

The Global Rise of Chronic Diseases: Why Broaden the Paradigm to Include Tick-borne Illness and Environmental Toxin Exposure?

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The incidence of chronic diseases is rapidly increasing worldwide. It has been calculated that, in 2001, chronic diseases contributed to approximately 46% of the global burden of disease and 60% of the total reported deaths with that number expected to increase to 57% by 2020, when chronic diseases will account for almost 75% of all deaths worldwide [1,2]. The role of obesity, poor nutrition, physical inactivity, tobacco use, the harmful use of alcohol, as well as elevated blood pressure and blood glucose levels have all been validated as important variables in chronic disease [3]. These risk factors account, in part, for the top ten causes of disability and death worldwide, including non-communicable diseases (ischemic heart disease, strokes, chronic obstructive pulmonary disease), cancer, Alzheimer's disease and dementia as well as communicable diseases including infections like tuberculosis [4].

We also are presently experiencing a global spread of Lyme and associated tick-borne diseases through the bite of *Ixodes* species, which include *Ixodes scapularis* and *I. pacificus* in the United States [5-7] and *Ixodes ricinus*, the primary vector in Europe. Over the last two decades, there has been a 300% increase in the number of US counties affected by Lyme disease [6], with record numbers of new cases of tick-borne diseases reported to the CDC [8] including seven new infectious agents that can cause illness. These include *Borrelia mayonii*, *Borrelia miyamotoi*, *Ehrlichia ewingii*, *Ehrlichia muris eauclairensis*, Heartland virus, *Rickettsia parkeri*, and *Rickettsia* species 364D [9]. The 2017 national data

capture only a fraction of the number of people suffering with tickborne illnesses, since current Lyme disease testing may underestimate the true number of individuals affected [10-13] and under-reporting of vector-borne diseases is common, so the number of people actually infected is much higher accounting for a larger health care burden [14].

Concomitantly, there has been a significant increase in exposure to environmental toxins during the past several decades. The initial CDC report [15] evaluated more than 116 different environmental toxins and found a significant number of Americans were affected [15]. An updated report ("The Fourth Report") contains testing information on 75 previously untested compounds, (for a total of 212 compounds measured) [16]. Outcomes include blood and urinary levels of heavy metals (mercury, arsenic and lead), 30 different solvents, as well as levels of acrylamides, bisphenol A, phthalates, chlorinated and organophosphate pesticides and aromatic hydrocarbons. Standard medical care does not routinely measure the burden of these environmental chemicals and may underestimate their importance and health consequences. Similarly, testing for tick-borne diseases like Lyme disease can underestimate the true incidence of individuals affected due to the organism evading an immune response [17-21]. Considering our high levels of risk and exposure, are there potential interactions between the rising burden of tick-borne infections and environmental toxins that could account in part for rising rates of chronic diseases worldwide?

Both infections and toxins may increase an inflammatory response in the body [22,23] and 'growing evidence suggests a close link between inflammation and many chronic health conditions including diabetes, metabolic syndrome, cardiovascular disease, cancer, rheumatoid arthritis, inflammatory bowel disease, asthma, and chronic obstructive lung disease' [24]. There have also been published associations with rising rates of fibromyalgia [25] and chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) [26,27], where both disorders (which affect approximately 11 million people in the US and 3-6% of the world's population) have been linked to infection [28-32], toxins [33], and inflammation [34]. Similar patterns have been seen with rising rates of autoimmune disease which now affect over 23 million Americans [35]. Several autoimmune conditions have been associated with infections (*Borrelia burgdorferi*) [36-41], environmental toxins [42-45] and inflammation [46]. The same pattern has been shown to exist for rising rates of autism spectrum disorder (ASD), now prevalent in 1/59 children (1-2% of children born in North America and Asia) [47,48], with 1 in 6 children in the United States now suffering from mild to serious developmental disabilities [49]. Infections (*Borrelia burgdorferi*) [50], environmental toxins (including but not limited to mercury, lead, manganese, methylene chloride, diesel exhaust, pesticides) [51-54] and inflammation [55-57] have all been shown to have an association with autism and ADD. Infections and fat soluble toxins with a propensity for the central nervous system may similarly play a role with ALS [58,59] and Alzheimer's disease [60-64] where inflammation increases symptomatology [65-67]. As the US population ages, Alzheimer's disease will become an enormous public health problem [68], since 47 million people have now been estimated to suffer with pre-clinical Alzheimer's in the United States [69].

As we search for answers to mitigate the rising rates of these and other chronic diseases, a one cause, one disease model (Koch's postulate) is inadequate. A precision medical approach which addresses multiple underlying sources of inflammation and their downstream effects in a multifactorial model has the potential to improve health care outcomes [70-73]. Multiple factors causing inflammation on the 16 point Multiple Systemic Infectious Disease Syndrome (MSIDS) model [71,72] such as chronic infections [30,74,75], dysbiosis of intestinal bacteria [76], leaky gut with food allergies and sensitivities [77], sleep disorders [78,79], environmental toxins [80] and nutritional deficiencies [81-83] may all increase underlying cytokine formation and lead to downstream effects including endocrine disorders (low testosterone, low adrenal function) [73,84,85], neurological and psychological dysfunction [86-88], dysautonomia with postural orthostatic tachycardia syndrome (POTS) [89-

91], mitochondrial dysfunction [92,93], liver dysfunction [94-96], pain syndromes [97-100] and autoimmune phenomenon [38]. These factors may contribute to chronic fatiguing, musculoskeletal pain syndromes with neurocognitive difficulties, part of the spectrum of symptoms seen in many emerging chronic diseases.

As Lyme disease approaches endemic proportions in the United States and Europe [101-103] with both diagnosed and undiagnosed patients suffering from disabling chronic symptoms [104], leading to rising rates of disability [105] and where a large portion of the US population (12.8% to 25.9%) now reports medically diagnosed multiple chemical sensitivity (MCS) [106], it is incumbent on our health care system to improve diagnostic and treatment parameters for tick-borne illness, and begin to account for the large number of environmental chemicals entering our bodies. A One Health approach [107,108] which promotes integrated solutions for complex problems that impact the health of animals, humans and the planet, while considering multiple potential causes of illness [73] is an essential paradigm shift if we are to responsibly address the 21st century medical challenges before us.

Disclaimer

The views expressed are those of Dr. Richard Horowitz, and do not represent the views of the Tick-Borne Disease Working Group, HHS or the United States.

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