ENVIRONMENTAL MEDICINE PART IV, Cardiovascular Disease and Cancer,
From the Clinical Environmental Medicine textbook, by Crinnion and Pizzorno
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Environmental pollutants play a huge role in the promotion of the two biggest killers, cardiovascular disease (CVD) and cancer. Along with the other common lifestyle recommendations for lowering the risks for these 2 scourges, we need to wake up to the dangers of these poisons in regard to those major diseases. CVD, the leading cause of death in the US, includes hypertension, stroke, myocardial infarction (m.i.), congestive heart failure, and stroke. Atherosclerosis is the major underlying mechanism in all these conditions. One of the best markers for atherosclerosis' development and progression is carotid intima-media thickness (CIMT). As CIMT increases, the risk of stroke increases 32% for each standard deviation, and that for m.i. increases 26%.

Environmental toxicants still have not been added to the standard list of risk factors, such as physical inactivity, diabetes, obesity, family history, etc., yet these primary toxicants head the list of pollutants that raise CVD risk: Air pollution from vehicular exhaust, tobacco smoke, PCB's, Bisphenol A, phthalates, and heavy metals.

Although the American Heart Association website does not list air pollution as a main modifiable cause of CVD, an AHA expert panel published a statement in 2004, concluding that short-term exposure to elevated particulate matter (PM) significantly contributes to CVD mortality, that hospital admissions for acute heart and lung disease increase in response to higher ambient PM levels, and that prolonged exposure to PM reduces life expectancy by several years.

Then after reviewing the research between 2004 and 2015, a more recent AHA panel with many of the same experts concluded, "There is now abundant evidence that air pollution contributes to the risk of cardiovascular disease and associated mortality, underpinned by credible evidence of multiple mechanisms that may drive this association. In the light of this evidence, efforts to reduce exposure to air pollution should urgently be intensified and supported by appropriate and effective legislation." What about the Clean Air Acts of 1970 and 1990? Well, the air still isn't so clean. Why is this info not part of the main established risk factors for CVD?

PM causes oxidative damage to tissues and is associated with increased mortality from not only CVD, but cancer and respiratory conditions. Adsorbed onto PM are multiple polycyclic aromatic hydrocarbons (PAH's) and other volatile organic compounds. One of these is benzo-a-pyrene, a combustion product. Urinary levels of its metabolite (1-OHP) are found in people with myocardial infarction, and with the inflammatory marker HS-CRP, associated with CVD, and lower levels of antioxidants. PM_{10} increases platelets, fibrinogen, and HS-CRP, all of which are risk factors for CVD.

People living in larger cities are 16% more likely to die premature death than people in cities with less polluted air. Each 10 mcg/m^3 of $PM_{2..5}$ increased the risk of heart disease by 43%, and death by m.i. by 64%. In people with acute m.i., those who lived within 100-200 meters from a major roadway were 19% more likely to die of their heart attack than someone living more than 1000 meters away. For those at high risk for acute m.i., exposure to vehicular exhaust triples the risk of having an m.i. within one hour after exposure.

Regarding the CIMT as a measure of atherosclerosis, areas with highest concentrations of $P_{2.5}$ in the air, for every 10 mcg/m^3, of $P_{2.5}$, the CIMT increases by 5.9%. Residents of Los Angeles with the

highest $P_{2.5}$ levels have 3 times the CIMT of people in cleaner areas of the county. Average annual progression of CIMT for urban dwellers is 2.04 µm per year, but for those living within 100 meters of a highway, the annual progression is double that amount, 5.62 µm per year. $P_{2.5}$ in indoor air (coming from the outside), also correlates with higher CIMT annual increase. Every decrease of 1 mcg/m^3 of $P_{2.5}$ is rewarded with 2.8 µm per year decrease in annual progression of CIMT. This shows the benefit of having a high quality air purifier, especially if living in an urban area or near a highway. $PM_{2.5}$ is also correlated with higher BP., as people moving from suburban to urban areas with high $PM_{2.5}$ show an increase in blood pressure.

Myocardial ischemia, lack of blood perfusing the heart muscle, can be monitored by the electrocardiogram (ECG), specifically depression of the ST segment. In Los Angeles, an area with very high pollution, people with coronary heart disease had their ST segments monitored. For every quartile increase of aromatic hydrocarbons in the air, they had a 15% increased risk of ST depression. When 20 men did moderate exercise, they had some ST depression. When they were exposed to diesel exhaust particulate (DEP) exposure during exercise, The ST depression was triple that with no exposure. They also had a greater measure of the tendency for blood clotting. Oxidized LDL is associated with plaque in the carotid arteries. The farther people lived from a busy roadway, the less oxidized LDL. Each doubling of the distance was accompanied by a 2.9U/L decrease in oxidized LDL.

Indoor air pollution contributes also to CVD risk. Solvents in hair salons increase risks. Elevated CRP indicates inflammation, and 8-hydroxy deoxyguanosine (8-OHdG) elevated means oxidative stress. On off days, workers at the salons had CRP average 1.1 mg/dL and 8-OHdG at 0.6 mcg/mL. On work days these numbers jumped to CRP of 10.9, and for 8-OHdG it was 4.5. Airborne volatile organic compounds (VOC's) was 44 PPB on non working days and 75 PPB on working days. Less than double the concentration resulted in many times more increase in the markers for health risk. Cleaning sprays, air "fresheners," and other scented home products reduced heart rate variability (HRV) significantly. Low HRV is associated with increase risk for CV events and mortality. Second hand smoke or environmental tobacco smoke (ETS) makes high risk for CVD. Minnesota had 33% reduction in acute m.i.'s, and sudden cardiac death declined by 17%, in the 18 months after enactment of a law forbidding smoking in public spaces.

Persistent organic pollutants (POP's, such as dioxins, PCP's, and chlorinated pesticides are called persistent because they stay in body fat for years and decades. Any amount of these substances detected in the blood shows increased CV risk, and of course, greater levels in the blood multiplied the risk level. The most common dietary sources for PCB's are farmed salmon and sardines. So much for eating fish to improve health! If salmon is labeled "Atlantic Salmon" or just plain "Salmon," you can bet that it is farmed. Otherwise, it has to specify "wild caught." Swedish seniors with higher levels of PCB's had more carotid artery atherosclerosis than those with lower levels, and higher levels were associated with lower left ventricular ejection fraction. PCB serum levels in residents of Annistan AL, living near a Monsanto plant that manufactured PCB's for decades, were correlated with higher systolic and diastolic BP.

Urinary Bisphenol-A (BPA) can increase by 1600% by drinking beverages from cans vs glass. Higher BPA levels correlate with higher BP. Maternal exposure to BPA confers risk of HBP to offspring. Some studies showed increase carotid atherosclerosis with increased BPA levels, and one showed that the risk of developing coronary artery disease (CAD) in the next 10 years was linked to BPA levels. Each 4.46ng/mL increase in urinary BPA increased the CAD risk by 13%.

Heavy metals also increase CVD. Lead increases BP by multiple mechanisms, including kidney damage, oxidative damage, reduction of available nitric oxide (NO), increasing vasoconstrictive prostaglandins and altering the renin-angiotensin system. Higher blood levels of lead correlate with higher systolic and diastolic BP. Blood lead and tibial bone lead levels also increase risk of ischemic heart disease. A twelve year study showed that people with blood lead levels greater than 3.62 µg/dL (approximately in the top 75th-90th %ile) were 55% more likely to die of CVD and 25% more likely to die of all causes.

Mercury increases CVD, BP, and atherosclerosis. Data from NHANES (National Health And Nutrition Examination Survey) 1999-2000 showed that for every 1.3 µg/L blood mercury level, systolic BP increased 2 points. Residents of Minimata, Japan, after that major spill of mercury into the bay in 1956, had a 60% greater likelihood of becoming hypertensive, and a 40% increased risk persisted 50 years later. As hair mercury increased, the CIMT also increased, indicating increased atherosclerosis. Increased hair mercury strongly correlates with a 56% greater risk of having coronary heart disease, and 60% increase for risk of acute m.i. The mercury in fish decreased the beneficial effects of the omega-3 oils in fish.

Data from 1999 to 2006 NHANES trial showed a clear correlation of blood cadmium levels with stroke and heart failure.

Higher urinary arsenic levels are correlated with higher rates of coronary heart disease and stroke.

Obesity and diabetes are also driven by pollutants, and they in turn drive CVD. See Dr. Crinnion's book Clean, Green, and Lean, and my article on that.

To assess exposure and toxic load of chemicals, urine and/or blood can reveal exposure to BPA, phthalates, arsenic, lead, mercury, and PCB's.

The most important intervention is avoidance. HEPA (high efficiency particulate air) face masks worn outside reduce $PM_{2.5}$ and improve cardiac function, and reduce blood pressure and cardiac symptoms. Indoor air purifiers that reduce PM burden by 98% are recommended. Avoid phthalates, parabens, and phenol-containing compounds, high mercury fish, and farmed salmon and sardines. Fish oil supplements appear to decrease adverse cardiac effects of PM's. Intravenous calcium EDTA can decrease lead levels, increase nitric oxide, and lower BP. Saunas can reduce P.O.P burden and lower the risk of fatal CVD and CAD, and improve cardiac function for those with heart failure.

Cancer is also an environmental disease. We want to focus on prevention and risk reduction, as it is a bit late after cancer has progressed, to remove the causative environmental insults. For secondary prevention after a small malignant tumor has been removed, presumably "cured," that is an excellent opportunity, a "teachable moment," to intervene with protective measures. Once a person has any form of cancer, the risk becomes much higher for the occurrence of a second or third type of cancer. That person likely has defective detoxification genes and enzymes and needs nutritional assistance in supporting those detoxification methods. Genetic tests are available to see which detox pathways are most affected.

Since treatment of cancer in general, although having more success in recent years, does not have very great odds for cure, it behooves us to focus on prevention. We could reduce the incidence of cancer in the population immensely by eliminating most exposure to toxicants. Most of the common types of cancer today were very rare before the beginning of the industrial age.

Conventional public conversation about preventing cancer mostly focuses on early detection with cancer screening, for early treatment. The American Cancer Society does emphasize nutrition and other lifestyle factors, but what is needed is a concerted effort to avoid exposure to toxic chemicals as much as possible, and to support and improve detoxification, especially for people with genetic detoxification defects.

Environmental risk factors for cancer are pollutants in air, water, and food, including cigarette smoking, solvents, pesticides, toxic metals, ionizing radiation, and biological toxins.

How toxins promote cancer is complex, and it involves oxidative stress and inflammation causing nuclear DNA and mitochondrial DNA damage. Cells can repair their DNA damage, but if reactive oxygen species (ROS) increase too much, they overwhelm the cellular antioxidant defense and capacity to repair. Oxidative stress can also up regulate oncogenes (which promote cancer) and can down regulate tumor suppressor genes.

The following are some of the various toxicants correlated with specific cancer types: For bladder cancer, arsenic has been established as causative. Cadmium exposure increases bladder cancer risk by a factor of 6. Trihalomethane (THM), a byproduct of water chlorination combining with pollutants, increases bladder cancer risk. Smoking is estimated to cause half of all bladder cancers, probably because the polycyclic aromatic hydrocarbons (PAH's), arsenic, and cadmium are excreted in the urine. Bone cancer (osteosarcoma) is highly correlated with arsenic exposure. Brain cancer is associated with pesticides and herbicides, such as chlorpyrifos, paraquat, and agents used in termite treatment, flea collars, pesticide bombs, and garden and yard herbicides and pesticides. Tobacco smoke, lead, and vinyl chloride also promote brain tumors.

Breast cancer, the most common malignancy among women throughout the world, has clear associations with chemical residues in food, applied chemicals in occupations, smoking, cosmetics, and water pollution. Especially organochlorines such as DDT, DDE, PCB's, lindane, etc., which stay deposited in body fat for years, are highly correlated with breast cancer, and are found at high concentrations in the tumors and in the surrounding tissue. Breast feeding reduces PCB levels in the mother, but sends it on to the unfortunate baby.

Parabens are also found at high levels in breast tissue, have estrogenic activity, and have been shown to induce growth of breast cancer cells in the laboratory. These are found in cosmetics and personal care products.

Colorectal cancer is related to trihalomethanes from chlorinated water, DDT, and DDE. Head and neck cancers are correlated with aluminum, arsenic, tobacco, and alcohol. Liver cancer's main toxicants are DDT, pyrethroid pesticides, and vinyl chloride. Lung cancer's main promoters are smoking, air pollution, especially diesel exhaust, radon, pesticides, and arsenic. Lymphohematopoetic cancers are mostly linked with pesticides, such as organophosphates, organochlorines, benzene from traffic pollution, and household use of solvents. Pancreatic cancer's main likely causes are smoking, cadmium, arsenic, and DDT. Prostate cancer: arsenic and smoking. Skin cancer: arsenic, and chronic sun exposure. Thyroid cancer: pesticides, herbicides, permanent hair dyes, and ionizing radiation.

Other factors related to cancers in general are chronic infections such as hepatitis B and C, schistosomiasis and other parasites, and helicobactor pylori. Alcohol, after it is converted to acetaldehyde, reduces the body's ability to repair DNA, and it increases risk of many digestive and

respiratory tract cancers, and breast cancer. Cannabis smoke with benzathrenes, and benzopyrene, higher than in cigarette smoke, can lead to many respiratory tract cancers and leukemia, although many of the constituents in marijuana itself have anti-cancer effects.

What I would add that is not itemized in the Clinical Environmental Medicine textbook is sugar and glucose/insulin dysregulation, with high insulin as a driver of cancer. Any caloric sweetener in excess can cause this dysfunction. Although these are considered foods, concentrated sugar could be considered a toxin, however natural, that drives cancer. High fructose corn syrup is specifically mentioned in the book as a toxin, since it is sourced from food in a way that it is an adulterated food product, and is thus an unnatural substance.

To assess toxic burden related to cancer risk, 8-OHdG (8-hydroxy-2'-deoxy guanosine) levels in the urine is a marker for oxidative stress, carcinogenesis, and degenerative disease, and detects oxidative damage to nuclear and mitochondrial DNA. This can be used to detect risk for developing many different types of cancer. Many people at high risk for cancer have genetic deficits in certain detoxification pathways, such as PON-1, (paraoxonase -1), and phase 1 or 2 detox pathways in the liver. Genetic tests are available for some of these variants.

The most important intervention is avoidance of those toxins that raise cancer risk. Previous articles cover specifics about avoidance methods.

This is the final installment that I plan to include on environmental medicine. This does not presume to be a complete coverage of the topic, but more would probable lead to readers' toxicant fatigue.

In summary, I think I will do a rant:

We wouldn't have to work with the enormous sickness caused by environmental toxins if we had better restriction of which chemicals were allowed to be released into the environment, like the precautionary principal that some countries have, requiring safety testing *before* chemicals are released for use, but unfortunately, due to regulatory capture by industry, we have very ineffective regulation, and many millions of people suffer illness, so we can have unhindered economic growth driven by the greed of a few billionaires. People seem to have a love affair with capitalism and don't seem to be too perturbed about wealth and income inequality, that drives many of our social, economic, and health problems. We seem to want more and more "stuff." This gives permission for industry continue to pollute. We have to take a look at a different kind of economy, one that would not be based on persistent "growth." Uncontrolled growth in the body is called cancer. We need to stop worshiping the sacred cow of economic growth. To have infinite appetite with finite resources is insane.

Let's take a fresh look at how we run our economy, and take a look at our personal needs and wants. Do we really need all that stuff? How about becoming more "Clean, Green, and Lean," to remember Dr. Crinnion's book by that title. Good Luck.