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## **The Shoemaker Protocol**

The Shoemaker Protocol is an evidence based approach to biotoxin illness. It is a structured, step-by-step method that relies on well-designed studies. Every step is peer-reviewed. The Shoemaker Protocol identifies those sickened from biotoxin illness and uses rigorously tested interventions to help them recover. The implications for the prevention and treatment of Chronic Inflammatory Response Syndrome are profound for individuals as well as for public health. If the lessons learned from The Shoemaker Protocol were put into practice universally, we could prevent illness and suffering for many.

A differential diagnosis is formulated by taking a thorough history, including a review of past medical history and labs. An environmental history includes questions about past and present living conditions, buildings the patient has occupied at school or work, HERTSMI/ERMI tests of the buildings, travel history, rashes, tick or spider bites, consumption of fish, yellow-jacket stings, exposure to fresh water with fish kills, and algae blooms. The history should include medications taken such as fluoroquinolones, corticosteroids, and gadolinium contrast. The patient is interviewed regarding 37 symptoms in 13 clusters. Chronic Inflammatory Response Syndrome (CIRS) patients typically have symptoms of 8 clusters or more. A physical exam may demonstrate dehydration with hypotension and tachycardia, red eyes, muscle fatigue, rales, S3 or S4 upon cardiac auscultation, edema, tremor, dermatographia/rashes, increased BMI, evidence of brain fog (which may include word-finding difficulties), difficulty following directions, and frequent patient interruptions due to difficulty with executive functions.

Ninety five percent of patients with CIRS will have susceptible human leukocyte antigens (HLAs). This is one of the most helpful lab tests available. Only about 5% of CIRS patients

have non-susceptible HLAs. About 24% of the population is susceptible to illness from water damaged buildings and 21% is vulnerable to illness from Lyme disease after treatment with antibiotics. The susceptible HLA signifies a flaw in antigen presentation. The body recognizes a threat exists but cannot properly form antibodies which can remove it. Therefore, the innate immune system amplifies inflammation without clearing the biotoxin. It's like one person calling 911 about a fire, but instead of the fire being put out by firemen more and more people call to report a fire that the firemen can't find. There is ever-increasing inflammation and vigilance with no resolution.

A screening Visual Contrast Sensitivity (VCS) test can detect capillary hypoperfusion in the retina and optic nerve by testing the patient's ability to differentiate shades of grey. VCS is a highly effective test which identifies 92% of sick patients and only has a 1% false positive rate. Individuals who have a false negative test tend to be young women or people trained in art, photography, or have vision-intensive careers like pilots which calls for close attention to detail. The small population with a false positive VCS may have been exposed to hydrocarbons or solvents. The test is non-invasive, fast, inexpensive, accurate and can be performed at home by the patient. VCS should be performed during the protocol period to measure both progress and re-exposure. This can be performed at home on a computer and verified with a hand-held VCS in the doctor's office. A negative VCS is required for initiation of vasoactive intestinal polypeptide (VIP) treatment. Occasionally, the VCS may not completely normalize, but it should stabilize. Passing the VCS means both eyes (if testable) see correctly 7 or more patterns in row C and 6 or more in row D. Failure in one eye means the patient failed the VCS. In instances when someone only has one eye or limited acuity, the test is valid if the one eye is able to see 20:50 or better.

A stress echocardiogram can identify elevated pulmonary artery systolic pressures. An elevation of PASP of > 8 mm Hg during exercise is abnormal and must be treated. These

patients can experience heart palpitations, find exercise difficult and may be short of breath. It is important to ask specifically for the PASP to be quantified by the cardiologist. This is another objective marker which helps confirm diagnosis and can be measured afterward to demonstrate response to the protocol.

A cardiopulmonary exercise test can be used to measure VO<sub>2</sub> max. A normal value is >35 ml of oxygen consumed per kilogram per minute. A CIRS patient may have a VO<sub>2</sub> max of <20 ml of oxygen consumed per kilogram per minute. To put into context, a VO<sub>2</sub> max of 15 ml of oxygen consumed per per kilogram per minute is consistent with Stage IV cardiac failure.

Pulmonary function tests (PFTs) should be performed on all patients but especially ones experiencing shortness of breath. These patients may appear to have asthma, but PFTs often show restrictive lung disease instead of obstructive lung disease. Restrictive lung disease happens in conjunction with abnormalities in TGFB-1, MMP-9, VEGF and T regulatory cells in the form of remodeling.

NeuroQuant is an important test added to a traditional MRI which shows small variances in volume in select areas of the brain. NeuroQuant shows a unique fingerprint for biotoxin illness which can easily distinguish cases from controls. NeuroQuant can also distinguish Lyme disease from mold exposure. This provides excellent evidence of biotoxin illness and can be repeated after treatment to demonstrate the efficacy of the protocol.

GENIE (Genomic Expression: Information Explained) testing can track genetic expression associated with illness from CIRS, help tailor treatment, and demonstrate resolution of illness. This test can be used to demonstrate hypometabolism through transcriptomics. GENIE has advanced our knowledge of CIRS and demonstrated marked response to endotoxins and actinomycetes. For \$725 patients can obtain state-of-the-art, individualized information on their health.

ACTH and cortisol levels may initially rise and then fall as the patient becomes more ill. Every effort must be made to avoid systemic corticosteroids such as prednisone unless absolutely required. Topical and inhaled corticosteroids may be used safely. This dysregulation occurs in about 65% of patients with low MSH levels.

### **Step 1: Removal from Exposure**

*Action:* PCR test with ERMI or HERTSMI. Leave and avoid all environments with unacceptable levels.

*Goal:* All environments should be ERMI < 2 and/or HERTSMI <11. This is one of the requirements before VIP treatment.

This simple-sounding step is deceptively difficult. It starts with identifying the sources of exposure. A PCR test such as an ERMI or a HERTSMI should be performed in each area where the patient spends time. Mycometrics Lab performs these reliably. This means home, school, and work. A test should be performed at locations like a family member's house (where the patient regularly spends time), church, or any other building they might frequent routinely. If the patient is renting a water damaged apartment or house it is best and easiest to move into a new home with an acceptable ERMI (less than 2) or HERTSMI (under 11) and remediate all belongings. If an individual has an MSH of < 35 and a C4 > 20,000 the ERMI must be -1 or less. If the patient owns a water damaged building, the home may be remediated by an expert who regards improvement in human health as the ultimate goal instead of an arbitrary spore count. The patient may need to temporarily vacate the environment during remediation, though sometimes moving out and selling is the best option. The items in the water damaged building must be carefully evaluated. Anything that is porous needs to be disposed of or placed in air-tight containers. Non-porous items such as glass, metal, finished wood and leather can be

cleaned with HEPA vacuums and quaternary solutions such as Windex, Fantastic, 409 or Clorox Clean-up (this is NOT the same as bleach). For the very sensitive, it is better to use paper towels and disposable dusting cloths (e.g., Swiffers) than rags to permanently remove contaminated material from the home. Reusable rags and mop-heads can spread the biotoxins. It may be necessary to wear HEPA respirators and protective gear while cleaning. Some of the most sensitive patients may need to abandon possessions altogether. Failure to remediate the old belongings before bringing them into a new environment will bring the patient back to square one.

Rugs, curtains, thick bedding and upholstered furniture are all reservoirs for inflammagens and must be discarded. Mattresses may potentially be salvageable with impermeable covers. Clothes can be cleaned with detergent, borax and quaternary cleaners. In general, the thicker the fabric, the more difficult it is to clean. Sometimes, depending on the person's sensitivities, cleaning fabric is ineffective and it's just better to buy new items. Every effort should be made to reduce the number of items in a home as a sparse aesthetic translates into a healthier environment with fewer reservoirs and less need for cleaning. Car interiors should also be considered. If a vehicle has been flooded or there is a longstanding leak from the window, this could cause illness and the upholstery and carpet can act as a reservoir and make the patient ill. Under these conditions, performing a HERTSMI may be advisable. The car can be cleaned with HEPA vacuuming and quaternary cleaners. Air Oasis is the best option in air purifiers and can be used in a car after cleaning.

The patient must not attend school or work at a water damaged building. In most cases, after someone has been sickened, it is best to find another school or workplace. Health cannot be regained if the patient continues to be exposed to water damaged buildings. When a school or workplace cleans the environment the remedial action is often insufficient or much too late for an already ill patient. Unfortunately, the patient is unlikely to find organizations that take full or

appropriate responsibility for their compromised buildings and the resulting damage to health. The patient should perform an ERMI or HERTSMI at a prospective school or job before beginning. Spore sampling is inherently flawed and has no bearing on human health per the World Health Organization's stance (2009). Intact mold spores account for about 0.2% of the problem and for this reason PCR is the only valid method to ensure safety. ERMI/HERTSMI PCR has been validated by studies of human health and re-exposure trials.

According to NIOSH, more than half the buildings in America are water damaged. Once the patient has determined that none of the buildings in question are water damaged, he/she must, never-the-less, remain cautious and vigilant when entering any other untested building. That means grocery stores, banks, pharmacies, movie theaters, big box stores, and restaurants must be safe if the patient is to regain health. If your local post office or shipping distribution center is moldy, online shopping can be a source of exposure. It is impractical to test each building you enter, so here are some general guidelines: if the building has a stucco facade and a flat roof there is a higher likelihood of water intrusion. Buildings at bottoms of hills or in a known flood-zone are likely to be unsafe. A quick glance at the roof and fascia can give you a clue about the condition of the building. If you see water stained ceiling tiles, stained carpet, smell musty odors, or see active leaks, find the exit quickly. If a basement has visible water, musty smells or visible mold, get out in a hurry. Many people have a "gut feeling" about a building. Trust that instinct if you feel unwell or uneasy about being there: you are most likely right! The symptoms can vary from person to person, but learn to recognize the first signs of feeling unwell.

Often as your living/working environment becomes progressively cleaner, you may notice these symptoms may occur more quickly in unclean environments. This points to the "sicker, quicker" pattern which may be associated with mannose-binding lectin serine protease 2 (MASP-2). In time, smaller exposures make the patient sicker and for longer periods. This is

very confusing to the patient and their loved ones who haven't studied CIRS. It baffles many people why they could work somewhere for years but then eventually not be able to spend a few minutes in the same building. Some people may get headaches, feel dizzy, become hoarse, feel short of breath, have nausea, and experience ringing or fullness in the ears. It varies from person to person, but know your signs of an exposure. Often it is very subtle. I have noticed people have different ways of describing a water damaged building. It may be characterized as “stuffy, dark, stale, dank, musty, run-down, cheap” or “dirty.” Sometimes the way someone describes a building provides information that they are not consciously processing.

After remediation and the home has an acceptable ERMI or HERTSMI, HEPA filters can remove particles down to 0.3 microns. For smaller fragments Air Oasis filters are a good choice. There is also an exciting product called Aero Solver which uses a fogging solution to take the smallest fragments and inflammagens out of the air to be wiped up permanently. Dehumidifiers can also be used to discourage mold growth. These are wonderful adjuncts but will never be adequate alone until water intrusion has been stopped and proper remediation performed.

Pets can also become sick from water damaged buildings and your veterinarian is highly unlikely to know about mold-exposure. There is a case study from 2007<sup>1</sup> which describes two Himalayan cats that died from pulmonary hemorrhage after *Stachybotrys* exposure. Does your pet spend time where you don't? If their doggy day-care, groomer or petsitter has mold, your pet could be bringing it home to you. If your basement has water damage, it is not good for your pets to spend time down there. Having litter boxes or relegating animals to areas where you can't be is bad for the pets and, ultimately, their humans. Basements typically have worse

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<sup>1</sup> Mader, Douglas & Yike, Iwona & Distler, Anne & Dearborn, Dorr. (2007). Acute pulmonary hemorrhage during isoflurane anesthesia in two cats exposed to toxic black mold (*Stachybotrys chartarum*). *Journal of the American Veterinary Medical Association*. 231. 731-5. 10.2460/javma.231.5.731.

ERMIs and HERTSMIs. Things to note are cough, lethargy, vomiting, diarrhea, vocalized pain, unexplained weight-loss/anorexia, neurologic issues like dizziness, ataxia or confusion, unexplained behavioral changes, and paw-shaking when no other sources of injury are apparent.

Children may spend time at day-care, extra-curricular lessons, or with family members outside of school. Each of these places can be a source of exposure and contamination. Make sure each of these places is safe by using PCR testing such as ERMI or HERTSMI.

Other sources of biotoxin illness to avoid include ciguatera from fish, Lyme and Babesia from ticks, algae blooms and cyanobacteria, Pfiesteria from waterways, Mediterranean spider bites, and lionfish. Even if WDB exposure was not the event which made a person sick, anyone with a low MSH (who has had the same final common pathway of inflammation triggered) can be made sicker with mold exposure. This is common with people who have had chronic illness from Lyme disease. They are frequently made ill from moldy buildings and may not know it. Instead, they can find themselves on unnecessary courses of antibiotics when, in fact, their home is causing continued inflammation.

## **Step 2: Cholestyramine and Welchol**

*Action:* Cholestyramine 4 grams four QID or Welchol 625 mg- two pills TID with food.

*Goal:* Reduce Biotoxin load to pass VCS.

Pediatric Considerations: Cholestyramine 60 mg/kg TID, 60 -120 lbs children 4 mg TID.

Biotoxins are small, negatively charged compounds which continuously cycle through the bile in a process called enterohepatic circulation. The bile is conserved in this process and because the biotoxins remain in the bile, they are not eliminated by normal physiologic

processes. Cholestyramine is cholesterol medication which has a positively charged side chain structure that grabs the negatively charged biotoxins as the bile enters the small intestine. The biotoxin and cholestyramine can then be eliminated via the digestive system. Each dose of cholestyramine will reduce the amount of biotoxins in the body. Pre-medicating with a week's worth of high dose fish oil (EPA 2.4 grams and DHA 1.8 grams) and for the first five days after initiation of cholestyramine can reduce the intensification reaction that can occur as these biotoxins are removed from the body. Four grams of cholestyramine is to be taken four times a day.

Cholestyramine can cause nausea, reflux, and constipation. It is a very safe medication as it doesn't absorb into the body. The gastrointestinal side-effects can be difficult to tolerate. Cholestyramine is mixed with water. One may eat 30 minutes after taking cholestyramine. It is also important to fast for at least 60 minutes after eating before taking a dose of cholestyramine. If the patient has difficulty tolerating the pharmaceutical formulation, a compounded version of cholestyramine without sugar, aspartame or additives can be used.

Cholestyramine is a cholesterol binder called a bile acid sequestrant. It should be dosed 4 hours after medications like Synthroid, digitalis, beta-blockers, valproic acid, coumadin and antibiotics. It can also bind to fat-soluble vitamins A,C,D, and E. The use of this medication to remove biotoxins is off-label and the physician should have the patient sign a consent.

Welchol is an alternative for those who cannot tolerate cholestyramine, but is about 1/4 as effective because it has less positive charges to bind the biotoxin. Welchol can be used for those with Multiple Chemical Sensitivity. It can be dosed with food and comes in pill form so it can be taken more easily.

Ultimately, the goal of this step is to remove as much of the biotoxin load as possible and pass the VCS. If there is no improvement, look for another source of biotoxin exposure and

check for patient compliance. The following step of eliminating MARCoNS may be needed for continued improvement of symptoms.

If you are entering a new and unknown building, pre-medicating with cholestyramine is advisable. Dosing with full strength cholestyramine for several days afterwards, as described above may be needed if the building is water damaged. Look for resolution of symptoms and improvement of the VCS.

### **Step 3: MARCoNS**

*Action:* 0.2% EDTA 2 sprays each nostril TID for 6-8 weeks, or BEG spray 2 sprays in each nostril TID for one month and re-culture.

*Goal:* Eradicate MARCoNS with EDTA, or BEG spray and confirm absence of MARCoNS with culture from MicrobiologyDX. This is needed before VIP treatment can be started.

*Pediatric Concerns:* Test after 15 years of age, BEG spray 1 spray 2X per day.

MARCoNS are multiple antibiotic resistant coagulase negative staphylococci which reside in the deep nasopharynx. The bacteria form a biofilm which provides protection for the bacteria and can encourage differential gene activation. MARCoNS then cleave MSH and form exotoxins. MARCoNS are very common in CIRS patients with low MSH. The presence of MARCoNS will reduce MSH and prevent the patient from healing. Children will usually not have MARCoNS before the age of 15.

0.2% EDTA has recently been added to the protocol. This can be used as a first-line medication.

BEG spray consists of Bactroban (Mupirocin) 0.2%, EDTA (Edetate Disodium) 1%, and Gentamicin 0.025%. This combination penetrates and kills the bacteria in the biofilm.

Re-acquisition of MARCoNS can occur if patients have close contact with dogs or individuals with low MSH and MARCoNS. It is recommended that dogs not sleep in bed with patients and patients should wash their hands after petting their dogs. If needed, a veterinarian can culture for MARCoNs through MicrobiologyDX and treat with BEG spray. Cats rarely harbor MARCoNS.

If the patient feels worse during treatment, high-dose fish oils can be administered in the manner we use during cholestyramine treatment (7 days prior and 5 days after with EPA 2.4 grams and DHA 1.8 grams). After treatment, repeat culture and VCS test. Most MARCoNS will be eliminated with BEG spray. A negative MARCoN test is needed to proceed with VIP.

#### **STEP 4: Correct Anti-Gliadin Antibodies**

*Action:* Eliminate gluten and retest anti-gliadin antibodies (AGA).

*Goal:* Negative AGA or continued avoidance of gluten.

CIRS patients can have positive AGAs and not be able to tolerate gluten well. If the patient has a positive AGA, the patient should avoid gluten for at least 3 months and be retested. If the AGA is normal, gluten can be reintroduced if desired. Many people will not feel as well on gluten and for these individuals gluten should be permanently eliminated. A positive TTG signifies celiac disease and gluten must be entirely eliminated for life.

#### **Step 5: Correct Androgens**

*Action:* Use VIP or DHEA 25 mg TID and monitor estradiol.

*Goal:* Normalize androgens and aromatase.

Problems with androgens are seen somewhere between 40-50% of CIRS patients. Aromatase must be checked along with DHEA, testosterone, and estradiol. Because aromatase converts testosterone to estradiol, replacing testosterone in a high aromatase patient will produce increased estradiol in men. For these reasons, testosterone replacement can be counterproductive and may exacerbate symptoms. VIP can normalize the androgens. If VIP does not optimize the androgens, DHEA can be used with caution while closely monitoring estradiol.

#### **STEP 6: Correct ADH/Osmolality**

*Action:* Desmopressin 0.2 mg every other night for a total of 5 doses. Monitor electrolytes and ADH/osmolality closely.

*Goal:* Normalize ADH/Osmolality.

*Pediatric Concerns:* DDAVP 1-2 sprays per day if absolutely needed (for example patient has POTS or acquired von Willebrand's disease).

ADH and osmolality dysregulation is very common in CIRS and affects about 60-80% of patients. The most common manifestation of this is low ADH which is accompanied by increased thirst, headaches which mimic migraines, static shocks, frequent urination and dehydration. The sweat chloride of some individuals with low ADH can actually exceed the sweat chloride of people with cystic fibrosis. Desmopressin can be used. ADH/osmolality, electrolytes, weight and ankle swelling must be closely monitored.

Acquired von Willebrand's factor can also normalize with this step. Acquired von Willebrand's deficiency can cause a patient to bleed profusely and have an inability to clot

normally. Acquired von Willebrand's deficiency is the loss of the ability to form clots via the formation of von Willebrand's multimers (Low ristocetin associated cofactor, low multimer formation and low von Willebrand's antigen are seen on labs). The multimers are polymers of monomers which cannot form in some individuals with elevated C4a and in patients with hematologic cancers.

### **STEP 7: Correct Elevated MMP-9**

*Action:* Use EPA 2.4 grams/DHA 1.8 grams or Actos 45 mg per day for 30 days with the no-amylose diet. VIP, when indicated in the protocol, will improve MMP-9.

*Goal:* Decrease MMP-9 and increase PPAR.

The next step is normalizing MMP-9. MMP-9 causes inflammation of the nervous system, lungs, muscles, blood vessels and joints. Reduction of high MMP-9 can be safely done with high dose fish oil (EPA 2.4 grams/DHA 1.8 grams). This is the same dosage discussed above in premedication for the cholestyramine and MARCoN steps. Actos has been used along with an amylose-free diet to reduce MMP-9 in individuals with a leptin over 7. There is concern regarding long-term Actos use in regard to bladder cancer which makes its use less appealing. This medication would only be used in the short-term; metabolic studies and fasting blood sugar should be monitored during the short course. TNF, PAI-1, leptin and VEGF may also normalize in this step.

A low amylose diet should be initiated which excludes gluten, rice, bananas, and all vegetables grown under-ground (except garlic and onions).

### **STEP 8: Correct VEGF**

*Action:* Use high dose fish oil (EPA 2.4 grams/DHA 1.8 grams) to increase low VEGF, or Actos 45 mg for 30 days with the no-amylose diet. VIP, when indicated in the protocol, will improve VEGF.

*Goal:* Normalize VEGF by raising a low VEGF or lowering a high VEGF.

Abnormal VEGF is frequently corrected by the same means as MMP-9. Correcting VEGF will improve breathing, fatigue, cognition, and reduce muscle cramping. Patients with low VEGF will have capillary hypoperfusion which must be corrected.

### **STEP 9: Correct High C3a**

*Action:* Use a high dose statin (like atorvastatin 80 mg) and pre-medicate with 10 days of Coenzyme Q10, 150-300 mg per day and monitor patients on coumadin.

*Goal:* reduce high C3a.

It is important to do a Complete Metabolic Panel with a fasting glucose to monitor liver function and detect hyperglycemia. C3a rises with presence of bacterial membrane. C3a rises within 12 hours of a tick bite in those who develop Lyme disease.

Proper antibiotic treatment for Lyme for 3 weeks must take place before reduction of C3a. Labs are repeated after antibiotic treatment. Non-HLA susceptible patients may obtain resolution of C3a, C4a and VCS after antibiotics alone. For those who do not obtain resolution, cholestyramine and high dose fish oil/Actos is used for one month. Cholestyramine and Actos treatment is then ceased. No change in C3a and a rise in C4a one week after treatment

indicates mold exposure. This is very common and must not be overlooked. A rise in C3a and C4a one month after treatment signifies active Lyme disease and the need for additional antibiotic treatment. This may take the form of continued oral antibiotic or IV antibiotics.

The patient must be premedicated with Coenzyme Q10 for ten days and then given a high dose statin such as atorvastatin 80 mg to reduce C3a afterwards.

### **STEP 10: Correct High C4a**

*Action:* Use VIP to reduce high C4a (or use Procrit if needed).

*Goal:* reduce high C4a.

One of the many things VIP corrects is high C4a. Before VIP was formulated, Procrit was routinely used. It has a black box warning and needs patient consent. It should not be given to patients with a high risk for blood clots or uncontrolled hypertension. It is also expensive and not covered by insurance for this purpose. It is dosed at 8,000 units twice a week for 5 doses. This is contraindicated in individuals with a history of blood clots and neck and throat cancer. D-dimer, CBCs, and blood pressure must be closely monitored. This is for short-term use only.

Use of VIP is safe, fast-acting and effective and has a lower cost. If a patient meets criteria and tolerates VIP, it is a great way to approach lowering C4a.

### **STEP 11: Reduce High TGFB-1**

*Action:* Use VIP or losartan 25 mg BID to reduce TGB-1 and monitor blood pressure.

*Goal:* reduce high TGFB-1.

*Pediatric Considerations:* losartan 0.6-0.7 mg/kg/day divided BID.

High TGFB-1 causes a number of pathologic conditions. High TGFB-1 and MMP-9 cause tissue remodeling by epithelial to mesenchymal transformation (EMT), including restrictive lung disease. This basically transforms a normal cell into one which is fibrotic and ineffective. Patients may acquire neurologic conditions such as multiple sclerosis, tics, tremor, and even a Parkinson-like illness. Autoimmune disorders like Crohn's disease and rheumatoid arthritis can respond to reduction of inflammation via reduced TGFB-1. Nasal and vocal cord polyps may develop, but gastrointestinal polyps are not associated with high TGFB-1. TGFB-1 can be lowered by either VIP or losartan.

### **STEP 12: Replace low VIP**

*Action:* VIP 50 mcg QID supplementation after all requirements are met, higher or lower doses may be appropriate.

*Goal:* normalize transcriptomics and NeuroQuant. Improve patient's symptoms.

This step can be taken after the patient no longer experiences mold exposure, registers an ERMI of less than 2 or a HERTSMI of less than 11, has a negative VCS test, a negative MARCoNS test, and a normal lipase. This is done in the office after a baseline TGF-B1. Then one spray of VIP is given followed by a second TGF-B1 test performed fifteen minutes later. The TGF-B1 should not rise. If lipase rises at 30 days, the patient could develop pancreatitis and VIP is contraindicated. Rising TGF-B1 is associated with ongoing mold exposure. The doctor must check for rashes, changes in blood pressure, and improvements in breathing and cognition which can be seen within minutes.

VIP corrects many steps of the protocol and can normalize NeuroQuant studies and transcriptomics. VIP can correct vitamin D, T regulatory cells, androgens, aromatase, MMP-9, VEGF, C4a, TGF-B1 and, of course, VIP levels. Treatment with VIP should also normalize PASP. It can also reduce extreme hypersensitivity to the inflammagens found in water damaged buildings by normalizing MASP2. For example, some sensitive individuals may be sickened by minute exposures found in air near water damaged buildings. VIP can increase endorphin production and reduce symptoms of Multiple Chemical Sensitivities and Chronic Fatigue Syndrome.

VIP is made by Hopkinton Drug and ships cool and should not be not be frozen. The medication should be refrigerated and stored upright (placing it in a mug that will not tip over is a good idea). It can be stored for 90 days and diluted for those who need to titrate up to the recommended dose. The typical dose is 4 times a day. This is generally done for 6 months while monitoring lipase, then tapered down to low maintenance doses which may be administered less than once per day.

### **Graded Exercise**

An exercise regimen to increase anaerobic threshold should be begun. The patient should work up to 15 minutes of cardiovascular work, 15 minutes of weights and 15 minutes of abdominal exercise to be performed daily. It should be slowly titrated as tolerated and performed every day without exception.

## **Re-exposure trials**

A re-exposure trial can be performed to prove that the building in question caused the clinical symptoms. This calls for the patient to be adequately treated. At that point the medications are stopped for 3 days while baseline VCS and labs (C4a, MMP-9, TGF-B1, VEGF and factor VIII) are measured. The patient is re-exposed to the building for 8 hours at a time for 3 consecutive days. Labs are performed the morning of the first day before exposure and for the next 3 mornings following exposure. C4a and TGF-B1 will increase on Day 1. VEGF will increase on Day 1 and fall by Day 3. Factor VIII decreases on Day 1 and normalizes by Day 3. Leptin increases and VCS becomes abnormal on Day 2. By Day 3, vW antigen and ristocetin cofactor may drop and bleeding can begin. On Day 3, MMP-9 increases as well. The patient should also record their symptoms. These labs follow a predictable pattern and can prove that a particular building is the cause of illness. The patient is then re-treated using the protocol to restore health.