**Foodborne Pathogens**

**Occurrence of Salmonella in Ready-to-Eat Meat and Poultry Product Samples from U.S. Department of Agriculture-Regulated Producing Establishments. II. Salmonella in Ready-to-Eat Pork Barbecue Products, from 2005 to 2012**


**Significance:** The USDA Food Safety and Inspection Service has issued guidelines to minimize foodborne infection of pork barbeque.

Ready-to-eat (RTE) meat and poultry product samples from the random ALLRTE and risk-based RTE001 sampling projects of the Food Safety and Inspection Service (FSIS) were tested for both *Listeria monocytogenes* and *Salmonella*. In the course of analyzing *Salmonella* data for calendar years 2005 to 2012, it was observed that 8 (17.0%) of 47 positive samples were from pork barbeque. The eight *Salmonella*-positive samples, from seven establishments in a single state, were from 1,085 pork barbeque samples tested nationwide (0.74% positive) and from 296 samples tested from that one state (2.7% positive). The seven establishments represented 30.4% of 23 federal establishments in that state that had pork barbeque samples tested for *Salmonella*. A follow-up sample from intensified verification testing at one of the seven establishments also was positive for *Salmonella*. Upon further examination, contamination appeared to be influenced by regional differences in production methods. Notably, the style of pork barbeque that tested positive for *Salmonella* used a vinegar- and pepper-based sauce in which the ingredients were mixed without cooking. All the establishments with *Salmonella*-positive samples followed the practice of first cooking the pork and then adding the barbeque sauce ingredients (vinegar, pepper, other spices, etc.) after cooking (postlethality exposure). In addition to the sauce ingredients, other possible sources of contamination included employee hygiene and food handling practices and cross-contamination from other *Salmonella*-contaminated products and from commonly used equipment. Based on these findings, the FSIS issued guidelines recommending changes in production methods that would minimize or eliminate pork barbeque as a potential source of foodborne *Salmonella* infections.

**Food Processing Safety**

**Foodborne Viruses: Detection, Risk Assessment, and Control Options in Food Processing**


**Significance:** A description of foodborne virus characteristics and response to control measure technologies is provided.

In a recent report by risk assessment experts on the identification of food safety priorities using the Delphi technique, foodborne viruses were recognized among the top rated food safety priorities and have become a greater concern to the food industry over the past few years. Food safety experts agreed that control measures for viruses throughout the food chain are required. However, much still needs to be understood with regard to the effectiveness of these controls and how to properly validate their performance, whether it is personal hygiene of food handlers or the effects of processing of at-risk foods or the interpretation and action required on positive virus test result. This manuscript provides a description of foodborne viruses and their characteristics, their responses to stress and technologies developed for viral detection and control. In addition, the gaps in knowledge and understanding, and future perspectives on the application of viral detection and control strategies for the food industry, along with suggestions on how the food industry could implement effective control strategies for viruses in foods. The current state of the science on epidemiology, public health burden, risk assessment and management options for viruses in food processing environments will be highlighted in this review.

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Radio-Frequency Processing for Inactivation of *Salmonella enterica* and *Enterococcus faecium* NRRL B-2354 in Black Peppercorn


**Significance:** Radio-frequency heating is an effective treatment for *Salmonella* inactivation without compromising the quality of back peppercorn.

Several *Salmonella* outbreaks linked to black pepper call for effective inactivation processes, because current decontamination methods result in quality deterioration. Radio-frequency (RF) heating provides a rapid heating rate and volumetric heating, resulting in a shorter come-up time. This allows for choosing a high-temperature and short-time combination to achieve the desired inactivation with minimal quality deterioration. The objectives of this study were to evaluate RF heating for inactivation of *Salmonella enterica* and *Enterococcus faecium* in black peppercorn and evaluate quality changes of RF-treated black peppercorn. Black peppercoms were inoculated with a five-strain cocktail of *Salmonella* or *E. faecium* to attain initial population levels of 6.8 and 7.3 log CFU/g, respectively, and were then adjusted to a moisture content of 12.7% (wet basis) and a water activity of 0.60 at room temperature. A stability test was performed to quantify the microbial reduction during inoculation and equilibration before RF heating inactivation. During RF heating, the cold spot was determined to be at the center on the top surface of the treated sample. In addition to inoculating the entire sample, an inoculated packed sample was placed at the cold spot of the tray. An RF heating time of 2.5 min provided a 5.31- and 5.26-log CFU/g reduction in the entire sample contained in the tray for *Salmonella* and *E. faecium*, respectively. Color parameters (L*, a*, b*), piperine content, total phenolics, scavenging activity, and most of the volatile compounds of 2.5-min RF-treated samples were not significantly different from those of the control samples. These data suggest that RF heating is a promising thermal inactivation treatment for *Salmonella* without significant quality deterioration, and *E. faecium* seems to be a suitable surrogate for *Salmonella* to validate the efficacy of RF heating of black peppercorn.

**Food Packaging**

**Scientific Advances and Challenges in Safety Evaluation of Food Packaging Materials: Workshop Proceedings**


**Significance:** The state of the science regarding the safety of food packaging, including research gaps and challenges, is discussed. This work was supported by the ILSI North America Food & Chemical Safety Committee. Subsequent work on this topic is being undertaken by the Food Packaging Safety Committee.

Packaging is an indispensable component of the food manufacturing and food supply process. This scientific workshop was convened to bring together scientists from government, academia, and industry to discuss the state of the science regarding the safety of food packaging, prompted by rapidly advancing research to improve food packaging that continues to impact packaging technology, toxicology, exposure, risk assessment, and sustainability. The opening session focused on scientific challenges in the safety assessment of food packaging materials. Experts discussed migration of contaminant residues from food packaging, presented emerging analytical methods for safety evaluation, and highlighted the use of improved exposure assessment models and new packaging technologies. The workshop then focused on recycled packaging and sustainability. Experts also discussed application of recycled materials in food packaging, recycling processes, identification of contaminant residues from recycled packaging, and challenges in safety assessment of recycled materials. The workshop concluded with panel discussions that highlighted the challenges and research gaps in food packaging. Overall, there is a need to better understand and define “contaminants in food packaging” for developing appropriate testing methods needed to establish the significance of the migration levels of these contaminants and conduct appropriate safety assessments in this rapidly evolving field.

**Risk Assessment for Migration of Styrene Oligomers into Food from Polystyrene Food Containers**


**Significance:** Dimers and trimers of styrene in polystyrene food packaging present a low risk for consumers.

Regulation EU 10/2011 requires a risk assessment of Non Intentionally Added Substances (NIAS) migrating into food for food contact plastics within the EU. Styrene oligomers are important potential components of NIAS in polystyrene used for food packaging and so far only dimers and trimers have been identified. They are not genotoxic in vitro, and there is good evidence that they are not endocrine disruptors. Hazard characterization to establish “safe” exposure levels is based on 1. The No Adverse Effect Level (NOAEL) of 1 mg/kg bw/d in an oral rat study during pregnancy and lactation and 2. The concept of Threshold of
Toxicological Concern (TTC). Likely human exposure is derived from 1. The concentrations of dimers and trimers in food simulants or 2. Food and 3. The probabilistic FACET exposure estimation based on dimer and trimer concentrations in polystyrene and their potential for migration. The Margin of Safety as the relation of potential consumer exposure and the “safe” exposure level was always above 1 (apart from migration with 95% ethanol which is no longer recommended as an official food simulant for overall migration into fatty food) demonstrating that dimers and trimers in PS food packaging present a low risk for consumers.

Natural Biomaterial-Based Edible and pH-Sensitive Films Combined with Electrochemical Writing for Intelligent Food Packaging

Significance: A composite film was developed for use in monitoring food spoilage as part of an intelligent packaging system.

An edible and pH-sensitive film combined with electrochemical writing was developed by using gelatin, gellan gum, and red radish anthocyanins extract for intelligent food packaging. The composite film showed an orange red-to-yellow color change in the pH range of 2-12. The tensile strength, ductility, and barrier abilities to ultraviolet (UV) light and oxygen of the films were improved as the concentration of red radish anthocyanins increased. Multicolor patterns were successfully drawn on the films by using the electrochemical writing method. The composite films, which acted as gas sensors, presented visible color changes in the presence of milk and fish spoilage, while the written patterns were well-preserved. Accordingly, this composite film with written patterns could be an easy-to-use indicator with great potential for monitoring food spoilage as a part of an intelligent packaging system.

Risk Assessment
One Science-Driven Approach for the Regulatory Implementation of Alternative Methods: A Multi-Sector Perspective

Significance: The challenges faced by different industry sectors in the implementation of alternative methods to animal testing in risk assessment are discussed.

EU regulations call for the use of alternative methods to animal testing. During the last decade, an increasing number of alternative approaches have been formally adopted. In parallel, new 3Rs-relevant technologies and mechanistic approaches have increasingly contributed to hazard identification and risk assessment evolution. In this changing landscape, an EPAA meeting reviewed the challenges that different industry sectors face in the implementation of alternative methods following a science-driven approach. Although clear progress was acknowledged in animal testing reduction and refinement thanks to an integration of scientifically robust approaches, the following challenges were identified: i) further characterization of toxicity pathways; ii) development of assays covering current scientific gaps, iii) better characterization of links between in vitro readouts and outcome in the target species; iv) better definition of alternative method applicability domains, and v) appropriate implementation of the available approaches. For areas having regulatory adopted alternative methods (e.g., vaccine batch testing), harmonised acceptance across geographical regions was considered critical for broader application. Overall, the main constraints to the application of non-animal alternatives are the still existing gaps in scientific knowledge and technological limitations. The science-driven identification of most appropriate methods is key for furthering a multi-sectorial decrease in animal testing.

Existing Regulatory Approaches to Reducing Exposures to Chemical- and Product-Based Risk and Their Applicability to Diet-Related Chronic Disease

Significance: This analysis found precedent for mandatory regulatory approaches that could address harms related to exposure to unhealthy diets.

We aimed to identify and categorize the types of policies that have been adopted to protect Americans from harmful exposures that could also be relevant for addressing diet-related chronic diseases. This article examines and categorizes the rationales behind government regulation. Our interest in the historical analysis is to inform judgments about how best to address newly emergent risks involving diet-related chronic disease within existing regulatory and information-based frameworks. We assessed exemplars of regulation with respect to harmful exposures from air, water, and food, as well as regulations that are intended to modify voluntary behaviors. Following the comparative analysis, we explored how exposures that lead to diet-related chronic
diseases among the general population fit within models of regulation adopted for other comparable risks. We identified five rationales and five approaches that protect people from harmful exposures. Reasons for regulation include: protection from involuntary exposure to risk, high risk of death or chronic illness, ubiquity of risk, counteraction to limit compulsive behaviors, and promotion of population health. Regulatory approaches include: mandatory limits on use, mandatory limits on exposure, mandatory controls on quality, mandatory labeling, and voluntary guidance. In contrast to the use of mandates, the prevention of diet-related chronic diseases thus far has largely relied on information-only approaches and voluntary adoption of guidelines. There is ample precedent for mandatory regulatory approaches that could address harms related to exposure to unhealthy diets, but several barriers to action would need to be overcome.

**Heavy Metals**

A State-of-the-Science Review of Mercury Biomarkers in Human Populations Worldwide between 2000 and 2018


**Significance:** Populations for concern of mercury exposure are identified.

**BACKGROUND:** The Minamata Convention on Mercury provided a mandate for action against global mercury pollution. However, our knowledge of mercury exposures is limited because there are many regions and subpopulations with little or no data. **OBJECTIVE:** We aimed to increase worldwide understanding of human exposures to mercury by collecting, collating, and analyzing mercury concentrations in biomarker samples reported in the published scientific literature. **METHOD:** A systematic search of the peer-reviewed scientific literature was performed using three databases. A priori search strategy, eligibility criteria, and data extraction steps were used to identify relevant studies. **RESULTS:** We collected 424,858 mercury biomarker measurements from 335,991 individuals represented in 312 articles from 75 countries. General background populations with insignificant exposures have blood, hair, and urine mercury levels that generally fall under [Formula: see text], [Formula: see text], and [Formula: see text], respectively. We identified four populations of concern: a) Arctic populations who consume fish and marine mammals; b) tropical riverine communities (especially Amazonian) who consume fish and in some cases may be exposed to mining; c) coastal and/or small-island communities who substantially depend on seafood; and d) individuals who either work or reside among artisanal and small-scale gold mining sites. **CONCLUSIONS:** This review suggests that all populations worldwide are exposed to some amount of mercury and that there is great variability in exposures within and across countries and regions. There remain many geographic regions and subpopulations with limited data, thus hindering evidence-based decision making. This type of information is critical in helping understand exposures, particularly in light of certain stipulations in the Minamata Convention on Mercury. [https://doi.org/10.1289/EHP3904](https://doi.org/10.1289/EHP3904).

**Food Allergy**

Multicenter, Randomized, Double-Blind, Placebo-Controlled Clinical Trial of Vital Wheat Gluten Oral Immunotherapy


**Significance:** The efficacy and safety of vital wheat gluten oral immunotherapy was evaluated.

**BACKGROUND:** Wheat is a common food allergen that can cause anaphylaxis. **OBJECTIVE:** We sought to determine the efficacy and safety of vital wheat gluten (VWG) oral immunotherapy (OIT). **METHODS:** After baseline double-blind, placebo-controlled food challenge (DBPCFC), 46 patients with wheat allergy (median age, 8.7 years; range, 4.2-22.3 years) were randomized 1:1 to low-dose VWG OIT or placebo, with biweekly escalation to 1445 mg of wheat protein (WP). After a year 1 DBPCFC, active subjects continued low-dose VWG OIT for another year and underwent a year 2 DBPCFC and, if passed, a subsequent off-therapy DBPCFC. Placebo-treated subjects crossed over to high-dose VWG OIT (maximum, 2748 mg of WP). **RESULTS:** The median baseline successfully consumed dose (SCD) was 43 mg of WP in both groups. At year 1, 12 (52.2%) of 23 low-dose VWG OIT-treated and 0 (0%) of 23 placebo-treated subjects achieved the primary end point of an SCD of 4443 mg of WP or greater (P < .0001); median SCDs were 4443 and 143 mg, respectively. At year 2, 7 (30.4%) of 23 low-dose VWG OIT-treated subjects were desensitized to an SCD of 7443 mg of WP; 3 (13%) achieved sustained unresponsiveness 8 to 10 weeks off therapy. Among placebo-treated subjects who crossed over to high-dose VWG OIT, 12 (57.1%) of 21 were desensitized after 1 year (median SCD, 7443 mg of WP;
nonsignificant vs low-dose VWG OIT). At year 1, skin prick test responses and wheat- and omega-5 gliadin-specific IgE levels did not differ between groups; the low-dose VWG OIT median specific IgG4 level was greater than placebo (wheat, $P = .0005$; omega-5 gliadin, $P = .0001$). Year 1 SCDS correlated with wheat-specific ($\rho = 0.55$, $P = .0003$) and omega-5 gliadin-specific ($\rho = 0.51$, $P = .001$) IgG4 levels in all subjects. Among 7822 low-dose VWG OIT doses in year 1, 15.4% were associated with adverse reactions: 0.04% were severe, and 0.08% subjects received epinephrine. Among 7921 placebo doses, 5.8% were associated with adverse reactions; none were severe. CONCLUSIONS: Low- and high-dose VWG OIT induced desensitization in about one half of the subjects after 1 year of treatment. Two years of low-dose VWG OIT resulted in 30% desensitization, and 13% had sustained unresponsiveness.

The IgE Memory Reservoir in Food Allergy

**Significance:** Alternative explanations for allergic persistence are explored.

IgE is a central effector component of TH2 immune responses toward helminths and allergens. With regard to food allergens, the clinical manifestations of food allergy are primarily mediated by IgE. Certain food allergies, such as those to peanut, tree nuts, fish, and shellfish, are lifelong in the majority of patients, and their persistence has been attributed to long-lived, IgE-secreting plasma cells (PCs). This led to the proposition that these cells are potential therapeutic targets in patients with food allergy. However, several lines of evidence have disputed this concept and have compelled researchers to search for alternative explanations for allergic persistence.

Nanomaterials

**A Review on Silver Nanoparticles-Induced Ecotoxicity and the Underlying Toxicity Mechanisms**

**Significance:** The toxicity mechanisms of silver nanoparticles are discussed.

Silver nanoparticles (Ag-NPs) are increasingly being applied in many consumer products due to their unique properties. Widespread use of Ag-NPs leads to an increasing human exposure to Ag-NPs in many different pathways. This review summarized the toxicity mechanisms of Ag-NPs based on various environmentally relevant test species, such as bacteria, cells, plants, aquatic animals and mammals, in both in vitro and in vivo experiments. Nanoparticles were usually exposed to combination chemicals but to single chemicals in the environment and thereby exert combined toxicities to the organisms. Therefore, the joint effects of nanomaterials and their co-existing characteristics were also discussed. The current knowledge gaps and safe product designs of Ag-NPs have been discussed in detail. The limited and existing data implied that understanding the toxicity mechanisms is crucial to the future research development of nanomaterials.

Caffeine

**Associations of Maternal Caffeine Intake with Birth Outcomes: Results from the Lifeways Cross Generation Cohort Study**

**Significance:** This prospective observational study found adverse birth outcomes associated with maternal caffeine intake from coffee and tea.

BACKGROUND: Maternal caffeine intake is associated with adverse birth outcomes, but in most studies the primary caffeine source is coffee; the influence of tea caffeine remains unclear. OBJECTIVE: The aim of the study was to examine the association between maternal caffeine intake and birth outcomes in a population with tea as the predominant caffeine source. DESIGN: Data from 941 Irish mother-child pairs of the Lifeways Cross Generation Cohort Study were examined. Maternal dietary intakes in early pregnancy were assessed using a validated food-frequency questionnaire. Caffeine intake was derived from coffee, tea, soft drinks, and cocoa-containing foods and beverages. Associations of maternal caffeine intake with continuous (birth weight, birth length, and gestational age) and binary (low birth weight (LBW) (<2500 g) and preterm birth (PB) (<37 wk gestational age)) birth outcomes were investigated using multiple linear and logistic regressions, respectively, with adjustment for potential confounders. RESULTS: Tea was the predominant caffeine source (48%), followed by coffee (39%). In the fully adjusted model, maternal caffeine intake was associated with lower birth weight [95% CI]: -71.9 (-105.4, -38.4) g · 100 mg-1 · d-1 caffeine increment],
shorter birth length [-0.30 (-0.49, -0.11) cm], smaller head circumference [-0.12 (-0.24, -0.01) cm], and shorter gestational age [-0.13 (-0.25, -0.02) wk]; higher risks for LBW [OR (95% CI): 1.47 (1.14, 1.90)] and PB [1.36 (1.07, 1.74)] were also observed (all P < 0.05). The associations were robust to the exclusion of participants with pregnancy complications and in never smokers. Similar higher risks of adverse birth outcomes were observed for the highest caffeine intake categories from coffee [ORLBW: 3.10 (1.08, 8.89); ORPB: 2.74 (1.05, 7.16)] and tea [ORLBW: 2.47 (1.02, 6.01); ORPB: 2.56 (1.14, 5.75)], compared with the lowest intake categories (all P < 0.05). CONCLUSIONS: Maternal caffeine intake from both coffee and tea is associated with adverse birth outcomes. This prospective observational study was registered at ISRCTN Registry as ISRCTN16537904.

Daily Patterns of Caffeine Intake and the Association of Intake with Multiple Sociodemographic and Lifestyle Factors in US Adults Based on the NHANES 2007-2012 Surveys

Significance: The daily pattern of caffeine intake and its relationship to demographic variables were examined.

BACKGROUND: Caffeine increases alertness when consumed in single servings of various products including coffee, tea, soft drinks, and energy drinks. Although not a nutrient, caffeine is consumed by 90% of the adult population in the United States. OBJECTIVE: This study examined the daily pattern of caffeine intake and its relationship to multiple demographic variables. METHODS: Data from the National Health and Nutrition Examination Survey (NHANES) 2007-2012 (adults aged 19+ years; n=16,173) were used to determine the time of day at which caffeine is consumed and demographic factors associated with intake. Regression analyses characterized factors associated with caffeine intake including sex, age, ethnicity, education, smoking status, physical activity, employment status, total work hours, alcohol, and energy intake. RESULTS: Mean adult per capita caffeine intake was 169±4 mg/d (mean±standard error). Most caffeine (70%) was consumed before noon, often at breakfast, and intake decreased progressively over the day, with little consumed after 9:00 pm. Intake was associated with age, ethnicity, smoking status, total calorie intake, and work hours (P<0.01) but not physical activity, economic status, education level, or employment status. Variables with the largest associations with intake were, respectively, ethnicity and age. Non-Hispanic black individuals consumed the smallest amounts (80±2 mg/d), non-Hispanic white individuals consumed the greatest amounts (194±3 mg/d), and Asian individuals (126±7 mg/d) and Hispanic individuals consumed intermediate amounts (127±3 mg/d). Middle-aged individuals (aged 50 to 54 years) consumed more caffeine (211±6 mg/d) than younger (107±4 mg/d, aged 20 to 24 years) and older individuals (153±4 mg/d, aged 75 to 79 years). CONCLUSION: Most caffeine is consumed in the morning, when alertness is lowest, and very little in the evening before sleep. Ethnicity and age were the variables most strongly associated with intake; work hours, occupation, energy and alcohol intake, and smoking were also associated with intake. Because caffeine increases alertness, it is not surprising that its pattern of consumption and factors associated with its intake vary from those of most other food constituents.