NUTRITIONAL MODULATION OF POP TOXICITY AND IMPLICATIONS IN PUBLIC HEALTH

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Introduction

Persistent organic pollutants (POPs), including dioxin-like chemicals can generate both short- and long-term health challenges for affected community members. Due to these prevalent health concerns, it is vital that public health professionals working with at-risk populations not only help monitor the ongoing health of exposed communities but also promote healthy practices and behaviors in order to prevent or reduce the potential for disease pathology. The pathologies of chronic diseases are complex and may be influenced by exposure to environmental pollutants throughout the lifespan. While a sedentary lifestyle and/or poor dietary habits can exacerbate the deleterious effects resulting from such exposure, much emerging evidence suggests that positive life-style changes (e.g., healthful nutrition, exercise) can modulate the toxicity of environmental pollutants[1,2]. Diet may serve as either an agonist or an antagonist of the health impacts associated with exposure to environmental pollutants. Thus, healthful nutrition may reduce human health risks associated with toxicant exposures and vulnerability to diseases linked to environmental toxic insults[3]. There is a significant need to further explore the paradigm of nutrition in environmental toxicology and to improve our understanding of the relationship between lifestyle modifications and toxicant-induced diseases. Relevant factors include the timing, from early development through adulthood, and duration of exposure to environmental toxicants, as well as potential nutritional interventions and the etiology of non-communicable diseases. Understanding mechanistic relationships among positive lifestyle changes, modulation of environmental toxicants, and susceptibility to disease development are important for both cumulative risk assessment and the design and implementation of future public health programs and behavioral interventions.

As a result of their long half-lives, POPs are ubiquitous in the environment for decades. Thus, exposure to POPs continues and occurs mostly through the food chain and atmospheric inhalation[1,2]. In fact, due to their lipophilic properties, many POPs, like polychlorinated biphenyls (PCBs), are prevalent in fatty foods, including fatty meats and fish[1]. Furthermore, many POPs are also stored long-term in bodily tissues, such as in human adipose tissue, making it difficult to avoid and especially reduce body burdens of POPs. Assuming that everyone has some degree of environmental pollutant body burden that can trigger disease pathologies, the development of prevention strategies to address environmental chemical-induced diseases needs to be a high priority. There is emerging evidence that healthful nutrition intervention is a substantive means of both disease prevention and disease risk mitigation following exposure to environmental pollutants[1,4]. Public health professionals will have an opportunity to monitor the health of exposed communities while also promoting healthy practices and behaviors designed to prevent or reduce exposure-related disease pathologies. The following discussion summarizes the recent literature about nutritional modulation of POP toxicity, with implications in risk assessment and public health paradigms.

Materials and methods

Detailed methods can be found within the references listed in this extended abstract. This extended abstract is intended to represent a review of the current literature.

Results and discussion

Exposure to POPs can be significant, especially near Superfund sites. Superfund chemicals have adverse health effects which require a concerted effort of both remediation of sources of pollutants as well as prevention of disease occurrence among exposed populations. Given the abundance of POP contamination (e.g., from water, soil, air, food, etc.) and widespread distribution in the ecosystem, it is unlikely that remediation alone will be sufficient to address POP-associated health problems. PCBs are a model toxicant of POPs to study

mechanistic relationships of chronic diseases with risks to environmental insults. PCBs are persistent and widely dispersed in the environment. The toxicity of PCBs and other chlorinated organics may be mediated by signal transduction following receptor binding, and the myriad effects that follow as part of overall disease development. A large part of PCB toxicity has been associated with non-ortho-chlorine-substituted or so-called coplanar PCBs, which are aryl hydrocarbon receptor (AhR) ligands and inducers of CYP1A1 enzymes, and thus elicit toxic and biological responses typical of dioxin (TCDD)[1]. Because of their lipophilic properties and long half-lives, PCBs are easily sequestered into adipose tissue, influencing the PCB burden during weight gain leading to obesity. PCBs are known to compartmentalize in selected tissues and are in dynamic equilibrium within the general circulation, thus making PCBs model Superfund pollutants for vascular diseases, including atherosclerosis, diabetes and obesity. In other words, persistent organic pollutants like PCBs have broad adverse effects and may contribute to the pathology of these diseases. Many of these diseases can also be classified as inflammatory diseases, which develop over a long period of time and thus can be easily modulated by environmental exposures, specifically to POPs. There is sufficient evidence that POPs contribute to inflammation by activating oxidative stress-sensitive transcription factors such as nuclear factor kappa-light-chain-enhancer of activated B cells (NFκB)[5]. For example, our studies suggest that PCBs, and in particular coplanar PCBs, can increase cellular oxidative stress and induce inflammatory parameters such as inflammatory cytokines, chemokines, and adhesion molecules in the vascular endothelium, which are metabolic events that foster an inflammatory response and atherosclerosis[1]. Through these pro-inflammatory mechanisms, PCBs and related environmental toxicants have been correlated with increased risk of multiple human chronic disease phenotypes including diabetes and heart disease[1,2]. Since many populations susceptible to toxicant-induced diseases are often also afflicted by diet-induced diseases, future human studies and integrated risk assessment and public health paradigms should better investigate the interaction between nutrition and toxicology[4]. The contribution of environmental pollutants in these processes and the possibility that their initiation and/or progression could be manipulated by appropriate dietary interventions is of great public health potential.

The diet is a major route of exposure to chlorinated organics, including PCBs and other persistent organic pollutants. Since these compounds are fat-soluble, fatty foods usually contain higher levels of persistent organics, such as PCBs, than vegetable matter[1,2]. Once absorbed, PCBs distribute themselves in tissues, especially adipose, where they are in dynamic equilibrium with the blood. Nutrition can also influence the cellular lipid milieu, oxidative stress/antioxidant status, and vascular inflammation, and thus modulate mechanisms of cytopathology and cytotoxicity mediated by Superfund pollutants.

The paradigm of nutrition as a key factor modifying Superfund chemical (e.g., PCB) toxicity is of considerable interest to populations at risk, i.e., populations residing near Superfund sites or areas of contamination and populations with poor dietary habits. In addition to novel environmental remediation technologies associated with nanoparticles, biosensors, etc., nutrition could be considered as a means of "biological remediation" by modulating the cytopathology and cytotoxicity of Superfund toxicants and thus affecting related issues of health and disease[2]. Proper nutrition counseling should be considered by health officials and the medical community to reduce the overall risk for Superfund chemical toxicity and disease development. At present, very little is known about the interaction of diets and cytotoxicity of environmental pollutants such as Superfund chemicals. Our data clearly show that nutrition can modulate PCB toxicity[1, 3]. For example, specific fatty acids present in plant oils, such as linoleic acid (the parent omega-6 fatty acid), can amplify PCB toxicity in vascular endothelial cells, an event which can be down-regulated by vitamin E[1]. Additionally, polyphenols and omega-3 polyunsaturated fatty acids have been shown to decrease toxicant-induced maladies including liver diseases, tumor formation and growth and endothelial cell[1]. Our work has shown that plant-derived flavonoids such as epigallocatechin-3-gallate (EGCG), and long-chain omega-3 fatty acids such as docosahexaenoic acid (DHA) can protect cellular systems by decreasing pro-inflammatory lipid raft signaling domains called caveolae and by simultaneously upregulating antioxidant defenses through increased nuclear factor (erythroid-derived 2)-like 2 (Nrf2) activation[1, 2]. Most recently we have elucidated novel cross-talk mechanisms between caveolae and Nrf2 pathways and have shown that nutrients and/or bioactive food compounds may protect against vascular dysfunction, oxidative stress and inflammation by downregulating caveolae and simultaneously upregulating Nrf2 target antioxidant genes[1]. In addition to reducing POP-induced oxidative stress and inflammation using bioactive food components such as polyphenols, multiple studies have also shown that diets high in fiber can alter the absorption and excretion rates of pollutants such as PCBs to reduce overall body burden[2]. Mechanistically, multiple dietary fibers have been shown to

effectively bind pollutants such as dioxins, which may help to explain increased fecal excretion rates, decrease in body burden, and observed protection[2]. Increasing excretion of lipophilic toxicants through other nutritional compounds such as fat substitutes may also effectively decrease risk[6]. For example, much emphasis including human clinical trials has been placed on the interactions between the non-absorbable fat substitute olestra and environmental toxicants[6]. A recent study by Jandacek at al. demonstrated that the dietary substitute olestra can safely reduce body burdens of PCBs in communities living near Anniston, AL, a Superfund site highly contaminated with PCBs[6]. All these studies suggest that nutrition intervention, and especially healthful nutrition, is a sensible means to address preventive measures against diseases associated with exposure to POPs. These discoveries have implications in cumulative risk assessment and public hearth paradigms.

The role of nutrition in cumulative risk assessment is being further substantiated not only as an important modulator of inflammatory and antioxidant pathways, especially associated with environmental insult, but also due to its link to obesity related diseases. It is plausible that individuals who are compromised nutritionally (e.g., because of poor dietary habits) are more vulnerable to hazardous chemicals throughout their life span. In contrast, diets rich in antioxidants and anti-inflammatory nutrients can improve health and decrease vulnerability to additional chemical stressors. Thus, healthy nutrition intervention should be considered as early in life as possible. We recommend that nutrition be included as a critical variable in risk assessment methodologies, and that this incorporation should emphasize nutrition as a powerful intervention tool for lowering health risks related to environmental toxicants. In fact, healthful nutrition could markedly buffer the body against chemical, biological, and physical stressors that humans are exposed to on a daily basis. Thus, positive dietary behaviors can potentially reduce health risks associated with hazardous substances, clearly placing nutrition within the paradigm of risk assessments[4].

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References:

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