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Risk Assessment

An Approach to Assessing the Influence of Environmental and Occupational Cancer Hazard Identification on Policy Decision-Making

Suril S Mehta, Isabelle Morin, Kimberly Osborn, Courtney R Lemeris, Michael Conti, Ruth M Lunn. *Environ Health Perspect.* 2023 Dec;131(12):125001. doi: 10.1289/EHP12681. [Article link](#)

Significance: Assessing the influence of cancer hazard identification on science-based public health policies is feasible, informative and needed.

Background: Cancer hazard identification is critical to informing decisions on preventive actions. However, the influence of cancer hazard assessments on the creation of health-protective regulations is poorly understood. Although prior studies have measured the health and economic benefits of regulatory actions in general, we are not aware of efforts to explicitly study the influence of cancer hazard identification on policy decisions in the United States.

Objectives: In this commentary, we present an approach to examine whether formal identification of a substance as a human carcinogen may prompt a regulatory action to reduce exposure to carcinogens and enhance public health. Further, we discuss the broader implications of cancer hazard identification on policy decision-making, including identifying gaps and providing recommendations. **Methods:** Using the Report on Carcinogens (RoC) as a test case, we systematically searched U.S. federal and state databases for notices of regulations mentioning the RoC from 1995 to 2023. For each regulation, we extracted information on the carcinogen(s) regulated, the regulatory agency, the regulatory purpose, the economic sector exposure sources, and the analyzed public health benefits and costs. We created a publicly available, web-based interactive tool to visualize the data. **Discussion:** U.S. regulatory agencies have been using cancer hazard evaluations, such as the RoC, for decades to inform public health policy actions to prevent or mitigate cancer risks. Specifically, nonregulatory cancer hazard assessments have been used to prioritize chemical evaluations, support regulatory-based assessments, and trigger regulatory action. Our approach showed that assessing the influence of cancer hazard identification on science-based public health policies is feasible, informative, and needed, and our study is a first step in this direction. We recommend expanding this approach to other cancer and noncancer hazard assessments to ultimately inform our understanding of the influence of hazard classifications on policymaking.

Foodborne Pathogens

Levels and Types of Microbial Contaminants in Different Plant-Based Ingredients Used in Dairy Alternatives

Alina Kyrylenko, Robyn T Eijlander, Giovanni Alliney, Elly Lucas-van de Bos, Marjon H J Wells-Bennik. *Int J Food Microbiol.* 2023 Dec 16;407:110392. doi: 10.1016/j.ijfoodmicro.2023.110392. [Article link](#)

Significance: Insight into microbial contaminants in plant-based ingredients effective design of plant-based food processing conditions and formulations to ensure food safety and prevent spoilage.

In this study levels and types of microbial contaminants were investigated in 88 different plant-based ingredients including many that are used to manufacture dairy alternatives. Studied ingredients encompassed samples of pulses (pea, faba bean, chickpea, and mung bean), cereals/pseudocereals (oat, rice, amaranth and quinoa) and drupes (coconut, almond and cashew). The microbial analysis included: i) total viable count (TVC), ii) total aerobic mesophilic spore count (TMS), iii) heat resistant aerobic thermophilic spore count (HRTS), iv) anaerobic sulfite reducing *Clostridium* spore count (SRCS), and v) *Bacillus cereus* spore count (BCES). Microorganisms isolated from the counting plates with the highest sample dilutions were identified using 16S rRNA and MALDI-TOF MS analyses. Many of the investigated ingredients showed a high proportion of spores as part of their total aerobic mesophilic counts. In 63 % of the samples, the difference between TVC and TMS counts was 1 Log₁₀ unit or less. This was particularly the case for the majority of pea isolates and concentrates, faba bean isolates, oat kernels and flakes, and for single samples of chickpea isolate, almond, amaranth, rice, quinoa, and coconut flours. Concentrations of TVC ranged between <1.0 and 5.3 Log₁₀ CFU/g in different samples, and TMS varied between <1.0 and 4.1 Log₁₀ CFU/g. Levels of HRTS, BCES and SRCS were generally low, typically around or below the LOD of 1.0 Log₁₀ CFU/g. In total, 845 individual bacterial colonies were isolated belonging to 33 different genera. *Bacillus licheniformis* and *B. cereus* group strains were most frequently detected among *Bacillus* isolates, and these species originated primarily from pea and oat samples. *Geobacillus stearothermophilus* was the main species encountered as part of the HRTS. Among the *Clostridium* isolates, *Clostridium sporogenes/tepidum* were predominant species, which were mostly found in pea and almond samples. Strains with potential to cause foodborne infection or intoxication were typed using the PCR-based method for toxin genes detection. In the *B. cereus* group, 9 % of isolates contained the *ces* gene, 28 % contained *hbl*, 42 % *cytK*, and 69 % were positive for the *nhe* gene. Absence of the *boNT-A* and *-B* genes was confirmed for all isolated *C. sporogenes/tepidum* strains. Nearly all (98 %) *B. licheniformis* isolates were positive for the *lchAA* gene. Insight into the occurrence of microbial contaminants in plant-based ingredients, combined with knowledge of their key inactivation and growth characteristics, can be used for the microbial risk assessment and effective design of plant-based food processing conditions and formulations to ensure food safety and prevent spoilage.

Foodborne Illness

Reduction of Nontyphoidal *Salmonella enterica* in Broth and on Raw Chicken Breast by a Broad-spectrum Bacteriophage Cocktail

Thomas Brenner, Danielle Morgan Schultze, David Mahoney, Siyun Wang. *J Food Prot.* 2023 Dec 22;87(1):100207. doi: 10.1016/j.jfp.2023.100207. [Article link](#)

Significance: A phage cocktail was effective at reducing a diverse set of prominent nontyphoidal *Salmonella* strains in broth and on raw chicken breast.

Globally, nontyphoidal *Salmonella* (NTS) causes approximately 150 million foodborne illnesses annually; many of which are linked to poultry products. Thus, improving food safety interventions in the poultry sector can reduce foodborne illness associated with prevalent NTS serotypes. Bacteriophages (phages) have shown promise as food-safe alternatives to current antimicrobial practices. However, challenges such as limited host range, bactericidal effectiveness in practical production settings, and the risk of developing host resistance remain as barriers for the widespread use of phages in commercial poultry operations. A broad-spectrum three-phage cocktail was evaluated against *S. enterica* subsp. *enterica* serotypes Enteritidis, Typhimurium and Kentucky. The impact of multiplicity of infection (MOI) on NTS growth was assessed in broth at 22°C for 18 hours (h). Then, phage cocktail efficacy was evaluated on raw chicken breast samples inoculated with the NTS cocktail and stored at 10°C or 22°C for 0, 1, and 5 days or 0, 4, 8, and 16 h, respectively. Most probable number (MPN) calculations were performed for NTS counts on chicken after phage treatment and storage at 10°C to account for samples with NTS counts below the detection limit. In general, a higher MOI corresponded to reduced NTS growth; however, residual nutrition in growth media and initial NTS contamination level affected samples treated with the phage cocktail at identical MOIs. On chicken, phage cocktail treatment significantly reduced NTS counts at 10°C and 22°C. After storage at 10°C for 5 days, NTS counts were reduced by >3.2 log compared to the control. After storage at 22°C for 16 h, NTS counts were reduced by >1.7 log compared to the control. Overall, the phage cocktail was effective at reducing a diverse set of prominent NTS strains in broth and on raw chicken breast, highlighting its potential for commercialization and use alongside other hurdles in poultry production.

Mycotoxins

Recent Advances in the Detection of Food Toxins Using Mass Spectrometry

Vishal Ahuja, Amanpreet Singh, Debarati Paul, Diptarka Dasgupta, Petra Urajová, Sounak Ghosh, Roshani Singh, et. al. *Chem Res Toxicol.* 2023 Dec 18;36(12):1834-1863. doi: 10.1021/acs.chemrestox.3c00241. [Article link](#)

Significance: This review discusses the application of Mass Spectrometry in detecting food toxins - including mycotoxins, marine biotoxins and plant-derived toxins - to enhance our understanding of potential hazards in the food supply chain.

Edibles are the only source of nutrients and energy for humans. However, ingredients of edibles have undergone many physicochemical changes during preparation and storage. Aging, hydrolysis, oxidation, and rancidity are some of the major changes that not only change the native flavor, texture, and taste of food but also destroy the nutritive value and jeopardize public health. The major reasons for the production of harmful metabolites, chemicals, and toxins are poor processing, inappropriate storage, and microbial spoilage, which are lethal to consumers. In addition, the emergence of new pollutants has intensified the need for advanced and rapid food analysis techniques to detect such toxins. The issue with the detection of toxins in food samples is the nonvolatile nature and absence of detectable chromophores; hence, normal conventional techniques need additional derivatization. Mass spectrometry (MS) offers high sensitivity, selectivity, and capability to handle complex mixtures, making it an ideal analytical technique for the identification and quantification of food toxins. Recent technological advancements, such as high-resolution MS and tandem mass spectrometry (MS/MS), have significantly improved sensitivity, enabling the detection of food toxins at ultralow levels. Moreover, the emergence of ambient ionization techniques has facilitated rapid in situ analysis of samples with lower time and resources. Despite numerous advantages, the widespread adoption of MS in routine food safety monitoring faces certain challenges such as instrument cost, complexity, data analysis, and standardization of methods. Nevertheless, the continuous advancements in MS-technology and its integration with complementary techniques hold promising prospects for revolutionizing food safety monitoring. This review discusses the application of MS in detecting various food toxins including mycotoxins, marine biotoxins, and plant-derived toxins. It also explores the implementation of untargeted approaches, such as metabolomics and proteomics, for the discovery of novel and emerging food toxins, enhancing our understanding of potential hazards in the food supply chain.

Heavy Metals

Arsenic Exposure and Epigenetic Aging: The Association with Cardiovascular Disease and All-Cause Mortality in the Strong Heart Study

Enoch X Jiang, Arce Domingo-Reloso, Ahlam Abuawad, Karin Haack, Maria Tellez-Plaza, M Danielle Fallin, Jason G Umans, et. al. *Environ Health Perspect.* 2023 Dec;131(12):127016. doi: 10.1289/EHP11981. [Article link](#)

Significance: Arsenic exposure was associated with measures of older biological age. Furthermore, accelerated biological aging measured from DNA methylation accounted for a relevant fraction of As-associated risk for cardiovascular disease and all-cause mortality.

Background: Inorganic arsenic (As) may increase the risk of cardiovascular disease (CVD) and all-cause mortality through accelerated aging, which can be estimated using epigenetic-based measures. **Objectives:** We evaluated three DNA methylation-based aging measures (PhenoAge, GrimAge, DunedinPACE) (epigenetic aging measures) as potential mediators of the previously reported association of As exposure with CVD incidence, CVD mortality, and all-cause mortality in the Strong Heart Study (SHS), an epidemiological cohort of American Indian adults.

Methods: Blood DNA methylation and urinary As levels were measured in 2,323 SHS participants (41.5% men, mean age of 55 years old). PhenoAge and GrimAge values were calculated using a residual-based method. We tested the association of urinary As with epigenetic aging measures using linear regression, the association of epigenetic aging measures with the three health outcomes using additive hazards models, and the mediation of As-related CVD incidence, CVD mortality, and all-cause mortality by epigenetic aging measures using the product of coefficients method. **Results:** SHS participants with higher vs. lower urinary As levels had similar PhenoAge age, older GrimAge age, and faster DunedinPACE. An interquartile range increase in urinary As was associated with higher of PhenoAge age acceleration [mean difference (95% confidence interval) = 0.48 (0.17, 0.80) years], GrimAge age acceleration [0.80 (0.60, 1.00) years], and DunedinPACE [0.011 (0.005, 0.018)], after adjusting for age, sex, center location, genetic components, smoking status, and body mass index. Of the 347 incident CVD events per 100,000 person-years associated with a doubling in As exposure, 21.3% (9.1, 57.1) and 22.6% (9.5, 56.9), were attributable to differences in GrimAge and DunedinPACE, respectively. **Discussion:** Arsenic exposure was associated with older GrimAge and faster DunedinPACE measures of biological age. Furthermore, accelerated biological aging measured from DNA methylation accounted for a relevant fraction of As-associated risk for CVD, CVD mortality, and all-cause mortality in the SHS, supporting the role of As in accelerated aging. Research of the biological underpinnings can contribute to a better understanding of the role of aging in arsenic-related disease.

Food Packaging

Active and Intelligent Biodegradable Packaging Based on Anthocyanins for Preserving and Monitoring Protein-Rich Foods

Bifen Zhu, Yu Zhong, Danfeng Wang, Yun Deng. *Foods*. 2023 Dec 15;12(24):4491. doi: 10.3390/foods12244491. [Article link](#)

Significance: This film, which achieves high stability and the continuous release of anthocyanins on demand, may become a key tool in packaging applications for protein-based foods.

Currently, active and intelligent packaging has been developed to solve the spoilage problem for protein-rich foods during storage, especially by adding anthocyanin extracts. In such a film system, the antioxidant and antibacterial properties were dramatically increased by adding anthocyanins. The physicochemical properties were enhanced through interactions between the active groups in the anthocyanins and reactive groups in the polymer chains. Additionally, the active and intelligent film could monitor the spoilage of protein-rich foods in response to pH changes. Therefore, this film could monitor the sensory acceptance and extend the shelf life of protein-rich foods simultaneously. In this paper, the structural and functional properties of anthocyanins, composite actions of anthocyanin extracts and biomass materials, and reinforced properties of the active and intelligent film were discussed. Additionally, the applications of this film in quality maintenance, shelf-life extension, and quality monitoring for fresh meat, aquatic products, and milk were summarized. This film, which achieves high stability and the continuous release of anthocyanins on demand, may become an underlying trend in packaging applications for protein-rich foods.

Chemical Contaminants

Linking Prenatal Environmental Exposures to Lifetime Health with Epigenome-Wide Association Studies: State-of-the-Science Review and Future Recommendations

Kelly M Bakulski, Freida Blostein, Stephanie J London. *Environ Health Perspect*. 2023 Dec;131(12):126001. doi: 10.1289/EHP12956. [Article link](#)

Significance: It is expected that larger epigenome-wide association studies with enhanced coverage of epigenome and exposome will expand mechanistic understanding of causal links between environmental exposures, the epigenome and health outcomes over the life course.

Background: The prenatal environment influences lifetime health; epigenetic mechanisms likely predominate. In 2016, the first international consortium paper on cigarette smoking during pregnancy and offspring DNA methylation identified extensive, reproducible exposure signals. This finding raised expectations for epigenome-wide association studies (EWAS) of other exposures. **Objective:** We review the current state-of-the-science for DNA methylation associations across prenatal exposures in humans and provide future recommendations. **Methods:** We reviewed 134 prenatal environmental EWAS of DNA methylation in newborns, focusing on 51 epidemiological studies with meta-analysis or replication testing. Exposures spanned cigarette smoking, alcohol consumption, air pollution, dietary factors, psychosocial stress, metals, other chemicals, and other exogenous factors. Of the reproducible DNA methylation signatures, we examined implementation as exposure biomarkers. **Results:** Only 19 (14%) of these prenatal EWAS were conducted in cohorts of 1,000 or more individuals, reflecting the still early stage of the field. To date, the largest perinatal EWAS sample size was 6,685 participants. For comparison, the most recent genome-wide association study for birth weight included more than 300,000 individuals. Replication, at some level, was successful with exposures to cigarette smoking, folate, dietary glycemic index, particulate matter with aerodynamic diameter <10µm and <2.5µm, nitrogen dioxide, mercury, cadmium, arsenic, electronic waste, PFAS, and DDT. Reproducible effects of a more limited set of prenatal exposures (smoking, folate) enabled robust methylation biomarker creation. **Discussion:** Current evidence demonstrates the scientific premise for reproducible DNA methylation exposure signatures. Better powered EWAS could identify signatures across many exposures and enable comprehensive biomarker development. Whether methylation biomarkers of exposures themselves cause health effects remains unclear. We expect that larger EWAS with enhanced coverage of epigenome and exposome, along with improved single-cell technologies and evolving methods for integrative multi-omics analyses and causal inference, will expand mechanistic understanding of causal links between environmental exposures, the epigenome, and health outcomes throughout the life course.

Caffeine

Is Coffee and Tea a Threat or Ally to Cardiovascular Health?

Vaidehi Mendpara, Shreya Garg, Priyanshi Shah, Jill Bhavsar, Fnu Anamika, Meet Patel, Ripudaman S Munjal, et. al. *Cureus*. 2023 Dec 5;15(12):e49991. doi: 10.7759/cureus.49991. [Article link](#)

Significance: Along with having a generally cardioprotective profile, coffee and tea have also demonstrated a favorable impact on insulin resistance and reduced risk of diabetes mellitus.

Tea and coffee have become ingrained in our daily lives and have become the most widely consumed drinks after water. Their effects vary on an individual basis depending upon the amount of daily consumption, genetic polymorphisms, and the presence of comorbidities. Non-habitual individuals experience an initial, brief increase in blood pressure due to caffeine's vasoactive effects. Caffeine also appears to be protective against arrhythmias and heart failure. Along with having a generally cardioprotective profile, they have also demonstrated to have a favorable impact on insulin resistance and reduced risk of diabetes mellitus. Physicians often practice caution and advise patients with known cardiovascular diseases to refrain from drinking caffeine; however, studies have shown that drinking two to three cups a day has either no or some beneficial effects on both patients with or without cardiac disorders like arrhythmias. This article focuses on the effects of tea and coffee on the cardiovascular system as well as the potential mechanisms involved.

Food Allergens

Feast for Thought: A Comprehensive Review of Food Allergy 2021-2023

Irene Bartha, Noorah Almulhem, Alexandra F Santos. *J Allergy Clin Immunol*. 2023 Dec 12:S0091-6749(23)02414-4. doi: 10.1016/j.jaci.2023.11.918. [Article link](#)

Significance: Early introduction of allergenic foods appears to be the most effective intervention, but other options are being studied, and will hopefully lead to modification of the epidemiological trajectory of food allergy.

This review covers the latest publications in food allergy over the last couple of years. Food allergy is a major public health concern, affecting about 8% of children and 10% of adults in developed countries. The food allergy prevalence varies around the world, with environmental factors mainly driving the increase, possibly together with genetical susceptibility to environmental changes. A precise diagnosis of food allergy is extremely important - both new tests (e.g. basophil activation test) and improved optimization of information provided by existing tests (e.g. skin prick test and specific IgE) can contribute to improving the accuracy and patients' comfort of food allergy diagnosis. Understanding the underlying immune mechanisms is fundamental to designing allergen-specific treatments that can be safe and effective in the long-term. New discoveries have emerged at various levels of the immune response to food allergens, including T cell and B cell responses. Novel therapeutic approaches are being trialed at various stages of development and will hopefully allow for more active intervention to treat food allergy. Prevention is key to reduce the increase in prevalence. Early introduction of allergenic foods seems to be the most effective intervention, but others are being studied, and will hopefully lead to modification of the epidemiological trajectory of food allergy over time.

Emerging Science Areas

Emerging Topic: Safe Manganese Levels

Scientific Opinion on the Tolerable Upper Intake Level for Manganese

EFSA Panel on Nutrition, Novel Foods and Food Allergens (NDA), Dominique Turck, Torsten Bohn, Jacqueline Castenmiller, Stefaan de Henauw, Karen-Ildico Hirsch-Ernst, et. al. *EFSA Journal*, 8 Dec. 2023. doi.org/10.2903/j.efsa.2023.8413. [Article link](#)

Significance: European regulators adopted a safe level of Manganese intake at 8 mg/day for adults (≥ 18 years including pregnant and lactating females), and 2-7 mg/day for other groups.

Following a request from the European Commission (EC), the EFSA Panel on Nutrition, Novel Foods and Food Allergens (NDA) was asked to deliver a scientific opinion on the tolerable upper intake level (UL) for manganese. Systematic reviews of the literature of human and animal data were conducted to assess evidence regarding excess manganese intake (including authorised manganese salts) and the priority adverse health effect, i.e. manganese-induced neurotoxicity. Available human and animal studies support neurotoxicity as a critical effect, however, data are not sufficient and suitable to characterize a dose-response relationship and identify a reference point for manganese-induced neurotoxicity. In the absence of adequate data to establish an UL, estimated background dietary intakes (i.e. manganese intakes from natural dietary sources only) observed among high consumers (95th percentile) were used to provide an indication of the highest level of intake where there is reasonable confidence on the absence of adverse effects. A safe level of intake of 8 mg/day was established for adults ≥ 18 years (including pregnant and lactating women) and ranged between 2 and 7 mg/day for other population groups. The application of the safe level of intake is more limited than an UL because the intake level at which the risk of adverse effects starts to increase is not defined.

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