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Marine Science Review - 241 Human health



In this review:

- A. Recent articles no abstract available
- B. Recent articles with abstracts

O/A denotes an open access article or journal

A. Recent articles – no abstract available

Weiss, B. Why methylmercury remains a conundrum 50 years after Minamata. Toxicological Sciences 97(2): 223-225, 2007.

Trasande, L., Landrigan, P.J., Schechter, C.B., and Bopp, R.F. Methylmercury and the developing brain. *Environmental Health Perspectives* 115(8): A396-A397, 2007. O/A

Griffiths, C., McGartland, A., and Miller, M. Methylmercury and the brain: Griffiths *et al.* respond. *Environmental Health Perspectives* 115(8): A397-A398, 2007. **O/A**

Lowry, T. and Smith, S.A. Zoonosis update - Aquatic zoonoses associated with food, bait, ornamental, and tropical fish. *Journal of the American Veterinary Medical Association* 231(6): 876-880, 2007.

B. Recent articles with abstracts

Sexton, K. and Hattis, D. Assessing cumulative health risks from exposure to environmental mixtures - Three fundamental questions. *Environmental Health Perspectives* 115(5): 825-832, 2007. O/A

Notes: Differential exposure to mixtures of environmental agents, including biological, chemical, physical, and psychosocial stressors, can contribute to increased vulnerability of human populations and ecologic systems. Cumulative risk assessment is a tool for organizing and analyzing information to evaluate the probability and seriousness of harmful effects caused by either simultaneous and/or sequential exposure to multiple environmental stressors. In this article we focus on elucidating key challenges that must be addressed to determine whether and to what degree differential exposure to environmental mixtures contributes to increased vulnerability of exposed populations. In particular, the emphasis is on examining three fundamental and interrelated questions that must be addressed as part of the process to assess cumulative risk: a) Which mixtures are most important from a public health perspective? and b) What is the nature (i.e., duration, frequency, timing) and magnitude (i.e., exposure concentration and dose) of relevant cumulative exposures for the population of interest? c) What is the mechanism (e.g., toxicokinetic or toxicodynamic) and consequence (e.g., additive, less than additive, more than additive) of the mixture's interactive effects on exposed populations? The focus is primarily on human health effects from chemical mixtures, and the goal is to reinforce the need for improved assessment of cumulative exposure and better understanding of the biological mechanisms that determine toxicologic interactions among mixture constituents.

Tittlemier, S.A., Pepper, K., Seymour, C., Moisey, J., Bronson, R., Cao, X.L., and Dabeka, R.W. **Dietary exposure of Canadians to perfluorinated carboxylates and perfluorooctane sulfonate via consumption of meat, fish, fast foods,**

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and food items prepared in their packaging. Journal of Agricultural and Food Chemistry 55(8): 3203-3210, 2007.

Notes: Human exposure to perfluorinated compounds is a worldwide phenomenon; however, routes of human exposure to these compounds have not been well-characterized. Fifty-four solid food composite samples collected as part of the Canadian Total Diet Study (TDS) were analyzed for perfluorocarboxylates and perfluorooctanesulfonate (PFOS) using a methanol extraction liquid chromatography tandem mass spectrometry method. Foods analyzed included fish and seafood, meat, poultry, frozen entrees, fast food, and microwave popcorn collected from 1992 to 2004 and prepared as for consumption. Nine composites contained detectable levels of perfluorinated compounds -- four meat-containing, three fish and shellfish, one fast food, and one microwave popcorn. PFOS and perfluorooctanoate (PFOA) were detected the most frequently; concentrations ranged from 0.5 to 4.5 ng/g. The average dietary intake of total perfluoro-carboxylates and PFOS for Canadians was estimated to be 250 ng/day, using results from the 2004 TDS composites. A comparison with intakes of perfluorocarboxylates and PFOS via other routes (air, water, dust, treated carpeting, and apparel) suggested that diet is an important source of these compounds. There was a substantial margin of exposure between the toxicological points of reference and the magnitude of dietary intake of perfluorinated compounds for Canadians ≥ 12 years old.

Kiljunen, M., Vanhatalo, M., Mantyniemi, S., Peltonen, H., Kuikka, S., Kiviranta, H., Parmanne, R., Tuomisto, J.T., Vuorinen, P.J., Hallikainen, A., Verta, M., Ponni, J., Jones, R.I., and Karjalainen, J. Human dietary intake of organochlorines from Baltic herring: Implications of individual fish variability and fisheries management. *Ambio* 36(2-3): 257-264, 2007.

Notes: This study examines the extent to which Finnish human dietary intake of organochlorines (PCDD/Fs and PCBs) originating from Northern Baltic herring can be influenced by fisheries management. This was investigated by estimation of human intake using versatile modeling tools (e.g., a herring population model and a bioenergetics model). We used a probabilistic approach to account for the variation in human intake of organochlorines originating from the variation among herring individuals. Our estimates were compared with present precautionary limits and recommendation for use. The results show that present consumption levels and frequencies of herring give a high probability of exceeding recommended intake limits of PCDD/Fs and PCBs. Furthermore, our results clearly demonstrate that in the risk management of dioxin-like organochlorines, regulating fishing (in this case increasing fishing pressure) is a far less effective way to decrease the risk than regulating the consumption of herring. Increased fishing would only slightly decrease organochlorine concentrations of herring in the Finnish fish market.

Wilkinson, P., Smith, K.R., Joffe, M., and Haines, A. A global perspective on energy: health effects and injustices. *The Lancet* 370(9591): 965-978, 2007. O/A

Notes: The exploitation of fossil fuels is integral to modern living and has been a key element of the rapid technological, social, and cultural changes of the past 250 years. Although such changes have brought undeniable benefits, this exploitation has contributed to a burden of illness through pollution of local and regional environments, and is the dominant cause of climate change. This pattern of development is therefore unsustainable at a global level. At the same time, about 2 4 billion of the world's population, disadvantaged by lack of access to clean energy, are exposed to high levels of indoor air pollutants from the inefficient burning of biomass fuels. Even in high-income countries, many people live in fuel poverty, and throughout the world, increasingly sedentary lifestyles (to which fossil-fuel-dependent transport systems contribute) are leading to chronic disease and injuries. Energy security is also an issue of growing concern to many governments in both the developed and developing world, and a potential source of international tension and conflict. In this Series, we examine the opportunities to improve health, reduce climate effects, and promote development through realistic adjustments in the way energy and food are produced and consumed.

Ilback, N.G. and Friman, G. Interactions among infections, nutrients and xenobiotics. *Critical Reviews in Food Science and Nutrition* 47(5): 499-519, 2007.

Notes: During recent years there have been several incidents in which symptoms of disease have been linked to consumption of food contaminated by chemical substances (e.g., 2,3,7,8-tetrachlorodibenzo-*p*-dioxin, TCDD). Furthermore, outbreaks of infections in food-producing animals have attracted major attention regarding the safety of consumers, e.g., Bovine

Spongiform Encephalitis (BSE) and influenza in chicken. As shown for several xenobiotics in an increasing number of experimental studies, even low-dose xenobiotic exposure may impair immune function over time, as well as microorganism virulence, resulting in more severe infectious diseases and associated complications. Moreover, during ongoing infection, xenobiotic uptake and distribution are often changed resulting in increased toxic insult to the host. The interactions among infectious agents, nutrients, and xenobiotics have thus become a developing concern and new avenue of research in food toxicology as well as in food-borne diseases. From a health perspective, in the risk assessment of xenobiotics in our food and of environment, synergistic effects among microorganisms, nutrients, and xenobiotics will have to be considered. Otherwise, such effects may gradually change the disease panorama in society.

Drake, S.L., DePaola, A., and Jaykus, L.A. An overview of Vibrio vulnificus and Vibrio parahaemolyticus. Comprehensive Reviews in Food Science and Food Safety 6(4): 120-144, 2007. O/A

Notes: The Vibrionaceae are environmentally ubiquitous to estuarine waters. Two species in particular, *V. vulnificus* and *V. parabaemolyticus*, are important human pathogens that are transmitted by the consumption of contaminated molluscan shellfish. This document provides a comprehensive review of the current state of knowledge about these important foodborne disease agents. Topics include the epidemiology of human disease; biotypes and virulence factors; cultural and molecular-based detection methods; phenotyping and genotyping approaches; microbial ecology; and candidate control strategies. Recent international risk assessment efforts are also described. The reader will gain an understanding of why these organisms pose a public health risk and how improving our understanding of their behavior in the environment and the host can aid in reducing that risk in the future.

David, S.T., McIntyre, L., MacDougal, L., Kelly, D., Liem, S., Schallie, K., McNabb, A., Houde, A., Mueller, P., Ward, P., Trottier, Y.L., and Brassard, J. An outbreak of norovirus caused by consumption of oysters from geographically dispersed harvest sites, British Columbia, Canada, 2004. *Foodborne Pathogens and Disease* 4(3): 349-358, 2007.

Notes: *Objectives*: In January 2004, an increase in gastrointestinal illness following oyster consumption was reported in British Columbia. An investigation was initiated to explore the association between norovirus infection and consumption of British Columbia oysters and to identify the source of oyster contamination. *Methods*: The outbreak investigation included active surveillance for human cases, two cohort studies, trace-back of oysters, and laboratory testing of oysters and human stools. *Results*: Enhanced surveillance identified 26 confirmed and 53 clinical cases over 3 months. Oyster consumption was associated with illness in one cohort and suggestive in the other. Oysters were traced to 14 geographically dispersed harvest sites, 18 suppliers, and 45 points of purchase. Norovirus BCCDC03-028 (genotype I.2) was detected in 50% of human specimens. Experimental methods detected norovirus in 12 oyster samples. Sequencing identified mixed clonal patterns in the oysters with one direct sequence match between an oyster sample and the associated human specimen. *Conclusions*: The consumption of raw oysters led to norovirus infection. The source of oyster contamination remained unidentified. The geographical dispersion of implicated harvest sites was unusual. *Applications*: This outbreak is unlike most shellfish outbreaks that can be traced back to a common source and challenges conventional thinking that all oyster-related norovirus outbreaks of are a result of point source contamination.

Sunnotel, O., Snelling, W.J., McDonough, N., Browne, L., Moore, J.E., Dooley, J.S.G., and Lowery, C.J. Effectiveness of standard UV depuration at inactivating *Cryptosporidium parvum* recovered from spiked Pacific oysters (*Crassostrea gigas*). *Applied and Environmental Microbiology* 73(16): 5083-5087, 2007.

Notes: When filter-feeding shellfish are consumed raw, because of their ability to concentrate and store waterborne pathogens, they are being increasingly associated with human gastroenteritis and have become recognized as important pathogen vectors. In the shellfish industry, UV depuration procedures are mandatory to reduce pathogen levels prior to human consumption. However, these guidelines are based around more susceptible fecal coliforms and *Salmonella* spp. and do not consider *Cryptosporidium* spp., which have significant resistance to environmental stresses. Thus, there is an urgent need to evaluate the efficiency of standard UV depuration against the survival of *Cryptosporidium* recovered from shellfish. Our study found that in industrial-scale shellfish depuration treatment tanks, standard UV treatment resulted in a 13-fold inactivation of recovered, viable *C. parvum* oocysts from spiked (1 x 106 oocysts liter¹) Pacific oysters. Depuration at half power also

significantly reduced (P < 0.05; ninefold) the number of viable oocysts recovered from oysters. While UV treatment resulted in significant reductions of recovered viable oocysts, low numbers of viable oocysts were still recovered from oysters after depuration, making their consumption when raw a public health risk. Our study highlights the need for increased periodic monitoring programs for shellfish harvesting sites, improved depuration procedures, and revised microbial quality control parameters, including *Cryptosporidium* assessment, to minimize the risk of cryptosporidiosis.

Graczyk, T.K. and Fried, B. Human waterborne trematode and protozoan infections. *Advances in Parasitology* 64: 111-160, 2007.

Notes: Waterborne trematode and protozoan infections inflict considerable morbidity on healthy, i.e., immunocompetent people, and may cause life-threatening diseases among immunocompromised and immunosuppressed populations. These infections are common, easily transmissible, and maintain a worldwide distribution, although waterborne trematode infections remain predominantly confined to the developing countries. Waterborne transmission of trematodes is enhanced by cultural practices of eating raw or inadequately cooked food, socio-economical factors, and wide zoonotic and sylvatic reservoirs of these helminths. Waterborne protozoan infections remain common in both developed and developing countries (although better statistics exist for developed countries), and their transmission is facilitated via contacts with recreational and surface waters, or via consumption of contaminated drinking water. The transmissive stages of human protozoan parasites are small, shed in large numbers in feces of infected people or animals, resistant to environmental stressors while in the environment, and few are (e.g., *Cryptosporidium* oocysts) able to resist standard disinfection applied to drinking water.

Guo, J.Y., Zeng, E.Y., Wu, F.C., Meng, X.Z., Mai, B.X., and Luo, X.J. **Organochlorine pesticides in seafood products** from Southern China and health risk assessment. *Environmental Toxicology and Chemistry* 26(6): 1109-1115, 2007.

Notes: Seafood consumption is an important route of human exposure to organic contaminants. Residual levels of organochlorine pesticides (OCPs), including DDTs, hexachlorocyclohexanes (HCHs), heptachlor, aldrin, α -endosulfan, β -endosulfan, dieldrin, endrin aldehyde, endrin ketone, methoxychlor, endosulfan sulfate, and heptachlor epoxide, were determined in a wide variety of seafood products collected from 11 coastal cities in southern China in June and October 2005. The results indicated that OCPs were predominated by DDTs and HCHs. The concentrations of other OCP components generally were low and were detectable in a small number of seafood samples only, probably reflective of the generally low levels of these OCPs in the study region and low bioaccumulation potentials in the species under investigation. Risk assessment against various standards clearly showed that seafood products were highly contaminated by DDTs and may pose health threats to local residents and consumers all over the world. Furthermore, other OCP components, such as dieldrin and heptachlor, also impose lifetime cancer risk, especially to residents of coastal regions who often consume more seafood than those living inland. Therefore, continual monitoring of OCPs in various environment compartments, including biota and abiota, urgently is needed to mitigate effectively the impact of OCPs, particularly DDTs, on human health and the ecological environment.

Sunderland, D., Graczyk, T.K., Tamang, L., and Breysse, P.N. Impact of bathers on levels of *Cryptosporidium parvum* oocysts and *Giardia lamblia* cysts in recreational beach waters. *Water* Research 41(15): 3483-3489, 2007.

Notes: Recreational beach water samples collected on weekends and weekdays during 11 consecutive summer weeks were tested for potentially viable *Cryptosporidium parvum* oocysts and *Giardia lamblia* cysts using the multiplexed fluorescence in situ hybridization (FISH) method. The levels of oocysts and cysts on weekends were significantly higher than on the weekdays (P<0.01). Concentrations of oocysts in weekend samples (n = 27) ranged from 2 to 42 oocysts/L (mean: 13.7 oocysts/L), and cyst concentration ranged from 0 to 33 cysts/L (mean: 9.1 cysts/L). For the samples collected on weekdays (n = 33), the highest oocyst concentration was 7 oocysts/L (mean: 1.5 oocysts/L), and the highest cyst concentration was 4 cysts/L (mean: 0.6 cysts/L). The values of water turbidity were significantly higher on weekends than on weekdays, and were correlated with the number of bathers and concentration of *C. parvum* oocysts and *G. lamblia* cysts (P<0.04). The study demonstrated positive relationships between number of bathers and levels of waterborne *C. parvum* oocysts and *G. lamblia* cysts and *G. lamblia* cysts in recreational beach water. It is essential to test recreational waters for *Cryptosporidium* and *Giardia* when numbers of bathers are greatest, or limit the number of bathers in a recreational beach area.

Stern, A.H. **Public health guidance on cardiovascular benefits and risks related to fish consumption.** *Environmental Health* 6: art. 31, 2007. O/A

Notes: Historically, concerns with fish consumption have addressed risks from contaminants (e.g., methylmercury (MeHg), and PCBs). More recently public health concerns have widened in appreciation of the specific benefits of fish consumption such as those arising from polyunsaturated fatty acids (PUFAs) in fish oil. Fish contains varying levels of PUFAs and MeHg. Since both address the same health outcomes (in opposite directions) and occur together in fish, great care must be exercised in providing public health guidance. Mozaffarian and Rimm in a recent article (JAMA. 2006, 296:1885-99) have made a strong case for the beneficial effects of PUFAs in reducing the risk of coronary heart disease, but at the same time, have also broadly discounted the increased risks of coronary heart disease posed by MeHg in fish, stating that "... among adults... the benefits of fish intake exceed the potential risks." This conclusion appears to be based on an inaccurate and insufficiently critical analysis of the literature. This literature is re-examined in light of their conclusions, and the available and appropriate public health options are considered.

Smith, K.F., Sax, D.F., Gaines, S.D., Guernier, V., and Guegan, J.F. **Globalization of human infectious disease.** *Ecology* 88(8): 1903-1910, 2007.

Notes: Globalization has facilitated the spread of numerous infectious agents to all corners of the planet. Analysis of the Global Infectious Disease and Epidemiology Network (GIDEON) database quantitatively illustrates that the globalization of human infectious agents depends significantly on the range of hosts used. Infectious agents specific to humans are broadly and uniformly distributed, whereas zoonotic infectious agents are far more localized in their geographical distribution. Moreover, these patterns vary depending on transmission mode and infectious agent taxonomy. This dichotomy is unlikely to persist if certain aspects of globalization (for example, exotic species introductions) continue unabated. This raises a serious concern for public health and leaves nations with the task of determining the infectious agents that have the greatest potential to establish within their borders. At the advent of a century characterized by an apparent increase in emerging infectious diseases, these results have critical implications for public-health policy and future research pathways of infectious disease ecology.

Gilron, G., Archbold, J., Goldacker, S., and Downie, J. Issues related to chemical analysis, data reporting, and use: Implications for human health risk assessment of PCBs and PBDEs in fish tissue. *Human and Ecological Risk Assessment* 13(4): 773-791, 2007.

Notes: Recent reports in the scientific literature and the media, related to elevated levels of polychlorinated biphenyls (PCBs) and polybrominated diethyl ethers (PBDEs) in farmed and wild salmon have had significant impacts on public opinion and consumer behavior, influencing the sales of farmed salmon in North America and Europe. The assessment of contaminants in fatty fish, an important source of omega-3 fatty acids, is therefore an exercise in balancing risks and benefits. Human health risk assessors and risk managers will benefit from an understanding of the level of uncertainty that is integrated into all aspects of evaluating risk in this context. Significant variability exists in the way in which analyses are conducted, how data are reported, and how they are used in risk assessments. We conducted an analytical review of PCB and PBDE data in farmed and wild salmon, and identified critical issues having implications on human health risk assessment from fish consumption. These issues include: analytical methodologies used, quantification issues, reporting of QA/QC information, tissue sampling, nature of tissue analyzed, and laboratory competence. This article reviews and outlines these issues, discusses their implications for human health risk assessment, and recommends the consistent application of analytical fish tissue data in human health risk assessment.

Graczyk, T.K., Sunderland, D., Tamang, L., Lucy, F.E., and Breysse, P.N. **Bather density and levels of** *Cryptosporidium*, *Giardia*, and pathogenic microsporidian spores in recreational bathing water. *Parasitology Research* 101(6): 1729-1731, 2007.

Notes: The study demonstrated that the resuspension of bottom sediments caused by bathers and their direct microbial input resulted in elevated levels of *Cryptosporidium parvum* oocysts, *Giardia lamblia* cysts, and microsporidian spores, particularly *Enterocytozoon bieneusi*, in recreational beach water on days deemed acceptable for bathing by fecal bacterial standards.

Domingo, J.L. Omega-3 fatty acids and the benefits of fish consumption: Is all that glitters gold? *Environment International* 33(7): 993-998, 2007.

Notes: In recent years, a number of studies have clearly remarked the nutritional benefits of fish consumption: proteins, vitamins, minerals, and especially omega-3 polyunsaturated fatty acids (PUFAs), which may protect against several adverse health effects, including coronary heart disease mortality and stroke. However, some concerns about potential health risks derived from the environmental contaminants found in fish have been also raised. Therefore, balancing adequately the risks and benefits of fish consumption is currently a nutritional/environmental health key issue. In this paper, the most recent available scientific information concerning this issue is reviewed. It is concluded that although it seems evident that fish must be an important part of a balanced diet, to choose the most suitable species in terms of levels of PUFAs and pollutants, the frequency of consumption, and the meal size are essential aspects to balance benefits and risks of a regular consumption.

Yamahara, K.M., Layton, B.A., Santcro, A.E., and Boehm, A.B. Beach sands along the California coast are diffuse sources of fecal bacteria to coastal waters. *Environmental Science and Technology* 41(13): 4515-4521, 2007.

Notes: Fecal indicator bacteria (FIB) are nearly ubiquitous in California (CA) beach sands. Sands were collected from 55 beaches along the CA coast. Ninety-one percent of the beaches had detectable enterococci (ENT) while 62% had detectable E. coli (El.) in their sands. The presence of a putative bacterial source (such as a river), the degree of wave shelter, and surrounding land use explained a significant (p < 0.05) fraction of the variation in both ENT and EC densities between beaches. Sand characteristics including moisture content, organic carbon, and percent fines, significantly (p < 0.05) influenced only EC densities in beach sand. We assayed 34 of 163 sand samples for salmonellae, but did not detect this bacterial pathogen. The potential for FIB to be transported from the sand to sea was investigated at a single wave-sheltered beach with high densities of ENT in beach sand: Lovers Point, CA (LP). We collected samples of exposed and submerged sands as well as water over a 24 h period in order to compare the disappearance or appearance of ENT in sand and the water column. Exposed sands had significantly higher densities of ENT than submerged sands with the highest densities located near the high tide line. Water column ENT densities began low, increased sharply during the first flood tide and slowly decreased over the remainder of the study. During the first flood tide, the number of ENT that entered the water column was nearly equivalent to the number of ENT lost from exposed sands when they were submerged by seawater. The decrease in nearshore ENT concentrations after the initial influx can be explained by ENT die-off and dilution with clear ocean water. While some ENT in the water and sand at LF might be of human origin because they were positive for the esp gene, others lacked the esp gene and were therefore equivocal with respect to their origin. Follow-up sampling at LP revealed the presence of the human specific Bacteroides marker in water and sand.

Covaci, A., Voorspoels, S., Vetter, W., Gelbin, A., Jorens, P. G., Blust, R., and Neels, H. Anthropogenic and naturally occurring organobrominated compounds in fish oil dietary supplements. *Environmental Science and Technology* 41(15): 5237-5244, 2007.

Notes: Fish oil dietary supplements (FODS) are recommended to increase the intake of polyunsaturated fatty acids (PUFAs), renowned for their beneficial effects on human health. However, FODS also contain anthropogenic contaminants, such as polychlorinated biphenyls and polybrominated diphenyl ethers (PBDEs). Sixty-nine (n = 69) PUFA-enriched FODS from 37 producers were collected in 2006 and then analyzed for their levels of organobrominated compounds. Levels of the sum of trito hepta-BDEs (BDEs 28, 47, 49, 66, 85, 99, 100, 153, 154, and 183) were typically below 5 ng/g oil, while only a few had higher values of up to 44 ng/g oil. Several peaks in the chromatograms were identified as methoxylated PBDEs (MeO-PBDEs) and polybrominated hexahydroxanthene derivatives (PBHDs). These two groups of compounds have been suggested to be produced by marine organisms (e.g., algae and sponges) and have also been reported in marine samples, such as fish and marine mammals. Median concentrations of MeO-PBDEs and PBHDs (6.2 and 5.3 ng/g oil, respectively) were higher than median concentrations of PBDEs (0.6 ng/g oil), and their maximum values were 1670 and 200 ng/g oil, respectively. FODS

are intended to be consumed on a daily basis, and the median daily intakes of MeO-PBDEs and PBHDs from FODS were 3 and 6 times higher than the median intake of PBDEs (3 ng/day). Consumption of FODS does not appear to substantially increase the total dietary intake of PBDEs since the median daily intake from FODS was 8 and 16 times lower than the intake from either fish consumption alone or from total diet. These findings indicate that FODS might be a suitable alternative to fish consumption for certain segments of the population for which fish consumption advices have been issued. The present study also strongly supports the need for not only the inclusion of new anthropogenic contaminants (e.g., PBDEs) but also of naturally occurring compounds in monitoring schemes of marine products destined for human consumption.

She, J.W., Holden, A., Sharp, M., Tanner, M., Williams-Derry, C., and Hooper, K. Polybrominated diphenyl ethers (PBDEs) and polychlorinated biphenyls (PCBs) in breast milk from the Pacific Northwest. *Chemosphere* 67(9): S307-S317, 2007.

Notes: Breast milk samples from 40 first-time mothers from the Pacific Northwest of the US and Canada were analyzed for polybrominated diphenyl ethers (PBDEs) and polychlorinated biphenyls (PCBs). Total PBDEs (Σ PBDEs), calculated by summing values for the 12 PBDEs congeners analyzed, ranged from 6 to 321 ppb (lipid weight) (mean = 96 ppb; median = 50 ppb). In similar to 40% of the women (15/40), Σ PBDEs > 100 ppb lw in their milk, and four samples had levels > 250 ppb lw. PBDE 47 was the dominant congener in most samples, whereas PBDE 153 was predominant in a few (3/40). Σ PCBs were calculated by summing values for the 82 PCB congeners analyzed, and ranged from 49 to 415 ppb (lipid weight) (mean = 147 ppb; median = 126 ppb). ~ 30% of the mothers (13/40) have Σ PBDEs > Σ PCBs in their milk samples, and ~ 65% (25/40) have BDE 47 > PCB 153 in breast milk samples, with BDE 47 averaging 3-fold greater levels than PCB 153. Clearly, the lower brominated PBDEs are surpassing PCBs as a major environmental concern in North America, and are likely affecting significant portions of the populations in these regions. PBDEs have become a major persistent organic pollutant. However, there are no positive correlations between levels of Σ PBDEs and Σ PCBs, or between levels of PBDE 47 and PCB 153, suggesting there may be some differences in exposure pathways for PBDEs and PCBs in humans.

Nagayama, J., Tsuji, H., Iida, T., Nakagawa, R., Matsueda, T., Hirakawa, H., Yanagawa, T., Fukushige, J., and Watanabe, T. Immunologic effects of perinatal exposure to dioxins, PCBs and organochlorine pesticides in Japanese infants. *Chemosphere* 67(9): S393-S398, 2007.

Notes: Effects of perinatal exposure to dioxins, PCBs and organochlorine pesticides on lymphocyte subsets were investigated in the peripheral blood from 101 Japanese infants with approximately 10 months of age. Perinatal exposure to these organochlorine compounds were estimated by their contamination levels in the breast milk of the mothers. Lymphocyte subsets such as CD16+, HLA-DR+, CD4+, CD4+8+, CD8+, CD3+ and CD20+ cells in peripheral venous blood were assessed in a subgroup of 92 infants. Greater exposures to HCE, chlordane and dioxins were significantly associated with the increase in the percentages of CD8+ and CD3+ T lymphocytes and CD4+/CD8+ T cell ratios, respectively. In addition, higher HCH exposure was also associated with a decrease in the percentage of HLA-DR+ T lymphocytes. Furthermore effects of dioxins, DDT and PCBs on the percentage of CD16+ T lymphocyte were more pronounced by the combined exposure of DDT and PCBs. Effects of HCE on the percentages of CD8+ T lymphocyte were also more pronounced by the combined exposure of HCE and chlordane. In conclusion, our study suggests that greater exposures to dioxins, PCBs and organochlorine pesticides determined in this study (except dieldrin) influence the immune system of Japanese infant, although the clinical significance of these changes is uncertain.

Domingo, J.L., Bocio, A., Falcó, G., and Llobet, J.M. Benefits and risks of fish consumption Part I. A quantitative analysis of the intake of omega-3 fatty acids and chemical contaminants. *Toxicology* 230(2-3): 219-226, 2007.

Notes: In recent years, and based on the importance of fish as a part of a healthy diet, there has been a notable promotion of fish consumption. However, the balance between health benefits and risks, due to the intake of chemical contaminants, is not well characterized. In the present study, edible samples of 14 marine species were analyzed for the concentrations of omega-3 fatty acids, as well as a number of metals and organic pollutants. Daily intakes were specifically determined for a standard adult of 70 kg, and compared with the tolerable/admissible intakes of the pollutants, if available. Salmon, mackerel, and red mullet were the species showing the highest content of omega-3 fatty acids. The daily intakes of cadmium, lead, and mercury through

fish consumption were 1.1, 2.0, and 9.9 g, respectively. Dioxins and furans plus dioxin-like polychlorinated biphenyls (PCBs) intake was 38.0 pg WHO-TEQ/day, whereas those of polybrominated diphenyl ethers (PBDEs), polychlorinated diphenyl ethers (PCDEs), polychlorinated naphthalenes (PCNs) and hexachlorobenzene (HCB) were 20.8, 39.4, 1.53, and 1.50 ng/day, respectively. In turn, the total intake of 16 analyzed polycyclic aromatic hydrocarbons (PAHs) was 268 ng/day. The monthly fish consumption limits for human health endpoints based on the intake of these chemical contaminants were calculated for a 70 years exposure. In general terms, most marine species here analyzed should not mean adverse health effects for the consumers. However, the type of fish, the frequency of consumption, and the meal size are essential issues for the balance of the health benefits and risks of regular fish consumption.

Domingo, J.L., Bocio, A., Martí-Cid, R., and Llobet, J.M. Benefits and risks of fish consumption Part II. RIBEPEIX, a computer program to optimize the balance between the intake of omega-3 fatty acids and chemical contaminants. *Toxicology* 230(2-3): 227-233, 2007.

Notes: In recent years, and based on the importance of fish as a part of a healthy diet, there has been a notable promotion of fish and seafood consumption. However, a number of recent studies have shown that fish may be a potential source of exposure to chemical pollutants, some of them with well known adverse effects on human health. Recently, we determined in 14 edible marine species the concentrations of eicosapentaenoic acid (EPA) and docosohexaenoic acid (DHA), as well as those of a number of chemical contaminants: Cd, Hg, Pb, polychlorinated dibenzo-*p*-dioxins and furans, polychlorinated biphenyls, hexachlorobenzene, polycyclic aromatic hydrocarbons, polychlorinated naphthalenes, polybrominated diphenylethers and polychlorinated diphenylethers. To quantitative establish the intake of these pollutants (risks) versus that of EPA+DHA (benefits), we designed a simple computer program, RIBEPEIX. The concentrations of EPA, DHA, and the chemical pollutants were introduced into the program. We here present how RIBEPEIX may be used as an easy tool to optimize fish consumption: most suitable species, frequency of consumption, and size of meals. RIBEPEIX can be useful not only for professionals (cardiologists, general physicians, nutritionists, toxicologists, etc.), but also for the general population. It is available at: http://www.fmcs.urv.cat/portada/ribepeix/.

Gochfeld, M. Framework for gender differences in human and animal toxicology. *Environmental Research* 104(1): 4-21, 2007.

Notes: Differences in exposure, anatomy, physiology, biochemistry, and behavior between males and females are a dominant theme in biology, transcending the plant and animal kingdoms. Yet differences due to sex and gender have not received adequate attention in human or animal toxicology nor always in epidemiology. Generalizations are often made about species' responses to xenobiotics, without data or consideration of female/male differences. Despite the leading role that pharmacology and drug development play in elucidating toxicokinetics, gender studies are relatively recent. Phenomenologic or clinical observations of sex differences often go unexplored, but pharmaceutical companies recognize the importance of enhanced understanding of toxicokinetics and toxicodynamics and emphasize the value of translational or integrational research-bringing laboratory findings to bedside applications and bedside questions to laboratory study. However, for many years Food and Drug Administration guidelines specifically precluded participation of females in many drug studies. Many occupational epidemiology studies, on which much of our understanding of toxic effects is based, begin by excluding women and minorities. Sex differentiation begins in the embryo under genetic and hormonal control. Changes affecting exposure, susceptibility, risk, and health continue throughout life. This paper provides a framework for analyzing-the level(s) at which gender differences arise. The framework addresses exposure, toxicokinetics, toxicodynamics, and modulating influences. Men and women differ in many aspects of vulnerability to xenobiotics and other stressors, beginning with their opportunities for exposure. Toxicokinetic differences mainly involve metabolism, with few differences in absorption yet demonstrated. In addition, lifestyle, psychosocial, and hormonal factors modify the kinetics and responsiveness. Some phenomena fit the Classic Sex Hormone Paradigm in which castration (with and without hormone replacement) and administration of the opposite sex hormone demonstrate the primary regulatory role of sex hormones. Many phenomena, however, differ between males and females without showing a clear-cut relationship with the sex hormones. Since every cell both has a sex chromosome (X or Y) and is exposed to hormones, elegant techniques are just beginning to tease apart genetic from hormonal influences. Wherever possible, studies should use balanced gender and gender x age designs and should analyze data by sex and interactions, rather than simply adjusting for (discarding) gender. Power should be adequate, or lack of power (if inevitable) should be clearly stated.

Vahter, M., Gochfeld, M., Casati, B., Thiruchelvam, M., Falk-Filippson, A., Kavlock, R., Marafante, E., and Cory-Slechta, D. **Implications of gender differences for human health risk assessment and toxicology.** *Environmental Research* 104(1): 70-84, 2007.

Notes: This paper from The Human Health working group of SGOMSEC 16 examines a broad range of issues on gender effects in toxicology. Gender differences in toxicology begin at the gamete and embryo stage, continuing through development and maturation and into old age. Sex influences exposure, toxicokinetics, and toxicodynamics. The effects of sex have often been overlooked in both epidemiology and toxicology. In addition to the obvious modifying effects of the sex hormones and conditions affecting the male and female reproductive organs and sex roles, both genetic and hormonal effects influence many aspects of life and toxic responses. All aspects of toxicology should consider gender-balanced designs so that a more comprehensive understanding of differences and similarities can be obtained. Differential gene expression is a new frontier in toxicology. Risk assessment should account for gender and life cycle differences. The biological basis for altered sex ratios observed in several populations should be sought in animal models, and expanded to other compounds that might exert sex-selective effects. Wherever possible and feasible, toxicologic and environmental epidemiological studies should be designed and have sufficient statistical power to quantify differential gender-based exposures and outcomes.

Falk-Filipsson, A., Hanberg, A., Victorin, K., Warholm, M., and Wallen, M. Assessment factors - Applications in health risk assessment of chemicals. *Environmental Research* 104(1): 108-127, 2007.

Notes: We review the scientific basis for default assessment factors used in risk assessment of nongenotoxic chemicals including the use of chemical- and pathways specific assessment factors, and extrapolation approaches relevant to species differences, age and gender. One main conclusion is that the conventionally used default factor of 100 does not cover all interspecies and inter-individual differences. We suggest that a species-specific default factor based on allometric scaling should be used for inter-species extrapolation (basal metabolic rate). Regarding toxicodynamic and remaining toxicokinetic differences we suggest that a percentile from a probabilistic distribution is chosen to derive the assessment factor. Based on the scarce information concerning the human-to-human variability it is more difficult to suggest a specific assessment factor. However, extra emphasis should be put on sensitive populations such as neonates and genetically sensitive subgroups, and also fetuses and children which may be particularly vulnerable during development and maturation. Factors that also need to be allowed for are possible gender differences in sensitivity, deficiencies in the databases, nature of the effect, duration of exposure, and route-to-route extrapolation. Since assessment factors are used to compensate for lack of knowledge we feel that it is prudent to adopt a "conservative" approach, erring on the side of protectiveness.
