ENVIRONMENTAL MEDICINE PART III, IMMUNOTOXICITY

David G. Schwartz, M.D. September 27, 2020

The immune system is an incredibly complex system, probably as complex as the brain. We often think of the *endocrine* system as a symphony conductor, for the dance and the music, for all systems to work in harmony. The immune system *also* seeks to maintain harmony. It is too often seen in simplistic terms, as an army that seeks to kill off anything that is not the body, not the self, discerning between "self and non-self." To the contrary, it is sublimely complex. Matt Richtel, author of <u>An Elegant Defense</u>, portrays the immune system as both a bouncer and a ballet dancer. Another author described it as a panel of attorneys deciding which things belong where and when and how.

When the immune system is working well, we can enjoy excellent health. Occasionally the immune system goes awry, with chaos and disorder introduced into the system, and we may see autoimmune diseases, allergies, cancer, or sepsis.

So to simply say we want to "boost" the immune system is far afield from what our goal should be. To harmonize or modulate the immune system would be a better approach. This system can be overactive in one aspect, and under-active in another, at the same time. It is one of the marvels of nature that such a complex system is so finely tuned when working well. To use a drug to block antibodies for autoimmune conditions or to stimulate antibody production for cancer can sometimes work well, but at other times it can act like a baseball bat in a candy store. A simple method trying to solve a complex problem. Vaccines have done wonders to stop many deadly infections, but too many vaccines repeatedly for less serious infections may be providing more "stimulation" of the immune system than is desirable, considering that most of the chronic diseases are caused by inflammation, a result of an activated immune system.

This gives us some appreciation for how marvelously the immune system works naturally, and it would seem that the most natural agents such as plant substances, with which the immune system is familiar, which also work in complex ways, might be more compatible with a complex human immune system. Yet when life or limb are at stake, we have to resort to drugs, which work more quickly, in spite of their complications, as "side effects."

Given that background, let us observe that many of the immune disorders previously mentioned were uncommon or rare 100 years ago. What has happened that has derailed this beautiful, incredibly intelligent system to render it subject to chaos and disorder? When something naturally is in such a delicate balance, it may not take much to throw it off; however, this system is incredibly resilient, so that if it is thrown out of balance, it is often able to correct itself. So when it is out of balance, what must have been the major repeated assaults that drove it to the situation it is in?

Our frantic pace of modern materialistic lifestyle and poor food choices do not support the resilience of a healthy immune system, but the major "elephant in the living room," is very likely the inundation of our planet with thousands of toxic chemicals that are disturbed, mined, or manufactured by humans, and with which our bodies are not familiar.

First of all, it would make sense to clean up our planet (first do no harm). Meanwhile, we have to deal with the mess we are in.

Enter environmental medicine.

The environmental medicine textbook describes immunotoxicity that has high prevalence in the population, and what we can do about it.

Allergies occur when the immune system thinks that a usually benign substance (or not so benign) is a threat, and it tries to attack it with histamines, cytokines, and antibodies. In the process, it can harm many other systems. Common substances that provoke the development of allergies are: vehicular exhaust, second hand tobacco smoke, chemicals from indoor building materials, perfluorocarbons, phthalates, organophosphate (OP) pesticides, solvents, cleaning supplies, lead, chlorinated pesticides, PCB's, and mold.

Allergies are more common in people with family histories of allergies, but environmental chemicals are often the trigger that leads to sensitivity to these natural substances. Asthma, atopic dermatitis, allergic rhinitis, conjunctivitis, eosinophilic esophagitis, anaphylactic reactions to foods, and celiac disease, all have increased around the world in the last few decades.

Vehicular exhaust creating carbon monoxide (CO), "coarse" particulate matter, particles with size less than 10 micrometers (P₁₀), and less than 2.5 micrometer particle size (P_{2.5}), resulting in elevated indoor levels of these pollutants, are related to higher levels of allergic rhinitis and asthma. As children continue to be exposed to exhaust, by age 4, the rates of food allergies double, and pollen allergies increase by 80%. Children living within 200 meters of a major roadway have much higher rates of allergic rhinitis than those living farther away.

The highest risk for allergic disorders occur near roadways with high diesel truck traffic. Diesel exhaust particles (DEP) are the worst of the vehicular exhaust in its effects on the immune system, which are not only allergic disorders, but weakened defenses against infections. The antiviral cytokine IFN-γ (interferon gamma) is reduced by DEP more than by the immunosuppressing drugs dexamethasone and cyclosporine. DEP exposure increases the rate of respiratory infections due to decreased natural killer cell activity, a Th 1 function. The Th 2 functions associated with allergies is also increased. Most pollutants cause this shift from Th 1 dominance to Th 2 dominance, resulting in more allergies *and* infections, and more Th 17, which promotes autoimmune conditions. (The T-lymphocytes are categorized into Th 1, Th 2, etc.) The DEP exposure, for example, results in increased reactivity to ragweed, cedar pollen, birch pollen, and egg protein. The increased use of diesel engines worldwide is probably a major factor in the global increase in asthma.

Indoor air pollutants, mold, environmental tobacco smoke (ETS), building and yard chemicals, solvents, perfluorocarbons, phthalates, and trichlorethylene increase rates of allergies and asthma, many increasing the Th 2 response and decreasing Th 1.

Mold illness has been extensively covered in the book report on <u>Break The Mold</u>, in the archives. This is a much more devastating illness than mere allergies. In this context, we see mold as increasing asthma, rhinitis, and eczema.

Other indoor air pollutants that increase allergies and/or asthma include synthetic carpets, new wall covering, recent painting, new furniture, plasticizers, and pesticide treatment, as well as lead, PCB's, and dioxins.

Household cleaning sprays used 4x weekly resulted in double the risk of asthma. The greatest association was found in kitchen cleaning and furniture polishing. People who clean other people's houses are 3x more likely to develop asthma. The solvents in cleaning supplies, paints, and building materials that lead to allergies are commonly toluene, xylene, ethyl benzene, and chlorobenzene.

Perfluorooctane sulfonate (PFOS) in Scotchguard treatment of clothing, carpeting, and upholstery, is released into the air and is found in the urine of most people, also creating a Th 2 dominance and increased allergic reactivity.

Phthalates are added to plastics to make them more flexible, but they are weakly bound to the plastics and are easily released into the surroundings, and they can be carried by dust throughout the house. They are in shower curtains, toys, PVC flooring, furniture polish, plastic food wrap, liquid personal care products, nail polish, fragrances, etc. They increase Th2 dominance and are associated with increased allergies and asthma. Trichlorethylene (TCE) has contaminated ground water in many areas and is associated with higher rates of allergies, asthma, and other chronic conditions.

At least 20 different contaminants are known to decrease Th 1 and increase Th 2 activity. PM, diesel exhaust, cigarette smoke, TCE, PCB's, and Paraquat are linked to increased Th 17, which is connected to autoimmunity. Autoimmune conditions such as Lupus, Rheumatoid Arthritis, type I diabetes, and thyroiditis, to name a few, are correlated with pollutants. Some of the main toxicants are vehicular exhaust, heavy metals, (especially mercury), PCB's, pesticides, TCE, lead, and OP (organophosphate) pesticides.

Average rates of Lupus erythematosis vary from 15 to 50 cases per 100,000 populatuion, but the rates in an African American community near a local industry go up to 1000/100,000. The residents of a 2 block area where oil field waste had been previously stored had rates of 872/100,000, had high exposure to benzene, xylene, toluene, polycyclic aromatic hydrocarbons (PAH's), and high blood levels of mercury. Hair dye, nail polish, and paints are all related to high rates of Lupus. TCE from contaminated municipal drinking water, smoking, PCB'S, pesticides, PM_{2.5}, NO₂ and CO are risk factors for developing Lupus.

Reumatoid Arthritis risk is increased by vehicular exhaust, PCB's, and cadmium, nickel, and lead in hair and blood.

Type I Diabetes has higher risk with PM, and autoimmune thyroiditis antibodies are increased with higher blood mercury levels and PCB's.

Neurological autoimmune diseases such as MS, Guillian Barre, and antibodies to myelin basic protein with symptoms of headaches and neuropathies, are related to PM and lead.

Conversely, when the immune system shows weakness, such as difficulty defending against infections, with a diminished Th1 response, often caused by pollutants, this increases the risk of chronic cytomegalovirus, chronic hepatitis C, RSV, HIV, and Lyme.

Diminished Th1 from exposure to chlorinated pesticides, solvents, arsenic, and other heavy metals also result in increased risk for Herpes Zoster (shingles), and chronic Epstein-Barr Virus (EBV) infection.

PCB's in mother's milk are connected with increased childhood infections. Likewise prenatal exposure to DDE, dieldrin, and hexachlorobenzene increase the risk of ear infections. Blood mercury, and exposure to PCB's and perfluorocarbons result in lower levels of post vaccine antibodies against measles and diphtheria.

Chemical sensitivity (CS), also called by many other names, including multiple chemical sensitivity (MCS), now occurs in 20% of the population. People with this get adverse physical, emotional, or mental symptoms upon exposure to a variety of common environmental chemicals, at doses far lower than those that cause symptoms in the general population. Characteristics of this syndrome: Symptoms are reproducible with repeated chemical exposure, the condition is chronic, symptoms improve when exposure is removed, and symptoms involve multiple organ systems. The immune system is dysregulated, and neural sensitization, and limbic kindling (a recurrent, excess emotional response) occur. Studies show elevated production of T-cell-derived antigen binding molecules, that increase with increased exposure, inflammatory cytokines, neuroinflammation, asthma, and allergies.

The most common exposures that initiate the development of this syndrome are pesticides and solvents. The people with this syndrome often have a genetic deficiency of paraoxonase 1 (PON1), an enzyme for the breaking down of OP pesticides and solvents.

So this is another immune disruption that can be very debilitating, and previously found mostly in adults, unfortunately now in very young children. So if you know someone who reacts to almost everything, when other people do not, believe them. It's not a hypochondriacal or psychiatric or imaginary condition. It is real, and it is caused by chemical pollution.

How to protect and heal the immune system? Avoidance is always the first step. First, eliminate off-gassing home products, especially solvent-containing cleaners and PFO's and phthalate containing products. Removing shoes before coming into the house reduces PM and PAH's. Electrostatic pleated air filters on HVAC systems with a minimum efficiency rating value (MERV) of 7 reduces PM and also household dust, on which many semi-volatile pollutants "catch a ride." In addiction, high quality air purifiers reduce indoor pollution as well as that from the outside air, and they have been shown to reduce hsCRP, a blood marker for inflammation in the inhabitants. Use of face masks outside in urban areas has been shown to improve endothelial (artery inner lining) function. Remediate any moldy drywall or other household structures and avoid inhaling in areas that smell moldy.

In areas with arsenic or TCE in groundwater, a reverse osmosis (RO) water filter is needed, for drinking and cooking.

Avoid mercury by not eating high-mercury fish, and don't get mercury (silver) fillings in teeth. Eat only organic foods, or at least the vegetables and fruits that are not on the "dirty dozen" list by the Environmental Working Group.

Cleansing or depuration techniques have been proven to be highly effective for improving the conditions of people with CS, autoimmune conditions, and allergy.

The most effective dietary interventions are the Mediterranean Diet (MD), wild caught small fish, cruciferous vegetables, turmeric, and green tea.

The MD seems to be the most powerful anti-inflammatory diet available. People who ate the MD had much lower rates of asthma and allergies, and those who switched to the MD improved their

conditions markedly. The brassica family of vegetables have several sulfur-containing compounds that help the removal of toxicants and reduce their damage. Especially sulfurophane promotes increased production of glutathione, needed for detoxification of many chemicals, and this decreases inflammatory cytokines from Th2 and Th17 dominance.

Curcumin, in turmeric, enhances glutathione activity, reduces Th 2 dominance, restores Th 1 function, and reduces inflammatory markers. Green tea also enhances glutathione and reduces Th 17 activity and autoimmunity markers.

Supplements are also useful. NAC, (n-acetyl cysteine) increases glutathione levels, and reduced airway reactivity to diesel exhaust in volunteers. Vitamins A and D reduce inflammatory cytokines. Several different probiotics have been found to reduce allergic symptoms.

Read Dr. Walter Crinnion's book, Clean, Green, and Lean, or my book report on it in the archives.

Our health vitally depends on a well-functioning immune system. Let's keep things as clean as possible. If you haven't read Parts I and II, they can give an overall view of environmental medicine. And be an environmental activist to change public policy to limit the polluting.

Next month I will take a break from environmental medicine and talk about fiber and the microbiome. Sounds boring? Not. An amazing fuel for the immune system and all other parts of the body.