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A HEALTH CRISIS? TOXIC BURDEN IN THE 21ST CENTURY

Mainstream medical organizations have begun to acknowledge environmental toxins' impact on human health and disease. For example, the World Health Organization (WHO) recognizes that at least 24 percent of the global chronic disease burden is due to preventable environmental factors, including environmental toxin exposure.[1] Common environmental toxins to which we are exposed daily include, but are not limited to:

- Heavy metals, such as mercury, cadmium, and lead
- Toxic air pollutants, including PM2.5, microscopic mixtures of solid and liquid particles found in the air and emitted by construction, combustion, and automobiles
- Per- and poly-fluoroalkyl substances (PFAS)
- Pesticides, such as organochlorine pesticides
- Herbicides, such as glyphosate
- Polychlorinated biphenyls (PCBs)
- Phthalates
- BPA
- Mycotoxins

Environmental toxins exert far-ranging effects on our health, impacting our mitochondria and numerous body systems, including the cardiovascular, immune, neurological, gastrointestinal, and endocrine systems.

Mitochondrial and Metabolic Dysfunction

Toxins do a number on our mitochondria, the powerhouses of our cells. By damaging mitochondria, toxins can also compromise our metabolic health, including blood sugar and lipid homeostasis. In addition, environmental toxins can compromise mitochondrial function by inhibiting the mitochondrial electron transport chain (ETC), uncoupling oxidative phosphorylation, and reducing mitochondrial antioxidant capacity.[2] Inhibition of these mitochondrial elements impairs ATP generation and has downstream effects on aspects of our metabolism, including insulin sensitivity.[3] A reduction in insulin sensitivity is associated, in turn, with body fat accretion, prediabetes, and type 2 diabetes.[4]

Various toxins can also alter lipid homeostasis, including cholesterol levels inside the body.

Cardiovascular Dysfunction

The cardiovascular system, consisting of the heart, blood vessels, and blood, is susceptible to the effects of environmental toxins.

Research indicates that fine particulate matter (PM2.5) promotes atherosclerosis by damaging the vascular endothelium, the single layer of cells that constitutes the inner cellular lining of arteries, veins, and capillaries.[5] PM2.5 refers to particulate matter with a diameter of less than 2.5 µm and is derived primarily from the combustion of fossil fuels, diesel exhaust, and indoor cooking activities.[6]

Injury to the vascular endothelium may make it more prone to plaque accumulation, a characteristic feature of atherosclerosis.[7]

Heavy metal exposure may also drive cardiovascular dysfunction. Research indicates that elevated cadmium, lead, and mercury levels are associated with a heightened 10-year risk of cardiovascular disease (CVD). Heavy metals may drive CVD by triggering dysfunction of the renin-angiotensin system, resulting in a rise in systolic blood pressure that strains the cardiovascular system.[8] Heavy metals can also disturb redox balance, the balance between oxidative stress and antioxidant activity in the body, resulting in excessive oxidative stress that harms vascular endothelial cells.

Environmental endocrine disruptors (EEDs), chemicals that interfere with any aspect of hormone action, may also drive cardiovascular disease.[9] EEDs such as BPA, phthalates, and organochlorine pesticides may also drive cardiovascular dysfunction. For example, BPA may drive cardiovascular dysfunction by affecting nuclear receptor and calcium ion channel signaling, causing oxidative stress and atherosclerosis.[10] Exposure to phthalates found in vinyl flooring, air fresheners, and personal care products may drive CVD by altering the body's lipid profile.[11]

Organochlorine pesticides, which are widely used worldwide, may precipitate CVD through reactive oxygen species (ROS) generation and depletion of nitric oxide (NO), though more research is needed to elucidate the potential mechanisms of action.[12] Nitric oxide is needed to regulate vascular tone and platelet aggregation and inhibit the adhesion of white blood cells to the vascular endothelium; without sufficient nitric oxide, blood pressure and clotting mechanisms are impaired, thereby driving cardiovascular disease.

Immune Dysfunction

The subject of toxins and their impact on immunity is germane to our society today, in light of the recent global pandemic. Exposure to toxic substances degrades the immune system, rendering the body more susceptible to exploitation by pathogens. Therefore, toxicology-focused strategies, including detoxification strategies, should be implemented for optimal long-term immune system health and resilience.[13]

Toxins degrade and dysregulate the immune system through multiple mechanisms. For example, mycotoxins can suppress innate and acquired immunity, immobilizing critical immune defenses and upregulating sterile inflammation, effectively distracting the immune system from more pressing threats.[14]

Perfluoroalkyl and polyfluoroalkyl substances (PFAS) may also degrade immune function. PFAS are synthetic molecules that contain fluorine, a member of the halogen element family, which also includes iodine. PFAS are a product of the "better living through chemistry" movement that began in the 1930s when chemical manufacturing behemoth DuPont developed this catchy slogan. Unfortunately, PFAS has ultimately led to "environmental degradation chemistry" due to their high resistance to degradation in the environment, giving them the nickname of "forever chemicals." PFAS are ubiquitous in stain-resistant fabrics, non-stick pots and pans, and other consumer goods designed to repel water and grease.

Research demonstrates that higher levels of PFAS in the body are associated with higher rates of infectious diseases in children, including stomach flu, bronchitis, and pneumonia.[15] The proposed mechanism of action is that PFAS targets antibody-producing B cells in the body, reducing antibody production to pathogens and thus the antibody response to infection, making the body less capable of fighting infections. In some situations, PFAS may also overactive the immune system, driving immune conditions such as asthma.[16] The U.S. National Toxicology Program has gone so far as to suggest that PFAS are "presumed to be an immune hazard to humans."[17] Furthermore, "forever chemicals" can take what seems like "forever" to be eliminated from the body; the half-life of PFOA in humans is over the timespan of years.[18]

Chemical plasticizers, including BPA and phthalates, also demonstrate harmful effects on immune function. For example, during fetal development, BPA exposure induces epigenetic and cell signaling changes in branches of the immune system that drive allergies, asthma, and autoimmune disease.[19] Phthalates stimulate innate immune cells, which elicit an inflammatory response while suppressing adaptive immune cells that mediate long-term immunity to pathogens and other environmental compounds.[20,21]

Furthermore, metabolic dysfunction is a driver of immune system dysfunction.[22] And both types of dysfunctions can be initiated by toxins, suggesting a need to focus on supporting a healthy metabolism to maintain optimal immunity.

Neurological Dysfunction

Neurological conditions, including neurodegenerative diseases like Alzheimer's and Parkinson's, and disabilities such as ADD and autism, are rising. For example, an estimated 6.2 million Americans ages 65 and older are currently living with Alzheimer's disease (AD), which is projected to grow to 13.8 million by 2060.[23] Furthermore, these figures don't account for individuals with mild cognitive impairment (MCI), the precursor to AD. According to the CDC, autism has risen to a shocking prevalence of 1 in 45 children.[24] and about 9.4 percent of children between the ages of 2 and 17 have been diagnosed with ADHD.[25] A growing body of research indicates that an assortment of toxins may drive neurological dysfunction.

Mycotoxins, substances produced by toxic molds, are implicated in Alzheimer's disease development.[26] Mycotoxins are small enough to cross the blood-brain barrier (BBB), a semipermeable layer of endothelial cells that regulates the entry of substances into the central nervous system (CNS).[27] Mycotoxins may drive neurodegeneration by increasing oxidative stress in neurons, which causes neurotoxicity and impairments in brain function.[28]

Mercury is a well-known neurotoxin; in fact, the saying "mad as a hatter" is derived from dementia and insanity that beset many in the hat-making industry in the 19th century, when mercury was used for preparing pelts and hats. Through its neurotoxic mechanisms, methylmercury exposure may accelerate brain aging and promote early-onset cognitive decline in exposed individuals.[29]

Exposure to fine particulate matter in air pollution and inhalational exposure to pesticides may promote the accumulation of beta-amyloid and hyperphosphorylated tau, two malformed proteins involved in the pathogenesis of AD that form plaques between neurons and disrupt neuronal function.[30,31]

GI Dysfunction

The gastrointestinal (GI) system is the primary interface between the interior of our bodies and our external environment. Therefore, anything that we ingest, including toxins, must pass through the GI system; the GI system is thus highly susceptible to the adverse effects of toxin exposures.

Environmental toxin exposures can degrade GI health by altering the gut microbiota, the collection of microorganisms colonizing the GI tract.[32] Toxins that alter the gut microbiota include arsenic, pesticides, and the synthetic antibacterial agent triclosan.[32] Mycotoxins degrade the gut by increasing intestinal permeability, thereby driving leaky gut and altering the gut microbiota.[33]

Finally, the pervasive herbicide glyphosate is designed to disrupt a biochemical pathway called the shikimate pathway in many weeds. However, the shikimate pathway is evolutionarily conserved and found in many commensal gut bacteria. Thus, glyphosate exposure through ingestion of contaminated food and environmental contamination may drive undesirable gut microbiota alterations.[34]

Hormone Dysfunction

The neuroendocrine system encompasses the hypothalamic-pituitary-adrenal (HPA), hypothalamic-pituitary-thyroid (HPT), and the hypothalamic-pituitary-gonadal (HPG) axes. The hypothalamus, a small gland in the brain, is the central regulator of the neuroendocrine system, ultimately coordinating the activity of nearly every hormone in our bodies.

Many toxins interfere with our neuroendocrine system; collectively, these chemicals are called "endocrine disruptors."

Two ubiquitous endocrine-disrupting chemicals, BPA and dioxin (dioxin is no longer manufactured in the U.S. but persists in the environment), accelerate reproductive system aging, shortening the reproductive life cycle.[35,36] These toxins exert epigenetic effects that change how hormones are synthesized and metabolized inside the body.

Phthalates, another endocrine disruptor commonly found in consumer goods, are linked to various adverse hormonal outcomes, including altered puberty, testicular dysgenesis, premature ovarian failure (POF), and altered ovarian and uterine function.[37]

Conclusion

Environmental toxins are pervasive; even the most "pristine" environments are now affected. These omnipresent substances can impact every system in the body, leaving no aspect of our physiology unscathed. This compilation of data shows that the more exposure and accumulation of toxins in the body, the greater the likelihood of those toxins exerting a dangerous combination of effects to long-term health.[38,39,40]

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