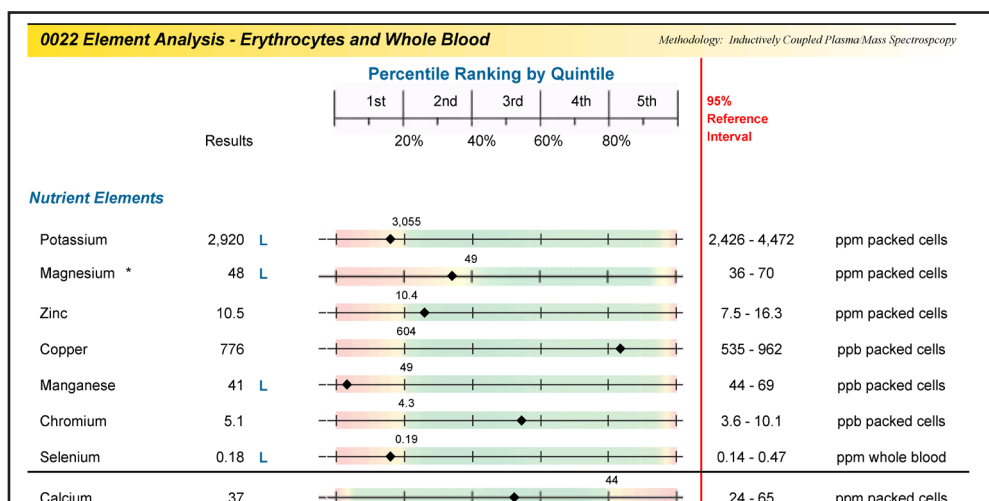


Low Erythrocyte Manganese & High Arsenic in Unresponsive Hypertensive Female Patient

Manganese superoxide dismutase (Mn-SOD) plays a pivotal role in endothelial vasodilation via its control of superoxide levels. Moreover, genetic polymorphisms in Mn-SOD have been linked with hypertension. Long-term, low-level arsenic exposure has also been linked with hypertension. High-dose manganese, removal of arsenic exposure and a concurrent detoxification protocol may therefore represent a novel strategy for controlling hypertension in this patient.

Case History

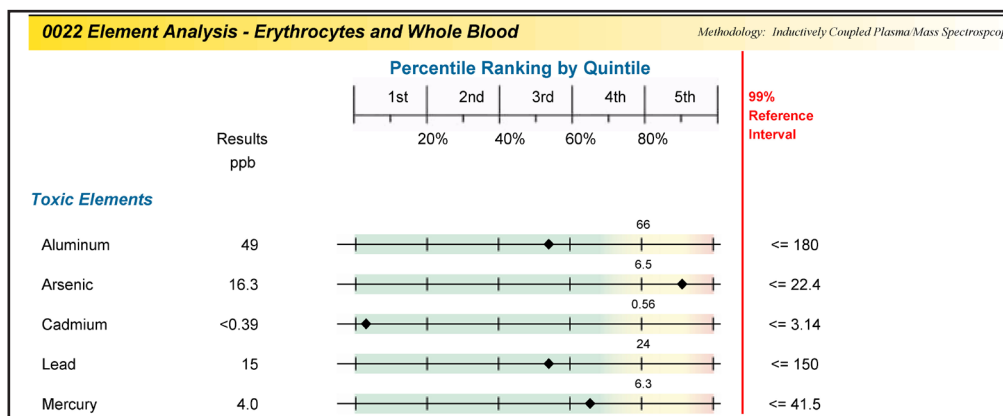
SC is a 42 y/o female with unresponsive hypertension. She lives on a rural property in far western Queensland with her husband. The entire population in her area rely on bore water obtained from the Artesian Basin for their drinking water. As such, there are reasonable grounds to suspect SC may be exposed to low levels of arsenic (a common contaminant of bore water in Australia¹). Her husband who suffers from unexplained very high ferritin levels has been tested for arsenic and found to have borderline high levels. SR is on a calcium-channel blocker and ACE-inhibitor for management of her blood pressure, albeit with little effect. Below are the results of her red blood cell element analysis.



Manganese-Superoxide Dismutase & Nitric Oxide Mediated Vasodilation

Mn-SOD is one of the three isoforms of SOD, which acts in the mitochondria. The other two isoforms of SOD, namely, zinc copper SODs act in the cytosol and extracellularly. Superoxide dismutases are enzymes that function to catalytically convert superoxide radical ($O_2^{\cdot-}$) to oxygen and hydrogen peroxide. Endothelium-

dependent, nitric oxide (NO)-mediated arteriolar dilation is known to be impaired in hypertensive patients due to increased generation of reactive oxygen species (ROS) such as superoxide.² Moreover, manganese has been shown both in vitro and in vivo to potentiate the activity of NO.³ It is possible, therefore, that genetic polymorphisms in the Mn-SOD gene may modify the ability of mitochondria to defend against oxidative stress, which in turn would negatively affect regulation of vasodilation.



Arsenic Exposure and Hypertension Risk

A number of research studies and review articles have linked arsenic exposure with an increased incidence and risk of hypertension and associated cardiovascular disease.⁴⁻⁶ One of the most common sources of low-level chronic arsenic exposure is through drinking water. In particular, artesian well water is a well-known source of inorganic arsenic. A group of researchers from Taipei, Taiwan have conducted a number of studies measuring the relationship between arsenic exposure and vascular disease in southwestern coastal areas of Taiwan, where residents have used high-arsenic-containing artesian well water for more than 50 years.^{7,8} One of these studies measured the association of four genetic polymorphisms in NAD(P)H oxidase, manganese superoxide dismutase, catalase and endothelial nitric oxide synthase (e-NOS) with arsenic-related hypertension risk.⁷ Relevant to this case study, the most significant finding to emerge from their research was that the Mn-SOD polymorphism was the most significant predictor of an increased risk of hypertension regardless of arsenic exposure.⁷ More specifically, the Mn-SOD gene polymorphism was found to modify the ability of mitochondria to defend against low-dose arsenic-induced oxidative stress, but play a less important role with high arsenic exposure.⁷

Mn-SOD Polymorphism & Low-Dose Arsenic Exposure Manifest as an Explanation for Unresponsive Hypertension...

The level of arsenic on SC's **Erythrocyte Element Analysis** can be considered to be borderline high or high-normal. Such levels may be reflective of long-term, low-dose arsenic exposure via drinking water at the patient's rural residence in regional Queensland. The very low levels of manganese may be a reflection that CR is carrying a genetic polymorphism in the Mn-SOD gene, which lowers the binding affinity of manganese and/or places SC at a higher requirement for manganese. The referring clinician may consider targeted high-dose manganese supplementation and use of a water filter to compensate for the possible polymorphic Mn-SOD gene and waterborne arsenic exposure respectively. Additional supplementation with selenium is also warranted due to the low erythrocyte levels and the vital protective role that selenium has been shown to play in individuals with arsenic exposure.^{9,10} A long-term detoxification protocol may also be required as individuals with previous arsenic exposure via artesian well water still show elevated urinary levels of arsenic even having stopped drinking well water for two to three decades.⁵

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