AGA is negative on retesting, gluten can be reintroduced into the diet without consequences.

The fifth step is correction of abnormal androgens typically caused by an up regulated aromatase enzyme. Treatment may consist of DHEA (dihydroepiandrosterone) 25 mg taken three times a day, HCG (human chorionic gonadotropin) injections of 125 mg per week (or sublingually) for 5 weeks or VIP (vasoactive intestinal polypeptide) nasal spray 4 times a day for 30 days.

Step 6 is to correct antidiuretic hormone/osmolality problems. Often antidiuretic hormone (ADH) is absolutely high or low. Often the osmolality is absolutely high or low. Because a functional feedback loop exists between these measures, there can also be relative highs and lows. For instance, if the osmolality is 305, one would expect the ADH to be in the high normal range or even higher than normal. Put another way, considering the osmolality, proper functioning of the feedback system would require the ADH to be high normal or even high. If ADH were in the low normal range, that would be relatively low for the measured high normal osmolality. Treatment consists of desmopressin 0.2 mg every other night for 10 nights. Electrolytes and ADH/osmolality are followed. This corrects the labs but also the polyuria, polydipsia, orthostatic hypotension, recurrent headaches and static shocking that patients have. I have also used desmopressin 0.2 mg BID for 30 days with success, although it is more likely to cause side effects. In children, I use DDAVP spray at 1-4 sprays per night depending on weight and age.

The seventh step is to correct MMP-9 (matrix metalloproteinase 9). This treatment entails using Actos (pioglitazone) 45 mg once daily for thirty days in conjunction with the "No Amylose" diet for the same time period. The goal is to up regulate PPAR-gamma production and subsequently reduce MMP-9 expression. Care should be taken with diabetic patients as this might interfere with their other therapies. At times, communication with the patient's PCP is warranted. For those with a leptin < 7, those under 18 years or those who cannot obtain or tolerate Actos, 2.4 g/day of EPA and 1.8 g/day of DHA can be used in its place. As with all steps, the abnormal labs should be repeated at the end of the therapeutic trial. This therapy also usually corrects abnormal VEGF.

Step 8 is the correction of high C3a. C3a and C3b are the split products of activating C3 in the complement system. High dose statins are used to clear elevated C3a. Co-administration of CoQ10, 150 mg qd, beginning 10 days before starting the high dose statins will help prevent CoQ10 deficiency secondary to decreased HMG-CoA reductase function.

Step 9 is the correction of elevated C4a. This split product of the MBL (mannose binding lectin) pathway of the complement system is a key marker of how severe a patient's CIRS is. Procrit (erythropoietin) is used to reduce C4a. Procrit has a black box warning so care is taken not to use this if any of the conditions indicated are present. Informed consent is obtained. Complete blood count and iron studies (as well as C4a, TGF beta-1, d-dimer and T regulatory assays) are obtained before each dose and after completion of the trials to insure

no polycythemia develops, potentially increasing risk of thrombus formation, as well as to document efficacy. Five shots of 8000 units are given in a supervised manner, twice a week over a 15 day period. Patients are to keep track of symptoms as they go. At the end, patient and provider go over the data to assess the benefit. If sufficient improvement exists, i.e., the patient is feeling better, breathing easier, mentally clearer and the C4a has dropped significantly from the baseline, a second trial could be started. Here the goal is to titrate to the best dose (8000, 6000 or 4000 units) over the optimal timing of dosing (q3, 4, or 5 days). There is no established Procrit dosing for children. For those recalcitrant to Procrit, VIP therapy can also be used at 4 sprays a day. There is no established VIP dosing for children.

Step 10 is the correction of TGF-B1 (transforming growth factor beta 1), an innate immune cytokine which is also a key marker of illness severity. Reduction is actuated by giving Cozaar (Losartan) up to 25 mg twice a day for 30 days in adults or 0.6-0.7 mg/kg/day divided BID for children. As many adult patients are on multi-therapy for hypertension, care should be given when using this and communication with the patient's PCP is warranted. Self-monitoring of blood pressure should occur daily and with the start of symptoms such as orthostasis. As with all other therapies, abnormal labs should be redrawn at the completion of therapy. For those recalcitrant to Cozaar, VIP therapy can also be used at 4 sprays a day.

The final step, step 11, is at the pinnacle of the pyramid (see Figure 1). By this time, most patients will already have become much better with reduction or resolution of at least 75% of their baseline symptoms. Some will require this last effort. VIP is the crown of therapy but can be misused. VIP is not appropriate for patients who still have significant exposures or MARCoNS. It won't work. As such, an Environmental Relative Moldiness Index (ERMI) of < 2 or an updated Health Effects Roster Type Species Mycotoxin and Inflammagen test (HERTSMI-2) not > 10 is required to prove lack of exposure. Further, the patient should have a negative nasal swab and a normalized VCS screen. These document the patient's body has been relatively cleared of toxin, that there is no major exposure and, indirectly, that MSH is moving in the right direction (though MSH seems to be the last of the compounds to correct and may need VIP therapy instead, in some cases, to reach normal levels, if possible). Passing these three tests demonstrates the effectiveness of the previous 10 steps. VIP is given as a nasal spray currently made only at Hopkinton Drug in Massachusetts. The dosage is 1 spray (50 micrograms) 4 x daily (typically in alternating nares). VIP therapy should be

maintained at QID for at least 2-3 months and then titrated to optimum dosing by decreasing one spray a day each month. Candidates for VIP administration should meet one of the following criteria: 1) decreased VIP levels per blood testing (through Quest); 2) increased pulmonary artery pressure (an increase of more than 8 mmHg during provocative testing; or 3) failure to regain immunoregulatory control after completing steps 1-10, as indicated.

VIP also appears to down regulate MASP2, an auto-activating receptor involved in C4a production. This may end the sicker-quicker phenomenon and also allow CIRS patients to stay well even if exposed. It is a marvelous drug when used properly.

Appropriate use of VIP also requires diligent monitoring. Lipase levels should be checked monthly. VIP administration should be discontinued at the first sign of lipase elevation or with the onset of abdominal pain. Per published clinical trials, abdominal pain has been found exceedingly rarely with VIP usage, however, the clinician should pay close attention to its advent.

Finally, labs should be repeated off all meds (except continuing VIP) to insure therapy is complete!

The pyramid was designed based on the following principle. Imagine all the ill patients huddled together at the lowest step. Of all those who remove all the toxins from their environments, some will get completely better from this alone. Treating all the remaining with 1 month of CSM will cause a certain percentage to get completely better. Still others of the diminishing crowd of ill people will find resolution by eradicating MARCoNS. And so it goes on with a smaller number of people at each step, hence the pyramid. The labs dictate which steps are to be followed; rarely is every step required, but each required step must be treated in the order given.

Following the 11 step protocol can be a rigid process. It requires painstaking attention to the sequence of therapies and the repeating of labs. It is not cheap and requires significant patient cooperation. However, the steps are laid in their order for logical and tested reasons. Attempts to cut corners, shorten the process or treat items out of sequence will usually end in failure. Alternatively, following the steps leads to a success rate that hovers around 90%. This author uses the Shoemaker 11 Step Treatment Protocol because it works and because he has hundreds of patients who will attest to that! Most of those patients have seen 8-10 other doctors. Many have been to the Mayo Clinic or similar temples of modern medical diagnostic prowess and come away with no

diagnosis and no hope. Others have been misdiagnosed. Yet both groups find relief of symptoms, pain and disability by following the pyramid!