NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCEINCES
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Concept Clearance

Dietary Influence on the Human Health Effects of Environmental Exposures

Overview:

Research conducted over the past several decades clearly indicates that disease risk is influenced by multifactorial elements that include exposure to environmental agents, diet/nutrition, and genetic susceptibility. From a pathophysiological standpoint many environmental exposures affect common biological pathways leading to disease, such as oxidative stress and inflammation; these same pathways are also likely to be influenced by diet and nutritional status. Thus, variability in disease risk in response to environmental exposures within populations may be at least partially attributable to components of diet and/or nutritional status. This suggests that by (1) more clearly identifying those nutritional or dietary components that influence the trajectory or onset of disease and (2) understanding mechanisms underlying the interplay between diet/nutrition and exposure to environmental agents and disease risk, more informed intervention or prevention strategies could be developed. Therefore additional research is needed to address these gaps in knowledge and will be of significant public health importance.

Background:

At the Comorbidity of Environmental Induced Diseases workshop, held in 20006, NIEHS extramural and intramural scientists along with invited scientists discussed potential disease modifying factors other than genetics that may determine the trajectory of environmentally-induced diseases. At the conclusion of this workshop several recommendations were made including the need to: (1) develop disease models that included other environmental factors such as psychosocial, circadian rhythm, and diet, (2) define the disease, and the cofactors of interest, (3) develop, relevant animal models as well as generate good exposure data.

Recent evidence from epidemiological and basic research studies suggests that disease onset and trajectory can be influenced both positively and negatively not only by diet and nutritional factors but the interplay between these and environmental exposures. It has long been known that pregnancy outcomes are related to maternal nutrition, and that fish consumption during pregnancy has been thought to be protective on birth outcomes For example, a diet rich in Omega-3 fatty acids has been shown to reduce the harmful effects of maternal mercury-contaminated fish consumption on child cognitive and behavioral performances.[1] Other studies have shown that fish consumption during the last trimester mitigates the harmful developmental effects of prenatal exposure to fine air particulate matter. Conversely, a poor

diet can have a negative influence on disease onset. Investigators at Johns Hopkins recently showed that an urban diet rich in fat and sugar appears to exacerbate the effects that ambient air pollution has on asthma symptoms. They also observed that this effect could be reduced by vitamin D supplementation.[2] These examples highlight the importance of nutrition-toxicant interactions in modulating disease risk across the life-span.

Adding another layer of complexity to the nutrient-toxicant-disease paradigm is the role of anthropometric attributes in influencing these relationships. For example, environmental chemicals in the diet or other sources may contribute to obesity through their perturbation of biologic pathways linked to endocrine signaling. Regardless of whether obesity originates from exposure to endocrine active compounds and/or from a high fat diet, the changes in endocrine and other signaling pathways that accompany obesity may themselves provide a biologic substrate that alters susceptibility to the same or to different environmental exposures (e.g., La Merrill et al, 2009). In this manner, obesity can be viewed not only as an outcome of interest linked directly to exposure and/or nutrition, but also as a mediator of the effects of exposure(s) on other disease endpoints. Robust study designs and analytic methods are needed to accommodate and provide insight into such complexities that may exist in nutrition-toxicant-disease relationships

Studies in model systems are also underway to explore mechanisms underlying the effects of diet and nutrition on biological pathways affected by environmental toxicants. A recent study in mice used dietary supplements of beta carotene or lycopenes to determine their effects on lung transcriptome as it relates to cigarette smoke.[3] This study was developed in response to conflicting epidemiological data on the role of these nutrients on the risk of lung cancer. This study concluded that mice can offer a viable model to study bioavailability and bioactivity of synthetic and natural carotenoids and their possible role in modulating environmentally induced lung pathobiologies. Furthermore, these studies prove that mouse models are useful for the interrogation of key pathways of environment-nutrient interaction in lung tissues. [4]

Objectives:

The main objective of supporting research in this area is to develop studies that would identify potential pathways and estimate variaibility in environmentally induced-disease in human populations by exploring the modulating effects of dietary and/ or nutritional factors.. A better understanding of mechanisms underlying these complex interactions will enable the development of effective primary prevention and intervention strategies to mitigate environmentally induced diseases.

To meet this objective, a multi-phased approach is envisioned. An initial funding opportunity announcement will be used to support small scale exploratory human and basic science projects pilot projects to identify relevant cohorts and biological pathways for possible future interventions. A later announcement will build upon the scientific evidence gained from the first phase to support studies that more fully explore the feasibility nutritional interventions to that inform the development of dietary/nutritional strategies to prevent or mitigate the harmful effects of toxicant exposure using both human and animal models.

Epidemiology studies will be encouraged that build on existing cohorts to examine the joint contribution of diet and environment on health outcomes. Examples of studies that could be considered include:

- Expansion of existing studies to look at the interplay between nutrition (ie. nutrient intake, supplement use, anthropometry) and environmental exposure on health outcomes, including secondary data analysis in on-going studies.
- Feasibility studies to test or develop tools or protocols for future studies that will look at diet and nutrition and environment, such as the refinement of dietary/nutritional assessment to add on to an existing environmentally characterized population or the addition of a new environmental measure or assay to an existing nutritional study like NHANES.
- Pilot studies to produce preliminary data to support and aid in the design of future studies testing diet- environment interaction.

Laboratory-based studies will be encouraged that identify and evaluate molecular targets and mechanisms that underlie the interaction of diet/nutrition with environment. Examples of studies that could be considered include:

- Identify and evaluate nutritional factors (ie. macro and micro-nutrient intake, dietary supplements, anthropometry) that modulate the health effects of environmental chemicals
- Identify critical life stages where the effects of dietary parameters will have the most pronounced effects on health outcomes.
- Use of well established animal models of environmentally induced disease to study the interaction of diet and nutrition with environmental toxicants.
- Identify key molecular targets in relevant biologic pathways that could be useful in prevention/intervention studies

Program Management, Implementation, and Budget:

NIEHS will encourage the development preliminary data of studying the interaction of diet and environmental exposures and will propose to develop opportunities that would expand the scope of work by supporting future large scale projects. Program will work with other agencies within NIH to support and promote the development of this diet and environment interaction program through informal discussions, seminars and workshops to integrate the various disciplines and to share tools and knowledge in this field, and lastly to develop and support complementary funding opportunities to capitalize on existing programs and infrastructure. Other Institutes within NIH with common interest include National Cancer Institute, National Heart Lung Blood Institute, National Institute Childe Health, Office of Dietary Supplements, Office Behavioral Social Science and National Center for Minority Health and Health Disparities.

1. Maternal fish intake during pregnancy, blood mercury levels, and child cognition at age 3 years in a US cohort, Oken Oken E, Radesky JS, Wright RO, Bellinger DC, Amarasiriwardena CJ, Kleinman KP, Hu H, Gillman MWE. Am J Epidemiol. 2008 May 15;167(10):1171-81. Epub 2008 Mar 18.
2. Does higher body mass index contribute to worse asthma control in an urban population? (Clerisme-Beaty EM, Karam S, Rand C, Patino CM, Bilderback A, Riekert KA, et al J Allergy Clin Immunol 2009;124:207-12.

3. Apo-10'-lycopenoic acid inhibits lung cancer cell growth in vitro, and suppresses lung tumorigenesis in the A/J mouse model in vivo. Lian F, Smith DE, Ernst H, Russell RM, Wang XD. Carcinogenesis. 2007 Jul;28(7):1567-74. Epub 2007 Apr 9.

4. beta-carotene-induced changes in RARbeta isoform mRNA expression patterns do not influence lung adenoma multiplicity in the NNK-initiated A/J mouse model. Goralczyk R, Bachmann H, Wertz K, Lenz B, Riss G, Buchwald Hunziker P, Greatrix B, Aebischer CP.Nutr Cancer. 2006;54(2):252-62.

5. Association of endocrine disruptors and obesity: perspectives from epidemiological studies, Hatch, Elizabeth et al. Journal of International Andrology: Volume 33 Issue 2 pages 324-344, May 2009.)