

EPI - SPECIAL SESSION: Defining the Impact of Endocrine Disruptors (EDCs) on Metabolic Disease and Obesity through Epidemiologic Research

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Abstract

Emerging epidemiological evidence linking organochlorine compounds and polyfluoroalkyl substances with type 2 diabetes

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Organochlorine compounds (OCs) and polyfluoroalkyl substances (PFASs) are persistent organic pollutants (POPs) that have strong endocrine disrupting potentials. Although most of these POPs have been banned or phased out in the US, Americans are continuously exposed to these chemicals through contaminated drinking water and foods and use of consumer products. Because the excretion of POPs in human body is slow, these chemicals can accumulate in human body and exert detrimental effects on cardiometabolic and endocrine functions. To illustrate the health effects among humans, we have conducted a series of studies on the associations of plasma POPs with body weight and T2D risk in several cohort studies and have explored major demographic, lifestyle and dietary determinants of POP exposure and elimination. In the National Health and Nutrition Examination Survey, we found that plasma levels of lipophilic OCs showed stronger associations with trunk fat than leg fat, which possibly explains more detrimental effects of visceral body fat storage on cardiometabolic disorders. In the POUNDS-LOST trial, participants with higher baseline PFAS concentrations had lower basal metabolic rates and more weight regain after the initial weight loss upon energy restriction. To add to the limited epidemiological evidence linking POPs and T2D risk, we conducted a case-control study of type 2 diabetes (T2D, n=793 pairs) nested in the Nurses' Health study II. We observed strong positive associations of plasma OCs (e.g., polychlorinated biphenyls) and PFASs (e.g., perfluorooctanesulfonic acid and perfluorooctanoic acid) with T2D risk over a mean follow-up of 6.7 years. These findings were largely independent of established T2D risk factors, and the positive associations between OCs and T2D risk were stronger among nurses with lower body weight gain before blood draw. Among possible determinants of POP exposure and elimination, older age and shorter lifetime breastfeeding history were associated with higher plasma levels of most POPs, and concurrent body mass index and previous weight changes were inversely associated with OCs. In addition, we found that popcorn and fish intake was associated with higher PFAS levels. Collectively, our findings highlight an independent role of low-dose POP exposure in the etiology of weight gain and T2D risk. These results also illustrate the role of body fats, breastfeeding, and diet in POP storage and elimination in human body.

Chronic disease management and prevention Environmental health sciences Epidemiology

Abstract

Potential role of lipophilic chemical mixtures in adipose tissue in the development of type 2 diabetes

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In the current paradigm for type 2 diabetes (T2D), obesity from energy imbalance, insulin resistance from obesity, and exhaustion of pancreatic beta cells from overproduction of insulin to compensate for insulin resistance ultimately progresses to T2D. However, various environmental chemicals have recently received attention as possible contributors to the development of T2D in vitro or in-vivo studies. Among them, persistent organic pollutants (POPs), strong lipophilic chemical mixtures stored in adipose tissue and released to circulation by lipolysis, have demonstrated the most consistent results in human studies, compared to other chemicals. In particular, a recent study reported that the chronic exposure to low-dose POPs primarily affected insulin secretory function of beta-cells in humans and in vitro cells, not insulin resistance. As beta-cell dysfunction is an essential step for the development of T2D, these findings strongly support a critical role of low dose POPs in the development of T2D. Although POPs are well-known endocrine disrupting chemicals (EDCs), recent human findings on low dose POPs cannot be attributed to endocrine disrupting properties of POPs because the net effect of EDC mixtures with diverse activities such as POPs is unpredictable. On-going researches suggest that mitochondrial dysfunction would be a possible underlying mechanism linking POPs to T2D. As there is no adipose tissue without contamination of POPs and toxicodynamics of POPs are mechanistically linked to dynamics of adipose tissue, the current paradigm linking obesity and T2D should be reevaluated from the viewpoint of POPs.

Chronic disease management and prevention Environmental health sciences Epidemiology

Abstract

Positive association of prenatal DDT exposure and obesity among women in their fifties: Findings from the Child Health and Development Studies

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Dichlorodiphenyltrichloroethane (DDT) was used extensively to control infectious disease worldwide in the mid-century, and its use in malaria control continues in some countries according to recommendation by the World Health Organization. Our meta-analysis indicates that maternal exposure to the metabolite of DDT, dichlorodiphenyldichloroethylene (DDE), is positively associated with childhood obesity in the majority of prospective epidemiology studies. We evaluated whether prenatal DDE and DDT exposures had a positive association with obesity in 511 aging women of the Child Health and Development Studies (CHDS), a hospital-based prospective birth cohort with over 50 years of follow-up. We found that o,p'-DDT exposure in the prenatal period had a positive association with risk of obesity defined by either waist circumference or body mass index (RR = 1.2-1.3). These positive associations remained after adjustment for confounders throughout the life-course and for known risk factors such as exercise (RR wc=1.24 (95% CI: 1.05, 1.46); RR BMI=1.27 (95% CI: 1.03, 1.56)). There were no such associations found for either p,p'-DDT or p,p'-DDE in this study. This study adds a novel investigation to the obesogen literature by identifying a positive association of prenatal DDT exposure with risk of obesity in adulthood. The available evidence indicates that prenatal exposure to DDT and its metabolites may be positively associated with obesity throughout life.

Basic medical science applied in public health Environmental health sciences Epidemiology

Abstract

Dietary modifiers in the association between inorganic arsenic and blood glucose levels

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Nutrients involved in one-carbon metabolism methylation reactions are thought to influence the metabolism of inorganic arsenic (iAs). Recent studies have examined how dietary methyl donors and co-factors may associate with urinary concentrations of iAs metabolites, but fewer studies have examined whether and how these nutrients may influence iAs associated health risks. This study examines whether dietary intakes of folate, vitamin B12, riboflavin, niacin, vitamin B6 and choline modify associations between water iAs and plasma glucose levels. Methods: Data came from a cross-sectional study of 1,160 adults >18y in Chihuahua, Mexico, a setting where wheat and corn flour are fortified with folate. Household drinking water samples were used to estimate iAs exposure, dietary intakes were estimated from a food frequency questionnaire (FFQ), and an oral glucose tolerance test was administered to all participants. Interactions were used to evaluate the combined effect of iAs exposure and nutrient intakes on 2h plasma glucose in multivariable linear regression models. Water arsenic was dichotomized at 50 ppb, approximately the median, as were energy-adjusted nutrient intakes. Models adjusted for age, sex, smoking, alcohol, BMI, energy intake, and nutrients and food groups correlated with the nutrient of interest. Results: Elevated drinking water arsenic was associated with significant increases in 2h glucose. Except for folate, higher intakes of other B vitamins attenuated these iAs-associated increases in 2h glucose. In contrast, 2-hour glucose was highest among participants with both high iAs exposure and high intakes of folate. Conclusions: Findings suggest that increasing intakes of numerous B vitamins may have beneficial effects on cardio-metabolic outcomes such as diabetes associated with iAs exposure. However, more research is needed to better understand potential effects of elevated folate, and possible imbalances in nutrient intake.

Administer health education strategies, interventions and programs Chronic disease management and prevention Environmental health sciences Epidemiology Public health or related education Public health or related research

