

## Commentary

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# Nephrology should Trail Blaze the End of Chronic Disease

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If history can serve as a guide quite some time can lapse between the inception of a concept and its proof. For instance, Einstein had described the special theory of relativity in 1905, but he published the general theory of relativity only after thinking about the problems for 10 years. On March 29, 1919, the opportunity to get proof came. British Astronomer Sir Arthur Eddington had traveled to Príncipe Island off the western coast of Africa. His team photographed star fields during the eclipse and compared the photos with those of the same star field taken when the sun was not present. Eddington found the apparent location of the stars had shifted, just as was predicted by Einstein's theory. That 15-year delay between conception and proof did not cause suffering or deaths as was the case with the germ theory of Semmelweis, who did not live to see his momentous insight being accepted. He was declined reappointment and admitted to an asylum where he died after only two weeks with the following on his mind "When I look back upon the past, I can only dispel the sadness which falls upon me by gazing into that happy future when the infection will be banished . . . The conviction that such a time must inevitably sooner or later arrive will cheer my dying hour".<sup>1</sup>

The author postulates based on his personal experience and strive with cancer that the end of chronic disease is near. He postulates that chronic disease arises whenever the innate immune system turns on the body. He feels that he cannot justify to wait until the editor of a prestigious medical journal decides to allow his manuscript to get peer reviewed until he let his unified theory of the cause of chronic disease become known. Too much is at stake, patients suffer unnecessarily and great cost is added to our overburdened health care system. So he takes the occasion of the Einstein's anniversaries, 100 years relativity theory<sup>2</sup> and his 60<sup>th</sup> death anniversary together with the generous invitation of Nephrology open journal editor Ms. K. Jessie to publish his theory. He bases his theory on four facts (1) he had managed to suppress the pain of his chemotherapy-induced peripheral neuropathic pain by attenuating the activity of the complement system with the mega dosed antioxidants Pyrroloquinoline quinone (PQQ) and N-acetylcysteine (NAC). They create a reactive oxygen radical-free state that prevents the activation of Transient Potential Receptor ion channels which serve as pain receptors; (2) that the metabolic syndrome of his wife resolved when taking PQQ/NAC; there is an obvious explanation for this reversal of diabetes. In the absence of attack by the complement system on the insulin producing beta cells they can recover and repopulate from resident stem cells to respond to physiological stimuli again. We hypothesize that similar mechanisms may be at work in other chronic disease states like Multiple Sclerosis, Alzheimer's disease, Parkinson's, Macular Degeneration, and Amyotrophic Lateral Sclerosis; (3) that the severity and frequency of migraine attacks decreased with PQQ/NAC intake; (4) that the pathophysiology underlying diabetes and migraine both involve Transient Receptor Potential (TRP) ion channels. It appears that the use of PQQ/NAC in Nephrology will most quickly yield the results to support our hypothesis as a dysfunctional immune system has been shown to be involved in causing renal damage.<sup>3</sup> Based on this insight the highly potent complement inhibitor compstatin was designed.<sup>4</sup> However, the toxicity of this compound does not allow it to be administered to patients for prolonged periods of time. In contrast, PQQ/NAC are well tolerated, the author has used them to suppress his pain from peripheral neuropathy for over three years without experiencing any adverse side effects. According to the literature TRP ion channels have beneficial effects in some thirty medical conditions for many of which there currently exist no efficient therapies. Preventative long-term intake of PQQ/NAC is therefore a good way to swart off chronic dis-

ease and correct non-life threatening medical inconveniences. The challenge is now to quickly make PQQ/NAC available to as many people as possible in order to see chronic disease disappear within our lifetime. It took over a year to reverse diabetes but complement activity following dialysis is quickly assessed. The benefits of PQQ/NAC on the outcome of hemodialysis should be apparent after a few rounds of hemodialysis. If it turns out that we are correct with our assumption, PQQ/NAC has to be made available to as many people as possible in the shortest time feasible. Enforcing the food supply with PQQ/NAC is one way to do so, introducing gut resident bacteria that are able to produce high enough quantities of PQQ and NAC is another. We are pursuing both options and will bring our product, Novapyrin™, which contains both PQQ and NAC on the market. We are pursuing this option vigorously as it obviously is the final fix for a problem that Nature could not satisfactorily solve. Nature has put in place the superoxide dismutases to protect from damage from the superoxide radicals but could not find a way to handle the hydroxyl radical efficiently through enzymatic deactivation, likely because it would be difficult to bind. The efficiency of small molecule hydroxyl radical scavengers like glutathione or polyphenols is not strong enough to deal with this reactive small radical.

Our manuscript stating just the facts was apparently not exiting enough to catch the fancy of editors.<sup>5</sup> The thought that we need a sexier title occurred to me when I picked up the Science issue celebrating the 100 year anniversary of the Theory of Relativity. A Unified Theory of Chronic Disease could be put forward without the conclusive evidence in hand and would imply that there is a single therapeutic solution which I already had found. I saw this solution to my problem and to a pressing health issue with great clarity. This is was my idol ETH-Zürich Organic Chemistry Professor Vladimir Prelog must have experienced when he had his insight about chirality that brought him the 1975 Nobel Prize in Chemistry which was divided equally between John Warcup Cornforth “for his work on the stereochemistry of enzyme-catalyzed reactions” and Vladimir Prelog “for his research into the stereochemistry of organic molecules and reactions”.<sup>6,7</sup> There are other reasons why to publish this material. The birthday of genius author William Shakespeare falls on the 23<sup>rd</sup> as does that of my wife who wondered why my neuropathy was relatively mild while a much severe condition was sketched in a television ad for a product promising relief from neuropathic pain. She noted that I had unintentionally been on a diet rich in PQQ (green vegetables, yogurt, milk, vinegar-based salads) in preparation and after the cell stem transplant. She had some 20 years ago helped me in the laboratory with performing pyrroloquinoline determinations and still remembered the samples with high readings. So I ordered PQQ gel caps and experienced some relief the first night after taking it. As the dose of 10 mg was certainly a mega dose I expected full relief and had to experiment for a while until I found the formulation giving full relief.

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