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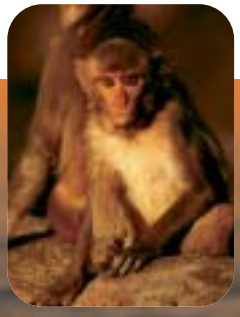
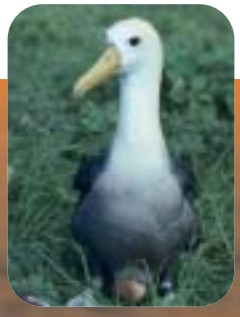


CAUSES FOR CONCERN: CHEMICALS AND WILDLIFE

TOXIC CHEMICALS

A THREAT TO WILDLIFE AND HUMANS

WWF DETOX CAMPAIGN

Prepared for WWF

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SAFER CHEMICALS
FOR A HEALTHIER FUTURE

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I. INTRODUCTION

Over the past half a century, scientists have uncovered a multitude of risks to wildlife and humans posed by toxic chemicals. Some of the most notorious chemicals have been taken off the market and others have been restricted to a narrower range of uses. Yet while a handful of these chemicals are slowly disappearing from the environment, new research is revealing that many other chemicals could be even more harmful than the infamous ones. Wildlife and humans are simultaneously suffering contamination by chemicals no longer in production, as well as chemicals currently in use – the dangers of which are becoming increasing clear.

Although manufacture and use of some chemicals has been tightly regulated, the "body burden" of chemicals in wildlife and humans is more worrying than ever. A recent study noted that only five organochlorines compounds and mercury were found in marine mammals in the 1960s. Today over 265 organic pollutants and 50 inorganic chemicals have been found in these species.[1]

Since the early 1990s, WWF has been concerned about the impacts of toxic chemicals on biodiversity. Wildlife, people, and entire ecosystems around the world are threatened by chemicals that can alter sexual, neurological, and behavioral development; impair reproduction; and undermine immune systems. Urgent and precautionary action is required to address threats from the most hazardous industrial chemicals and pesticides.

Existing regulation is neither comprehensive nor effective enough in protecting wildlife and human health. Despite the widespread contamination of wildlife and people and the discovery of harmful chemical effects, there is a shocking lack of publicly available safety data on chemicals currently in use. However, in the European Union (EU) reforms are underway that could fundamentally change the way chemicals are managed in Europe, with possible global implications (see box on REACH). Ensuring the success of the proposed reforms known as REACH (Registration, Evaluation and Authorization of Chemicals), which embraces the precautionary principle as an important part of chemicals management, is a priority for WWF.

REACH is a critically important addition to existing and ongoing efforts to improve effective chemicals management. At present, several international instruments, including the Stockholm Persistent Organic Pollutants Convention (POPs), the Rotterdam Prior Informed Consent Convention, and the Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and their Disposal, address specific chemical issues. REACH cuts across the spectrum of voluntary and regulatory initiatives that currently exist, helping to ensure that substances are used safely at all stages of their life cycle – by requiring all those manufacturing, importing, or using substances to fulfill certain obligations.

This "Causes for Concern" paper examines scientific findings concerning exposure and effects of various chemicals on wildlife, as well as research on related human health impacts. While not intended to be exhaustive, this review of recent science illustrates the magnitude of the problem, the ongoing threat some chemicals pose to wildlife and people, and the need for improved regulation of chemicals.

II. CHEMICALS OF CONCERN – WHAT DO THEY DO TO WILDLIFE?

The picture that is emerging from new scientific research on wildlife and chemicals is a disturbing one, and it does little to reassure us that chemical effects are benign. Many animals are known to pass chemicals to their offspring, mammals through the placenta and during suckling, and reptiles and birds through their eggs. In the last decade, a great deal of research has concentrated on unraveling the possible effects of chemicals on the endocrine system, particularly the reproductive hormones such as estrogens and androgens.

Recent research has focused on how chemicals affect the thyroid and pituitary systems. Some chemicals have been identified as endocrine disrupters because they can interfere with the body's own hormones, which are secreted by the endocrine glands.

It is also emerging that endocrine disrupters can have many physiological effects not directly associated with the primary system. For example, the thyroid system is well known to regulate metabolism, but it is also a crucial component in fetal brain development in mammals, and too much or too little thyroid hormone at crucial points can do permanent damage. The immune system is also vulnerable to hormone-mediated disruption. Chemicals can cause neurological problems, reproductive and developmental abnormalities, and cancers as well.

And researchers are only just beginning to disentangle the questions about the effects of chronic low-level exposure (as opposed to brief high doses of chemicals), combinations of chemicals, and interactions between chemicals and other physiological and environmental factors.

"The Relevance of REACH"

This new evidence of chemical contamination in wildlife, coupled with corresponding information on widespread human exposure, underscores the urgency of international policy reform. The European Commission estimates there are now slightly over 30,000 chemicals on the European market produced or imported at over 1 tonne per annum. Existing European Union rules allow continued use of chemicals that were put on the market prior to 1981, without submission of safety data. Such chemicals still make up over 90% of the market, and research has shown that for the vast majority of chemicals now in use there is inadequate publicly available scientific date to assess their safety.

The European Union is currently considering the most sweeping chemicals regulation legislation in the world to date. The proposal, called REACH (Registration, Evaluation, and Authorisation of CHemicals) will, for the first time, require manufacturers and importers to provide safety information on those industrial chemicals annually marketed in Europe in volumes of 1 tonne or more. Much of the resulting information will be publicly available in a database to be administered by a new chemicals agency. The required amount of safety data, including information on toxicity, environmental fate, and usage will be determined by the amounts of the chemical produced and the level of concern. Manufacturers, importers and downstream users will have to ensure that chemicals they produce, import or use do not adversely affect human health or the environment.

REACH will go beyond existing regulation of chemicals in other parts of the world, including the United States. It will require industry to obtain prior authorisation before using chemicals of very high concern. These are defined as:

- carcinogens, mutagens or reproductive toxins (categories 1 & 2);
- chemicals that are persistent, bioaccumulative and toxic;
- chemicals that are very persistent and very bioaccumulative irrespective of their currently known toxicity; and
- chemicals that are of a similar level of concern, such as endocrine disrupters.

  NB: The draft regulation published by the European Commission in October 2003 'raised the bar' for the addition of such chemicals by changing this requirement to "causing serious and irreversible effects to humans or the environment which are equivalent to..."

  This proposal would mean that serious or irreversible effects would have to be demonstrated prior to a chemical being added to authorisation - this will not be an effective precautionary action.

Despite the progress in controlling chemicals that REACH represents, it is not sufficiently protective with regard to these chemicals of very high concern, as it allows continued use of such chemicals even if safer alternatives are available. Following the adoption of draft legislation by the European Commission on October 29, 2003, REACH is now being considered in the European Parliament and by the Council of Ministers. Depending on decisions taken by these bodies REACH is expected to be adopted as a binding regulation throughout the European Union by late 2005 or early 2006.

A. NEW CAUSES FOR CONCERN

Many chemicals in wide use today are assumed to be safe by consumers and other downstream users. However, some of the chemicals used to produce a variety of products such as clothing, food containers, computer equipment, and toys are contaminating the environment and can have dangerous effects.

1. Perfluorooctanes

Over the past four years, perfluorooctanoic acid (PFOA), perfluorooctane sulfonate (PFOS) and similar compounds have emerged as an important class of persistent global pollutants referred to as perfluorochemicals (PFCs). The first public indication that PFOS and PFOA were problematic came on May 16, 2000 when 3M, the primary global manufacturer of many perfluoroalkanesulfonates and PFOA, announced plans to phase out by the end of 2001 the production of perfluorooctanyl chemistry that underpinned their extremely successful Scotchgard™ and Scotchban™ product lines.[2] 3M took this course of action, under pressure from the U.S. Environmental Protection Agency (EPA)[3] after learning that PFOS, PFOA and other perfluorooctanylsulfonate degradation products of chemicals used in Scotchgard™ and Scotchban™ could readily be found in blood samples from the general population in the United States and/or wildlife specimens from across the globe. These compounds, like other perfluorochemicals (PFCs), are chains of fully fluorinated carbon atoms of varying lengths, yielding chemicals that are extremely resistant to heat, chemical stress, and that repel both water and oil.

Because of these properties PFCs, or chemicals that degrade into PFCs, have been widely used since the 1950s by industry as surfactants and emulsifiers and in commercial products, including stain or water protectors for carpet, textiles, auto interiors, camping gear and leather; food packaging; folding cartons and other paper containers; floor polishes; photographic film; shampoos; dental cleaners; inert pesticide ingredients; and lubricants for bicycles, garden tools and zippers. Neither PFOS nor PFOA are major ingredients in commercial products. Instead, the products typically contain fluorochemicals that degrade into PFOS and PFOA. In addition, PFOA is manufacturing aid used to produce polytetrafluoroethylene, a compound more commonly recognized as Teflon and Gortex. Their persistence is extreme—there is no evidence that they ever fully degrade, and they have been found in animals, humans and ecosystems worldwide.

The EPA is currently negotiating a consent agreement with 3M and DuPont, which has led to the disclosure of a great deal of the companies' own research, much of which is only now being made public.

Exposures

Of the perfluorinated compounds, PFOS appears to have the widest distribution. A 2002 European study of PFOS, PFOA and PFHxS, a related compound, detected these compounds in bottlenose, common and striped dolphins, whales, bluefin tuna, swordfish and cormorants in the Mediterranean, and in ringed and gray seals, sea eagles and Atlantic salmon in the Baltic.[4] PFOS was the predominant compound. Other research shows that this chemical is now contaminating many wildlife species around the world, including polar bears in the Arctic, seals in Antarctica, dolphins in the river Ganges in India, albatrosses from Midway Atoll in the Pacific, turtles in the United States, gulls in Korea, cormorants in Canada,[5] and fish in Japan.[6]

Fluorinated telomers are used to keep grease from soaking through fast food containers such as pizza boxes, French fry holders, and food wrapping paper. The digestive system can break telomers down into PFOA and related chemicals. Newly revealed tests conducted by 3M showed that a metabolite specific to the telomers was found in 85 per cent of the children tested.[7] Telomers are not regulated, so manufacturers are not obligated to disclose their presence to consumers or any downstream users.

A 2003 study of PFOS and PFOA in the U.S. Red Cross blood banks, conducted by a team including scientists from the 3M Company, estimated the average concentrations in humans to be 30-40 parts per billion (ppb), with males having higher levels.[8] By comparison, levels in wildlife have been measured at 940 ppb in common dolphin liver; 1100 ppb in ringed seals from the Bay of Bothnia; and 270 ppb in long-finned pilot whale liver from the North Thyrrenian Sea.[9] This study noted that PFOS concentrates in the liver and lowers cholesterol levels in the blood.

Effects

3M has known for decades that perfluorinated compounds were not the benign, inert chemicals it claimed they were. In 1979, 3M administered four doses of PFOS to monkeys and all the monkeys in all treatment groups died within weeks. Typically, when a study like this is conducted, the researchers predict that the lowest dose will not cause any harmful health effects.[10] In 1981 both DuPont and 3M reassigned women of childbearing age working in their production plants after they learned that PFOA caused developmental abnormalities in laboratory animals. Within weeks of this discovery, DuPont found PFOA in the women's blood. Eventually they returned the women to the plants, and both companies continue to downplay adverse consequences even as demonstrated by their own research of perfluorinated compounds. It was known as early as 1975 that fumes from hot pans coated with polytetrafluoroethylene can kill pet birds,[11] and broiler

chicks have died after exposure to polytetrafluoroethylene-coated light bulbs.[12] Laboratory experiments reported in 2003 showed that in rats, PFOS exposure can lead to loss of appetite, interrupted estrus cycles, and elevated stress hormone levels. PFOS was found to accumulate in brain tissue, particularly the hypothalamus, suggesting that PFOS crosses the blood-brain barrier and may interfere with reproductive hormones through the pituitary-hypothalamus process that stimulates their production.[13] Recent laboratory studies with PFOA involving rats show low birth weight, small pituitary gland, altered maternal care behavior, high pup mortality, and significant changes in the brain, liver, spleen, thymus, adrenal gland, kidney, prostate, testes and epididymides.[14] Several studies indicate PFOA increases estrogen and leads to testosterone dysfunction in males. There is even more evidence that PFOA as well as chemicals that metabolize to PFOs and PFOA lead to underactive thyroid; thyroid dysfunction during pregnancy can lead to many developmental problems, including faulty brain development and neurological and behavioral problems that affect not only infants and young animals (or humans) but continue into adulthood. The EPA considers both PFOS and PFOA to be a carcinogen in animals, with testicular, pancreatic, mammary, thyroid and liver tumors most frequent in exposed rats.

All studies to date indicate perfluorinated compounds damage the immune system. In one experiment, a chemical very similar to PFOA called PFDA resulted in such atrophy of the thymus gland, (the source of T cells that attack bacteria, viruses and cancer cells) that the gland was undetectable upon clinical examination.

Although every species has its individual profile of vulnerabilities and protections from exposures to chemicals, there is no reason to believe that the pathologies exhibited by laboratory animals are confined to one or two species; both wildlife and humans are likely to suffer similar effects.

PFOs are a perfect example of the need for REACH. The chemical industry claims that REACH's testing requirements will be financially burdensome, yet 3M and DuPont were obviously willing to conduct detailed research on PFOs voluntarily for 30 years; they just were not willing to share the results. If REACH's transparency provision had been in place during that time, the public would have known the risks of such perfluorinated compounds in time to make informed decisions about their use before exposures had reached such high levels.

2. Phthalates

Exposures

Phthalates are a group of chemicals used as softeners in a variety of plastic products, including the ubiquitous polyvinyl chloride (PVC). Products containing phthalates include medical devices (intravenous tubing, blood bags, masks for sleep apnea devices), building products (insulation of cables and wires, tubes and profiles, flooring, wallpapers, outdoor wall and roof covering, sealants), car products (car under-coating, car seats etc.) and children's products (teething rings, squeeze toys, clothing and rainwear). They are also used in some lacquers, paints, adhesives, fillers, inks and cosmetics. The most common phthalate in the environment is di-(2-ethylhexyl)phthalate (DEHP), which comprises half of all phthalates produced in Western Europe, with 450,000 tonnes used per year. Concern about children's exposure to phthalates prompted the EU to ban six types of phthalate softeners in PVC toys designed to be mouthed by children under three years of age.

Both humans and wildlife may be exposed to various phthalates. For example, a 2003 study of two groups of pregnant women, one in New York City and one in Krakow, Poland, compared the levels of four phthalates in the women's personal ambient air and measured the levels of the metabolites of these phthalates in the urine of the New York women.[15] All four phthalates were present in all the air samples, but air concentrations of DBP, di–isobutyl phthalate and DEHP were higher in Krakow than in New York. The study found that air was a significant source of exposure, that some women receive doses high enough to cause concern, and that there was a correlation between air and urine levels of some phthalates.

Other studies in the EU have also raised concerns with regard to current exposure levels. A recent study in Germany, for example, has concluded that exposure to DEHP may be far higher than previously thought. It reported that in 12 per cent of the Germans studied, phthalate levels exceeded the tolerable daily intake (TDI) used by the EU Scientific Committee for Toxicity, Ecotoxicity and the Environment. Exposure to DBP and BBP was also ubiquitous.[16]

Effects

Some phthalates appear to exert endocrine disrupting effects, and can act against the male hormone, androgen, through pathways other than binding to androgen or estrogen receptors. While there is little research on the effects of phthalates on wildlife per se, some studies suggest that there may be serious consequences for both wildlife and humans. Of particular concern is phthalate exposure in pregnant females: some researchers have proposed that the anti-androgenic properties of phthalates *might* be linked to testicular dysgenesis syndrome, the manifestations of which range from birth defects in males, including undescended testes, to low sperm counts and testicular cancer.[17]

Numerous Laboratory studies underpin the concern. For example, a study has shown that DEHP, BBP, and DINP administered to pregnant rats induced feminized breasts in the male offspring, as well as other reproductive malformations, including small testes in the case of the DEHP and BBP.[18]

There are also worries that exposure to man-made chemicals with hormone disrupting properties may be affecting the age of puberty. A study of Puerto Rican girls with premature breast development suggested a possible association with exposure to certain phthalates.[19] U.S. researchers recently reported the effects of DEHP on Leydig cells (testosterone-producing cells in the testes) in rats.[20] They found that pro-

longed exposure to DEHP caused the number of Leydig cells to increase by 40 per cent-60 per cent while simultaneously reducing testosterone production. At the same time, blood levels of both testosterone and estrogen increased by 50 per cent. It is known that males with high levels of serum testosterone and luteinizing hormone (a hormone that triggers testosterone production) are at higher risk of early puberty and testicular tumors.

With regard to cancer, a recent study supported other research associating DEHP with liver cancer in rodents.[21] A 2003 Harvard study suggested another mechanism for carcinogenic effect of phthalates. The researchers measured levels of eight phthalates in subjects and found an association between monoethyl phthalate (MEP) and increased damage to the DNA in the subjects' sperm.[22] This is the first study showing that phthalates can induce such damage at levels presently found in the environment.

Other studies with phthalates show that additive effects can occur when there is exposure to more than one phthalate.[23] This underlines the growing concern with real life exposures to multiple pollutants, and the increasing realisation that current regulatory practices, based on testing chemicals in isolation, may not be protective.

3. Phenols

The first study showing that certain phenolic compounds produced estrogenic effects was published in 1936,[24] but only recently have researchers begun to explore its implications. Evidence for endocrine disruption by the widely used phenol compounds bisphenol A (BPA) and nonylphenol is mounting. BPA is mostly used to make polycarbonate plastic, which has a diverse range of application in making bottles, computer and electronics shells, CDs, crash helmets, and many other consumer products. Certain compounds that can leach BPA are also used in the plastic linings of food cans and in dental fillings, through which people can ingest small quantities. In December 2003, concerned about BPA in the plastic linings of food cans, the EU reduced the amount of BPA migration permitted by 80 percent to 0.6 milligrams per kilogram of food.[25] However, BPA remains widely distributed in consumer products.

Nonylphenolic compounds have been used in degreasing solutions, and in leather and textile processing, as well as in de-icing fluid, paints, plastics, and pesticides. The EU has imposed restrictions on the marketing and use of nonylphenol and nonylphenol ethoxylates to a certain extent in cleaning products, textile and leather processing, agricultural teat dips, metal working, pulp and paper, cosmetics including shampoos, and personal care products except spermicides.[26]

Fish have been shown to be susceptible to the endocrine disrupting effects of both nonylphenol[27] and BPA.[28] Exposure to either of these chemicals can cause male fish to make vitellogenin (an estrogen-regulated protein produced by female egg-laying vertebrates and not normally produced by males or juveniles), and can also affect the formation of sperm. Before improved regulation, male fish in the river Aire in England were found to be feminised downstream of a wastewater treatment plant discharge containing alkylphenol ethoxylates from the textile industry. Many male fish were found with egg producing cells in their testes, and reduced testis growth rate and size.[29] [30]

Aquatic invertebrates seem particularly sensitive to these chemicals. For example, nonylphenol affects the freshwater algae, *Scenedesmus subspicatus* at levels of 3.3 micrograms per litre.[31] Molluscs in particular have shown effects at very low dose levels. For example, in the mollusc *Potamopyrgus antipodarum*, BPA and octylphenol, as well as a mixture of these and other chemicals in treated sewage effluent, stimulated egg and embryo production at low doses and inhibited such production at high doses.[32] This work supported a 2000 study by some of the same researchers showing that extremely low levels of BPA and octylphenol triggered malformed genitals of female ramshorn (freshwater) snail, *Marisa cornuarietis*, and the (saltwater) dogwhelk *Nucella lapillus*.[33] In some of the freshwater snails, the excessive growth of the female glands and the egg masses ruptured the egg tube, and the snails died. This syndrome was referred to as superfeminisation. A number of other adverse changes were observed in both species. Another important finding was that in the freshwater snails, the medium doses of octylphenol produced more changes than either the highest or lowest doses.

Other researchers have shown that a single 48-hour exposure to 1 microgram per litre of nonylphenol, comparable to environmental levels, altered the sex ratio of oysters, reduced the survival of offspring, and caused some oysters to become hermaphroditic.[34] A 2001 study exposing barnacles to concentrations of nonylphenol similar to those in the environment (0.01-10 micrograms per litre) disrupted the timing of larval development.[35]

In addition to fish, other vertebrates also show effects when exposed to BPA. For example, in 2003, researchers reported that BPA at environmentally comparable doses resulted in sex-reversals and altered gonadal structures in the broad-snouted caiman, an alligator relative native to mid-latitude South America.[36] In another study, the offspring of pregnant mice exposed to BPA showed changes in ovarian and mammary gland tissues and disrupted fertility cycles as adults.[37] BPA was reported for the first time in 2001 to induce reproductive malformations in birds—specifically, in female quail embryos and male chicken embryos. The female embryos' oviducts developed abnormally, and the males' testes were feminized.[38]

The exact mechanism by which BPA and nonylphenol exert their effects is not clear, but a recent *in vitro* study demonstrated a molecular mechanism by which BPA and nonylphenol interfere with both the activation and function of cellular androgen receptors.[39] In a 2002 study, nonylphenol tested on barnacle larvae induced DNA damage, possibly including mutations, and the authors speculate that this effect may be a mechanism by which higher-level reproductive abnormalities are caused.[40]

Despite evidence from these and other studies, the low dose effects of BPA are still in dispute. Regulators in the EU have been reluctant to act, and further studies have been demanded.

4. Polybrominated Flame Retardants

Brominated flame retardants (BFRs) in furniture, building material, and clothing have become a serious concern, as their levels are showing sharp increases in living organisms. The first BFRs were taken off the market in the early 1970s after a spill led to poisonings of livestock and farm families in Michigan.[41] Three BFRs now dominate the market: TBBPA, the most widely used, primarily in printed circuit boards and in some plastics; HBCD, and the deca-BDEs. The other commercial PBDEs (octa-BDE and penta-BDE) will be banned in the EU as of August 2004,[42] and the state of California has taken similar action. However, because of their alarming spread and rate of accumulation in humans and animals, Europe's ban does not provide complete reassurance, particularly regarding the penta-BDE form used as a flame retardant in polyurethane foam elsewhere in the world.

Researchers recently reported levels of PBDEs in U.S. breast milk.[43] Forty-seven Texas women had an average level of 73.9 ng/g lipid; such levels are sharply higher than those found in European studies. There are serious concerns about the transfer of BFRs to nursing infants, and some scientists are worried that BFRs might affect fetal development, including disruption of the thyroid system's role in fetal brain development.[44] In 2003 a WWF-UK biomonitoring program found deca-BDE in the blood of seven per cent of those tested.[45]

New research from Sweden has found high levels of several brominated flame retardants in the eggs of peregrine falcons from 1987-1999. The eggs of falcons living in the wild had significantly higher concentrations of the essentially unregulated deca-BDE than eggs of captive falcons. The fact that deca-BDE was found in eggs demonstrates that the chemical can cross cell membranes, contrary to what scientists had previously thought. The peregrine study represents the first time that the deca formulation has been found in wildlife. [46]

In 2002, one research team predicted that within 10 to 15 years, concentrations of BFRs in Great Lakes herring gull may be higher than those of PCBs.[47] BFRs have also been found in sperm whales,[48] ringed seals from the Canadian Arctic,[49] mussels and several kinds of fish in Norwegian waters, and harbour seals in San Francisco Bay,[50] among other wildlife. Essentially, BFRs are being found wherever we look.

Effects

Laboratory studies show that certain BFRs are highly toxic to aquatic animals (crustaceans),[51] and suggest effects on pubertal development, thyroid and liver in rats, as well as developmental neurotoxicity in mice.[52] A recent paper reported behavioral effects in mice pups at a relatively low dose.[53] In 1999 Swedish researchers reported that PBDEs and HBCD may have health effects similar to those of DDT and PCBs because of their ability to induce genetic recombination.[54]

While there are no published epidemiological studies on effects of BFRs on humans, the possible thyroid effects, based on tissue culture and animal studies, are a red flag. As with other chemicals, anything that affects fetal development merits particular study because of the profound, long-term, and often irreversible influence that early exposures have on the entire life of an organism.

The Precautionary Principle

In the context of chemicals, the precautionary principle responds to the complexity of environmental health problems, the paucity of information and subsequent uncertainty about cause-effect relations, and the slow pace of testing and government decision making. At its core, the principle calls for preventive, anticipatory measures to be taken when an activity raises threats of harm to the environment, wildlife, or human health, even if some cause-and-effect relationships are not fully established scientifically.

The precautionary principle has taken root in international statements of policy and legally binding agreements dealing with high stakes environmental concerns of low scientific certainty. From UNEP's Governing Council Report on its 15th Session (1989), to the Rio Declaration on Environment and Development (Principle 15), Ozone Layer Protocol, Climate Change Convention, London (Dumping) Convention, OSPAR and North Sea-related decisions, UN Fisheries Agreement, and the Stockholm Persistent Organic Pollutants Convention (POPs), among many other agreements, the principle has gained widespread international acceptance as a guiding principle for decision making.

Although there is no universally agreed upon, specific definition that fits all situations, acceptance of the principle nonetheless reflects a significant paradigm shift in the environment-development realm of decision making.

B. LESSONS FROM THE PAST

There is continuing evidence of widespread contamination and impacts on wildlife of chemicals that are now banned or restricted. This growing body of scientific evidence should act as a warning: unless action is taken now other chemicals in widespread use today will leave a similar legacy.

1. DDT/DDE and PCBs

Because of the persistence and bioaccumulative properties of the many pesticides and PCBs known collectively as organochlorines or chlorinated hydrocarbons, animals at the top of the food web tend to have high levels of these chemicals in their tissues. This is especially true of animals whose diet is mostly fish, including mink, otter, polar bears, whales, dolphins, and birds such as eagles, ospreys, gulls, and skuas (a predatory and scavenging gull-like seabird).

Because of temperature and circulation patterns in the atmosphere and oceans, many chemicals tend to concentrate at the poles. Most is known about the consequences in the Arctic, but the Antarctic is by no means exempt. One recent study documented for the first time the presence of PCNs (polychlorinated naphthalenes) in Antarctic silverfish, adelie penguins, South polar skua, and Weddell seals from the Ross Sea.[55] These chemicals have been used as insulating fluids in electrical equipment and in paints, lubricants and preservatives. The study also showed that adult female penguins and skua, like many other birds, transfer chemicals to their eggs, and thus to their offspring.

Polar Bears The polar bear rates as one of the wildlife species most threatened by chemicals.

As the apex of the Arctic food web, polar bears collect the highest doses of many chemicals. They also undergo periods of fasting or starving during ice melts and breeding, which may mobilize the toxic chemicals they retain. Most is currently known about the effects of the PCBs, but in future it is likely that concern will also focus on other chemicals or interactive effects due to the many contaminants now found in this species.

A comparison of polar bears from Svalbard in the Norwegian Arctic with those in less polluted areas in the Canadian Arctic found very high concentrations of PCBs in older male bears.[56] Females have lower levels because they pass the chemicals on to their young through their fat-rich milk.

PCBs reduce the ability of the immune system of Svalbard bears to combat common infections such as influenza, REO virus and herpes virus. This poses a particular threat to these long-living, slowly reproducing animals which have few offspring. Bears with higher PCB contamination also produce lower levels of the male sex hormone testosterone. Similarly, in females, those with the highest concentrations of PCBs have higher levels of progesterone in their blood.[57] Other research into Svalbard bears found four of 269 females to be masculinised. Some researchers consider that this pseudohermaphroditism could result from excessive androgen excretion by the mother caused by a tumor, or it could be a result of endocrine disruption from environmental pollutants.[58]

Levels of newer-generation chemicals such as brominated flame-retardants[59] and artificial musks[60] are also rising in the Arctic. The toxic properties of these flame retardant chemicals are similar to PCBs and if the current trend of increasing global production is not halted, levels will surpass those of PCBs within the next 50 years.[61] Although a direct link between these chemicals and adverse effects on artic wildlife has yet to be established, it is becoming increasingly clear that the wildlife of the Arctic may face a new PCB-like problem from chemicals that can disrupt thyroid hormone function, affect the immune system, disrupt brain development and affect coordination, learning abilities and memory.

Mink and Otter In 1999 a correlation was found between the PCB mixture Aroclor 1260 and short baculum (penis bone) length in wild juvenile mink in the Canadian Fraser River and U.S. Columbia River systems.[62] Scientists have suggested that baculum length may be a factor in breeding success. Similarly, a study in the polluted lower Columbia River revealed young otter with shorter bacula and smaller testes compared to otters in less polluted areas.[63]

Salmon A new laboratory study of Chinook salmon indicates that even brief exposures to low doses of DDE can impair the fish's immune systems.[64] Newly fertilized salmon eggs were immersed in a 10 parts per million solution of DDE for one hour and then again at hatching for two hours. When the fish were a year old, their spleens were significantly impaired in their ability to produce white blood cells, a major component of the immune system. Salmon are high in the food web and can accumulate significant levels of toxic chemicals in their fat. An alarming study published in January 2004 indicates that consumption of

salmon and other fish high in essential fatty acids may pose serious health risks for humans.[65] Researchers measured a total of 14 contaminants, including PCBs, dieldrin, dioxins, furans, toxaphene, lindane and DDT/DDE. The highest levels of PCBs, dioxins, toxaphene and dieldrin were found in salmon from Scotland and the Faroe Islands. The concentrations of these contaminants were significantly higher in all European fish than in the comparison salmon from Chile and Washington State in the U.S. The researchers suspect that the fish used to make the salmon feed were taken from European waters that are more contaminated than pacific waters. They also note that under U.S. regulations, the levels found in European fish would trigger advice to consumers to eat less than half a meal of salmon per month.
This study starkly illustrates the magnitude and ubiquity of the contaminant problem and underlines the fact that humans cannot insulate themselves from a dangerous cocktail of chemicals.

Seals In the 1970s, common seals in the Wadden Sea (the eastern part of the North Sea) produced few pups and the population went into decline. The animals were heavily polluted with PCBs. Seals fed on contaminated Wadden Sea herring had only half the breeding success of those feeding on less contaminated North Atlantic herring. Embryos failed to attach to the womb, and while this phenomenon can be associated with low levels of the female hormone, PCBs are known to stimulate the production of enzymes that break down that hormone. The seals' immune systems were also affected, and this combination is believed to have contributed to the mass deaths of common seals in the North Sea and Baltic by distemper in the late 1980s. Those areas where the seals were most exposed to pollution, such as the Wadden Sea, had the highest death rates.[66]

Few now doubt that the decline of Baltic ringed and grey seals was the result of pollution. Many spontaneous abortions and deformed wombs were observed. Seventy per cent of ringed seals and 30 per cent of grey seals had problems reproducing. An analysis of PCB and DDT levels in grey seals between 1969 and 1997 implicated PCBs as the leading cause of reproductive failure. The grey seals also suffered an impaired immune system, associated with high PCB and DDT levels. Other pathologies included hyperactivity of hormonal glands, bone degeneration, intestinal ulcers, claw malformations, arthritis, cancer of the womb and skin thinning.
Researchers are now also looking at the role of chemicals in the disruption of Vitamin A (also known as retinol) physiology.[67] Laboratory studies have shown that many contaminants, including PCBs, polychlorinated dibenzo-para-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs), can disrupt vitamin A and alter the distribution of its essential metabolites. Field studies also suggest that complex environmental mixtures of chemicals disrupt vitamin A in wild marine mammals and other fish-eating wildlife. Vitamin A is important in immune function, growth and development, reproduction, vision, and other bodily processes.[68] It has also been noted that many of the symptoms of contaminant exposure resemble those of vitamin A deficiency, including stunted growth and impaired reproductive function, implying that vitamin A disruption may be a mechanism by which contaminants interfere with normal physiology.[69]

Lake Apopka wildlife Lake Apopka, Florida, has been the subject of extensive study since a chemical spill in 1980 dumped a number of DDT-related compounds into the water, after which the alligator population declined sharply. Runoff from farming in the area has also added several other pesticides, including dieldrin and toxaphene. Ongoing research continues to reveal aspects of chemical endocrine disruption in wildlife.

Alligators Many studies have reported reproductive disorders in Lake Apopka alligators as well as an overall decline in the alligator population. For example, compared with less polluted waters, fewer viable eggs were found, and juvenile survival was lower. Also Lake Apopka

alligators had reproductive effects including smaller phalli in males.[70] The pesticides polluting the lake are generally accepted as the cause.

Mosquitofish In 2003 researchers reported a study comparing male mosquitofish in Lake Apopka with those in two other nearby lakes which had not been affected by the 1980 chemical spill. Male fish from Lake Apopka had slightly shorter gonopodia and on average 32 per cent and 47 per cent fewer sperm cells per milligram testis, when compared with the fish collected from the other two lakes.[71]

Human cancer. New research shows how chemicals long banned can still exert harmful effects. A 2003 Swedish study measured levels of PCBs, hexachlorobenzene and chlordanes in the mothers of men with testicular cancer.[72] Most of the men in the study were born in the 1970s, the period when these chemicals reached their highest concentrations in the population. Testicular cancer incidence has been rising in Western countries, with Swedish rates rising 2.2 per cent between 1980 and 1999.[73] Because testicular cancer is thought to begin in the fetus, and because mothers are known to transfer POPs to their offspring, maternal levels during pregnancy and lactation would be an important source of exposure. The study found that concentrations of the chemicals were significantly higher in the mothers of men with testicular cancer than in the control group.

2. PAHs

Beluga whales The approximately 650 remaining beluga whales in the St. Lawrence River estuary are subjected to multiple and severe chemical threats from the highly industrialized Great Lakes system. In 2002 researchers published the results of a study of 129 carcasses of beluga stranded between 1983 and 1999. More

than a quarter of the animals suffered from cancer, and cancer accounted for 18 per cent of the deaths in the whales studied.[74] Tumors and cancer in general are very rare in cetaceans. Intestinal cancer, the most common found in the belugas, was seen at rates exceeding those for humans, domestic cats, and cattle; the overall cancer rate was higher than that reported for any other wild animals. The researchers found three cases of breast cancer among the belugas—the first ever reported for cetaceans.

The St. Lawrence beluga whales are contaminated with a variety of heavy metals, PCBs and DDT compounds, including polycyclic aromatic hydrocarbons (PAHs), of which some 36,000 tonnes were released into the St. Lawrence watershed from aluminium smelters upstream between 1937 and 1980. Benzo(a)pyrene, a PAH known to be a human carcinogen, is suspected as a possible culprit in the cancers, although the belugas' immune systems may also have been stressed by PCBs and other chemicals, perhaps in interaction with high natural hormone levels during the relatively long pregnancy and lactation periods of cetaceans. It is likely that the belugas ingest the contaminants as they dig into sediments and feed on bottom invertebrates.

3. Atrazine

Atrazine is a very commonly used herbicide; in the U.S., 27,000 tonnes are applied every year to farmland to kill weeds. It is so widespread that it has been measured in rainwater in parts of the world where it is not used. Although atrazine and simazine use is to end in the EU,[75] their ubiquity in the environment and the emerging evidence of effects at relatively low ambient environmental concentrations leave little room for complacency.

Frogs Frogs around the world have suffered catastrophic declines in population, as well as a number of malformations including extra limbs and limbs growing in the wrong places. Researchers have investigated a number of causes ranging from increased UV exposure as a result of a depleted ozone layer, chemical exposures, and infectious and/or parasitic agents. The explanation for the global phenomenon is likely to involve a combination of factors, but chemicals remain suspect, and atrazine is high on the list of likely chemical culprits.

The scientific evidence concerning the threshold of atrazine's effects on organisms has evolved dramatically. A laboratory study published in 2001 using frog embryos, larvae and adults showed a dose-dependent increase in larval deformations, as well as respiratory distress in adults.[76] Despite this evidence, the researchers concluded that atrazine concentrations in the environment were significantly lower than those necessary to harm amphibian embryos and adults and therefore that atrazine was probably not a major factor in amphibian declines.

However, just a year later, another group of researchers published work which challenges that assertion.[77] They exposed a large number of African clawed frog tadpoles to varying concentrations of atrazine ranging from .01 ppb to 200 ppb. Then they measured changes in the frogs' bodies after metamorphosis. They found that tadpoles exposed to as little as 0.1 ppb developed reproductive abnormalities, exhibiting characteristics of both sexes, and at concentrations of 1.0 ppb the larynges of the males were significantly smaller. In a second experiment, they exposed adult frogs directly to atrazine and then measured testosterone and estrogen levels, finding a 10-fold decrease in testosterone in the adult males exposed to 25 ppb of atrazine. The males' vocal cords were also much smaller than normal. In 2003 the same team published a study of American leopard frogs both in the wild and in the laboratory which supported their earlier research.[78] Exposures at 0.1 ppb produced retarded gonadal development and hermaphroditism in laboratory tests on the frogs. Frogs living wild in atrazine-contaminated sites exhibited similar characteristics.

A two-year study of northern red-legged frogs along the northwest coast of California found male frogs producing vitellogenin, an egg yolk protein normally produced only by females, in nine of 13 populations sampled.[79] The researchers noted the previous research that had raised concerns about atrazine but the study did not identify an estrogenic agent in the red-legged frogs' environment.

4. Tributyltin

Tributyltin (TBT) belongs to a group of chemicals called organotins that are used to kill both microbes and fungi and to keep barnacles and other organisms from sticking to ship hulls. TBT is a known endocrine disrupter, and has been show to be toxic in a wide variety of aquatic organisms, including dog whelks, barnacles, mud snails, newts, sea anemones, coral, crabs and prawns.[80]

In certain gastropods (a type of mollusc including snails, whelks, limpets and slugs), tributyltin causes a condition called imposex, in which the females develop male sexual organs. Imposex has been documented in 140 species

of snails.[81] Although the International Maritime Organization (IMO) has agreed to eliminate TBT-based paints on ships' hulls by 2008,[82] and TBT levels in marine biota have begun to decline, there is still significant endocrine disruption among gastropods in heavily used shipping lanes and harbors. A 2003 study of whelk in the Skagerrak region of the North Sea between Norway, Denmark and Sweden indicated high levels of imposex in common whelk *(Buccinum undatum)* living in areas with the highest ship traffic and the most thoroughly mixed water.[83] A survey of snails in Sicilian coastal waters published in 2003 found that in four of the five sample sites almost all female snails showed signs of imposex even though the organotin concentrations in both the snails and the sediment were low.[84] Despite the IMO ban on organotin biocides, some researchers are concerned that new chemical substitutes may be just as damaging as those removed from the market.[85]

Research on mammals is more limited. Japanese researchers reported in 2002 that exposure of cells from Dall's porpoises, bottlenose dolphins, California sea lion, larga seal and humans to tributyltin and dibutyltin significantly suppressed cell processes important in immune response.[86] The researchers suggested that butyltins could also pose a serious threat to immune functions in free ranging marine mammals and humans. Experiments also show that TBT may disrupt mammalian thyroid hormones.[87]

C. CHEMICAL MIXTURES IN EFFLUENTS

Effluents from sewage treatment plants, cattle feedlots, and paper mills have been implicated in endocrine disruption, although researchers have not always been able to identify all the specific compounds at work. Endocrine-disrupting chemicals in these environments are likely to be naturally-occurring ones, such as natural hormones excreted by humans and farm animals, and phytoestrogens from plant material. However, some sewage treatment effluents also include industrial chemicals such as BPA and nonylphenol as well as nitrates found in fertilizers and animal excrement.

Cattle Feedlot Effluent

Feedlot effluents have been under suspicion for some time because livestock in the United States are treated with, and excrete, significant amounts of androgens and estrogens. Concern about their effects on wildlife is building.[88] The EU took action in the 1980s to ban growth promoters with steroid-like action.[89] New research is emerging showing that fish living in feedlot effluent undergo reproductive alterations.[90] One new study of fathead minnows living in water contaminated with such effluent found demasculinised males and defeminised females.[91] The researchers suspect there are either potent androgens or a complex mixture of androgens and estrogens in the effluent.

Sewage and Wastewater

A number of studies in the UK have established that treated sewage effluent exerts pronounced estrogenic effects on fish. Freshwater Roach from several river systems showed increased vitelligenin levels, as well as intersex (ovotestis). Studies of flounder in the UK estuaries also showed high vitellogenin levels. Researchers think the presence of industrial chemicals as well as natural female hormones and synthetic steroid oestrogens ('The Pill') from sewage effluent contributes to the estrogenic effects.[92]

Later work on the European continent is consistent with the UK freshwater results. A 2002 study of freshwater bream and estuarine flounder in The Netherlands found that 37 per cent of the male bream exhibited gonads with both male and female parts, as well as elevated levels of vitellogenin in bream and male flounder, with the highest levels found in bream taken from a stream near a municipal wastewater treatment plant.[93] This study did not identify the estrogenic agents in the water. In a 2003 study of rainbow trout caged in effluent from two municipal sewage treatment plants and in Rhine River water, significant levels of estradiol compounds derived from fecal material, as well as phytoestrogens and other compounds, were identified in the samples.[94] The male fish in the effluent showed vitelligenesis. Although fish kept in Rhine River water did not, the researchers identified fecal steroids and phytoestrogens in it as well, concluding that all water sampled contained biologically relevant concentrations of estrogenic compounds.

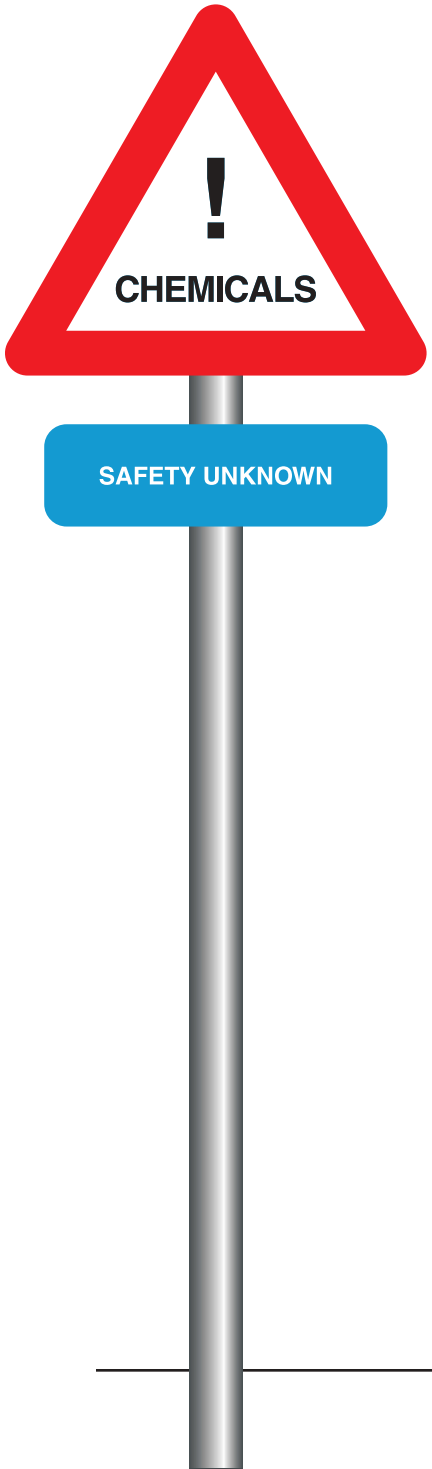
Nitrates and nitrites may also be contributing to endocrine disruption in sewage treatment effluent. A retrospective study of alligators in seven Florida lakes receiving sewage runoff found that as nitrate-nitrogen compounds rose above 10 ppm (the U.S. limit in drinking water), testosterone levels fell by 50 per cent and penis size shrank.[95] The alligators' testosterone levels in lakes high in nitrogen but low in pesticides were similar to those of alligators in lakes with high pesticide levels.

Paper Pulp Mill Effluent

Paper mill effluent contains a complex brew of chemicals, only a few of which have been identified, including polychlorinated dibenzofurans and dibenzothiophenes.[96] In a 2003 study, 80 per cent of the wild female mosquitofish living in a river downstream from paper mills were shown to be partially masculinised, with altered anal fins, a feature known to be androgen-dependent; 10 per cent of the fish were fully masculinised.[97] Although the researchers did not identify a specific androgenic compound in the pulp mill effluent, tests of the effluent produced a variety of androgen receptor reactions.

Household Chemical Effluent

Wastewater effluent carries hundreds, probably thousands, of ordinary household chemicals. The study of their distribution and effects in the environment is just beginning, but the implications of early research are unsettling. A laboratory study of two compounds used in many household products and an antibiotic were found to reduce the biodiversity of algae found in a river receiving wastewater effluent.[98] The compounds are triclosan, a microbicide used in kitchen cleaners and toothpaste; tergitol NP10, a nonylphenol ethoxylate surfactant used in hair dye and spermicidal lubricants; and ciproflaxin, a widely used antibiotic. This illustrates the potential ecological impact of chemicals in personal care products.



III. CONCLUSION

There is considerable and growing scientific evidence of damage to wildlife from chemical exposures, and even more indications of widespread contamination. A large amount of research has focused on the most notorious historical contaminants such as PCB and DDT. The fact that these chemicals continue to have an impact clearly demonstrates the long-term threats posed by persistent and bioaccumulative chemicals: even after they are banned it takes many years for environmental contamination to decline.

Research has begun on chemicals of concern that have yet to gain broad public attention, such as brominated flame retardants and perfluorinated compounds. However, scientists are already demonstrating that these chemicals are contaminating wildlife across the globe, and there are many indications of potential impacts. It took a long time to identify conclusive evidence that PCBs have an impact on wildlife and humans; it will similarly take a long time to prove impacts from these newer chemicals of concern.

We know that globally chemical production is increasing, wildlife contamination is widespread, and a variety of troubling threats to species health are becoming more prevalent. Scientific research is only just beginning to uncover the extent of the chemical threat. To suggest there is no link between these developments, and to give chemicals the benefit of the doubt, is reckless. To assume a link and to begin an immediate precautionary phase-out of certain chemicals in the face of unknown risks before it is too late is prudent and necessary—because the safety of people and the environment is paramount.

The experience with specific chemicals already known to endanger humans and the environment should motivate action to confront new chemicals before they create a legacy of unintended consequences. Such an approach should help to avoid unpleasant surprises in the future. This represents a major improvement on the status quo where ignorance and short-sightedness have created long delays before problems were identified and remedied.

Existing chemicals that threaten the health of wildlife and people can be substantially reduced, and future dangers averted, by ensuring that no chemicals are allowed on the market without basic information on their impacts. Those that pose the greatest concern -- including especially persistent and bioaccumulative chemicals and those that disrupt endocrine systems, reproduction, and other essential biological functions, deserve the greatest scrutiny. The use of chemicals of very high concern should only be authorized when there is an overwhelming social need for the use and safer alternatives are not available. This will require new international regulations, such as REACH, that promise to disclose missing data, to promote the innovation of safer alternatives, and to demand environmental accountability in global trade.

The Johannesburg Summit's 2020 Challenge

In September 2002, the Johannesburg World Summit on Sustainable Development adopted a Plan of Implementation that contains over thirty targets – framing specific actions to be achieved by prescribed dates. With regard to the sound management of chemicals, the 191 participating governments agreed that the global community should renew its commitment, made in Rio de Janeiro in 1992:

"…to sound management of chemicals throughout their life cycle and of hazardous wastes for sustainable development and for the protection of human health and the environment, inter alia, aiming to achieve by 2020 that chemicals are used and produced in ways that lead to the minimization of significant adverse effects on human health and the environment…."

Achieving that 2020 target will be challenging, requiring a diverse mix of REACH and other regulatory and voluntary actions at global, regional, national, and local levels. Without enactment of effective REACH-type measures, in conjunction with other initiatives to phase out and replace toxic chemicals with safe alternatives, the 2020 target will likely be little more than a "paper tiger" that provided a false sense of future security while chemical contamination worsened.

WWF DETOX CAMPAIGN

REFERENCES

1 O'Shea, T.J., Tanabe, S., Persistent ocean contaminants and marine mammals: a retrospective overview. In: O'Shea, T.J. et al. (Eds.), 1999. Proceedings of the Marine Mammal Commission Workshop Marine Mammals and Persistent Ocean Contaminants, pp 87-92. (cited in Tanabe, S. Contamination and toxic effects of persistent endocrine disrupters in marine mammals and birds. Mar Pollut Bull 2002;45:69-77.)

2 3M. (2000) 3M phasing out some of its specialty materials, May 16, 2000 press release.

3 Barboza D. (2000) "EPA Says It Pressed 3M for Action on Scotchgard Chemical". New York Times, May 19, 2000.

4 Kannan, K., Corsolini, S., Falandysz, J., Oehme, G., Focardi, S., Giesy, J.P. Perfluorooctanesulfonate and related fluorinated hydrocarbons in marine mammals, fishes and birds from coasts of the Baltic and Mediterranean Seas. Environ Sci Technol 2002 Aug 1;36(15):3210-6.

5 Geisy J.P. and Kannan K. Global Distribution of Perfluorooctane sulfonate in wildlife.
Env Sci Technol 2001, 35:1339-42.

6 Taniyasu, S., Kannak, K., Horii, Y., Hanari, N., Yamashita, N. A survey of perfluorooctane sulfonate and related perfluorinated organic compounds in water, fish, birds and humans from Japan. Environ Sci & Technol 2003, 37:2634-2639.

7 Fields, S. Another fast-food fear. Environ Health Perspect 2003: 111:16:A162.

8 Olsen, G. W., Church, T.R., Miller, J.P., Burris, J.M., Hansen, K.J., Lundberg, J.K., Armitage, J.B., Herron, R.M., Medhdizadehkashi, Z., Nobiletti, J.B., O'Neill, E.M., Mandel, J.H., Zobel, L.R. Perfluorooctanesulfonate and other fluorochemicals in the serum of American Red Cross adult blood donors. Environ Health Perspect 2003:111:1892-1901. doi.10.1289/ehp.6316 via http://dx.doi.org.

9 Kannan, et al., 2002.

10 Organization for Economic Cooperation and Development (OECD). (2002) Hazard Assessment of perfluorooctane sulfonate (PFOS) and its salts (November, 21 2002). ENV/JM/RD(2002)17/FINAL. Available online http://www.oecd.org/dataoecd/23/18/2382880.pdf.

11 "PFCs: A Family of Chemicals that Contaminate the Planet," Part 6: PFCs in Animals Worldwide. Environmental Working Group, 2003. http://www.ewg.org/reports/pfcworld/part8.php. Accessed 3 January 2004.

12 Ibid.

13 Austin, M.E., Kasturi, B.S., Barber, M., Kannan, K., MohanKumar, P.S., MohanKumar, S.M.J. Neuroendocrine effects of perfluorooctane sulfonate in rats. Environ Health Perspect 2003:111:12:1485-1489.

14 Thayer, K., Klein, J. Gray, S., Houlihan, J., Wiles, R., Greenleaf, T., PFCs: A Family of Chemicals that Contaminate the Planet. Environmental Working Group 2003. http://www.ewg.org/reports/pfcworld/part4.php. Accessed 5 January 2004.

15 Adibi, J.J., Perera, F.P., Jedrychowski, W., Camann, D.E., Barr, D., Jacek, Ryszard, Whyatt, R.M. Prenatal exposures to phthalates among women in New York City and Krakow, Poland. Environ Health Perspect 2003:111:14:1719-1722.

16 Kock et al, 2003. An estimation of the daily intake of di(2-ethyl) phthalate (DEHP) and other phthalates in the general population. International Journal Hygiene and Environmental Health.

17 Sharpe R.M. (2003). The oestrogen hypothesis – where do we stand now? International Journal of Andrology 26:2-15; Skakkebaek, N.E. et al., (2001) Testicular dysgenesis syndrome: an increasingly common developmental disorder with environmental aspects. Human Reproduction 2001:16:5:972-978.

18 Gray, L.E. Jr., Ostby, J., Furr, J., Price, M., Veeramachaneni, D.N., Parks, L. Perinatal exposure to the phthalates DEPH, BBP, and DINP, but not DEP, DMP, or DOTP, alters sexual differentiation of the male rat. Toxicological Sciences 2000:58:350-565.

19 Colón, I., et al., Identification of phthalate esters in the serum of young Puerto Rican girls with premature breast development. Environmental Health Perspectives, 2000. 108(9): p. 895-900.

20 Akingbemi, B.T., Ge, R., Klinefelter, G.R., Zirkin, B.R., Hardy, M.P. Phthalate-induced Leydig cell hyperplasia is associated with multiple endocrine disturbances. Proceedings of the National Academy of Sciences 2004 (Early Edition). www.pnas.org/cgi/doi/10.1073/pnas.0305977101, accessed 31 December 2003.

21 Seo, K.W., Kim, K.B., Kim, Y.J., Choi, J.Y, Lee, K.T., Choi, K.S. Comparison of oxidative stress and changes of xenobiotic metabolizing enzymes induced by phthalates in rats. Food Chem Toxicol. 2004 Jan;42(1):107-14.

[22] Duty, S.M., Singh, N.P., Silva, M.J., Barr, D.B., Brock, J.W., Ryan, L., Herrick, R.F., Christiani, D.C., Hauser, R. The relationship between environmental exposures to phthalates and DNA damage in human sperm using the neutral comet assay. Environ Health Perspect 2003 111:9:1164-1169. http://ehp.niehs.nih.gov/members/2003/5756/5756.html, accessed 6 January 2004.

[23] Foster, P M. Turner K J, Barlow N J. Anti-androgenic effects of a phthalate combination on in utero male reproductive development in the Sprague-Dawley rat: additivity of response? Toxicologist 2000 Mar; 66(1-S), 233.

[24] Dodds, E.C., Lawson, W. Synthetic estrogenic agents without the phenanthrene nucleus. Nature 1936:137:996. Cited in Pulgar, et al., 2000.

[25] Environmental Data Services, Ends Daily 15th Dec 2003.

[26] DIRECTIVE 2003/53/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 18 June 2003 amending for the 26th time Council Directive 76/769/EEC relating to restrictions on the marketing and use of certain dangerous substances and preparations (nonylphenol, nonylphenol ethoxylate and cement), Official Journal L 178 17-7-2003

[27] Jobling S., Sheahan D., Osborne J., Matthiessen P., Sumpter J. (1996). Inhibition of testicular growth in rainbow Trout (Oncorhynchus mykiss) exposed to oestrogenic alkylphenolic chemicals. Environ. Toxicol. Chem., 15, 194-202.

[28] Sohoni et al, Reproductive effects of long term exposure to bisphenol A in the fathead minnow (Pimephales promelas), Environ Sci Technol 2001:35: 2917-2925.

[29] Environment Agency of England and Wales 1998; Endocrine Disrupting Substances in the Environment. What Should Be Done? The EA Bristol.

[30] Commission of the European Communities. Proposal for a Directive of the European Parliament and of the Council relating to the restrictions on the marketing and use of nonylphenol, nonylphenol ethoxylate and cement. COM (2002) 459, 2002/0206 (COD).

[31] Kopf W. Wirkung endokriner stoffe in biotests mit wasserogranismen. In Stoffe mit endokriner wirkung in wasser. Bayerisches landesamt für wasserwirtschaft, Institut für Wasserforschung München (ed) Oldenbourg (1997) (as detailed in the European Union Risk Assessment Report (2002) 4-NONYLPHENOL (BRANCHED) AND NONYLPHENOL, CAS Nos: 84852-15-3 and 25154-52-3 EINECS Nos: 284-325-5 and 246-672-0, Joint Research Centre, European Commission).

[32] Jobling, S., Casey, D. Rodgers-Gray, T., Oehlmann, J., Schult-Oehlmann, U., Pawlowski, S., Baunbeck, T., Turner, A.P., Tyler, C.R. comparative responses of molluscs and fish to environmental estrogens and an estrogenic effluent. Aquat Toxicol 2003 Oct 29;65(2):205-20.

[33] Oehlmann, J., Schulte-Oehlmann, U., Tillmann, M., Markert, B. Effects of endocrine disruptors on Prosobranch snails (Mollusca: Gastropoda) in the laboratory. Part I: Bisphenol A and octylphenol as xenoestrogens. Ecotoxicology 2000 9:383-397.

[34] Nice, H.E., Morritt, D., Crane, M. Thorndyke, Long-term and transgenerational effects of nonylphenol exposure at a key stage in the development of Crassostrea gigas. Possible endocrine disruption? M. Marine Ecology Progress Series, 2003 256:293-300.

[35] Billinghurst, Z., Clare, A.S., Depledge M.H. Effects of 4-n-nonylphenol and 17beta-oestradiol on early development of the barnacle Elminius modestus. J. Exper. Mar. Biol. Ecol. 2001: Mar 15;25(2);255-268.

[36] Stoker, C., Rey, F. Rodriguez, H., Ramos, J.G., Sirosky, P., Larriera, A., Luque Munoz-de-Toro, M. Sex reversal effects on Caiman latirostris exposed to environmentally relevant doses of the xenoestrogen bisphenol A. Gen Comp Endocrinol 2003 Oct 1;133(3)287-96.

[37] Markey, C.M., Coombs, M.A. Sonnenschein, C., Soto, A.M. Mammalian development in a changing environment: exposure to endocrine disruptors reveals the developmental plasticity of steroid hormone target organs. Evol Dev 2003 Jan-Feb;5(1):67-75.

[38] Berg, C., Halldin, K., Brunstrom, B. Effects of bisphenol A and tetrabromobisphenol A on sex organ development in quail and chicken embryos. Environ Toxicol Chem 2001 Dec;20(12):2836-40.

[39] Lee, H.J., Chattopadhyay, S., Gong, E-Y, Ahn, R.S, Lee, K. Antiandrogenic effects of bisphenol A and nonylphenol on the function of androgen receptor. Toxicological Sciences 2003 75:, 40-46.

[40] Atienzar, F.A., Billinghurst, Z., Depledge, M.H. 4-n-Nonylphenol and 17-beta estradiol may induce common DNA effects in developing barnacle larvae. Environ Pollut 2002;120(3):735-8.

[41] Dunckel (cited in Birnbaum, L., Staskal, D.F. Polybrominated flame retardants: cause for concern? Environ Health Perspect 2004:112:9-17. doi10.1289/ehp.6559. available via dx.doi.org. Accessed 5 January 2004.

42 Official Journal of The European Union, L 42/45 Feb. 15, 2003.

43 Schecter, A. Pavuk, M. Papke, O., Ryan, J.J., Birnbaum, L., Rosen, R. Polybrominated diphenyl ethers (PBDEs) in U.S. mothers' milk. Environ Health Perspect 2003:111:14:1723-1724.

44 http://www.ourstolenfuture.org/NewScience/oncompounds/PBDE/2003/2003-0807schecteretal.htm. Accessed 5 January 2004.

45 http://www.panda.org/about_wwf/where_we_work/europe/what_we_do/policy_and_events/epo/news.cfm?uNewsID=9941 Accessed 8 January 2004.

46 Lindberg, P., Sellström, U., Häggberg, L., and de Wit, C.A. Higher brominated diphenyl ethers and hexabromocyclododecane found in eggs of peregrine falcons (Falco peregrinus) breeding in Sweden. Environ Sci Technol 2004:38;(1): 93-96.

47 Norstrom RJ, Simon M, Moisey J, Wakeford B, Weseloh D.V. Geographical distribution (2000) and temporal trends (1981-2000) of brominated diphenyl ethers in Great Lakes herring gull eggs. Environ Sci Technol. 2002 Nov 15;36(22):4783-9.

48 De Boer, J., Wester, P.G., Klamer, H.J.C., Lewis, W.E., Boon, J.P. Do flame retardants threaten ocean life? Nature 1998:394:28-29; doi:10.1038/27798

49 Ikonomou et al., 2002a (cited in Birnbaum & Staskel, 2004).

50 Birnbaum & Staskal, 2004.

51 Birnbaum & Staskal, 2004.

52 Birnbaum & Staskal, 2004.

53 Darnerud, P.O. Toxic effects of brominated flame retardants in man and in wildlife. Environ Int 2003 Sep;29(6):841-53.

54 Helleday, T., Tuominen, K.L., Bergman, A., Jenssen, D. Brominated flame retardants induce intragenic recombination in mammalian cells. Mutat Res 1999:Feb 19;439(2):137-47.

55 Corsolini, S., Kannan, K., Imagawa, T., Focardi, S., Giesy, J.P. Polychloronaphthalenes and other dioxin-like compounds in Arctic and Antarctic marine food webs. Environ Sci Techno 2002:Aug 15;36(16):3490-6.

56 Derocher, A et al. (2000). Immune response and chlorinated organic pollution in polar bears. Norwegian Polar Institute. http://npolar.no/transeff/Effects/Polar_Bear/Polar_bear-NP.htm.

57 Haave, M., Ropstad, E., Derocher, A.E., Lie, E. Dahl, E. Wiig, O., Skaare, J.U., Jenssen, B.M. Polychlorinated Biphenyls and reproductive hormones in female polar bears at Svalbard. Environ Health Perspect. 2003:111:4:431-436. doi:10.1289/ehp.5553 available via http://dx.doi.org/.

58 Wiig O, Derocher AE Cronin MM, Skaare JU. Female Pseudohermaphrodite Polar Bears At Svalbard. J Wildl Dis 1998 Oct;34(4):792-6.

59 AMAP Assessment Report (2002) Arctic Pollution 2002 www.amap.no/assess/AP2002POPs.pdf.

60 Indian and Northern Affairs Canada NCP Home Page. New Persistent Chemicals in the Arctic Environment. www.ainc-inac.gc.ca/ncp/abio_e.html. Accessed 25 February 2003.

61 Ikonomou, M.G., Rayne, S., and Addison, R.F. (2002) Exponential Increases of the Brominated Flame Retardants, Polybrominated Diphenyl Ethers, in the Canadian Arctic from 1981 to 2000 Environ. Sci. Technol. 2002, 36, 1886-1892.

62 Harding L.E. et al. Reproductive and Morphological Condition of Wild Mink (Mustela vison) and River Otters (Lutra Canadensis) in Relation to Chlorinated Hydrocarbon Contamination, Environ Health Perspect 1999: 107:141-147.

63 National Biological Service 14 Feb 1996 Press Release: Male Otters From Columbia River Have Abnormally Small Reproductive Organs.

64 Milston, R.H., Fitzpatrick, M.S., Vella, A.T., Clements, S., Gundersen, D., Feist, G., Crippen, T.L., Leong, J., and Schreck, C.B. Short-term exposure of Chinook salmon (Oncorhyncus tshawytscha) to o,p'-DDE or DMSO during early life-history stages causes long-term humoral immunosuppression. Environ Health Perspect 2003: 111:1601-1607.

65 Hites, R.A., Foran, J.A., Carpenter, D.O., Hamilton, M.C., Knuth, B.A., Schwager, S.J. Global assessment of organic contaminants in farmed salmon. Science 2004 Jan 9;303:226-229.

[66] WWF Briefing (1999). Seals and Endocrine Disruptors. www.ngo.grida.no/wwfneap/Publication/briefings/Seal.pdf.

[67] Simms W, Ross PS. Vitamin A Physiology And Its Application As A Biomarker Of Contaminant-Related Toxicity In Marine Mammals: A Review. Toxicol Ind Health. 2001 Sep;16(7-8):291-302.

[68] Simms, W. and Ross, Peter. Vitamin A physiology and its application as a biomarker of contaminant-related toxicity in marine mammals: a review. Toxicology and Industrial Health 2001:(291) 16:6.

[69] Simms and Ross, 2001; Brouwer, A., Reijnders, J.H., Koeman, J.H. Polychlorinated biphenyls (PCB)-contaminated fish induces vitamin A and thyroid deficiency in the common seal Phoca vitulina. Aquatic Toxicology 1989 15:99-106.

[70] Guillette et al., 1994.

[71] Toft G, Edwards TM, Baatrup E, Guillette LJ Jr. Disturbed sexual characteristics in male mosquitofish (Gambusia holbrooki) from a lake contaminated with endocrine disruptors. Environ Health Perspect. 2003 May;111(5):695-701.

[72] Hardell, L., van Bavel, B., Lindstrom, G., Carlberg, M., Dreifaldt, A.C., Wijkstrom, H., Starkhammar, H., Eriksson, M., Hallquist, A., Kolmert, T. Increased concentrations of polychlorinated biphenyls, hexachlorobenzene, and chlordanes in mothers of men with testicular cancer. Environ Health Perspect 2003; 111:7:930-934.

[73] Hardell, et al., 2003.

[74] Martineau, D., Lemberger, K., Dallaire, A., Labelle, P., Lipscomb, T.P., Michel, P., Mikaelian, I. Cancer in wildlife, a case study: Beluga from the St. Lawrence Estuary, Quebec, Canada. Environ Health Perspect 2002: 110:285-292.

[75] World Crop Protection News, AGROW, No. 434 Oct. 17, 2003.

[76] Allran, J.W., Karasov, W.H. Effects of atrazine on embryos, larvae, and adults of anuran amphibians. Environ Toxicol Chemic 2001 Apr;20(4):769-75.

[77] Hayes, T.B., Collins, A., Lee, M., Mendoza, M., Noriega, N., Stuart, A.A., Vonk, A. Hermaphroditic, demasculinized frogs after exposure to the herbicide, atrazine, at low ecologically relevant doses. Proceedings of the National Academy of Sciences (US) 2002:9:5476-5480. [via www.ourstolenfuture.org]

[78] Hayes, T., Haston, K., Tsui, M., Hoang, A., Haeffele, C., Vonk, A. Atrazine-induced hermaphroditism at 0.1 ppb in American leopard frogs (Rana pipiens): laboratory and field evidence. Environ Health Perspect: 2003: 11:4; Apr:568-575.

[79] Bettaso, J.B., Welsh, H.H., Palmer, B.D. Northern red-legged frogs and endocrine disrupting compounds (EDCs). 2002 Froglog No. 52, August. (Newsletter of the Declining Amphibian Populations Task Force of the World Conservation Union's Species Survival Commission), http://www2.open.ac.uk/biology/froglog/FROGLOG-52-1.html, accessed 17 December 2003.

[80] Toxicity Studies for Tributyltin oxide on All Organism Groups – Toxicology studies on aquatic organisms from science journals. PAN Pesticides Database – Chemical Toxicity Studies on Aquatic Organisms. http://www.pesticideinfo.org/List_AquireAll.jsp?Rec_Id=PC4, accessed 17 December 2003.

[81] Gooding, M.P., Wilson, V.S., Folmar, L.C., Marcovich, D.T., LeBlanc, G.A. The biocide tributyltin reduces the accumulation of testosterone as fatty acid esters in the mud snail (Ilyanassa obsoleta) Environ Health Perspect 2003 April;111(4)::426-430; Mathiessen, P., Reynoldson, T., Billinghurst, Z., Brassard, D.W., Cameron, P., Chandler, G.T., et al. 1999. Field assessment for endocrine disruption in invertebrates. In: Endocrine Disruption in Invertebrates: Endocrinology, Testing and Assessment (deFur, P.L, Crane, M., Ingersoll, C., Tattersfield, L., eds.). Pensacola, FL:SETAC, 199-270.

[82] Birchenough, A.C., Evans, S.M., Moss, C., Welch, R. Re-colonisation and recovery of populations of dogwhelks Nucella lapillus (L.) on shores formerly subject to severe TBT contamination. Mar Pollut Bull 2002 Jul;44(7):652-9.

[83] ten Hallers-Tjabbes, C.C., Wegener, J.W., Van Hattum, B.A., Kemp, J.F. ten Hallers, E., Reitsemae, T.J., Boon, J.P. Imposex and organotin concentrations in Buccinum undatum and Neptunea antiqua from the North Sea: relationship to shipping density and hydrographical conditions. Mar Environ Res Apr;55(3):203-33.

[84] Chiavarini, S., Massanisso, P., Nicolai, P., Nobili, C., Morabito, R. Butyltins concentration levels and imposex occurrence in snails from the Sicilian coasts (Italy). Chemosphere 2003 Jan;50(3):311-9.

[85] Birchenough, A.C., Evans, S.M., Moss, C., Welch, R. Re-colonisation and recovery of populations of dogwhelks Nucella lapillus (L.) on shores formerly subject to severe TBT contamination. Mar Pollut Bull 2002 Jul;44(7):652-9.

[86] Nakata, H., Sakakibara, A., Kanoh, M., Kudo, S., Watanabe, H. Nagai, N., Miyazaki, N., Asano, Y., Tanabe, S. Evaluation of mitogen-induced responses in marine mammal and human lymphocytes by in-vitro exposure of butyltins and non-ortho-coplanar PCBs. Environ Pollut 2002;120(2):245-53.

87 Adeeko, A., Li, D., Forsyth, D.S., Casey, V., Cooke, G.M., Barthelemy, J., Cyr, D.G., Trasler, J.M., Robair, B., Hales, B.F. Effects of in utero tributyltin chloride exposure in the rat on pregnancy outcome. Toxicol Sci 2003 Aug:74(2):407-15.

88 Raloff, J. Hormones: Here's the Beef. Science News, January 1, 2002.

89 European Environment Agency, Late lessons from early warnings: the precautionary principle 1896-2000. Published by Office for the Official Publications of the European Communities. ISBN 92-9167-323-4, Luxembourg, 2001.

90 Wilson, V.S., Lambright, C., Ostby, J., Gray, L.E. In vitro and in vivo effects of 17beta-trenbolone: a feedlot effluent contaminant. Toxicological Sciences 2002:70:202-11; Jegou, B. sots, A., Sundlof, S. Stephany, R. Meyer, H., Leffers, H. Existing guidelines for the use of meat hormones and other food additives in Europe and USA. APMIS 2001:103(Suppl.) S551-S556; Raloff, J. Hormones: Here's the Beef. Science News, January 1, 2002.

91 Orlando, E.F., Kolok, A.S., Binzcik, G.A., Gates, J.L., Horton, M.K., Lambright, C.S., Gray, L.E., Soto, A.M., Guillette, L.J. Endocrine disrupting effects of cattle feedlot effluent on an aquatic sentinel species, the fathead minnow. Environ Health Perspect 2003 doi:10.1289/ehp6591 via http://dx.doi.org.

92 EU Scientific Committee on Toxicity Ecotoxicity and the Environment. CSTEE Opinion on Human and Wildlife Health Effects of Endocrine Disrupting Chemicals, with Emphasis on Wildlife and on Ecotoxicology Test Methods. DGXXIV, Consumer Policy and Consumer Health Protection, Brussels (1999), pp 42-43.

93 Vethaak, A.D., Lahr, J., Kuiper, R.V., Grinwis, G.C.M., Rankouhi, T.R., Giesy, J.P., Gerritsen, A. Estrogenic effects in fish in The Netherlands: some preliminary results. Toxicology 2002 Vol. 181-182, Issue 0, pp. 147-150.

94 Pawlowski, S., Ternes, T., Bonerz, M., Kluczka, T., van der Burg, B., Nau, H., Erdinger, L. Braunbeck, T. Combined in situ and in vitro assessment of the estrogenic activity of sewage and surface water samples. Toxicological Sciences 2003 75:57-65.

95 Orlando, E.F., Kolok, A.S., Binzcik, G.A., Gates, J.L., Horton, M.K., Lambright, C.S., Gray, L.E., Soto, A.M., Guillette, L.J. Endocrine disrupting effects of cattle feedlot effluent on an aquatic sentinel species, the fathead minnow. Environ Health Perspect 2003. doi:10.1289/3hp6591
(available at http://dx.doi.org online 1 December 2003. Accessed 3 January 2004.

96 CSTEE Opinion on Human and Wildlife Health Effects of Endocrine Disrupting Chemicals, with Emphasis on Wildlife and on Ecotoxicology Test Methods. European Union, DG XXIV, Consumer Policy and Consumer Health Protection. March 1999.

97 Parks, L.G., Lambright, C.S., Orlando, E.F., Guillette, L.J., Ankley, G.T., Gray, L.E., Jr. Masculinization of female mosquitofish in Kraft mill effluent-contaminated Fenholloway River water is associated with androgen receptor agonist activity. Toxicological Sciences 2001 62:257-267.

98 Wilson, B.A., Smith, V.H., Denoyelles, F., Larive, C.K. Effects of three pharmaceutical and personal care products on natural freshwater algal assemblages. Environ Sci Techno 2003:May 1;37:9:1713-1719.

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