HANDBOOK ON REDUCING CHEMICAL FOOTPRINTS

Chapter 4. Human Health and Environmental Impacts from Chemical Exposures

This chapter examines how exposure to chemicals of concern affect human and environmental health. Described in this chapter are known human health effects from exposure that can range from increased cancer risks, allergic reactions, and the possibility of increased antibacterial resistance. The discussion then highlights the impacts chemicals of concern have on the environment, including bioaccumulation, toxicity and the endocrine disruption of wildlife.

Increased Risk of Cancers

Cancer is a group of diseases involving abnormal cell growth. According to the American Cancer Society, more than one million Americans are diagnosed with cancer each year.[1] The causes of this complex group of diseases are diverse, many of which are unknown. However, exposures to some chemicals of concern have been linked with particular types of cancers. Exposures might be through direct use of a product containing a chemical of concern or through indirect environmental contact (such as through the water system, which carries trace levels of many contaminants). Some cancers may result from the endocrine disruption effects discussed in the previous section, while others occur under other biological processes.

Several of the chemicals of concern reviewed in this handbook are known or suspected carcinogens. The common plastic additive BPA has been linked to breast and prostate cancers.[2] Synthetic preservatives classified as parabens (common in a wide variety of personal care products as well as some foods, beverages and pharmaceuticals) have been linked to breast cancer. A 2004 study found five different parabens in 19 of 20 breast cancer tumors analyzed; a 2006 study found parabens in nearly all urine samples tested.[3] Butylated hydroxyanisole (BHA) is "reasonably anticipated to be a human carcinogen based on sufficient evidence of carcinogenicity from studies in experimental animals," according to the US Department of Health and Human Services National Toxicology Program.[4] Still, BHA is commonly used as an antioxidant and preservative in food, food packaging and cosmetics (especially lipstick and eye shadow).

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[1] American Cancer Society, "Learn About Cancer," 2015 (http://www.cancer.org/cancer/index).

[2] See the Breast Cancer Fund review of recent scientific literature, including studies linking BPA to breast and prostate cancers, "Abstracts of Selected Bisphenol A (BPA) Studies," November 2011 (http://www.breastcancerfund.org/assets/pdfs/tips-fact-sheets/bpa-abstracts.pdf); also see the Environmental Working Group's Human Toxome Project, "Bisphenol A" for a listing of scientific studies (http://www.ewg.org/sites/humantoxome/chemicals/chemical.php?chemid=100357).

[3] Recent research is briefly summarized in the Environmental Working Group's Human Toxome Project, "Parabens" (http://www.ewg.org/sites/humantoxome/chemicals/chemical_classes.php?class=Parabens).

[4] National Toxicology Program, US Department of Health and Human Services (HHS), "Butylated Hydroxyanisole," *13th Report on Carcinogens* (October 2, 2014), a cumulative report that includes 243 listings since 1980 (http://ntp.niehs.nih.gov/ntp/roc/content/profiles/butylatedhydroxyanisole.pdf). BHA was first listed in the *6th Report on Carcinogens* published in 1991.

Allergic and Contact Irritation Responses

Many chemicals of concern trigger allergic responses or irritant contact reactions in sensitive individuals. These two types of responses often appear similar, with skin inflammation or irritation of eyes and respiratory systems resulting from exposure to specific chemicals of concern.

Contact irritation responses result when the protective layer of skin and other tissues is damaged by chemical exposures. Some chemicals in products that come into direct contact with skin can remove the surface oils that protect the skin and result in irritant contact dermatitis, or inflammation of the skin (including rashes, blisters and itchiness). Antibacterials (triclosan), the insect repellent DEET, preservatives (parabens) and synthetic fragrance ingredients in a variety of personal care products that are applied to skin (such as soaps, lotions, shampoos and perfumes) can result in irritant contact dermatitis. Other chemical substances release airborne particles that cause irritation responses in the eyes or breathing passages. Both triclosan and synthetic fragrances (such as in perfumes and air fresheners) can cause these types of contact irritation responses. The insect repellent DEET has also been linked with eye irritation.[5]

Allergic responses involve the immune system. When exposed to an allergen, or a substance that causes an allergic reaction, the sensitive individual's immune system produces antibodies to fight off the allergen. The result is an inflammatory response (such as rashes, itchy skin, red and watery eyes, runny nose or constricted breathing). Allergic reactions can range from minor discomfort to life-threatening. Preservatives used in personal care products (parabens), BPA-containing plastics, and the sunscreen ingredient oxybenzone can penetrate the skin and cause allergic skin reactions. Phthalates added as softeners in personal care products such as cosmetics and shampoo and added to plastics (such as children's toys) to keep them flexible have been linked to allergic reactions and asthma.[6]

Antibacterial Resistance

Antibacterial substances eliminate or inhibit the growth of disease-causing microorganisms. Widespread commercial adoption of antibacterial ingredients in common personal care and household products increases the likelihood that bacterial pathogens will develop resistance to these substances, making them more difficult to inhibit or eliminate. Moreover, microbes that mutate in response to regular use of antimicrobial substances may cause infections in humans that cannot be treated with existing antibiotic drugs.

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[5] Contact irritation responses are identified in the human health research by Environmental Working Group for triclosan (http://www.ewg.org/skindeep/ingredient/706623/TRICLOSAN/); DEET (http://www.ewg.org/research/ewgs-guide-bug-repellents/repellent-chemicals#deet); parabens (http://www.ewg.org/skindeep/search.php?query=parabens); and synthetic fragrance (http://www.ewg.org/skindeep/ingredient/702512/FRAGRANCE/).

[6] Allergic responses are identified in the human health research by Environmental Working Group for parabens (http://www.ewg.org/skindeep/search.php?query=parabens); oxybenzone (http://www.ewg.org/skindeep/ingredient/704372/OXYBENZONE/); BPA (http://www.ewg.org/sites/humantoxome/chemicals/chemical.php?chemid=100357); and phthalates (http://www.ewg.org/enviroblog/2008/05/cheatsheet-phthalates).

The prevalence of triclosan in consumer products raises particular concerns with regard to this ingredient. Though there are many questions remaining, multiple laboratory studies over the past decade have identified triclosan resistance among microorganisms found on skin and in the intestines.[7] Ongoing studies are focusing on the association between triclosan resistance and resistance to other microbial substances that are critical to protecting public health.

Environmental Effects

Unregulated chemicals of concern found in common consumer products are often present and persistent in the environment through biomagnification, and have toxic and/or serious endocrine disrupting effects on other species. Biomagnification is the process by which a compound, such as a pollutant, increases its concentration in the tissues of organisms as it travels up the food chain. For example, fish accumulate mercury more rapidly than they excrete it, and every fish up the aquatic food chain contains more than the one it just ate. Specific effects vary by substance, but many chemicals found in common consumer products are of concern due to demonstrated or potential impacts to both human health and the health of other species. Some chemicals readily break down in the natural world while others may remain for long periods during which time they can be absorbed and consumed by surrounding animals and plants. The water system is the primary channel for transferring contaminants from products used by humans to the natural environment. For example, bioaccumulation in fish leads to biomagnification in the surrounding ecosystem and environment as a whole.

USGS Water Quality Sampling
Boulder Creek, Colorado

USGS scientist collecting a water-quality sample from Boulder Creek, Colorado, following a set of protocols to ensure the sample is representative of all the water flowing down the creek. Photo credit: Jennifer Beck, USGS

The environmental effects of these chemicals were historically underestimated because of faulty assumptions. If a substance was sold as a personal care or household product, it was assumed that any effects would be limited to direct contact. In conducting risk assessments, the EPA did not find it necessary to assess ecological risks for chemicals that were contained in products used primarily indoors. This was true with regard to the EPA's 1998 review of the insect repellent chemical DEET. The EPA found that because "DEET is only applied directly to the human body/clothing, cats, dogs, pet quarters and household/domestic dwellings, it is considered to be an 'indoor residential' use… [and] is not likely to adversely affect terrestrial wildlife or aquatic

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[7] S.P. Yazdankhan, et al., "Triclosan and Antimicrobial Resistance in Bacteria: An Overview," *Microbial Drug Resistance* 12, 2 (Summer 2006): 83-90 (http://www.ncbi.nlm.nih.gov/pubmed/16922622); Justin L. Copitch, Rebekah N. Whitehead and Mark A. Webbe, "Prevalence of Decreased Susceptibility to Triclosan in *Salmonella enterica* Isolates from Animals and Humans and Association with Multiple Drug Resistance, *International Journal of Microbial Agents* 36, 3 (September 2010): 247-251 (http://www.ijaaonline.com/article/S0924-8579%2810%2900200-1/abstract).

organisms."[8] More recent analyses have shown otherwise: "This compound has commonly been detected in aquatic water samples from around the world indicating that DEET is both mobile and persistent, despite earlier assumptions that DEET was unlikely to enter aquatic ecosystems."[9] DEET, along with numerous other chemicals of concern, has been detected at low levels in 75 percent of streams sampled across the US, and breaks down slowly in soil.[10] In other words, 'indoor residential use' does not contain the impacts of the chemicals of concern.

Tracking the Distribution and Transport of Contaminants

USGS scientist adding Rhodamine dye to Fourmile Creek, Iowa, during a dye-tracing test to determine travel times used to understand the distribution and transport of emerging contaminants in streams. Source: USGS http://toxics.usgs.gov/regional/emc/instream_processes.html

As discussed in Chapter 3, a wide variety of human and veterinary drugs, natural and synthetic hormones, detergent metabolites, plasticizers, insecticides, and fire retardants have been detected in streams across the US. In 2002, a study sponsored by the USGS reported, "One or more of these chemicals were found in 80% of the streams sampled. Half of the streams contained 7 or more of these chemicals, and about one-third contained 10 or more of these chemicals."[11]

The following discussion reviews several types of effects associated with contaminants found in the environment, including bioaccumulation, toxicity and endocrine disruption. Bioaccumulation affects ecological systems and individual species as chemical contaminants build up over time. Toxicity focuses on the degree of damage that results from direct exposure to a particular substance, dependent on dosage. Toxic reactions can affect whole organisms (animals or plants), or organism substructures (such as particular organs or cells). Endocrine disruption impacts in wildlife affect reproduction and survival of species. Each of these is discussed in turn, with examples describing how particular chemicals of concern are affecting the environment.

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[8] US Environmental Protection Agency, "R.E.D. [Reregistration Eligibility Decision] Facts: DEET," Office of Prevention, Pesticides, and Toxic Substances (EPA-738-F-95-010, April 1998; now archived and available at http://www.epa.gov/oppsrrd1/reregistration/REDs/factsheets/0002fact.pdf).

[9] S.D. Costanzo, A.J. Watkinson, E.J. Murby, D.W. Kolpin and M.W. Sandstrom, "Is There a Risk Associated with the Insect Repellent DEET (*N,N*-diethyl-*m*-toluamide) Commonly Found in Aquatic Environments?" *Science of the Total Environment* 384, 1-3 (October 2007): 214-220 (http://www.sciencedirect.com/science/article/pii/S0048969707006316). Also see Mark W. Sandstrom, "Widespread detection of *N,N*-diethyl-*m*-toluamide in U.S. Streams: Comparison with concentrations of pesticides, personal care products, and other organic wastewater compounds," *Environmental Toxicology and Chemistry* 24, 5 (May 2005): 1029-1034 (http://onlinelibrary.wiley.com/doi/10.1897/04-297R.1/abstract).

[10] US Environmental Protection Agency, "Diethyltoluamide (DEET) Chemical Summary," Toxicity and Exposure Assessment for Children's Health (TEACH), last revised 4/24/2007 (http://www.epa.gov/teach/chem_summ/DEET_summary.pdf).

[11] Dana W. Kolpin, Edward T. Furlong, Michael T. Meyer, E. Michael Thurman, Steven D. Zaugg, Larry B. Barber and Herbert T. Buxton, "Pharmaceuticals, Hormones, and Other Organic Wastewater Contaminants in U.S. Streams,

Bioaccumulation and Biomagnification through the Food Chain

Chemicals of concern can build up in plants as well as the bodies of fish, birds, humans and other mammals, with health risks rising as contaminant concentrations increase. Not all chemical substances bioaccumulate. Many contaminants quickly degrade or are easily excreted from the body and thus do not build up over time. However, some chemicals are known to build up in body tissues, especially fat cells, with consequences for the organism as chemical levels increase and are concentrated.

Bioaccumulation can also lead to biomagnification through the food chain. These processes occur when animals or plants with bioaccumulative substances in their tissues are eaten by animals higher in the food chain. Small crustaceans such as shrimp might be bioaccumulating pollutants from continued exposure to chemical substances in the water or through ingestion. Fish accumulate higher levels of pollutants from eating numerous shrimp over time. Larger species, such as bears, are exposed to concentrated levels of the pollutant by ingesting many fish as part of their regular food supply.

Bottlenose Dolphins

Triclosan is bioaccumulating in the blood plasma of these marine mammals residing off the South Carolina coast.

Source:
http://en.wikipedia.org/wiki/Bottlenose_dolphin

Several of the chemicals of concern covered in this handbook are known to bioaccumulate. Researchers have found the antibacterial agent triclosan bioaccumulating in algae and freshwater snails.[12] The first instance of triclosan bioaccumulating in marine mammals was found in blood plasma collected from wild bottlenose dolphins off the coast of Charleston, South Carolina.[13] Artificial fragrances, including synthetic musks, were found to be bioaccumulating at varying levels among fish species sampled in the pond of a municipal sewage treatment plant.[14] Moderate to high potential for bioaccumulation of the preservative BHA has

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1999-2000 – A National Reconnaissance," *Environmental Science and Technology* 36, 6 (2002): 1202-1211 (available at http://pubs.acs.org/doi/abs/10.1021/es011055j).

[12] Melinda A. Coogan, Regina E. Edziyie, Thomas W. La Point and Barney J. Venables, " Algal Bioaccumulation of Triclocarban, Triclosan, and Methyl-triclosan in a North Texas Wastewater Treatment Plant Receiving Stream," *Chemosphere* 67, 10 (May 2007): 1911–1918 (http://www.sciencedirect.com/science/article/pii/S0045653506017449); Melinda A. Coogan and Thomas W. LaPoint, "Snail Bioaccumulation of Triclocarban, Triclosan, and Methyltriclosan in a North Texas, USA, Stream Affected by Wastewater Treatment Plant Runoff, *Environmental Toxicology and Chemistry* 27, 8 (August 2008): 1788-1793 (http://onlinelibrary.wiley.com/doi/10.1897/07-374.1/abstract).

[13] Patricia A. Fair, et al., "Occurrence of Triclosan in Plasma of Wild Atlantic Bottlenose Dolphins (*Tursiops truncates*) and in their Environment," *Environmental Pollution* 157 8-9 (August-September 2009): 2248-2254 (http://www.sciencedirect.com/science/article/pii/S0269749109001833).

[14] R. Gatermann, S. Biselli, H. Huhnerfuss, G.G. Rimkus, M. Hecker and L. Karbe, "Synthetic Musks in the Environment. Part 1: Species-dependent Bioaccumulation of Polycyclic and Nitro Musk Fragrances in Freshwater Fish and Mussels," *Archives of Environmental Contamination and Toxicology* 42, 4 (May 2002): 437-46 (http://www.ncbi.nlm.nih.gov/pubmed/11994785).

been found with freshwater fleas (*cladoceran daphnia magna*), an important food source for other aquatic species, as well as algae and terrestrial plants.[15] Laboratory and field studies indicate that surfactants also have moderate bioaccumulation potential.[16] Nonylphenols, one of the surfactants of concern, accumulate in sediments lining streambeds and other water bodies and have been found to bioaccumulate in crustaceans (shrimps) and mussels.[17] They have also recently been observed to be bioaccumulating in land-based earthworms.[18] As these examples suggest, contaminants that bioaccumulate can move through the food chain, eventually affecting all levels of an ecosystem.

Toxicity

Toxicity focuses on the direct damaging effects of a substance on an organism. The damage can affect the organism as a whole (such as in increased rates of mortality) or to a substructure of the organism (such as injury to an organ or specific cell types). Because so many chemicals of concern enter the environment through the water system, much of the research has focused on the effects of chemicals on aquatic species, or aquatic toxicology studies. Analyses typically focus on either acute or chronic toxicity. Acute aquatic toxicity refers to "the intrinsic property of a substance to be injurious to an organism in a short-term aquatic exposure to that substance." [19] For fish, an acute toxic response (such as lethality) must be detected within 96 hours of exposure. Chronic aquatic toxicity focuses on adverse effects to aquatic organisms during aquatic exposures, which are determined in relation to the life cycle of the organism, such as early life stage, reproduction or growth inhibition effects.

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[15] A. Jos, et al., "Ecotoxicological Evaluation of the Additive Butylated Hydroxyanisole Using a Battery with Six Model Systems and Eighteen Endpoints," *Aquatic Toxicology* 71, 2 (January 2005): 183-92 (http://www.ncbi.nlm.nih.gov/pubmed/15642642).

[16] European Chemicals Agency (ECHA), "Member State Committee Support Document for Identification of 4-(1,1,3,3-TETRAMETHYLBUTYL)PHENOL, 4-TERT-OCTYLPHENOL, as a Substance of Very High Concern Because Its Endocrine Disrupting Properties Cause Probable Serious Effects to the Environment which Gives Rise to an Equivalent Level of Concern," Adopted on 9 December 2011 (http://ECHA.EUROPA.EU/DOCUMENTS/10162/13638/SUPPDOC_4_TERT_OCTYLPHENOL_20111211_EN.PDF); Charles A. Staples, John Weeks, Jerry F. Hall and Carter G. Naylor, "Evaluation of Aquatic Toxicity and Bioaccumulation of C8- and C9-alkylphenol ethoxylates," *Environmental Toxicology and Chemistry,* 17, 12 (December 1998): 2470-2480 (http://www.researchgate.net/publication/229450442_Evaluation_of_aquatic_toxicity_and_bioaccumulation_of_C8_and_C9alkylphenol_ethoxylates).

[17] S.A. Hecht, J.S. Gunnarsson, B.L. Boese, J.O. Lamberson, C. Schaffner, W. Giger and P.C. Jepson, "Influences of Sedimentary Organic Matter Quality on the Bioaccumulation of 4-nonylphenol by Estuarine Amphipods, *Environmental Toxicology and Chemistry* 23, 4 (April 2004): 865-73 (http://www.ncbi.nlm.nih.gov/pubmed/15095881); R. Ekelund, A. Bergman, A. Granmo and M. Berggren, "Bioaccumulation of 4-nonylphenol in Marine Animals – a Re-evaluation, *Environmental Pollution* 64, 2 (1990): 107-120 (http://www.ncbi.nlm.nih.gov/pubmed/15092296).

[18] Jun Shan, Ting Wang, Chengliang Li, Erwin Klumpp and Rong Ji, "Bioaccumulation and Bound-Residue Formation of a Branched 4-Nonylphenol Isomer in the Geophagous Earthworm *Metaphire guillelmi* in a Rice Paddy Soil," *Environmental Science and Technology* 44, 12 (May 2010): 4558-4563 (http://pubs.acs.org/doi/abs/10.1021/es100139w).

[19] United Nations, UN Economic Commission for Europe (UNECE), "Globally Harmonized System of Classification and Labelling of Chemicals (GHS)," Part IV, Environmental Hazards, 5th Revised Edition, 2013 (http://www.unece.org/fileadmin/DAM/trans/danger/publi/ghs/ghs_rev05/English/04e_part4.pdf).

Many of the chemicals of concern have known or suspected toxic effects on various species. Triclosan is especially toxic to algae, invertebrates and certain types of fish.[20] Studies have also shown that triclosan "by-products such as methyl-triclosan and other chlorinated phenols may be more resistant to degradation and have higher toxicity than the parent compound."[21] Recent laboratory research has linked triclosan with impaired muscle contraction, including reduced heart muscle function in mice, and lowered swimming effectiveness of fish (fathead minnows).[22]

Toxic Effect of Phthalates on Zebrafish Embryos

(A) control embryos, not exposed to phthalates; and (B) embryos exposed to phthalates and phthalate mixture. Toxicity symptoms include tail curvature (solid arrows), necrosis or cell death (empty arrows), cardio edema, or accumulation of fluid around the heart (arrowhead), and death. Source: Xueping Chen et al. (2014) http://www.mdpi.com/1660-4601/11/3/3156/htm

Phthalates are linked with acute and chronic toxicity in both freshwater and saltwater aquatic organisms, including algae, invertebrates (such as daphnids, or water fleas, shrimp and mollusks), and fish (such as blue gill, rainbow trout, fathead minnows and zebrafish). Increased mortality, tail curvature, cell death, growth inhibition, and decreases in organism abundance and diversity are some of the observed effects of phthalate exposure in aquatic environments.[23] Parabens have been linked with toxic effects in invertebrates and fish.[24] A number of organisms have been found to be sensitive to BHA, a preservative common in personal care products. Among other effects, BHA inhibits bioluminescence in luminescent bacteria (*vibrio fischeri* bacteria) common

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[20] A.B. Dann and A. Hontela, *op. cit.;* D.R. Orvos, D.J. Versteeg, J. Inauen, M. Capdevielle, A. Rothenstein and V. Cunningham, "Aquatic Toxicity of Triclosan," *Environmental Toxicology and Chemistry* 21, 7 (July 2002): 1338-49 (http://www.ncbi.nlm.nih.gov/pubmed/12109732); John M. Brausch and Gary M. Rand, "A Review of Personal Care Products in the Aquatic Environment: Environmental Concentrations and Toxicity, *Chemosphere* 82 (2011): 1518-1532 (http://jlakes.org/web/A-review-personal-care-products-aquatic-environment-C2011.pdf).

[21] A.B. Dann and A. Hontela, *op. cit.*

[22] Gennady Cherednichenko, et al., "Triclosan Impairs Excitation–Contraction Coupling and Ca^{2+} Dynamics in Striated Muscle," *Proceedings of the National Academy of Sciences of the United States of America* 109, 35 (August 28, 2012): 14158–14163 (http://www.pnas.org/content/109/35/14158.abstract).

[23] Charles A. Staples, William J. Adams, Thomas F. Parkerton, Joseph W. Gorsuch, Gregory R. Biddinger and Kevin H. Reinert, "Aquatic Toxicity of Eighteen Phthalate Esters," *Environmental Toxicology and Chemistry* 16, 5 (May 1997): 875-891 (http://onlinelibrary.wiley.com/doi/10.1002/etc.5620160507/full). Staples, et al. reviewed acute and chronic aquatic toxicity data for 18 phthalate esters for freshwater and saltwater aquatic microorganisms, algae, invertebrates and fish. They found the following lower molecular weight phthalates were associated with the highest aquatic toxicity effects: Dimethyl phthalate (DMP), Diethyl phthalate (DEP), Diallyl phthalate (DAP), Dibutyl phthalate (DBP) and Butylbenzyl phthalate (BBP). More recent laboratory applications of phthalates to zebrafish embryos observed several specific toxic and physical effects. See: Xueping Chen et al., "Toxicity and Estrogenic Endocrine Disrupting Activity of Phthalates and Their Mixtures," *International Journal of Environmental Research and Public Health* 11, 3 (March 14, 2014): 3156-3168 (http://www.mdpi.com/1660-4601/11/3/3156/htm).

[24] Laura L. Dobbins, et al., "Pharmaceuticals and Personal Care Products in the Environment: Probabilistic Ecological Hazard Assessment of Parabens Using Daphnia Magna and Pimephales Promelas," *Environmental Toxicology and Chemistry* 28, 12 (2009): 2744-2753.

to marine environments in colonies or in symbiotic associations with other marine species such as fish and squid.[25]

Surfactants have toxic effects on a variety of aquatic species as well. Alkylphenols were found to be especially harmful to the marine bacterium *vibrio fischeri*.[26]

The EPA recognizes nonylphenol as highly toxic to fish, aquatic invertebrates, and aquatic plants.[27] In October 2014, because of these effects, nonylphenol was added to a list of chemicals issued by the EPA that are subject to increased assessment under the Toxic Substances Control Act. The chemicals on this list are suspected of presenting a risk to human health or the environment based on a combination of hazard, exposure (including via uses), and persistence and bioaccumulation characteristics. Other chemicals added to the TSCA list are BPA and a group of seven phthalates.[28]

Sunscreen ingredients (including benzophenone-3, or oxybenzone) have direct effects on corals and on their symbiotic algae. The sunscreen ingredients build up in waterways popular for human recreational use and promote viral infection, one of the known causes of coral bleaching.[29] Both laboratory and field experiments found that sunscreens “cause the rapid and complete bleaching of hard corals, even at extremely low concentrations.”[30]

Chemical Sunscreens and Coral

Chemical sunscreens activate viruses that kill the symbiotic algae that feeds coral through photosynthesis. Without the algae, the coral turns bleach white and dies.
Source: http://www.redangppelangi.com/

The findings cited above focus on research to date. Not all of the chemicals of concern have been thoroughly analyzed for their toxic effects on various species. Synthetic musk fragrance is recognized as having the potential to cause adverse effects in wildlife. Some suspect that synthetic musk could be especially toxic to benthic invertebrates, the organisms that live on or

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25 A. Jos, et al., *op. cit.*

26 Kyungho Choi, Leonard I. Sweet, Peter G. Meier and Pan-Gyi Kim, “Aquatic Toxicity of Four Alkylphenols (3-tert-butylphenol, 2-isopropylphenol, 3-isopropylphenol, and 4-isopropylphenol) and their Binary Mixtures to Microbes, Invertebrates, and Fish,” *Environmental Toxicology* 19, 1 (February 2004): 45-50 (http://onlinelibrary.wiley.com/doi/10.1002/tox.10150/abstract).

27 US Environmental Protection Agency, “Nonylphenol (NP) and Nonylphenol Ethoxylates (NPEs) Action Plan,” 8/18/2010 (RIN 2070-ZA09), available at http://www.epa.gov/oppt/existingchemicals/pubs/actionplans/RIN2070-ZA09_NP-NPEs%20Action%20Plan_Final_2010-08-09.pdf.

28 US Environmental Protection Agency, Office of Pollution Prevention and Toxics, “TSCA Work Plan for Chemical Assessments: 2014 Update,” October 2014 (http://www.epa.gov/oppt/existingchemicals/pubs/TSCA_Work_Plan_Chemicals_2014_Update-final.pdf).

29 R. Danovaro, et al., “Sunscreens Cause Coral Bleaching by Promoting Viral Infections,” *Environmental Health Perspectives* 116, 4 (April 2008): 441-7 (http://www.ncbi.nlm.nih.gov/pubmed/18414624); John Tibbetts, “Bleached, But Not by the Sun: Sunscreen Linked to Coral Damage,” *Environmental Health Perspectives* 116, 4 (April 2008): A173 (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2291012/).

30 R. Danovaro, *op. cit.*

burrow under the surface of the sediments of rivers, streams and lakes.[31] Very little data exists pertaining to acute toxicity of the insect repellent DEET to aquatic organisms. However, there is some evidence that it is slightly toxic to fish, aquatic invertebrates, and birds.[32]

Endocrine disruption

Northern Leopard Frog

Exposure to the herbicide Atrazine is linked to physiological and reproductive changes in amphibians, such as deformities.

Source: US Fish and Wildlife Service

Hormones shape development, physiology and behavior across animal species. Specific developmental windows range from gestation, prenatal and early development stages through puberty, maturation, and reproduction. Exposures to chemicals of concern during these developmental windows can profoundly alter individual and population outcomes with a wide array of endocrine disruption effects. Many chemicals of concern have been identified as xenoestrogens, or chemicals that mimic estrogen in their effects on living organisms – such as triclosan, BPA, phthalates, atrazine and alkylphenols (including nonylphenol and octylphenol). These same chemical compounds are known to be present in aquatic ecosystems across the US. Numerous endocrine disrupting changes have been observed in various species in the environment. Tracking these effects to specific chemicals is much more difficult, with field studies and laboratory tests just beginning to identify some of these connections.[33]

Exposure to the herbicide atrazine has been linked to reproductive changes in amphibians. A 2003 study reported evidence that atrazine was causing male tadpoles to develop into female frogs, suggesting that such exposures were leading to declining amphibian populations.[34] Subsequent studies found additional adverse effects on amphibians, depending on when in the life cycle that exposure occurred.[35] Some of the effects include delayed developmental transition

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[31] John M. Brausch and Gary M. Rand, *op. cit.*

[32] US Environmental Protection Agency, "Reregistration Eligibility Decision (RED): DEET," Office of Prevention, Pesticides, and Toxic Substances (EPA-738-R-98-010, September 1998): 32-33; now archived and available at http://www.epa.gov/oppsrrd1/reregistration/REDs/0002red.pdf; John M. Brausch and Gary M. Rand, *op. cit.*

[33] US Environmental Protection Agency, Endocrine Disruptor Research, "Ecosystems & Environment: Aquatic Effects," last updated April 5, 2013 (http://www.epa.gov/research/endocrinedisruption/aqueff.htm); US Fish & Wildlife Service, Environmental Quality, "Endocrine (Hormone) Disruptors," last updated April 17, 2014 (http://www.fws.gov/contaminants/issues/endocrinedisruptors.cfm).

[34] T. Hayes, K. Haston, M. Tsui, A. Hoang, C. Haeffele and A. Vonk, "Atrazine-induced Hermaphroditism at 0.1 ppb in American Leopard Frogs (Rana pipiens): Laboratory and Field Evidence," *Environmental Health Perspectives* 111, 4 (April 2003): 568-575 (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1241446/).

[35] Jason R. Rohr and Krista A. McCoy, "A Qualitative Meta-Analysis Reveals Consistent Effects of Atrazine on Freshwater Fish and Amphibians," *Environmental Health Perspectives* 118, 1 (January 2010): 20-32 (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2831963/).

from tadpole to frog, immune suppression, sex organ abnormalities, and physiological abnormalities.

BPA-caused Color Change and Interspecies Mating Confusion

In this experiment with common river *Blacktail Shiner* fish, males that were exposed to BPA over a 2-week period lost some of their distinctive coloring that females use in mate choice. Mating with the wrong species was the result. The females were less choosy when it came to their mates and often paired with the *Red Shiner* competitor species that naturally exhibits fewer red color highlights. Source: *Scientific American* http://blogs.scientificamerican.com/science-sushi/mating-with-the-wrong-species-plastics-make-it-possible/

Endocrine-disrupting compounds also affect fish. Reproductive and developmental changes in fish have been linked to triclosan[36] exposure and BPA. In one study, Jessica L. Ward and Michael J. Blum found that environmental exposure to BPA can lead to declines in fish population, especially in regions under pressure from invasive species.[37] These researchers collected individuals from two species of fish found in rivers across the US: the blacktail shiner, a native species, and the red shiner, an invasive species. Some of the fish were exposed to BPA over a 14-day period. Following this exposure, both color and behavioral changes were observed. When the fish were brought together, changed male coloring appeared to alter female fish mate choice and the researchers observed increased interbreeding between the blacktail shiners and the red shiners. The authors concluded that exposure to endocrine-disrupting compounds "can lead to population declines via the erosion of species boundaries and by promoting the establishment and spread of non-native species via hybridization."

[36] A.B. Dann and A. Hontela, *op. cit.*

[37] Jessica L. Ward and Michael J. Blum, "Exposure to an Environmental Estrogen Breaks Down Sexual Isolation Between Native and Invasive Species," *Evolutionary Applications* 5, 8 (July 10, 2012): 901-912 (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3552407/).

Endocrine disruption from contaminants of concern also affects mammals. Numerous rodent studies have linked BPA exposure to altered development of the male and female reproductive tracts, mammary tissues, immune system, fat tissue, and thyroid, as well as heightened risk of mammary and prostate cancers.[38] BPA-exposed animals demonstrated altered brain development, increased aggression in adulthood, abnormal play and sexual behaviors, and decreased maternal behaviors.[39] Numerous studies have confirmed and strengthened these findings. A systematic review of the cumulative research record was published in 2014 finding "strong evidence" that BPA is an ovarian toxicant, uterine toxicant, and prostate toxicant, with other effects of BPA on mammal reproductive systems also observed and evident at doses below those generally considered safe.[40]

Alkylphenol Exposure and Lobster Shell Hardening Disease

Lobster showing symptoms of shell disease. Increasing numbers of New England lobsters exhibit this disorder, associated with alkylphenols together with increased presence of bacteria and higher concentrations of trace metals. Source: *UConn Today* http://today.uconn.edu/blog/2010/08/lobster-dieoffs-linked-to-chemicals-in-plastics/

Other species exhibit changes from exposure to endocrine-disrupting compounds. Freshwater snails exposed to low levels of BPA and octylphenol exhibited the formation of additional female organs, enlargement of sex glands, and malformations of sex organs, with increased mortality and changes in spawning production.[41] Alkylphenols have been associated with shell hardening in lobsters found in New England, with effects dependent on timing during molting. Research Professor Hans Laufer found that chemical exposures can slow lobster molting patterns and interfere with regular development, leading to body deformations,

[38] Catherine A. Richter et al., "*In Vivo* Effects of Bisphenol A in Laboratory Rodent Studies," *Reproductive Toxicology* 24, 2 (June 26, 2007):199–224 (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2151845/); Beverly S. Rubin, "Bisphenol A: An Endocrine Disruptor with Widespread Exposure and Multiple Effects," *The Journal of Steroid Biochemistry and Molecular Biology* 127, 1-2 (October 2011): 27-34 (http://www.sciencedirect.com/science/article/pii/S0960076011001063).

[39] Ibid.

[40] Jackye Peretz et al., "Bisphenol A and Reproductive Health: Update of Experimental and Human Evidence, 2007-2013," *Environmental Health Perspectives* 122, 8 (August 2014): 775-786 (http://ehp.niehs.nih.gov/1307728/).

[41] Jorg Oehlmann, Ulrike Schulte-Oehlmann, Michaela Tillman and Bernd Markert, "Effects of Endocrine Disruptors on Prosobranch Snails (Mollusca: Gastropoda) in the Laboratory, Part I: Bisphenol A and Octylphenol as

susceptibility to disease, and potential death.[42] Interest in this issue has grown due to large-scale lobster die-offs in Long Island Sound.

Summary

Chemicals of concern affect human and environmental health in numerous ways, but knowledge of these effects remains incomplete. Chemical characteristics are complex, with a variety of direct and interactive effects across species that are difficult to measure. Identifying the effects of chemical exposures also depends on research design and methods, with many suspected effects waiting for additional study. Nevertheless, a number of serious human health effects have been linked to exposures to chemicals of concern. Among these are endocrine disruption or hormonal effects, including reduced fertility, abnormalities and cancers in reproductive organs, and increased incidences of certain immune diseases, obesity and diabetes. Exposures to chemicals of concern are also associated with other cancers, skin sensitivities and allergies, and the possibility of increased antibacterial resistance. Other species are also being affected by exposures to chemicals of concern, particularly through the water system. Bioaccumulation and biomagnification of certain chemicals through the food chain have been identified. In addition, many of the chemicals of concern have toxic and endocrine disrupting effects on a wide variety of species.

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Xeno-Estrogens," *Ecotoxicology* 9 (2000): 383-397 (http://link.springer.com/article/10.1023/A:1008972518019#page-2).

[42] Hans Laufer, Ming Chen, Michael Johnson, Neslihan Demir and James Bobbitt, "The Effect of Alkylphenols on Lobster Shell Hardening," Department of Molecular and Cell Biology, University of Connecticut, accessed 2015 (http://www.researchgate.net/publication/268366090_THE_EFFECT_OF_ALKYLPHENOLS_ON_LOBSTER_SHELL_HARDENING); Hans Laufer, Bryan Baclaski and Uwe Koehn, "Alkylphenols Affect Lobster (Homarus americanus) Larval Survival, Molting and Metamorphosis," *Invertebrate Reproduction and Development* 56, 1 (March 2012): 66-71 (http://www.researchgate.net/publication/254244733_Alkylphenols_affect_lobster_%28Homarus_americanus%29_larval_survival_molting_and_metamorphosis).