



A Special Interview with Dr Ritchie Shoemaker, MD

How did you get to be the leading physician in the field of Chronic Inflammatory Response Syndrome (CIRS) and what is the history of CIRS?

Sometimes people just stand in the right place where something is going to happen. Others make things happen from the spot they are in.

Looking back at the beginnings of my work in the field of biotoxins and CIRS, maybe both ideas apply to me. My rural Family Practice (FP) was just in the right place at the right time to let me be on the riverside where Pfiesteria human illness syndrome was getting started. Pfiesteria is a fish-killing dinoflagellate, a single celled organism that makes a small toxin that can move from cell to cell (called an ionophore) without being metabolised. The toxin creates a multisystem, multisymptom illness not like anything anyone knew about back then. The toxin is not destroyed by the liver, for example, but is secreted against a gradient into bile.

Here is the critical basis for the C (for chronic) in CIRS: the toxin is excreted into the duodenum in bile but because it moves from cell to cell, it is rapidly reabsorbed by a process we call enterohepatic recirculation. Without fail, given the ongoing recirculation of a toxin, the illness won't go away on its own because of persistence of direct toxin effects. Stay with me; there is so much more to this story.

The Pfiesteria patients were so unique: no one had ever seen such an illness in the wild. The sickened people were just breathing the air that came off areas of fish kill. No, eating fish or clams or shrimp didn't do it. And people living within 300 yards of the fish kills (and even without fish kills but where fish kills would take place later)

were sickened as well. I had never seen such an illness: neither had any health officials in the US. My third patient seeking help I couldn't provide had terrible secretory diarrhoea as part of a syndrome with the typical findings of headache, memory impairment, cough and aching. I am no different from thousands of rural FPs. We all know that cholestyramine (CSM), an old FDA-approved cholesterol lowering drug works quickly and effectively to stop secretory diarrhoea. So I gave it to Number 3. Surprise! Not just her diarrhoea got better; the whole syndrome disappeared and didn't come back.

What did CSM do? It isn't absorbed and couldn't add to the body's defences. But it does bind to just about everything in the gut. So how did the toxin (back then no one even knew what the toxin structure was!) get into the gut? Inhalation to blood, to tissue, to liver, to bile, to duodenum. I then gave the drug to over 200 people, with incredibly good results. I wrote up the cases, published in September 1997, with treatment published in February 1998. These were the first cases published in the world's literature on diagnosis and certainly on treatment of cases acquired in the wild.

Needless to say the massive publicity from influential US newspapers and media drove the US public health community into defensive mode, (1) at first denying there was any illness, then (2) saying I was a wacko until finally (3) saying they knew it all along. Sound familiar?



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The “action” of the arguments about existence appealed to me but the questions were legion. Why did some people get sick and others didn’t?

Why did the illness affect so many tissues? What was the mechanism of illness? Were there people who were less affected than others who had a less dominant illness presentation? Were there other mechanisms of additional illness I didn’t know? Long term effects? And what kinds of diagnostic tests were helpful since everything I knew to order had been normal to date.

The ensuing months brought me to treat other dinoflagellate illnesses and cyanobacteria illnesses as well, especially in Florida. Then the human illness presented by exposure to fungi and other organisms in growing inside wet buildings (1998) followed. All these illnesses appeared the same: only different exposures separated the cases. Later in summer of 1998, along came visual contrast sensitivity, (VCS) the first objective test that ever showed us who was a case. All we had to go on was that the exposures were to biologically produced neurotoxins.

In 1999, Sam Donta, M.D. published his work on a neurotoxin made by *Borrelia burgdorferi* (Bb). He even obtained a US patent. So, I’m thinking, if Lyme made a neurotoxin, why not use the same fantastically successful protocol with it? Cases were confirmed and treated with reasonable courses of antibiotics, but 25% of patients stayed ill. VCS was positive, just like the other biotoxin illnesses. Symptoms were the same too.

I gave them CSM according to my nice neurotoxin model; I was stunned when about dose 6-10 the Lyme patients got horribly worse. When the data didn’t fit the CSM model, the model was wrong! What did I miss?

This was the first indication of the role of cytokines and what I was seeing was a cytokine storm. VCS fell in Row E and the Row D; MMP9, a measure of cytokine activity rose. This test was set up for me by Esoterix for the usual trade: cash.

Still my samples were the only ones the lab had. I was the only one who knew whether the patient was case or control. This same pattern occurs when Lyme patients experience worsening with use of antibiotics. What some in the Lyme community call a “Herx,” rarely actually is. VCS and MMP9 help shed needed light.

Use of protocols that block the intensification seen with CSM stopped the cytokine storm. After that hurdle was cleared, the Lyme patient progresses like any others using CSM, per the prior CSM model. We had now a basis to regard the Post-Lyme Syndrome as a CIRS.

Now the role of genetic susceptibility was identified. Strikingly, cases of mold illness had a marked “relative risk,” of the immune response genes or HLA DR. Sure enough Post-Lyme had their statistical association but different HLA haplotypes! This observation led to understanding the role of defective antigen presentation that underlies another element of chronicity. If the antigen isn’t presented properly then no antibody is formed. And if the antigen isn’t cleared by an antibody, then innate immune responses would persist. But those responses wouldn’t create illness if there were regulation of inflammation by melanocyte stimulating hormone (MSH) and vasoactive intestinal polypeptide (VIP). And look: those levels of regulatory neuropeptides were far too low.



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Now we are seeing the science of 2001. Genetic susceptibility leads to illness following exposures, governed by lack of regulation of inflammation and expanded innate immune inflammation. No wonder all our regular tests were normal: we hadn't done the ones that mattered! Since MSH also regulated ADH and ACTH, we looked at those hormones and sure enough, dysregulation was present in over 70% of cases.

Still some people stayed ill despite fixing all the newly confirmed elements. The plot shifts to Newcastle, NSW, Australia. There researchers, including Dr. Timothy Roberts, had told the world that supposedly benign coagulase negative staphs were bad actors in Chronic Fatigue Syndrome (CFS). Did we have these no-longer benign skin contaminants? For sure; they were multiply-antibiotic resistant and made biofilm. In biofilm, they differentiated to become functioning as a multi-celled creature, and not as the planktonic form of a free-living bacterium. These odd organisms (MARCoNS) made (1) antibiotic resistance factors just as fast as one could say "stop over-using antibiotics" and they (2) split MSH too. MSH eradicates MARCoNS and MARCoNS only lived in low MSH. Fascinating.

Missing pieces fell into place quickly; VEGF in 2002 to explain reduced anaerobic threshold and then the big one, split products of complement C3a and C4a told us about bacterial membranes (C3a) and capillary hypoperfusion (C4a).

But what about all the auto-immunity, especially in kids? I begged several labs to run a transforming growth factor beta-1 (TGF beta-1)

for me and finally in 2008, Cambridge Biomedical used my samples to validate a test that quickly was commercialised. We had an answer to hypermobility, restrictive lung disease, unusual neurologic illness and auto-immunity. Fascinating again.

Because of the interaction of TGF beta-1 with T-regulatory cells, once again a lab set up a test for me. Voila we had the basis for TH17/T reg imbalance.

Still, what did we know about genes? Since 2005 I had been collecting special tubes, called PAXgene tubes that blocked the breakdown of mRNA in white cells in peripheral blood. Once stabilised, these samples can stay in a frost-free freezer for years. Now that we can analyze the mRNA and indeed, using Next Generation sequences we can see thousands of genes, and not just protein coding genes, the age of genomic identification of a fingerprint of gene activation and gene suppression is upon us. Moreover, by using genomic therapies, we can show normalisation of changes in genes and normalisation of illness.

The journey has many more applications to guide us towards the future. Lyme is just one example of an illness with terrible diagnostic tests and much said about treatments that is simply guess and assumption. CIRS can lead us to the unveiling of the mysteries of Post-Lyme, but we must understand the nuances and clinical materials needed to stop guessing and start treating based on solid data.



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What are the symptoms of CIRS and how do they impact the body?

The symptoms of the various sources of CIRS are statistically indistinguishable. CIRS represents a final common pathway of all the pathways activated in CIRS (see Exhibit, symptoms by biotoxin illness). The impact on the body is profound as one might expect. Disability and cognitive impairment are common. Interestingly, the mystery of the common observation of “wacko” behaviour of some Post-Lyme patients, often labelled as psychiatric in origin is actually due to measurable changes in brain volumes and

atrophy of specific grey matter nuclei. These changes of microscopic edema and putamen atrophy seen in Lyme abate with CIRS therapies, but not with use of antibiotics.

The same kind of approach can be taken to understanding symptoms based on abnormal physiology. By defining the physiology, we define the illness. Use of symptom recording is required yet compared to genomics and proteomics, symptoms relative importance approaches zero.

Do you think many Australian’s are suffering from a combination of Post-Lyme and CIRS? If so, where can they obtain assistance?

Absolutely! Practitioners who have applied for certification in the Surviving Mold protocols include [Dr Sandeep Gupta](#); Dr Mark Westaway and [Dr Tania Ash](#). Dr. Gupta has completed his certification. He has a special section on the SM website dedicated to his understanding to the protocols.

Useful resources for patients and physicians from Dr Shoemaker

- View the [Biotoxin Pathway which outlines what Biotoxin \(such as Mold\) can do](#) for those who are genetically susceptible.
- View Dr Shoemaker’s presentation [Inflammation in Lyme disease only affects locations that receive blood flow](#) presented in 2014 at a Physician’s roundtable.
- [SurvivingMold.com](#) – Dr Shoemaker’s website has thousands of pages of materials that are free (for the most part) to users of the site.

The Lyme Disease Association of Australia has no financial interest or otherwise to declare regarding Dr Shoemaker’s visit or promotion of his resources.