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Epidemiological Analysis of Persistent Organochlorine Contaminants in Cetaceans

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Contents

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I. Introduction

Because of increasing evidence of the global distribution of persistent organochlorine chemicals and their potential to affect adversely a number of top predator species associated with aquatic systems, the role of chemical contaminants must be considered among the threats posed to cetaceans.

This review presents a synthesis of the literature relevant to the health of large cetaceans and the possible consequences of exposure to organochlorine contaminants. Besides the review of the cetacean literature, it includes information on the effects of organochlorine contaminants in other marine and freshwater species and humans. This analysis is not limited to direct effects or mortality but also considers the indirect effects of toxic chemicals on offspring as a result of maternal exposure. For any organism to survive, it must have a morphology and physiology that allows it to function and adapt to changes in its environment. Consequently, this review considers the potential deficiencies in structure and functionality in the offspring as well as the wider ramifications of large-scale changes within populations that could ultimately affect population stability.

Unfortunately, cause-and-effect relationships are difficult to establish in the environment, especially when they involve complex pathways, subtle shifts in effects, and species that are difficult to study. An alternative approach, therefore, is to infer or deduce causality using epidemiological criteria based on a set of scientific principles to test the hypothesis that these chemicals have no effect on direct lethality or reproductive dysfunction among cetaceans.

The environment is laden with a host of chemicals that have multiple effects, many of them similar, overlapping, or with unpredictable interactions. These chemicals have not been investigated with respect to their potential for affecting morphological and/or physiological damage in marine mammals. Only a few chemicals have been monitored and studied well enough to arrive at some conclusions about their impact on the health of living organisms. This information is used as an analogy of what will likely be occurring in whales. This review focuses on two groups of these widely dispersed chemicals, polychlorinated biphenyls (PCBs) and 1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane (DDT) and its metabolites, and provides information on what is known about their effects at the population, organism, tissue, and cellular levels among species.

In lieu of existing comprehensive studies on large whales, predictions of potential health threats can be made on the basis of the patterns and mechanisms of damage reported in other cetaceans and pinnipeds, other wildlife, laboratory animals, and humans exposed to the same chemicals. Parallel results from other wildlife, laboratory, and human studies can provide valuable insight about the health of wide-ranging vertebrate species (Colborn and Clement 1992), including marine mammals (Consensus Statement 1995). This is based on the assumption of shared and highly conservative

biochemical pathways and processes among vertebrate taxa. Applying what is known about concentrations of chemicals in individual animals and the impacts of these chemicals on cell, tissue, and organ function, an estimation of the potential risks to large whales is possible. To this end, a survey was undertaken of the literature on marine mammals that included the health of individuals and populations, behavior, and geographic distribution as it relates to chemical contamination.

II. Background Information on Cetaceans

A. Effects

An examination of the literature on marine mammals reveals that 16 species have experienced population instability, major stranding episodes, reproductive impairment, endocrine and immune system disturbances, organ damage, general health decline, and serious infectious diseases since 1968 (Table 1). Cancer has rarely been reported in marine mammals. Contaminant concentrations in the tissues of the affected animals were not reported in all of the studies in Table 1. Most of the studies in Table 1 are descriptive or morphological. However, in the case of the Dall's porpoises (*Phecoenoides dalli*), a biochemical marker identifies changes to physiological and functional processes. The concentration of one of the naturally produced male hormones, testosterone, was inversely proportional to the concentration of 1,1-dichloro-2,2,bis(*p*-chlorophenyl) ethylene (DDE), a metabolite of DDT, signaling an effect on the endocrine system (Subramanian et al. 1987).

DDT/DDE and a number of other organochlorine chemicals are lipophilic and, as a result, bioaccumulate in fatty tissue. They have been reported in animals from the Arctic to the Antarctic (Subramanian et al. 1983, 1988a,b; Tanabe and Tatsukawa 1986; Tanabe et al. 1983, 1986). Many are known disruptors of the endocrine, immune, and nervous systems (Colborn and Clement 1992). Individual animals whose endocrine, immune, or nervous systems are compromised in the presence of these persistent chemicals may appear normal but may suffer early mortality or, on reaching adulthood, may be infertile as a result of their exposure. Such alterations in functionality at the individual level can have a profound effect at the population level if the problem becomes widespread.

For example, the massive die-offs of seals in the Baltic Sea and North Sea (Dietz et al. 1989; Hall et al. 1992), dolphins along the Eastern coast of the United States (Geraci 1989), and striped dolphins (*Stenella coeruleoalba*) in the Mediterranean Sea (Aguilar and Borrell 1994; Aguilar and Raga 1993; Aznar et al. 1994; Domingo et al. 1992; Forcada et al. 1994; Kannan et al. 1993c) have prompted speculation that synthetic chemicals may have been involved by reducing the animals' immune competency and thus increasing their vulnerability to infection (Simmonds 1992, 1994). Likewise, burdens of chemical contaminants sequestered in the lipid re-

Table 1. Perturbations observed in marine mammals since 1968. Numbers refer to literature sources (see footnote).

Mammals	Population decline or dieoffs	Reproduction and endocrine impairment	Immune system compromised	Organ damage	Infection and health decline	Tumors
Whales						
beluga	19, 34, 35	33	32	32	18	17, 31
sperm	13					
humpback	42					
right	16	14, 15				
Porpoises						
harbor	37			28	27, 28	
Dall's		29				
Dolphins						
striped	30		25, 48	48	25, 26	
bottlenose	23, 38, 42		22, 36	41	20, 21, 22, 24	
Seals						
harbor	8, 11, 43	39, 40	12	28	8	
grey	11			10		
ringed	5, 11	12		9		
northern fur		49				
Baikal	7				6, 7, 8	
bearded	5					
Sea Lions						
Steller's	44, 45, 46	47			47	
California		1, 2			2, 3, 4	

Citations: (1) Delong et al. 1973; (2) Gilmartin et al. 1976; (3) Smith et al. 1974a; (4) Smith et al. 1974b; (5) Stirling et al. 1982; (6) Osterhaus et al. 1989; (7) Grachev et al. 1989; (8) Dietz et al. 1989; (9) Helle 1980; (10) Bergman and Olsson 1986; (11) Jensen et al. 1979; (12) Helle et al. 1976a; (13) Simmonds 1992; (14) Brown et al. 1994; (15) Knowlton et al. 1994; (16) Klinowska 1991; (17) De Guise et al. 1994b; (18) Martineau et al. 1988; (19) Beland et al. 1993; (20) Lipscomb et al. 1994b; (21) Lipscomb et al 1994a; (22) Kuehl et al. 1994; (23) Miller 1992; (24) Thompson and Hammond 1992; (25) Aguilar and Raga 1990; (26) Duinker et al. 1989; (27) Kuiken et al. 1994; (28) Schumacher et al. 1993; (29) Subramanian et al. 1987; (30) Tanabe et al. 1987a; (31) Martineau et al. 1985b; (32) De Guise et al. 1995b; (33) Beland et al. 1988a,b; (34) Sergeant and Hoek 1988; (35) Pippard 1985; (36) Lahvis et al. 1995; (37) Kannan et al. 1993a; (38) Kuehl et al. 1991; (39) Brouwer et al. 1989; (40) Reijnders 1986; (41) Cowan 1994; (42) Geraci 1989; (43) Miles et al. 1992; (44) Loughlin et al. 1984; (45) Merrick et al. 1987; (46) Loughlin et al. 1992; (47) Calkins and Goodwin 1988; (48) Domingo et al. 1992; (49) Trites and Larkin 1989.

serves can become a source of additional stressors when released into the blood of an infected animal as it fights viral or bacterial infections (Simmonds 1994). The die-offs also generated concern about the status of other marine species around the world. These events provided the impetus to seek information not merely on concentrations of the chemicals in marine mammals but on adverse health effects among these animals and to assess the status of regional populations.

Concentrations of DDT, DDE, PCBs, and other commercial synthetic chemicals have been reported in marine mammals since the 1960s (Table 2). More recently, adverse health effects have been reported as well: reproductive dysfunctions (Delong et al. 1973; Gilmartin et al. 1976; Reijnders 1986), immune suppression (Ross et al. 1994), tumors (De Guise et al. 1994b, 1995a; Martineau et al. 1985b), population instability (Beland and Martineau 1988; Beland et al. 1988; Prescott 1991), abnormal sexual development (De Guise et al. 1994a), and adrenal insufficiency (De Guise et al. 1995b), to mention only a few.

Current research provides some insight into the health of dolphins and porpoises. However, little is known about the status of the larger toothed whales, and even less about the baleen whales. What is known about contaminants in large whales is primarily limited to a few studies from opportunistic encounters with dead, beached whales, with most of these studies describing only a single sample from one dead whale.

B. Contaminant Burdens

A survey of the literature (see Table 2) reveals the relative lack of information on contaminants in whales and, in particular, baleen whales. Attempts at determining contaminant concentrations in individual species have been limited primarily to total PCBs (ΣPCB) and total DDT and its metabolites (ΣDDT). Only in rare instances were these chemicals not detected in samples. The analytical methodologies have been quite variable, which results in difficulties when comparing reported values in the literature (Hutchinson and Simmonds 1994; O'Shea and Brownell 1994). This variability is introduced through differing levels of precision in the equipment, use of internal standardization, sample preparation, and selection of the chemical or congeners. Truly representative comparisons of concentrations are limited to the reports from a single laboratory. Despite these limitations, reports from the literature must be compared to develop a global pattern of distribution and effects of chemical contaminants on species of marine mammals.

Organochlorine, such as PCBs and DDT, are dispersed worldwide as the result of agricultural and industrial activities. PCBs were first introduced in 1929; DDT was first synthesized in 1938. Massive production and use of these chemicals started in the 1940s. Atmospheric transport of contaminants is now recognized as a major pathway for their dispersion (Takeoka et al. 1991) and is the primary source of contaminants in polar regions

Table 2. Citations involving analysis of tissues for chemical contaminants arranged by species.

Species	DDT	DDE	DDD	ΣPCB	Chlordane[a]	Aldrin/dieldrin
Balaenoptera borealis (sei whale)	1		1	1		
Balaenoptera physalus (fin whale)	1, 48		1	1, 48		
Balaenoptera musculus (blue whale)						
Balaenoptera acutorostrata (minke whale)	39, 40, 50, 45, 44			39, 40, 50, 45, 44	50	
Balaenoptera mysticetus (bowhead whale)	50			50	50	
Eubalaena glacialis (right whale)	38	38	38	38	38	38
Megaptera novaengliae (humpback whale)	2	2, 34		2, 34	2, 34	2
Eschrichtius robustus (gray whale)	49, 43	49, 43	49, 43	49	49	49, 43
Physeter macrocephalus (sperm whale)	1, 2, 27, 46, 43, 28	2, 27, 46, 43, 28	1, 27, 46, 43, 28	1, 2, 27, 46	2	2, 27, 43
Orcinus orca (killer whale)				19, 26		
Delphinapterus leucas (beluga whale)	30, 31, 32, 33, 47	30, 31, 33	31, 33	30, 31, 47	32, 47	32
Monodon monoceros (narwhal)	21	21	21	21	21	21
Globicephala melaena (long-finned pilot whale)	1, 2, 36, 41, 50	2, 41, 34, 51	2	1, 2, 34, 36, 41, 50, 51	2, 34, 41, 50, 51	2, 41, 51

Mesoplodon densirostris (dense-beaked whale)	2	2		2	2	2
Globicephala macrorhyncha (Pacific pilot whale)	2, 25	2, 25, 37	25	2, 25, 37	2	2, 25
Lagenorhynchus obliquidens (Pacific white-sided dolphin)	2	2		2, 26	2	2
Lagenorhynchus acutus (Atlantic white-sided dolphin)	1	13	1	1, 18	13	13
Lagenodelphis albirostris (white-beaked dolphin)	41, 27	41, 27	27	41, 27	41	41, 27
Phocoena phocoena (harbor porpoise)	1, 2, 8, 9, 12, 23, 25, 27, 50, 35	2, 8, 9, 23, 25, 27, 34, 35	1, 8, 9, 23, 25, 27	1, 2, 8, 9, 12, 14, 23, 25, 27, 50, 34, 35	2, 12, 25, 34	2, 8, 9, 12, 23, 27, 35
Delphinus delphis (saddleback dolphin)	2, 25, 27	2, 13, 25, 27	25, 27	2, 25, 18, 27	2, 13, 25	2, 13, 25, 27
Stenella coeruleoalba (striped dolphin)	2, 3, 4, 15, 16, 17, 25, 42	2, 3, 4, 25	3, 4, 25	2, 3, 4, 15, 16, 17, 25, 42	2, 25	2, 25
Phocoenoides dalli (Dall's porpoise)		5, 6, 25	25	5, 6, 25, 26	25	25
Tursiops truncatus (bottlenose dolphin)	7, 10, 29, 25, 27, 20, 50, 22, 35	10, 13, 20, 25, 27, 29, 34, 24, 35	10, 25, 27, 35	7, 10, 13, 18, 25, 27, 29, 22, 50, 34, 20, 24, 35	13, 25, 20, 50, 34, 35	7, 13, 20, 25, 27, 22, 35
Stenella longirostris (spinner dolphin)	10	10	10	10		

(*continued*)

Table 2. (*Continued*)

Species	DDT	DDE	DDD	ΣPCB	Chlordane[a]	Aldrin/dieldrin
Sousa chinensis (humpback dolphin)	10	10	10	10		
Platanista gangetica (Ganges River dolphin)	11			11	11	11
Pontoporia blainvillei (La Plata dolphin)	25	25	25	25	25	25
Lagenodelphis hosei (Fraser's dolphin)	25	25	25	25	25	
Steno bredanensis (rough-toothed dolphin)	25	25	25	25	25	25
Neophocoena phocaenoides (finless dolphin)	25	25	25	25, 26	25	25

Species	HCH	HCB	Mirex	Lindane	Toxaphene	Dioxin/furan
Balaenoptera borealis (sei whale)						
Balaenoptera physalus (fin whale)						
Balaenoptera musculus (blue whale)						
Balaenoptera acutorostrata (minke whale)						
Balaenoptera mysticetus (bowhead whale)						
Eubalaena glacialis (right whale)						
Megaptera novaengliae (humpback whale)						
Eschrichtius robustus (gray whale)		49				
Physeter macrocephalus (sperm whale)	27					
Orcinus orca (killer whale)						19
Delphinapterus leucas (beluga whale)		32	32	32		
Monodon monoceros (narwhal)	21	21	21		21	
Globicephala melaena (long-finned pilot whale)	41		41		41	

(*continued*)

Table 2. (*Continued*)

Species	HCH	HCB	Mirex	Lindane	Toxaphene	Dioxin/furan
Mesoplodon densirostris (dense-beaked whale)						
Globicephala macrorhyncha (Pacific pilot whale)		25			25	
Lagenorhynchus obliquidens (Pacific white-sided dolphin)						
Lagenorhynchus acutus (Atlantic white-sided dolphin)		13		13		
Lagenodelphis albirostris (white-beaked dolphin)	41, 27		41		41	
Phocoena phocoena (harbor porpoise)	8, 9, 12	8, 9, 12, 12, 14, 23, 25, 35				
Delphinus delphis (saddleback dolphin)	27	13, 25		13		
Stenella coeruleoalba (striped dolphin)	3, 4	3, 4, 17, 25		25	25	
Phocoenoides dalli (Dall's porpoise)		25				
Tursiops truncatus (bottlenose dolphin)	10, 27	10, 13, 20, 25, 35	20	13, 20		13

Stenella longirostris (spinner dolphin)	10	10		
Sousa chinensis (humpback dolphin)	10	10		
Platanista gangetica (Ganges River dolphin)	11	11		
Pontoporia blainvillei (La Plata dolphin)		25		25
Lagenodelphis hosei (Fraser's dolphin)				
Steno bredanensis (rough-toothed dolphin)				
Neophocoena phocaenoides (finless dolphin)		25		25

PCB, Polychlorinated biphenyl.

[a]Chlordane includes estimates of heptachlor, heptachlor epoxide, oxychlordane, and *trans*-nonachlor.

Citations: (1) Borrell, 1993; (2) Taruski et al. 1975; (3) Tanabe et al. 1981b; (4) Tanabe et al. 1982; (5) Subramanian et al. 1987; (6) Subramanian et al. 1988b; (7) Cockcroft et al. 1989; (8) Kuiken et al. 1993; (9) Kuiken et al. 1994; (10) Tanabe et al. 1993; (11) Kannan et al. 1993b; (12) Kannan et al. 1993a; (13) Kuehl et al. 1991; (14) Falandysz et al. 1994; (15) Kawai and Fukushima, 1981; (16) Fukushima and Kawai, 1981; (17) Tanabe et al. 1981a; (18) Kuehl et al. 1994; (19) Ono et al. 1987; (20) Kuehl and Haebler, 1995; (21) Muir et al. 1992; (22) Law et al. 1995; (23) Duinker and Hillebrand, 1979; (24) Salata et al. 1995; (25) O'Shea et al. 1980; (26) Tanabe et al. 1987a; (27) Duinker et al. 1989; (28) Henry and Best, 1983; (29) Lahvis et al. 1995; (30) Masse et al. 1986; (31) Martineau et al. 1987; (32) Beland and Martineau, 1988; (33) Addison and Brodie, 1973; (34) Geraci, 1989; (35) Wells et al. 1994; (36) Borrell and Aguilar, 1993; (37) Tanabe et al. 1987b; (38) Woodley et al. 1991; (39) Tanabe et al. 1984; (40) Tanabe et al. 1986; (41) Muir et al. 1988; (42) Kannan et al. 1993c; (43) Wolman and Wilson, 1970; (44) Johansen et al. 1980; (45) Sergeant, 1980; (46) Aguilar, 1983; (47) Muir et al. 1991; (48) Saschenbrecker, 1973; (49) Varanasi et al. 1994; (50) Varanasi et al. 1993; (51) Simmonds et al. 1994.

and open ocean environments (Bacon et al. 1992; Ono et al. 1987). These chemicals persist in the environment. Some of them resist metabolism, and many are exceedingly lipophilic, so that when ingested they accumulate in fat reserves such as blubber and visceral fat in all vertebrates.

DDT. ΣDDT is the sum of DDT (the parent compound) and its breakdown or metabolic products, DDE and 1,1-dichloro-2,2,bis(*p*-chlorophenyl) ethane (DDD). The half-life of DDT and some of its metabolites is approximately 57.5 yr in temperate-zone soils (Cooke and Stringer 1982). However, little is known about the half-life of DDT in food webs. Because the half-life of a chemical is dependent on temperature, it would persist longer in the polar regions.

The odontocetes have some of the highest mean concentrations of ΣDDT reported in wildlife. The highest (225 ppm ΣDDT) was reported (Table 3) in a dead beluga whale (*Delphinapterus leucas*) from the St. Lawrence Estuary in northeastern Canada (Martineau et al. 1987). The mean was 58 ppm ΣDDT in this population. Belugas sampled from populations in northern Canada have lower concentrations of ΣDDT (mean, 1.9–6.8 ppm). Long-finned pilot whales (*Globicephala melaena*), another piscivorous species, sampled from various locations, have been reported with elevated concentrations of ΣDDT. Populations sampled from the Faroe Islands range from 2.1 to 82.0 ppm ΣDDT. It is not known where these highly mobile pods feed during a large part of the year (Aguilar et al. 1993). It has been suggested that the wide range of contamination among the Faroe Island populations may be explained by the differences in contaminant exposure in their respective feeding sites. Pilot whales from the eastern coast of Canada and the United States also carry elevated concentrations of ΣDDT (Muir et al. 1988; Varanasi et al. 1993), as do short-finned pilot whales (*Globicephala macrorhyncha*) in the Pacific Ocean (O'Shea et al. 1980).

Concentrations of ΣDDT in mysticetes vary from undetected to 587 ppm wet weight (Schafer et al. 1984, from O'Shea and Brownell 1994). The high value represents a single minke whale (*Balaenoptera acutorostrata*) collected from the Washington (U.S.) coast with an extreme burden and is not representative of this species. A minke from Greenland was reported with 2.6 ppm ΣDDT wet weight, and another individual off the coast of Washington had 8.25 ppm ΣDDT. Humpback whales (*Megaptera novaeangliae*) have concentrations ranging from 1.7 to 7.6 ppm ΣDDT in samples collected from the Caribbean to Nova Scotia (Taruski et al. 1975). The fin (*Balaenoptera physalus*), bowhead (*B. mysticetus*), sei (*B. borealis*), blue (*B. musculus*), and right (*Eubalaena glacialis*) whales cited in the literature surveyed for this review stand out distinctly as having lower concentrations of ΣDDT than other species.

The ratio of the tissue concentrations of DDT to DDE provides clues to the age of the chemical in the environment and, in some cases, to the prior exposure of the animals (Bacon et al. 1992). When released in the

Table 3. Concentrations of ΣDDTs and ΣPCBs reported as parts per million (ppm) in blubber from selected cetacean species.

Species	ΣDDTs	ΣPCBs	*n*	Locality	Source
Balaena mysticetus					
(bowhead whale)	0.11	0.44 ± 2	2	Alaska	Varanasi et al. 1993
Eubalaena glacialis					
(right whale)					
immature	0.16 (w)	0.20 (w)	5	Canada	Woodley et al. 1991
female	0.23 (w)	0.40 (w)	1	Canada	
male	0.10 (w)	0.20 (w)	3	Canada	
immature	0.07 (w)	0.90 (w)	3	Canada	
female	0.03 (w)	0.40 (w)	6	Canada	
male	0.21 (w)	0.70 (w)	6	Canada	
calf	0.01 (w)	0.30 (w)	1	Canada	
Eschrichtius robustus					
(gray whale)	nd–0.68 (w)	–	23	Pacific	Wolman and Wilson 1970
	0.078 ± 0.02 (w)	1.60 ± 45 (w)	22	Pacific	Varanasi et al. 1994
	(0.001–0.370)	(0.12–10.00)			
Balaenoptera acutorostrata					
(minke whale)	0.21–2.60 (w)	0.14–1.10 (w)	–	Greenland	Johansen et al. 1980
	1.10 (w)	27.00 (w)	–	St. Lawrence	Sergeant 1980
	–	4.80 (w)	–	Mediterranean	Alzieu and Duguy 1979
	nd–0.82 (w)	nd	–	S. Africa	Henry and Best 1983
	0.01–0.14 (w)	0.003–0.029 (w)	37	Antarctic	Tanabe et al. 1986
	5.50 (w)	3.70 (w)	2	Washington	Varanasi et al. 1993
	(2.75–8.25)	(2.05–5.35)			

(*continued*)

Table 3. (*Continued*)

Species	ΣDDTs	ΣPCBs	*n*	Locality	Source
Balaenoptera borealis (sei whale)					
male	0.40 ± 0.29 (1)	0.46 ± 0.26 (1)	14	Iceland	Borrell 1993
female	0.11 ± 0.07 (1)	0.18 ± 0.09 (1)	26	Iceland	Borrell 1993
Balaenoptera physalus (fin whale)	nd–0.48 (1)	nd (1)	–	S. Africa	Henry and Best 1983
	0.67–2.56 (w)	0.01–0.18 (w)	–	S. Africa	Saschenbrecker 1973
male	–	1.26 ± 0.61 (1)	48	Iceland	Borrell 1993
female	–	0.94 ± 0.12 (1)	3	Iceland	Borrell 1993
Megaptera novaeangliae (humpback whale)	1.70 (w) (1.40–2.10)	1.40 (w) (1.30–1.50)	2	Caribbean	Taruski et al. 1975
	7.60 (w)	6.00 (w)	1	New Jersey	Taruski et al. 1975
	23.10 (w)	5.40 (w)	1	Nova Scotia	Taruski et al. 1975
	– (6–44)	13 ± 12 (1)	8	eastern U.S.	Geraci 1989
Physeter macrocephalus (sperm whale)	8.30 (w)	2.35 (w)	2	Caribbean	Taruski et al. 1975
	8.90 (w)	2.10 (w)	1	eastern U.S.	Taruski et al. 1975
	4.20 (l)	8.32 (l)	14	Spain	Aguilar 1983
	4.17 (w)	10.20 (w)	10	Iceland	(in: Borrell and Aguilar 1993)
	5.80 (w)	–	6	western U.S.	Wolman and Wilson 1970
	0.45 (w)	nd	12	S. Africa	Henry and Best 1983
	@45.00 (l)	@12.00 (l)	1	Netherlands	Duinker et al. 1989

Globicephala melaena					
(long-finned pilot whale)	7.60 ± 1.00 (w)	1.70 ± 0.22 (w)	19	eastern U.S.	Varanasi et al. 1993
	16.30 (l)	25.80 (l)	114	Faroe Isl.	Aguilar et al. 1993
	(2.10–82.00)	(5.00–103.10)			
	18.78 (w)	27.40 (w)	90	Faroe Isl.	Borrell and Aguilar 1993
	26.17 (l)	33.39 (l)			
	42.00 (w)	39.00 (w)	–	Faroe Isl.	Bloch and Hoydal 1987
male	31.39 ± 19.23 (l)	48.81 ± 23.13 (l)	52	Faroe Isl.	Borrell 1993
female	13.40 ± 16.35 (l)	26.27 ± 23.12 (l)	159	Faroe Isl.	Borrell 1993
male	11.90 ± 6.09 (w)	9.03 ± 3.80 (w)	5	eastern Canada	Muir et al. 1988
	(6.45–22.30)	(4.33–14.70)			
female	4.70 ± 5.30 (w)	3.46 ± 3.34 (w)	9	eastern Canada	Muit et al. 1988
	(1.03–16.40)	(0.52–11.80)			
Delphinapterus leucas					
(beluga whale)	58.00 (w)	141.40 (w)	26	St. Lawrence	Martineau et al. 1987
	(1.20–225.60)	(5.60–576.00)			
	89.90 (w)	65.62 (w)	2	St. Lawrence	Masse et al. 1986
	(76.10–103.70)	(59.10–72.10)			
	6.83 ± 1.89 (w)	4.91 ± 0.25 (w)	6	Baffin Isl.	Muir et al. 1992
	1.96 ± 0.32 (w)	2.53 ± 0.57 (w)	8	Baffin Bay	
	2.27 ± 0.68 (w)	2.77 ± 0.51 (w)	8	Hudson Bay	
	101.00 ± 32.6 (w)	75.80 ± 15.3 (w)	4	St. Lawrence	
Monodon monoceros					
(narwhal)					
male	5.92 (w)	5.18 (w)	15	northern Canada	Muir et al. 1992
	(2.60–8.56)	(2.25–7.29)			
female	2.54 (w)	2.69 (w)	6	northern Canada	Muir et al. 1992
	(0.59–5.91)	(0.89–5.71)			

(*continued*)

Table 3. (*Continued*)

Species	ΣDDTs	ΣPCBs	*n*	Locality	Source
Tursiops truncatus (bottlenose dolphin)	–	81.29 (l) (17.4–195.0)	14	eastern U.S.	Kuehl et al. 1991
Delphinus delphis (common dolphin)	–	36.50 (l) (31.2–40.6)	4	eastern U.S.	Kuehl et al. 1991
Lagenorhynchus acutus (white-sided dolphin)	–	50.07 (l) (34.5–59.6)	3	eastern U.S.	Kuehl et al. 1991
Stenella coeruleoalba (striped dolphin)	139 ± 84 (w) (22–230)	393 ± 202 (w) (94–670)	10	Mediterranean	Kannan et al. 1993c

Wet weight, w; lipid weight, l; range, given in parentheses; standard deviation (SD, ±); not detected, nd; (@), based on 17 congeners.

environment, the pesticide is primarily DDT and, through weathering and metabolism, is converted principally to DDE and ultimately to DDD. Cetaceans inhabiting the coastal waters of northern Europe, eastern Canada, and the western U.S. began to show a decline in the proportion of DDT to its metabolites during the 1980s (Addison et al. 1984), possibly reflecting the decreases in newly applied DDT (Aguilar 1984) following restrictions on its use in the U.S. in the early 1970s. However, the ratio of DDT to DDE/DDD remains high in populations of cetaceans from the northwestern Pacific Ocean, the Indian Ocean, and Antarctic waters, reflecting the continued use of DDT in other parts of the world (Tanabe et al. 1986).

The concentrations and proportions of DDT and its metabolites in cetaceans vary among species (Table 4). For example, mean DDT for samples varies from not detected to 68 ppm, and DDE ranges from 0.02 to 310 ppm, depending on species and location. Gray whales from the western coast of North America had the highest concentrations of DDT (370 ppm) and DDE (2100 ppm) reported (Varanasi et al. 1994). The ratios of ΣDDT to ΣDDE vary for the subpopulations from 1 : 2.2 to 1 : 8 (Varanasi et al. 1994). It should be noted that the largest proportion of these animals were migrating north and presumably had been fasting. This would suggest that when the lipid reserves of these mammals were depleted, the contaminants became concentrated in the blubber.

There are two patterns of DDT partitioning in the whales from the northern Atlantic. Whales found along the eastern coastline of North America, the Caribbean, and the western coastline of Europe have lower ratios of DDT to DDE (1 : 3). However, cetaceans collected in the waters surrounding Iceland and the Faroe Islands have greater proportions of DDT to DDE (1.5 : 1 to 2 : 1), and the species comprising this group represent species (sei, fin, and pilot whales) with diverse prey bases. This suggests that fresh sources of DDT are moving into these whales as they feed in their food web. DDD is almost always found in the lowest proportion among the three chemicals in all of the samples (see Table 4). Concentrations of DDE in the samples may reflect in part the metabolic reduction of DDT to DDE in the animal. However, DDE concentrations in tissue are more likely the result of ingestion of DDE in the prey species consumed.

PCBs. PCB burdens are highest in fish-eating species such as dolphins, pilot whales, and belugas (see Table 3). The highest concentration of ΣPCB (mean, 141 ppm wet weight, $n = 26$; range, 5.7–576 ppm) has been reported in the belugas of the St. Lawrence Estuary (Martineau et al. 1987). Long-finned pilot whales from the Faroe Islands and sperm whales (*Physeter macrocephalus*) from the North Atlantic also have elevated concentrations of ΣPCB, probably reflecting the contaminant burdens in their diets. Baleen whales have comparable ΣPCB body burdens. For example, Geraci (1989) reported humpback whales (lipid basis) with a mean of 13 ppm ΣPCB and one individual with 44 ppm.

Table 4. Concentrations (ppm) of DDT and its metabolites on wet (w) or lipid (l) weight basis in blubber of selected cetacean species [range of values in parentheses; standard deviation, (±)].

Species	ΣDDT	DDT	DDE	DDD	*n*	Locality	Source
Eubalaena glacialis (right whale)							
male	0.21 (w)	0.04	0.16	0.01	6	eastern Canada	Woodley et al. 1991
female	0.03 (w)	nd	0.02	nd	6	eastern Canada	
Eschrichtius robustus (gray whale)	454 (w)	(68 ± 22) (1–370)	310 ± 96 (9–2100)	76 ± 24 (1–470)	22	eastern Pacific	Varanasi et al. 1994
Balaenoptera borealis (sei whale)							
male	0.58 (l)	0.40	0.21	0.09	14	Iceland	Borrell 1993
female	0.16 (l)	0.11	0.05	0.03	26	Iceland	
Balaenoptera physalus (fin whale)							
male	1.29 (l)	0.85	0.49	0.18	48	Iceland	Borrell 1993
female	1.25 (l)	0.61	0.34	0.12	3	Iceland	

Megaptera novaengliae							
(humpback whales)	7.6 (w)	3.3	3.3	1.0	1	eastern Canada	Taruski et al. 1975
	23.1 (w)	4.7	15.0	3.4	1	eastern U.S.	
Physeter macrocephalus							
(sperm whale)	10.23 (l)	7.80	4.16	1.10	10	Iceland	Borrell 1993
	8.30 (w)	2.10	5.35	0.85	2	Caribbean	Taruski et al. 1975
	4.20 (l)	1.27	2.28	0.36	14	Spain	Aguilar 1983
	5.80 (w)	1.66	3.62	0.52	6	California	Wolman and Wilson 1970
	0.45 (l)	0.23	0.22	nd	12	South Africa	Henry and Best 1983
Globicephala melaena							
(long-finned pilot whale)							
male	39.83 (l)	31.39	20.23	4.50	52	Faroe Isl.	Borrell 1993
female	17.00 (l)	13.40	7.97	1.89	159	Faroe Isl.	
Delphinapterus leucas							
(beluga)	58.0 (w) (2.5–225.6)	13.6 (0.2–53.8)	33.5 (0.5–136.0)	10.9 (0.4–35.8)	26	St. Lawrence	Martineau et al. 1987

Relationship Between ΣPCB and ΣDDT. Contaminant burdens vary greatly among species, with the beluga whale and long-finned pilot whales exhibiting the greatest uptake (Fig. 1A). The accumulation of ΣPCB and ΣDDT is less (Fig. 1B) among other odontocetes (sperm whales) and mysticetes (humpback and minke whales). The limited data on the concentrations of PCBs and DDT in baleen whales counter any speculation that balenids do not carry biologically important burdens because they feed lower in the food web (O'Shea and Brownell 1994; Tanabe et al. 1984). It appears that these species also have the potential to bioaccumulate notable concentrations of persistent chemicals.

The accumulation of ΣPCB and ΣDDT is not consistently proportional across species (Fig. 1) or geographic regions. A single minke whale (Fig. 1A) held 27 ppm ΣPCB and 1.1 ppm ΣDDT with a ratio of 24 : 1 as opposed to the 1 : 1 and 1 : 3 ratio in the other minke whales studied (Fig. 1B). The benthic feeding habits of gray whales (Varanasi et al. 1994) may be responsible in part for the 22 : 1 ratio between ΣPCB and ΣDDT.

PCB Congeners. Depending on the permutations and combinations of the positions of the chlorine atoms on the biphenyl rings, there are 209 possible configurations (congeners) of PCB. Only recently has the technology been available to quantify the individual PCB congeners. In some studies, only a selected number of the more commonly found congeners are quantified and are then compared to the proportions of these congeners in commercial mixtures to determine ΣPCB in a sample. In other cases, the congeners are quantified and summed to derive the ΣPCB in the sample. The various protocols used to estimate the concentrations of organochlorines, therefore, confound comparisons between studies. Rather than focusing on a specific quantity of a chemical reported in an animal, it is imperative to think in ranges and look across populations and species at relative concentrations.

The problem of comparability between studies is exacerbated by the cost of biological sample analysis, which is high for ΣPCB and ΣDDT: approximately US $450 per sample. Congener-specific analysis increases these costs considerably, to US $2000. It is not surprising, therefore, that there is little information available about these chemicals in free-ranging species over which there has been no jurisdictional responsibility for determining their contaminant burden. However, as technology has advanced, more has been learned about the health effects and mechanisms of action of those congeners that are found in wildlife and humans.

A limited number of tissue samples from cetaceans have been subjected to PCB congener analysis (Table 5). In some cases, the investigators selected several congeners for quantification, usually those that were detected in greatest abundance. In other cases, such as in harbor porpoises (*Phocoena phocoena*) (Falandysz et al. 1994) and pilot whales (Muir et al. 1988), a greater number of congeners were quantified.

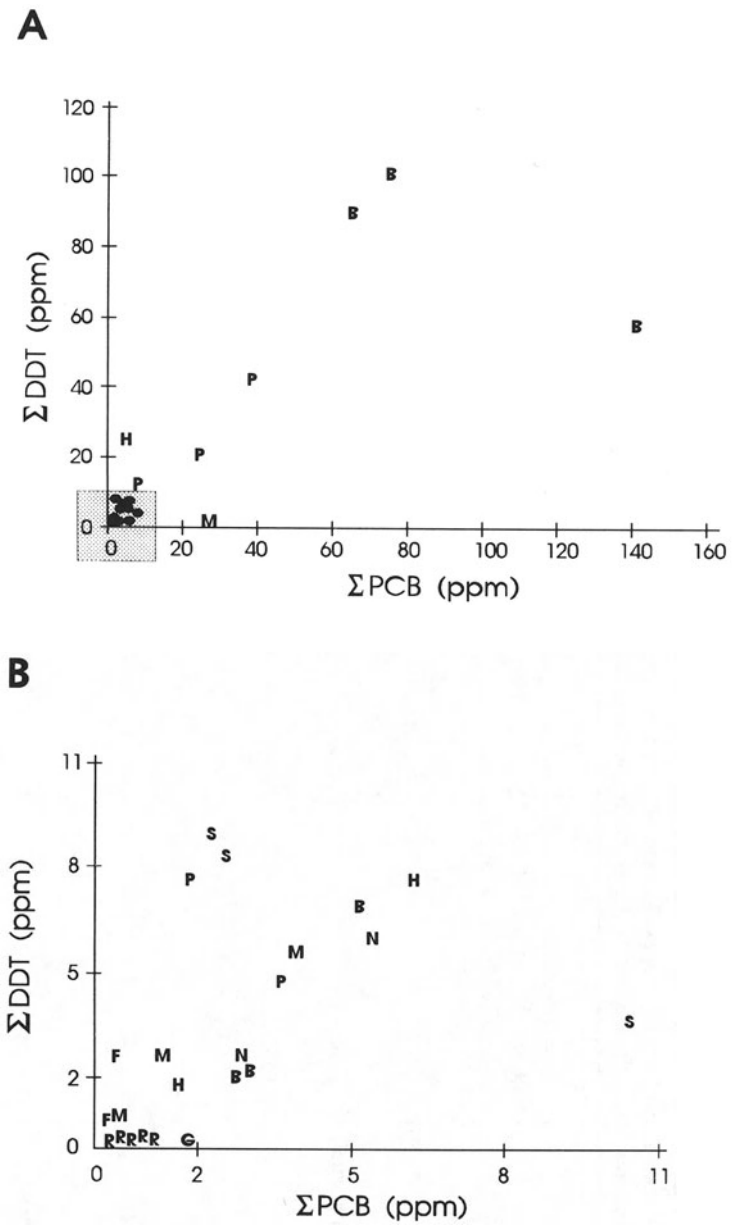

Fig. 1. Relationship among whales regarding concentrations on a wet weight basis of ΣPCB and ΣDDT using data listed in Table 3. A. Plot of full range of concentrations; the *shaded box* near the origins identifies the region plotted in B. B, Beluga; M, minke; P, long-finned pilot whale; S, sperm whale; H, humpback whale; G, gray whale; F, fin whale; N, narwhal; R, right whale.

Table 5. PCB congeners identified in tissues of cetaceans. The numbers of chlorine atoms on the biphenyl rings on each congener form the isomers: tri (3); tetra (4); penta (5); hexa (6); hepta (7); octa (8); nona (9); deca (10). Note: Because congeners must be specifically sought, the absence of an asterisk does not imply the absence of the isomer in the samples.

	PCB Congeners																										
	18	28	31	40	44	47	49	52	53	58	60	66	69	70	72	74	77	79	80	84	85	87	89	90	91	92	95	97
	tri			tetra													tetra		penta									
Delphinapterus leucas (beluga whale)																												
Masse et al. 1986					*			*										*	*				*		*			
Monodon monoceros (narwhal)																												
Muir et al. 1992								*				*															*	
Globicephala melaena (long-finned pilot whale)																												
Muir et al. 1988	*	*	*		*	*	*	*				*		*		*				*	*	*		*	*			*
Physeter macrocephalus (sperm whale)																												
Duinker et al. 1989					*		*	*																				
Phocoena phocoena (harbor porpoise)																												
Falandysz et al. 1994	*	*	*		*	*	*	*	*	*	*	*	*	*		*	*			*	*	*		*	*	*	*	
Morris et al. 1989		*						*																				
Boon et al. 1994								*									*							*				
Duinker et al. 1989					*		*	*																				

Tursiops truncatus (bottlenose dolphin)						
Morris et al. 1989	*		*			
Kuehl et al. 1991						
Stenella coeruleoalba (striped dolphin)						
Morris et al. 1989	*		*			
Kannan et al. 1993c				*		*
Delphinus delphis (common dolphin)						
Kuehl et al. 1991						
Lagenorhynchus acutus (Atlantic white-sided dolphin)						
Kuehl et al. 1991						

(*continued*)

Table 5. (*Continued*)

	99	101	102	105	106	108	110	117	118	119	126	128	129	132	133	135	136	138	144	147	148	149	151	153	156
	penta										penta	hexa													hexa
Delphinapterus leucas (beluga)	*	*	*		*	*			*			*	*	*		*		*	*	*	*	*		*	
Monodon monoceros (narwhal)	*	*							*									*						*	
Globicephala melaena (long-finned pilot whale)	*	*		*			*		*			*					*	*				*	*	*	*
Physeter macrocephalus (sperm whale)		*							*									*				*		*	
Phocoena phocoena (harbor porpoise)	*	*	*	*				*	*		*	*		*	*	*	*	*	*	*		*	*	*	
		*							*									*						*	
	*	*		*			*		*			*					*	*				*		*	
		*							*									*				*		*	
Tursiops truncatus (bottlenose dolphins)		*							*									*						*	
									*			*						*						*	
Stenella coeruleoalba (striped dolphin)		*							*									*						*	
				*					*		*							*						*	*
Delphinus delphis (common dolphin)									*			*						*						*	
Lagenorhynchus acutus (Atlantic white-sided dolphin)									*			*						*						*	

	161	163	165	169	170	172	173	176	177	178	179	180	183	185	187	190	194	195	198	199	200	201	202	206	208	209
	hexa.....			hepta.....												hepta	octa						octa	nona		deca
Delphinapterus leucas (beluga whale)	*	*	*		*		*				*	*		*	*											
Monodon monoceros (narwhal)												*								*						
Globicephala melaena (long-finned pilot whale)					*	*			*			*	*	*	*		*			*	*	*		*		
Physeter macrocephalus (sperm whale)												*		*		*										
Phocoena phocoena (harbor porpoise)				*	*	*	*	*	*	*		*	*	*	*		*	*	*		*	*	*			
									*																	
		*			*							*	*	*	*	*	*	*			*		*		*	*
						*			*			*	*		*		*									*
Tursiops truncatus (bottlenose dolphin)												*														
												*														
Stenella coeruleoalba (striped dolphin)												*														
					*	*							*					*								
Delphinus delphis (common dolphin)												*														
Lagenorhynchus acutus (Atlantic white-sided dolphin)												*														

Specific PCB Congeners with Dioxin-Like Effects. The concentration of a chemical in tissue alone provides little insight about its toxicity. In an effort to provide more meaning to quantitative chemical data, techniques have been developed to determine functional changes in vital biochemical and physiological systems that accompany the presence of chemicals. By combining quantitative chemical results with biochemical responses, the biological significance of the chemical's presence in the tissue becomes meaningful. In recent years, this technique has been applied in wildlife research using the level of activity of an enzyme system in the presence of a number of the organochlorines, such as dioxins, furans, and certain PCB congeners. The non-, mono-, or di-*ortho* chlorine-substituted PCB congeners 60, 77, 105, 126, 137, 138, 153, 156, 169, 170, 180, and 194 have planar configurations that facilitate binding to the aryl hydrocarbon hydroxylase (Ah) receptor for which the planar organochlorine chemical 2,3,7,8-TCDD (dioxin) also has a strong affinity. Upon binding to the receptor, these congeners can elicit the same receptor-mediated changes as dioxin but with less potency. The ability of dioxin to bind to the Ah receptor and activate the cytochrome P450 (cP450) system in rat liver hepatoma cells (H4IIE) has been established as a standard to which congeners can be compared and their toxicity determined. A linear association between Ah receptor-binding affinity and Ah-induced enzyme activity has been demonstrated for dioxin and the foregoing congeners.

Using standardized Toxic Equivalence Factors (TEFs) as determined by Safe (1990) for the planar PCBs, the sum of the activity of the congeners can be reported in terms of dioxin Toxic Equivalents (TEQs). Ah-induced enzyme activity has been associated with thymic atrophy (T-cell suppression), body weight loss (wasting), porphyria, and, in mice specifically, cleft palate (Safe 1987, 1990). Dioxin is not an estrogenic hormone mimic; it does not bind to the estrogen receptor but under certain conditions can block estrogenic action and act as an antiestrogen. Dioxin and some planar PCB congeners lower concentrations of male hormones (Haake et al. 1987), thyroid hormones, and insulin, thus affecting the endocrine system as well as the immune system (Birnbaum 1994; Keys et al. 1985).

Additional techniques for measuring cP450 activity have also been developed that provide more options for quantifying PCBs. One of these techniques (Tillett et al. 1991) employs a new cell line for *in vitro* assays and alternative systems, such as ethoxy resorufin-*O*-deethylase (EROD). This also leads to variations among the equivalence factors for some congeners and ultimately contributes to the confounding of direct comparisons.

In samples of cetaceans, these planar congeners have only been quantified in striped dolphins and harbor porpoises. Applying TEFs to these values, it can be estimated that the striped dolphins are carrying 6676 pg/g (ppt) TEQs and the harbor porpoises 526 pg/g (ppt) on a fat basis. PCB congeners 118, 138, 153, and 180 account for much of the toxicity in these two odontocetes, 63.3% and 75.5%, respectively (Table 6).

Table 6. Actual concentrations (ppb—ng/g) of PCB congeners reported in the literature. [Toxic Equivalent Factors (TEFs) in brackets are based on Safe (1990); Toxic Equivalents (TEQs) in parentheses are in ppt—pg/g.]

				PCB Congener (TEF)					
				77 [0.01]	126 [0.10]	169 [0.05]	60 [0.0001]	105 [0.0001]	118 [0.0001]
Species	Tissue	*n*	ΣPCB	PCB Concentration (TEQ)					
Phocoena phocoena (harbor porpoise)									
Falandysz et al. 1994	blubber	3	31333	1.74 (17)	0.5 (50)	0.72 (36)	11.8 (1.2)	128.67 (12.9)	890 (89.0)
Morris et al. 1989	blubber	3	49000						2290 (229.0)
Falandysz et al. 1994	liver	1	1200						63 (6.3)
Tursiops truncatus (bottlenose dolphin)									
Morris et al. 1989	blubber	1	290000						15800 (1580.0)
Kuehl et al. 1991	blubber	12	81392						4497 (449.7)
Kuehl et al. 1991	liver	1	253000						17900 (1790.0)
Kuehl et al. 1991	liver	1	51500						5200 (520.0)
Kuehl et al. 1991	liver	1	271000						16100 (1610.0)

(*continued*)

Table 6. (*Continued*)

Species	Tissue	*n*	ΣPCB	PCB Congener (TEF) 77 [0.01]	126 [0.10]	169 [0.05]	60 [0.0001]	105 [0.0001]	118 [0.0001]
				PCB Concentration (TEQ)					
Stenella coeruleoalba (striped dolphin)									
Morris et al. 1989	blubber	1	22000						1000 (100.0)
Kannan et al. 1993c	blubber	10	393000	43 (430)	68 (680)	7.8 (390)	160 (16.0)	2000 (200.0)	7900 (790.0)
Delphinus delphis (common dolphin)									
Kuehl et al. 1991	blubber	4	36500						2838 (238.8)
Lagenorhynchus acutus (Atlantic white-sided dolphin)									
Kuehl et al. 1991	blubber	3	50067						3270 (327.0)
Globicephala melaena (long-finned pilot whale)									
Muir et al. 1988	blubber	– ♂	9030				144 (14.4)	90.3 (9.0)	451.5 (45.1)
Muir et al. 1988	blubber	– ♀	3460				38.06 (3.8)	31.14 (3.1)	166.1 (16.6)

Monodon monoceros (narwhal)									
Muir et al. 1992	blubber	15 ♂	5180						
Muir et al. 1992	blubber	6 ♀	2695						
Halichoerus grypus (grey seal)									
Morris et al. 1989	blubber	1	17000						330 (33.0)
Phoca vitulina (harbor seal)									
Hall et al. 1992	blubber	89	16398						181 (18.1)
			156 [0.0001]	137 [0.00002]	138 [0.00002]	153 [0.00002]	170 [0.00002]	180 [0.00002]	194 [0.00002]	ng/g (ppb) [pg/g (ppt)]
Phocoena phocoena (harbor porpoise)			0 (0)	530 (11)	6200 (124)	7900 (158)	3 (0)	1300 (26)	71.67 (1)	15751 (526.1)
					3400 (68)	3780 (76)		1370 (27)		10840 (400.0)
					250 (5.0)	320 (6.4)		110 (2.2)		743 (19.9)
Tursiops truncatus (bottlenose dolphin)					33000 (660)	2900 (580)		11200 (224)		89000 (3044.0)
					5826 (116.5)	12160 (243.2)		6031 (120.6)		28514 (930.0)
					20200 (404)	43900 (878)		14600 (292)		96600 (3364.0)
					1700 (34)	4400 (88)		1400 (28)		12700 (670.0)
					20200 (404)	43100 (862)		20400 (408)		99800 (3284.0)

(*continued*)

Table 6. (*Continued*)

	156 [0.0001]	137 [0.00002]	138 [0.00002]	153 [0.00002]	170 [0.00002]	180 [0.00002]	194 [0.00002]	ng/g (ppb) [pg/g (ppt)]
Stenella coeruleoalba (striped dolphin)			1800 (36)	1800 (36)		810 (16.2)		5410 (188.2)
	3000 (300)	5500 (110)	60000 (1200)	73000 (1460)	12000 (240)	39000 (780)	4000 (80)	206617 (6676.0)
Delphinus delphis (common dolphin)			3085 (61.7)	5875 (117.5)		2142 (42.8)		13940 (505.8)
Lagenorhynchus acutus (Atlantic white-sided dolphin)			3797 (75.9)	7290 (145.8)		2543 (50.9)		16900 (599.6)
Globicephala melaena (long-finned pilot whale)	117.4 (11.7)	99.3 (2.0)	1038 (20.8)	903 (18.1)	135.4 (2.7)	442.5 (8.8)	45.2 (0.9)	3466 (133.5)
	27.7 (2.7)	34.6 (0.7)	359.8 (7.2)	363.3 (7.3)	65.7 (1.3)	190.3 (3.8)	38.1 (0.8)	1315 (47.3)
Monodon monoceros (narwhal)			481 (9.6)	443 (8.9)		133 (2.7)		1057 (21.2)
			237 (4.7)	274 (5.5)		85 (1.7)		596 (11.9)
Halichoerus grypus (grey seal)	1800 (3.6)			2400 (48)		970 (19.4)		5500 (104)
Phoca vitulina (harbor seal)			1763 (35.3)	2707 (54.1)		1157 (23.1)		5808 (130.6)

By using the contaminant concentrations available for PCB congeners 118, 138, 153, and 180, it is possible to estimate the relative dioxin toxicity of the contaminants among the other toothed cetaceans listed in Table 6. Applying TEQs to the PCB congeners that are dioxin-like provides some insight into the toxic burden of these animals. Based on the TEFs of the four PCB congeners, 9 of the 16 cetacean populations had estimated TEQs that exceeded 500 pg/g (ppt). Two bottlenose dolphin (*Tursiops truncatus*) liver samples had estimated TEQ values of more than 3000 pg/g (ppt). All of these estimates must be considered conservative because they only represent the presence of four PCB congeners with low enzyme inductive activity and do not take into consideration exposure to more highly active PCB congeners, furans, dioxins, and other synthetic chemicals that can induce Ah activity.

The proportions of congeners of PCBs, especially tetra-, penta-, and hexa-chlorinated forms, have been shown to be similar among closely and distantly related marine mammals (Bacon et al. 1992; Boon et al. 1994; Duinker et al. 1989; Tanabe et al. 1987a). Assuming a similar relationship among the congeners of PCBs among cetaceans, further analysis is possible. When the ΣPCBs are plotted in relationship to the estimated TEQs for four congeners (Fig. 2), a linear relationship is evident (slope = 0.988, intercept = 4.117, n = 14). Using the reported ΣPCB values for baleen

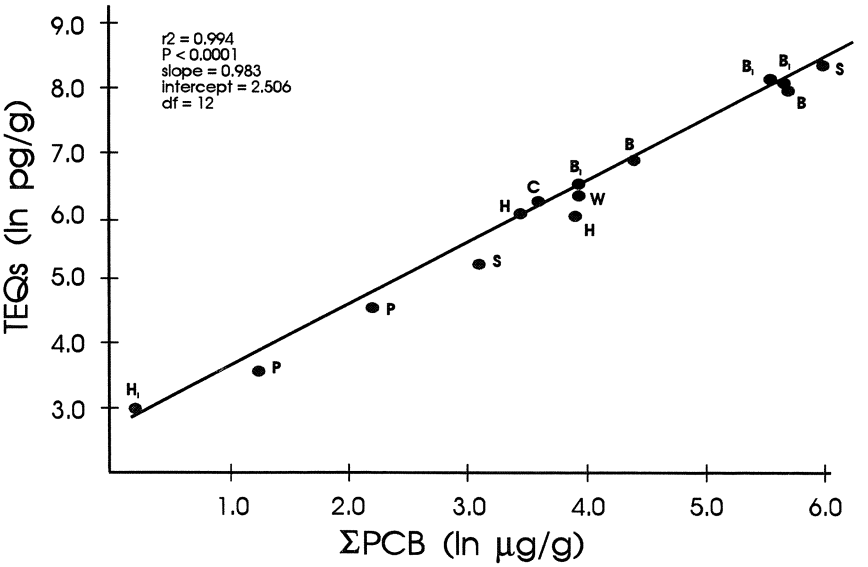

Fig. 2. Relationship between ΣPCB and TEQs as estimated from four congeners (118, 138, 153, and 180) for cetaceans listed in Table 7. P, Long-finned pilot whale; S, striped dolphin; H, harbor porpoise; B, bottlenose dolphin; C, common dolphin; W, Atlantic white-sided dolphin; subscript (l), liver sample.

whales in this regression formula (estimated TEQs = 4.117 + [0.988 *ΣPCB]), the relative TEQs for baleen and other large, toothed whales can be estimated (Table 7). The estimated TEQs for long-finned pilot and baleen whales are less than those of many of the small dolphins and porpoises from which exact TEQs could be computed. Sperm whales have estimated TEQs lower than pilot whales, ranging from 25 to 141 pg/g (ppt). Among the baleen whales, gray, fin, bowhead, and right whales have estimated TEQ values that range from 0 to 19. Humpback and minke whales show a wider variation in TEQs, with humpbacks ranging from 17 to 506 pg/g (ppt) and minkes ranging from 0 to 313 pg/g (ppt).

Persistent Organochlorine Contaminants: Others. Other lipophilic synthetic chemicals that bioaccumulate in marine mammals include the chlordanes, dieldrin/aldrin, hexachlorobenzene (HCB), mirex, toxaphene, and lindane, to name a few (Table 8). Additional sample preparation is required to quantify these chemicals, and, unless they are specifically sought during analysis, they are not identified. Although few reports include the presence of these chemicals in marine mammals (see Table 2), we know they are present in animal tissue because they can be measured. However, there are vast numbers of other persistent chemicals that may be present in wildlife tissue but have never been measured because of the current lack of technical ability to detect them.

In addition to the planar PCBs, dioxins, and furans, other chemicals known to or suspected to induce Ah activity because of their structure are the polycyclic aromatic hydrocarbons (PAHs) and the naphthalenes, diphenyltoluenes, diphenyl ethers, anisole, phenoxy anisoles, xanthenes, xanthones, anthracenes, fluorenes, dihydroanthracenes, diphenylmethanes, phenylxylylethanes, dibenzothiophenes, quaterphenyls, quaterphenyl ethers, biphenylenes, thioanthrenes, diphenyl ethers, and azoanthracenes (Giesy et al. 1994). The cost of sample preparation and chemical analyses limits our knowledge about these chemicals in all living tissue.

C. Blubber as a Repository for Organochlorines

Cetaceans are unique in terms of the vast storage capacity of their blubber. This lipid-rich tissue is a reservoir for ingested lipophilic chemical contaminants and, because cetaceans are long lived, it can accumulate sizable concentrations. The net effect is generally increased exposure of individuals as they age. Furthermore, because cetacean breast milk is rich in lipids, the calves ingest high concentrations of contaminants. During lactation, under most circumstances, their exposure will exceed anything they may encounter throughout later life. This exposure occurs during critical periods of growth when the endocrine, immune, and nervous systems are developing.

In species that fast, organochlorines mobilize from their fat into their blood and become more available for the embryo, fetus, and nursing calf.

Table 7. Sum of TEQs in cetaceans estimated using ΣPCB reported in the literature in the regression formula (TEQ_{est} = 4.117 + [0.983 × ΣPCB]). The formula is based on the relationship between known concentrations of ΣPCB and Toxic Equivalents computed for four coplanar PCBs (118, 138, 153, 180).

Species	ΣPCBs (ppm)	Estimated TEQs (pg/g)	Tissue	*n*	Locality	Source
Balaenoptera acutorostrata	27.00	313	blubber	1	St. Lawrence	Sergeant 1980
(minke whale)	0.14	2	blubber	1	Greenland	Johansen et al. 1980
	1.10	13	blubber	1	Greenland	Johansen et al. 1980
	3.70	44	blubber	2	Washington	Varanasi et al. 1993
	0.21	3	blubber	1	Washington	Varanasi et al. 1993
	0.023	0	blubber	20	Antarctic	Tanabe et al. 1986
	0.013	0	blubber	17	Antarctic	Tanabe et al. 1984
	0.005	0	blubber	29	Antarctic	Tanabe et al. 1984
Balaenoptera physalus	0.01	0	blubber	–	–	Saschenbrecker 1973
(fin whale)	0.18	2	blubber	–	–	Saschenbrecker 1973
male	1.26	15	blubber	–	Faroe Isl.	Borrell 1993
female	0.94	12	blubber	–	Faroe Isl.	Borrell 1993
Balaenoptera mysticetus						
(bowhead whale)	0.44	5	blubber	2	Alaska	Varanasi et al. 1993
Balaenoptera borealis						
(sei whale)						
male	0.46	6	blubber	14	Iceland	Borrell 1993
female	0.18	2	blubber	26	Iceland	Borrell 1993

(*continued*)

Table 7. (*Continued*)

Species	ΣPCBs (ppm)	Estimated TEQs (pg/g)	Tissue	*n*	Locality	Source
Eubalaena glacialis (right whale)	0.70	9	blubber	6	Canada	Woodley et al. 1991
	0.40	5	blubber	6	Canada	
	0.90	11	blubber	3	Canada	
	0.20	3	blubber	3	Canada	
	0.40	5	blubber	1	Canada	
	0.20	3	blubber	5	Canada	
Megaptera novaengliae (humpback whale)	1.40	17	blubber	2	Caribbean	Taruski et al. 1975
	6.00	71	blubber	1	New Jersey	
	5.40	64	blubber	1	Nova Scotia	
	13.00	153	blubber	8	eastern U.S.	Geraci 1989
	6.00	71	blubber	1	eastern U.S.	
	44.00	506	blubber	1	eastern U.S.	
Eschrichtius robustus (gray whale)	0.44	5	liver	1	Puget Sound	Varanasi et al. 1994
	0.63	8	liver	1	Puget Sound	
	0.74	9	liver	1	Puget Sound	
	0.27	3	liver	1	Washington	
	1.60	19	liver	1	Washington	
	0.37	5	liver	1	Washington	
	0.08	1	liver	1	Alaska	
	0.88	11	liver	1	Alaska	
	0.14	2	liver	1	California	
	0.21	3	liver	1	Port Angeles	
	0.59	7	liver	10	western U.S.	

Globicephala melaena						
(long-finned pilot whale)						
male	48.81	560	blubber	52	Faroe Isl.	Borrell 1993
female	26.27	305	blubber	159	Faroe Isl.	Borrell 1993
	33.39	386	blubber	90	Faroe Isl.	Borrell and Aguilar 1993
	16.95	198	blubber	39	Faroe Isl.	Simmonds et al. 1994
	28.68	332	blubber	23	Faroe Isl.	Simmonds et al. 1994
	25.8	299	blubber	114	Faroe Isl.	Aguilar et al. 1993
Delphinapterus leucas	141.40	1593	blubber	26	St. Lawrence	Martineau et al. 1987
(beluga whale)	65.60	749	blubber	2	St. Lawrence	Masse et al. 1986
	75.80	863	blubber	4	St. Lawrence	
	4.91	59	blubber	6	Baffin Isl.	Muir et al. 1992
	2.53	31	blubber	8	Baffin Bay	
	2.77	33	blubber	8	Hudson Bay	
Physeter macrocephalus	12.00	141	blubber	1	Netherlands	Duinker et al. 1989
(sperm whale)	2.35	28	blubber	2	Caribbean	Taruski et al. 1975
	2.10	25	blubber	1	eastern U.S.	Taruski et al. 1975
	8.32	98	blubber	14	Spain	Aguilar 1983
	10.20	120	blubber	10	Iceland	(in: Borrell and Aguilar 1993)

Table 8. Concentrations (ppm) of Σchlordane, dieldrin, mirex, lindane, toxaphene, and hexachlorobenzene (HCB) in blubber of cetaceans. Dash (–) identifies chemicals not analyzed in the study. ΣChlordane includes estimates of heptachlor, heptachlor epoxide, oxychlordane, and *trans*-nonachlor.

Species	ΣChlordane	Dieldrin	Mirex	Lindane	Toxaphene	HCBs	*n*	Locality	Source
Eubalaena glacialis (right whale)									
male	nd	0.03	–	–	–	–	6	eastern Canada	Woodley et al. 1991
female	nd	0.01	–	–	–	–	6	eastern Canada	
calf	tr	0.01	–	–	–	–	1	eastern Canada	
Eschrichtius robustus (gray whale)	0.27 ± 0.10 (0.01–2.20)	0.16 ± 0.07 (0.004–1.600)	–	–	–	0.35 ± 0.13 (0.02–2.90)	22	eastern Pacific	Varanasi et al. 1994
Balaenoptera acutorostrata (minke whale)	0.47 ± 0.40	–	–	–	–	–	2	eastern Pacific	Varanasi et al. 1994
Balaenoptera mysticetus (bowhead whale)	0.07 ± 0.01	–	–	–	–	–	2	eastern Pacific	Varanasi et al. 1994
Megaptera novaeangliae (humpback whales)	0.1 (nd–0.1)	–	–	–	–	0.1 (nd–0.1)	1	eastern Canada	Taruski et al. 1975
	0.2	–	–	–	–	1.2	1	eastern U.S.	
	nd					nd	1	eastern Canada	
Physeter macrocephalus (sperm whale)	–	0.00–0.02	–	–	–	–	6	California	Wolman and Wilson 1970

Globicephala melaena (long-finned pilot whale)	0.0017	–	–	–	–	–	19	eastern Pacific	Varanasi et al. 1993
male	1.65 ± 0.91 (1.04–3.19)	2.65 ± 1.13 (1.72–5.25)	–	–	11.7 ± 7.05 (4.39–19.9)	0.29 ± 0.22 (<0.01–0.31)	5	eastern Canada	Muir et al. 1988
female	0.68 ± 0.50 (0.25–1.85)	2.13 ± 0.50 (1.48–2.91)	–	–	2.22 ± 2.29 (0.44–7.94)	0.01 ± 0.10 (<0.01–0.31)	9	eastern Canada	Muir et al. 1988
Delphinapterus leucas (beluga)		0.11–7.06	nd–5.97	nd–1.04		0.05–10.69	26	St. Lawrence	Beland (personal communication)
	2.38 ± 0.04						6	Baffin Isl.	Muir et al. 1992
	1.87 ± 0.04						8	Baffin Bay	
	1.86 ± 0.03						8	Hudson Bay	
	7.43 ± 0.06						4	St. Lawrence	
Monodon monoceros (narwhal)									
male	1.92 ± 0.41 (0.94–2.51)	0.46 ± 0.09 (0.27–0.67)	0.014 ± 0.005 (0.007–0.022)				15	Baffin Isl.	Muir et al. 1992
female	1.40 ± 1.02 (0.55–2.82)	0.32 ± 0.26 (0.15–0.83)	0.021 ± 0.025 (0.000–0.072)				6	Baffin Isl.	Muir et al. 1992

Baleen whale calves would be especially vulnerable throughout gestation and lactation, not only because they are developing rapidly but because their mothers undergo fasting during these periods. Among whale species, therefore, in an environment contaminated with organochlorines the baleen whales would be more vulnerable than species that do not have extended periods of fasting.

The majority of reports on organochlorine contaminants in whales have been from blubber samples. These values vary among geographic regions, seasons of the year, sexes, and species. Blubber generally contains greater than 60% fat (Aguilar 1983; Tanabe et al. 1986; Woodley et al. 1991) and frequently as much as 80%–90% fat, with a report of 100% in belugas (Martineau et al. 1987).

Varanasi and co-workers (1994) reported that the lipid content of blubber varies in gray whales, ranging from 0.6% to 73%. The gray whale with the highest lipid content (73%) among those examined did not hold significantly more or even proportionally higher contaminants than whales with less lipid in their blubber (Varanasi et al. 1994). Varanasi and coworkers believed that the whales in their study were migrating from wintering grounds with low lipid levels in their blubber, whereas the individual whale with high lipids was leaving the feeding grounds. The actual contaminant content of the individual whale in relationship to lipid content was not provided in their report.

III. Epidemiological Analysis of Potential Threats to Whales from Organochlorines

To arrive at some conclusions concerning the potential threat of marine pollution to the health of whales, epidemiological criteria will be applied using the information in Section II plus relevant information from the literature on laboratory research, other animals, and humans. The criteria are used to infer causality where direct cause-and-effect relationships cannot be made (Fox 1991; Hill 1965; Susser 1986). The following are accepted tenets that can be applied (Consensus Statement 1995): "(1) time order (exposure must precede the effect); (2) strength of association (relative risk); (3) specificity of a compound to an effect (does X lead to Y?); (4) consistency on replication (results are supported across studies, geographic areas, species and over time); (5) coherence with biological theory (the relationship must be biologically plausible); and (6) performance on prediction (does the test stand up in field studies?)."

In most applications, not all of these tenets can be demonstrated. However, in situations where difficult decisions must be made concerning risk, such analyses can provide valuable insight into the levels of uncertainty in decision-making processes. These criteria have been successfully applied to the outbreaks of chemically induced diseases in fish and wildlife in the Great Lakes and are becoming accepted approaches by regulatory agencies and industry for inferring cause-and-effect relationships (Fox 1991).

The organochlorines most frequently reported in biological tissue (e.g., PCBs, dioxins, DDT/DDE, dieldrin, aldrin, chlordane, lindane) are generally not considered carcinogens at ambient concentrations. These chemicals are, however, developmental toxicants at extremely low concentrations and, when present from conception through postnatal or posthatching stages, can disrupt the development of the endocrine, reproductive, immune, and nervous systems in the offspring. The chemicals interfere with endogenous chemical messengers such as hormones, neurotransmitters, growth factors, and inhibiting substances as they direct development and regulate homeostatic control of the function of these systems (Colborn et al. 1993; Gray 1992). The embryo, fetus, and newborn are especially vulnerable to exquisitely low concentrations of maternal hormones and chemicals that interfere with these hormones; in most instances, the organizational effects are delayed and irreversible (Bern 1992; Guillette et al. 1995; Mori and Nagasawa 1988; vom Saal et al. 1992).

Because there is extensive chemical signaling among cells in developing systems, there are many targets for contaminants acting as chemical messengers, making it difficult to detect subtle effects and practically impossible to predict lesions or developmental modifications. For example, many effects may not be readily apparent at birth or hatching but can be manifested subsequently as diminished function leading to loss of immune competence, abnormal sexual development, malfunctioning reproductive systems, and neurological and behavioral changes that may be expressed from birth through puberty and even into later life (Colborn et al. 1993). There can thus be a long delay between exposure and effect whereby the latter may not be expressed until adulthood.

Outcomes of this nature are insidious and may not be recognized until they become widespread and result in changes discovered at the population level. Among wildlife populations, the death of a single animal is generally overlooked, and not until large numbers of animals are affected is a problem acknowledged (Consensus Statement 1995). Recognizing these delayed effects in species that are long lived and develop slowly, such as whales and humans, is even more difficult.

To compensate for the lack of specific studies directed at assessing the health status of large whales, epidemiological criteria are applied using parallels drawn from other marine mammals and a number of other species dependent on aquatic systems. Examples from the Great Lakes of North America, the U.S., Canada, Europe, and the Pacific Ocean will be used for comparison.

IV. Time Order

A. Marine Mammals

A first step in determining whether organochlorines pose a threat to marine mammals is the demonstration that the effects of concern were not prevalent before these chemicals were introduced into the marine ecosystem.

Historical information on marine mammals reveals several mass mortalities, although in the early years only in pinnipeds, that were widely separated over time and geographical location; for example, harbor seals (*Phoca vitulina*) in 1918 in Iceland and crabeater seals (*Lobodon carcinophagus*) in 1955 in Hope Bay, Antarctica (Lavigne and Schmitz 1990). However, the incidence of epizootics in the past 30 years is greater (see Table 1).

Since the early 1930s and especially following World War II, organochlorine chemicals (pesticides, industrial chemicals, plasticizers, fire retardants) have been produced in large amounts and widely used. The quantities that entered the terrestrial environment rose sharply, and over the years organochlorines gradually infiltrated freshwater systems and ultimately entered marine systems to become an integral part of the global marine environment. The recent seal, dolphin, and porpoise epizootics of the late 1980s occurred in a wide variety of aquatic systems: large, closed freshwater systems and coastal and semiclosed marine systems. The animals in some of these die-offs held the highest concentrations of organochlorines ever reported in animal tissue (Aguilar 1991; Tanabe and Tatsukawa 1991).

When looking for an explanation for the sudden onset of marine mammal die-offs almost 40 years after mass production of organochlorines commenced, it is important to keep in mind that the first generation of adult animals (F_0) directly exposed to developmental toxicants would not display obvious effects unless they were exposed to extremely high doses (McLachlan et al. 1992). Instead, the effects would be expressed in their offspring (F_1) as a result of embryonic and early postnatal exposure. The effects reported in Table 1 could be the result of this long-term chronic exposure or, more likely, the indirect exposure of subsequent generations through transplacental and lactational transfer.

F_1 effects that have been reported in humans and other animals as a result of exposure of the ovum, embryo, or fetus to developmental toxicants include functional changes in immune competence (Blair 1992; Blair et al. 1992), neurological damage (Jacobson and Jacobson 1988; Rogan et al. 1986), reproductive abnormalities (Guillette et al. 1994; Mori and Nagasawa, 1988), and damage to the endocrine system and reproductive tract (Gray et al. 1993; Guillette et al. 1995). [See Colborn and Clement (1992) for review.] This scenario predicts that top predator species with a shorter generation time would be among the first to show the effects, followed later by longer-lived species such as the large cetaceans and humans. This is clearly observed when one reviews the sequence of discoveries of transgenerational, developmental anomalies in Great Lakes wildlife commencing in the mid-1950s (Colborn et al. 1990) and described in the section that follows.

As synthetics slowly permeate the environment, the first aquatic systems to become contaminated are the large landlocked freshwater systems and coastal marine waters; the midoceans would be last. As the chemicals pene-

trate the marine environment, they slowly infiltrate the food web, bioaccumulating in the stored body fat and oil of all individuals in the system. With the onset of reproduction, females begin passing their accumulated chemicals on to their offspring, and in the case of marine mammals, via placental transfer during *in utero* development and via milk during lactation. Considering such a timeline, this raises the possibility that the pinnipeds and cetaceans that succumbed in the recent virus-related die-offs were F_1 generation or perhaps F_2 and F_3 generation individuals whose endocrine, reproductive, immune, and nervous systems were compromised because of *in utero* exposure to synthetics.

B. The Great Lakes Experience

Species in the Great Lakes conform to this time-order model of exposure and effects. Following World War II, a giant industrial and agricultural complex, from which vast amounts of chemicals were subsequently released into the environment, developed in the Great Lakes region. For years it was assumed, as with marine ecosystems, that the water resources of the region could dilute and assimilate the chemicals while maintaining the integrity of the system. However, reports started appearing in the literature by the late 1950s suggesting that all was not well within the wildlife community.

A review of the literature (Colborn et al. 1990) concerning wildlife health in the Great Lakes revealed that populations of 16 top predator species had suffered severe declines or instability since the mid-1950s. The underlying problem was a suite of adverse developmental effects, many of which are under the control of the endocrine system. The effects were in most cases expressed in the offspring and related to parental exposure. These effects often led to early mortality, or loss of fecundity if the animals reached adulthood. As concentrations of some of the chemicals in the Great Lakes system abated, following restrictions on their use, the incidence and severity of the effects, such as eggshell thinning, high incidence of deformities, and outright mortality, were also reduced though they have not completely ceased.

Less visible effects on the endocrine, immune, and nervous systems persist. Even today, bald eagles (*Haliaeetus leucocephalus*) have difficulty reproducing after establishing residency along the shoreline of the Lakes, and recruitment from within the population is negligible (Best et al. 1992; Colborn 1991). Similar problems with nest fidelity have been reported for Forster's terns (*Sterna forsteri*) and Caspian terns (*Sterna caspia*) nesting in the region (Kubiak et al. 1989; Mora et al. 1992). Another problem with a presumed endocrine basis, wasting, accounted for the loss of almost all of the Forster's tern chicks in 1983 on an island in Lake Michigan near Green Bay (Hoffman et al. 1987; Kubiak et al. 1989). Depending on the intensity of exposure, wasting can be expressed early as egg and/or chick mortality or as late as 17 d after hatching with mortality extending through day 31

(Harris 1990; Kubiak et al. 1989). In the 1983 field season, the investigators demonstrated that nest inattentiveness during incubation and reduced parental care after hatching contributed in part to the loss of chicks.

Biologists continue to report that 100% of the herring gulls (*Larus argentatus*) and adult salmon (*Salmo* sp.) observed in the Great Lakes are suffering from thyroid disturbances, including hyperplasia, hypertrophy, and shifts in thyroid hormone (T3 : T4) ratios (Leatherland 1992; Moccia et al. 1981, 1986). These researchers ruled out iodine deficiency as the problem. Despite the fact that the male salmon exhibit a precocial onset of sexual maturity, they do not become sexually mature and consequently are incapable of reproducing (Leatherland 1992). As a result, top predator salmonid species in the Great Lakes area can only be sustained through stocking programs. Leatherland (personal communication) also reported that almost all of the salmonids he has examined of either sex exhibit degrees of hermaphroditism; that is, they have all or part of both male and female organs.

In all of these studies, the effects described were discovered only because there was an unmistakable impact at the population level—the populations had been severely decimated (Colborn et al. 1990). Unfortunately, field observations such as those just mentioned require extensive resources and logistical planning and therefore are rarely undertaken. The difficulty of conducting comprehensive research of this nature in a coastal or marine environment in order to survey cetaceans would be almost insurmountable without extensive cooperation among governments and their agencies.

C. Humans

The Great Lakes wildlife studies revealed the importance of looking beyond the health of the directly exposed individuals to the health of their offspring and thus to the delayed manifestations of the effects compared with the time of actual exposure. Humans provide another example of transgenerational effects, especially relating to fertility. The prenatal and early postnatal exposure of an individual must be evaluated when seeking causal links for loss of fertility or fecundity.

The prenatal and early postnatal periods may have more influence on an individual's fertility than any other period throughout a lifetime (Sharpe and Skakkebaek 1993). At this time, tissues are formed that eventually become part of the mature reproductive system. For example, in the male, the Sertoli cells, which in adulthood control spermatogenesis, are formed at this time. The rate of sperm production, and ultimately sperm concentration, depends on the number of active Sertoli cells in the testes and the integrity of the rest of the male reproductive tract, which is also vulnerable during the early stages of development (Sharpe 1993).

Recently, it was discovered that not only has human sperm count decreased by approximately 50% over the past 50 yr but sperm quality and motility have also decreased significantly (Auger et al. 1995; Carlsen et al.

1992). Auger and co-workers compared sperm count, quality, and motility from 1973 to 1992 in 1351 healthy men who had previously fathered one child and found a 2.1%/yr sperm decrease from 89 $\times$ 10^6/mL to 60 $\times$ 10^6/mL ($p < .001$) and a reduction in motile sperm (0.6%/yr) and normal sperm (0.5%/yr). The younger men in this study produced the least sperm and sperm poorest in both quality and motility.

In a meta-analysis of 61 studies from around the world, Carlsen and co-workers (1992) showed a decline in mean sperm count from 113 $\times$ 10^6/mL to 66 $\times$ 10^6/mL between 1938 and 1990. Subsequent studies have supported these findings (Auger et al. 1994; Irvine 1994; Van Waeleghem et al. 1994), leading to the conclusion that sperm count is decreasing at the rate of approximately 1 $\times$ 10^6 sperm/(mL·yr), accompanied by reduced sperm quality and motility.

The authors of these sperm count papers have suggested that elevated exposure to environmental pollutants with estrogen-like activity during the prenatal and early postnatal stages could be the underlying cause of the male reproductive disorders (Auger et al. 1995; Carlsen et al. 1992; Sharpe and Skakkebaek 1993). The fact that age of the donor was inversely proportional to sperm count and quality provides additional evidence that environmental contaminants are a causal agent (Auger et al. 1995). The sperm count decline has been confirmed on several continents around the world and appears to be a global problem.

Increases in other problems of the developing male reproductive system have been reported, providing evidence of the number of vulnerable targets in a developing system when endocrine disruptors are present. A doubling of cryptorchidism (undescended testicles) occurred in the United Kingdom between 1970 and 1987 (Chilvers et al. 1984; Jackson et al. 1986). An increase in hypospadias (abnormal penis development) has been reported in several nations as well (Giwercman et al. 1993).

D. Cetaceans

The effects currently known to be associated with developmental toxicants are limited to changes in fertility, immune competence, and reproductive success, all parameters that have not been subject to careful scrutiny in large cetaceans. No trend information is available on sperm counts for wildlife species, including cetaceans. Consequently, risks cannot be determined concerning potential changes in cetacean fertility. Nevertheless, testicular samples should be collected from dead whales or harvested whales for histopathological examination of the Sertoli cells and spermatogonia to provide some insight into the reproductive status of the males. Similarly, necropsies of females should include gross and histopathological examinations of the entire reproductive tract. Examiners should look for Mullerian duct remnants in males and the presence of Wolffian duct remnants in females, which indicate abnormal development of the reproductive tract.

Researchers should also search archived tissue banks for samples that could provide comparative material for changes in gonadal tissues.

The widespread evidence of reduction in sperm numbers and quality among humans must be taken into consideration when estimating the hazard of exposure to environmental contaminants for marine mammals, especially since there is no indication that the decline in human sperm count is abating. There is no reason to believe that the marine mammals are not experiencing a similar reduction in reproductive potential, because the testes share similar ontogenetic processes.

V. Strength of Association

To strengthen the link between cause and effect, it is necessary to demonstrate that the incidence of effects in more highly contaminated populations is higher than in less contaminated populations. Unfortunately, studies from which epidemiological risk ratios can be generated are not available for most species of marine mammals. Studies generally are focused on describing specific events, such as massive die-offs, disease infestations, and disappearances, rather than differences among populations based on exposure levels before these populations are affected.

In light of current knowledge, several options are available for considering the relative risk to cetaceans from chemical exposure. First, comparisons can be made between stable and unstable populations of similar species to determine how much of the risk might be attributed to toxicants. Second, using what is known quantitatively about contaminant burdens in whales, comparisons can be made with other species that are similarly exposed for which associations have been made between adverse health effects and contaminant burdens. These comparative studies confirm that some species are far more sensitive than others.

Although nothing is known about where the cetaceans fall in the spectrum of sensitivity, these comparative or sentinel species can provide relative information on risk to cetaceans from exposure to synthetic chemicals. Finally, just the fact that the major die-offs of pinnipeds and small cetaceans have occurred in highly contaminated areas, as well as the inability of the St. Lawrence beluga whale population to recover in a highly contaminated habitat, provides evidence of increased risk to cetaceans in polluted areas.

A. Comparison of Stable and Unstable Beluga Whale Populations

The St. Lawrence/Saguenay River beluga whale (*Delphinapterus leucas*) population has been studied by a number of researchers for over ten years (Beland et al. 1987, 1988, 1993; Martineau et al. 1985a, 1986, 1987, 1988; Pippard 1985). However, because this is a protected species, biopsy sampling is not allowed and therefore only whales that were found dead have been available for necropsy. The whales are collected as soon as possible

after they are found and then are systematically examined. The information gained provides a basis for comparison with a relatively unexposed Arctic population of belugas.

Reproduction in the beluga whale population at the confluence of the St. Lawrence and Saguenay Rivers is 30%–40% lower compared with a control population in the Arctic (Sergeant 1986). It has been estimated that no more than 10% of the estimated 1885 population of 5000 belugas exists today (Reeves and Mitchell 1984). Despite rigid protection since 1980, the population has not recovered (Beland et al. 1988). Low calf production and increased mortality among young calves appears to be the underlying problem, paralleling the pattern of early mortality and reduced fertility among other Great Lakes vertebrates (Fox 1992). The number of reproductively capable females was more than half the number in a freshly harvested Alaskan population (Beland et al. 1993). No females among the St. Lawrence whales over the age of 21 yr were pregnant or showed evidence of a recent pregnancy. Mammary gland lesions that could have hindered breast feeding were discovered in 36% of the necropsied females (Beland et al. 1993).

In 1989, a bilateral hermaphroditic beluga whale was retrieved along the St. Lawrence River (De Guise et al. 1994a). An examination of his teeth revealed that he had been born in 1963. This animal's mother had been exposed to years of unregulated releases of chemicals into the St. Lawrence system. Other gross effects reported in these animals that were not visible until necropsy included: gastric ulcers, thyroid disorders, ankylosing spondylitis, secondary opportunistic bacterial infections, extreme cases of internal parasites, a high incidence of tumors (rare in cetaceans; see Table 1), and adrenal lesions (Beland et al. 1993; De Guise et al. 1995b; Martineau et al. 1988).

Because of their proximity to land-based industrial activities, the St. Lawrence animals experienced both earlier exposure to organochlorines, commencing in the 1940s, and heavier exposure than the Arctic animals (Martineau et al. 1987, 1988; Masse et al. 1986; Reeves and Mitchell 1984; Sergeant 1980, 1986; Sergeant and Hoek 1988).

This chronology of exposure and effects, and the comparison between the health status of an Arctic population of beluga whales and the St. Lawrence River belugas, provide evidence that toxic chemicals are in part involved in undermining the health and reproductive success in the St. Lawrence whales, thus putting the population at risk. However, it will be difficult if not impossible to determine which chemical(s) is responsible for their health problems.

B. Association with Disease or Reproductive Dysfunction

A series of recent studies state association between elevated organochlorines in the diets or bodies of seals, dolphins, and porpoises and a variety of dysfunctions. Marine mammal declines in the Baltic and Mediterranean

Sea, as well as apparently high incidence of growth deformities, tumors, and other pathologies, have been associated with these elevated body burdens of organochlorines or implied as a causal agent in those habitats with the high concentrations of chemical contamination. A recent study by Ross and co-workers (1995) specifically draws a close association between suppression of delayed-type hypersensitivity and antibody responses in harbor seals (*Phoca vitulina*). Seals with concentrations of 208.7 pg/g (ppt) TEQ lipid adjusted from serum had a measurable suppression when compared with seals that exhibited no suppression at 61.8 pg/g (ppt) TEQ (Ross et al. 1995). These studies are discussed in more detail later in this review; however, they provide strong support for the strength of association between concentrations of organochlorines and morphological and physiological perturbations.

VI. Specificity

The literature provides little information on a specific chemical(s) or a specific effect or physiological change in marine animals that could have caused these effects. Mixtures, rather than single compounds, are found in all animal tissue, thus obscuring the precision of association with the causal agent. Although a number of chemicals, including PCBs, dioxins, and DDT/DDE, have been measured in marine animals, this review focuses only on PCBs and DDT/DDE because little is known about the other chemicals that accompany them.

The effects of exposure to environmental contaminants are as obscure as the causal components; only recently have functional deficits been described in the wildlife and human toxicology literature. Traditionally, human health concerns were limited to cancer, acute toxicity, mortality, and mutations. More recently, it has been recognized that chemicals can affect development of vital physiological systems and that the effects vary depending on time of exposure, sex, age, and other chemicals present. In many cases, such as with neurological damage, neurotoxicological effects must be measured subjectively and in a large study cohort, compounding the difficulty of making associations.

A. Specificity of Effect

A growing list of organochlorines has been measured in marine mammal tissue. Most of them have not been as well studied in relation to marine mammal health as have DDT/DDE and PCBs. However, the other organochlorines cannot be ruled out as possible contributors to health problems in whales, especially in discrete areas where these chemicals are still found in elevated concentrations. The combinations and permutations of the mixtures of organochlorines are endless, varying within and among sampling sites, thus potentially confounding all ecological studies.

The cumulative effect of some of these chemicals has been demonstrated. Ten commonly encountered organochlorines were mixed at one-tenth their individually active dose, and an estrogenic effect on cell proliferation *in vitro* was reported for the mixture at 10 times the expected potency (Soto et al. 1994). These commonly encountered estrogenic organochlorines include endosulfan A and B, toxaphene, PCB congeners 61 and 136, dieldrin, methoxychlor, *p,p'*-DDT, *p,p'*-DDE and *p,p'*-DDD. The ultimate result(s) of a chemical that interferes with normal chemical messengers and, in this case, with cell proliferative capacity, is as obscure as the cause. Age, sex, timing of exposure, dose, season, nutritional status, and other stresses on the animal all determine the health outcome.

PCB Congeners with Endocrine Disruptive Effects. No PCB congener analyses are available for any baleen whale. However, a number of such analyses have been conducted on dolphins and porpoises (see Table 5). The commonly reported congeners in these species are 52, 101, 118, 128, 138, 153, and 180 (Table 5). Effects on the endocrine or reproductive system other than those related to Ah enzyme induction have been reported for some of these congeners. Congener 52, acting like an estrogen, induced uterine cell proliferation and weight gain ($p < 0.01$) in young female rats (Jansen et al. 1993). Prenatal exposure to congeners 118 and 153 reduces postnatal thyroid hormone (T4) levels and alters thyroid histology in rat pups (Ness et al. 1993). Congener 169, reported in a harbor porpoise, reduces plasma thyroid hormone levels and alters the metabolism of thyroid hormones in the brain of pregnant rats and their fetuses and pups when administered in a single dose (0.6 mg; $p < 0.01$) on day 1 of gestation (Morse et al. 1992).

Thyroid hormones are critical for the development of the brain during embryonic, fetal, and postnatal development. Interference with the thyroid hormone messages delivered to the brain during these early stages leads to intelligence loss and behavioral changes in human offspring (Hauser et al. 1993; Porterfield and Hendrich 1993). Only very low levels of free T4, approximately 10^{-12} g, are necessary to control development, making development vulnerable to exogenous chemicals (Porterfield and Hendrich 1993; Porterfield and Stein 1994).

Bush and co-workers (1986) found that concentrations of congeners 118, 138, and 153 were inversely associated with sperm motility in men with fertility problems (<20 million sperm/mL; $p < 0.005$, <0.001, <0.001). In this study, ΣPCB semen content was 5.8 ng/g, similar to the average serum content (6–7 ng/g) in adults from the U.S. (Miller et al. 1991). Bush and co-workers suggested that because these are the three PCB congeners most frequently found in human tissue, they may only be indicative of other contaminants such as furans or dioxins that generally accompany them. Congeners 153 and 138 are among those that comprise the highest percentage of total PCB congeners in whale tissue. Congener 153 comprises

approximately 20% of the PCB body burden of people living in industrialized temperate areas and 40%–50% of the body burden of native Americans living in eastern Arctic Canada (Dewailly et al. 1994).

ΣPCB and Associated Effects. Behavioral abnormalities have been linked with PCBs in a number of Great Lakes colonial nesting birds. Colony site tenacity was significantly less in those colonies of Caspian terns (*Sterna caspia*) from contaminated areas around the Great Lakes (Mora et al. 1992). There was a significant negative correlation between PCBs and the number of Caspian terns returning to where they fledged ($r^2 = 0.83$; $p < 0.001$). PCBs ranged from 2.5 to 3.5 ppm wet weight in plasma of adults and from 4.2 to 11 ppm in pooled, live eggs. Although some populations appeared normal, it was discovered that outside recruitment kept them in existence. Early reproductive failure and mortality among fledglings were undermining the populations in the more contaminated areas. It was also discovered that both PCBs and DDE were accumulated in the birds on the breeding ground and that the concentrations were not age related, suggesting quick mobilization of the contaminants from the mother to the chick.

B. Specificity of Cause

Marine Mammals. The harbor seal (*Phoca vitulina*) population in the westernmost part of the Wadden Sea collapsed from 3000 to 500 animals between 1950 and 1975 as a result of reduced pup production (Reijnders 1986). The westernmost part of the sea was highly polluted with PCBs from the Rhine River. To determine whether PCBs were playing a role in the decline, confined seals were held in two groups; one group was fed fish (plaice, flounder, dab, eelpout, and hooknose) from the Wadden Sea and the other group was fed fish (mackerel) from the North Atlantic. Average daily intake for 2 yr was 1.5 mg PCBs and 0.4 mg *p,p'*-DDE for the Wadden Sea group and 0.22 mg PCBs and 0.13 mg *p,p'*-DDE for the North Atlantic group. Seals fed Wadden Sea fish had significantly lower plasma thyroid hormones, total T4, free T4, free T3, and plasma retinols (Brouwer et al. 1989). There was no significant difference in progesterone and estradiol 17-β production in the two groups. However, reproductive success was significantly lower in the group fed Wadden Sea fish than in the group fed North Atlantic fish. The nonpregnant seals' reproductive difficulty occurred around the time of implantation. In a similar experiment conducted with American mink (*Mustela vison*), reproduction was inhibited at an average daily intake of 25 μg PCB in fish. Repeating the study with a pure PCB diet, the results were identical to those from mink eating the contaminated fish (den Boer 1983).

Questions have been raised about the role organochlorines have played

in the recent marine mammal die-offs. Mortality in each case was the result of opportunistic bacterial infections as the result of a morbillivirus infection. It has been argued that the animals' immune systems were compromised by morbillivirus, thus increasing their susceptibility to bacterial infections. In contrast to this hypothesis, it has also been argued that a contributing factor in the deaths was impaired immunological function as a result of exposure to organochlorines, thus setting up the series of events that led to mortality.

To test these hypotheses, Baltic Sea herring were fed to one group of harbor seals and Atlantic Ocean herring to another group of seals (Swart et al. 1994). The estimated Baltic Sea herring diet included 1.46 mg/d ΣPCBs with an estimated 203 ng/d TEQ, and the Atlantic herring diet included 0.26 mg/d ΣPCBs with an estimated 23 ng/d TEQ. Natural killer cell activity was significantly lower in the group fed Baltic Sea herring, which exhibited suppression of delayed-type hypersensitivity and antibody responses. In this study, the female's lymphocyte response was less than that of the male's (Ross et al. 1995). This study supports the hypothesis that organochlorine chemicals contributed in part to the seal and small cetacean epizootics that commenced in the late 1980s.

In another study to determine the role of organochlorines on marine mammal immune competency, blood was examined from a resident population of bottlenose dolphins (*Tursiops truncatus*) in the Gulf of Mexico off the coast of Florida, U.S. (Lahvis et al. 1993). Animals were sampled during a routine annual capture, sample, mark, and release project. Inverse correlations were discovered between Con A-induced lymphocyte proliferation and pentachlorinated and hexachlorinated PCBs (r^2 = 0.87 and 0.84, respectively) and between *o,p'*-DDT (r^2 = 0.73–0.79), *o,p'*-DDE (r^2 = 0.93 and 0.96), and *p,p'*-DDE (r^2 = 0.73 and 0.81). ΣPCBs ranged from 26.3 to 752 ng/g (ppb), and ΣDDT ranged from 12.7 to 562.93 ng/g (ppb) in whole blood (Lahvis et al. 1995). This study revealed a response to environmental contamination by a biological marker of immune competence in a stable dolphin population. Although these animals appeared to be healthy when sampled, the study provides evidence that some individuals' immune systems were affected by organochlorines, suggesting that susceptibility of this population to disease has increased.

Other Aquatic Species. The relationships between the presence of chemical contaminants and observed effects is also seen in other aquatic vertebrates. White croakers (*Genyonemus lineatus*) were collected from San Pedro Bay (ovarian DDT, 2.10 ± 0.85), off the coast of Los Angeles, California (U.S.), which was contaminated by industrial and municipal waste (Cross and Hose 1988). Fish from a control site, Dana Point, were used for comparison (ovarian DDT = 0.31 ± 0.18). These fish were induced to spawn in the laboratory (Cross and Hose 1988; Hose et al. 1989). San Pedro

females (41%) were not as successful as the Dana Point females (54%). Only 16% of the ovaries in the nonspawning fish from San Pedro were ready to spawn compared to 100% in the Dana Point females. Preovulatory atresia was reported in the San Pedro fish with immature or yolky oocytes. No croakers with more than 3.8 ppm ovarian DDT could be induced to spawn.

Concentrations of contaminants were also associated with effects in birds. In the mid-1970s, researchers began to notice female–female pairing, supernormal clutches, and reduced numbers of males in colonies of Lake Ontario herring gulls, accompanied by reduced nest attention in the adults (Fox et al. 1978; Shugart 1980). In these colonies, there was an increase in chick embryonic mortality, deformities, enlarged livers, porphyria, edema, wasting, and reduced fledging (Gilbertson 1983; Gilbertson and Fox 1977). After discovering that male gulls from both the Great Lakes and the California Pacific coast were being feminized and demasculinized, researchers set out to determine if there was any relationship between these effects and the concentrations of several pesticides in the environment (Fox et al. 1978; Fry and Toone 1981; Hunt and Hunt 1977). Using ambient concentrations of the chemicals found in the birds, Fry and co-workers induced the same effects in confined kestrels (*Falco sparverius*) and California (*Larus californicus*) and Western gulls (*Larus occidentalis*). Male kestrels, hatched from eggs of females fed *p,p'*-DDE at 0.3 mg/(kg·d) throughout courtship and egg laying, developed cortical localization of primordial germ cells in meiosis in the testes, resembling ovarian cortical and medullary tissue. The testes were flattened, with fewer or absent seminiferous tubules, and at adulthood the males were submissive. Under normal conditions, the testes have a thin, squamous epithelial cortex surrounding the seminiferous tubules. Histopathological examination showed that male chicks from California gull and western gull eggs injected with 2 and 5 ppm *o,p'*-DDT ($p < 0.01$) and 50 ppm *p,p'*-DDT/*p,p'*-DDE (4 : 1) ($p < 0.05$) developed both right and left oviducts (Fry and Toone 1981; Fry et al. 1987). In this series of studies, the severe effects were reported in animals receiving a lower dose. This is similar to reports by Peakall that eggshell thinning occurred only at the lower doses in his treatment regimens with DDT (Peakall 1970; Peakall 1993).

Researchers are just beginning to go back to the laboratory and explore the low-dose effects of chemicals that had traditionally been tested at high doses to monitor their effects on the function of the endocrine, immune, and nervous systems. In a receptor-mediated system, such as the endocrine system, there are 10,000 or more of one type of receptor within a cell, although only a small number of receptors need to be activated to trigger a cascade of events. For years, it was assumed that high-dose testing for cancer was protective from all other adverse health effects. It is now known that if a receptor system is overloaded with compounds that can bind to the receptor, the system is downregulated and the low-dose effects are not expressed (Gorski and Gannon 1976).

VII. Consistency

To meet the tenet of consistency, it is important to demonstrate that associations between cause and effect have been made across species, in different geographic locations, under various circumstances, and by different researchers. For that purpose, parallels can be cited from findings concerning other wildlife species in relation to historical changes in population stability, conditions of exposure and exposure pathways, and laboratory studies. Most of what was presented in Sections (V and VI) would naturally be included in *Consistency*; however, it is necessary to list them earlier in order to discuss the effects seen in cetaceans. Specific effects have been repeatedly observed across vertebrate species.

A. Aquatic Animals

A number of consistencies appear when comparing the literature about animals in the Great Lakes and animals in marine systems. Like the Great Lakes animals, a number of top predators in the marine system have experienced reproductive failure or population declines. In the case of marine animals, however, these problems were recognized in the late 1960s, a little more than ten years after the problems were recognized in the Lakes. This fits the timeline mentioned earlier in this review, allowing for the chemicals to reach the ocean.

Because of the mobility of marine populations and inability to track their whereabouts, it is difficult to determine where most of the populations spend the bulk of their time. However, recent findings from the North Pacific provide evidence that organochlorines have reached levels in black-footed albatrosses that are at or above the level at which effects are seen in Great Lakes birds in Saginaw Bay and Green Bay (Jones et al. 1995). Although the toxicity is similar, the organochlorines contributing to the toxicity in albatrosses do not exhibit the same pattern as those in the Great Lakes. The TEQs for dioxins and furans in black-footed albatross eggs, computed using the TEFs in Ahlborg et al. (1992), range from 297 pg/g (ppt) in adult fat to 17 and 37 pg/g (ppt) in composite egg samples. The sum of the 19 PCB congeners analyzed ranged from 2.75 ppm in adult fat to 0.2 and 0.64 ppm PCB in the composite egg samples. Total TEFs for dioxins, furans, and PCBs were 472 pg/g (ppt) in adult fat and 8.9–86.6 pg/g (ppt) in egg components, with approximately 40% of the toxicity from furans, 22% from dioxins, and 38% from the more highly chlorinated PCBs.

Eggshell abnormalities not previously reported in black-footed albatrosses are occurring in this species, which feeds in the northeastern Pacific (Ludwig, personal communication). Of the ΣDDT in the eggs, 35% was DDT compared to 1%–2% in Great Lakes birds, indicating recent production and release of the pesticide. DDE concentration was 0.297 ppm in the blood of the albatrosses and 1.8 ppm in the eggs. Wiemeyer and co-workers

(1984) reported 3 ppm DDE in bald eagle eggs as the critical concentration to maintain a stable population. Similarly, Cross and Hose (1988) reported that no female white croakers spawned with more than 3.8 ppm DDT in their ovaries. It appears that the black-footed albatrosses may be the most sensitive indicator of DDT exposure.

Albatrosses already serve as an excellent integrator of contamination over vast geographic regions and time. These birds feed on fish eggs and squid at the ocean surface, using the Midway Pacific Islands only to raise their young. The unexpected finding concerning the presence of furans in these birds must be taken into consideration when estimating risks to cetaceans. As mentioned earlier, Ono and co-workers (1987) reported furans ranging from Σ300 to Σ480 ppt in killer whales from the North Pacific, the same vast region where the albatrosses feed.

B. Humans

The position of the human mother in a food web as well as her unintentional exposure to organochlorines has been shown to affect the cognitive, motor, and behavioral development of her offspring (Jacobson and Jacobson 1993). For example, cord blood from mothers with at least 6 yr of exposure to contaminants in Lake Michigan fish held higher concentrations of PCB than the blood of women from the same communities who did not eat fish (Jacobson et al. 1990a). Although the concentrations of PCB were very low, cord serum levels were associated with a shorter gestational period, lower birth weight, and smaller head circumference in infants (Jacobson and Jacobson 1993). At age 4 yr, the children's lower weight continued to be associated with cord blood PCB levels. At 4 yr, the children most highly exposed *in utero* had difficulty with verbal and numerical memory. Mothers' breast milk concentrations were also associated with poorer performance on quantitative memory and verbal performance scores at age 4 yr; however, as the Jacobsons point out, this was more likely the result of high exposure during gestation.

Children whose mother's milk fat PCB levels exceeded 1.25 ppm and who breast fed for more than 9 mon scored 0.9 SD lower than others in the study. At age 4 yr, the children's PCB accumulation was primarily from their breast-feeding experience, which affected their activity level (Jacobson et al. 1990b). The paternal contribution to these effects was not measured and is thus unknown.

Arochlor 1260 (a commercial form of PCB) was used to measure residues in this study. These results parallel those of a study by Rogan et al. (1986) that found a correlation between PCB concentrations greater than 3.5 ppm in breast milk fat and loss of muscle tone, decreased activity, and abnormal reflexes in infants born in North Carolina. Again, in this study it was determined that the mothers' PCB breast milk concentrations depended on their lifetime exposure.

In both the Jacobson and Rogan studies, the concentrations of PCBs in

the mothers were similar to that of the general population. It is estimated that mothers of the children who, when tested using the Fagan test of infant memory recognition and infant intelligence, had impaired visual recognition at 7 mon and short-term memory problems at age 4 yr, were exposed to 0.093 μg/kg/(bw·d) PCB throughout their lifetime preceding their pregnancy. During lactation, they exposed their infants to 27 μg/kg/(bw·d) (Tilson et al. 1990), providing a model for the accumulation and mobilization of PCBs via a mother to her offspring.

In the case of the mothers who ate Lake Michigan fish, the common route of exposure was the aquatic food web. The effects in the children were not dependent solely on their mothers' exposure during pregnancy but also on their mothers' exposure prior to conception. Roncevic and co-workers (1987) found that at 3 and 6 mon after conception a continual drop in blood concentrations of PCB and DDE occurred compared to a control group of nonpregnant women. The reduction in maternal PCB and DDE levels suggested that fetal loading was dependent on the mother's lifetime accumulation. This concurs with findings in marine mammals (Addison and Stobo 1993; Cockcroft et al. 1989; Fukushima and Kawai 1981; Tanabe et al. 1982).

Although maternal transfer is significantly lower during placental transfer than during breast-feeding, the concentrations that reach the womb need only be extremely low to interfere with the delicate balance of chemicals that control development. For instance, free estradiol in the womb of a pregnant rat is in the range of $1\text{–}10 \times 10^{-13}$ g (1/10th of a trillionth of a gram). Slight shifts in this range can change the course of development of both male and female rat pups (vom Saal et al. 1992). Free estradiol in human cord blood is in the same range, fluctuating within an order of magnitude (vom Saal et al. 1995). The chemicals of concern in this review are found in human and wildlife serum at 6×10^{-12} to 10×10^{-9} g, giving them a competitive edge for the estradiol receptors if they do not bind to proteins in serum. In a competitive binding situation in which only a small number of receptors need to be activated to initiate DNA activity and trigger a subsequent cascade of biochemical events, the foreign material in the womb has an advantage even if it is only 10^{-4} times as active as estradiol. The added effect of a suite of foreign chemicals that invade the womb is unpredictable.

Rogan and co-workers (1987) discovered that the period of breast milk production (lactation) was markedly shorter in mothers with elevated DDE (>4.0 ppm) in their breast milk fat. There was a measurable decline in the lactation period as concentrations in breast milk fat exceeded 2.0 ppm DDE. In addition, they found that lactational failure, nursing for less than 1 mon, increased with ΣDDE concentrations (Rogan et al. 1987). Rogan and co-workers (1986) also confirmed that accumulation of PCBs and DDT by humans is the result of widespread exposure through low-level contamination in food.

The diet of Arctic Native Americans is rich in marine mammals and

fishes. In seven surveys of food consumption among the native communities, the women were exposed to 0.25–3.25 ($\mu g \cdot kg$)/(bw·d) ΣPCB (Kinlock et al. 1992). The range reflects the difference between a traditional subsistence diet and a diet that restricts some of the more highly contaminated meats. Eastern Arctic Inuit infants are exposed to concentrations of PCB in their mother's breast milk fat 7 times that of infants in Quebec and the U.S. on the basis of ten PCB congeners. These concentrations are similar to the concentrations in Arctic beluga whale blubber. The polar bear holds sevenfold more of the same PCBs than the Arctic human mother and the beluga (Dewailly et al. 1994).

It is important to point out that samples of Inuit breast milk (n = 24) collected in 1987 and 1988 were reported with 3.6 ppm (range, 0.5–14.7 ppm) ΣPCB on a fat basis using Arochlor 1260 as the standard (Dewailly et al. 1989). In 1989, with a larger cohort (n = 107), Inuit breast milk collected in the same region was reported with 1.052 ppm ΣPCB on a fat basis using the sum of ten PCB congeners commonly found in breast milk (Dewailly et al. 1994). In each case, when the Inuit breast milk was compared with breast milk from Quebec City mothers, there was a comparable difference between the two studies, 0.77 (range, 0.3–3.2) ppm ΣPCB and 0.157 ppm ΣPCB, respectively. In either case, the children in these Inuit populations experience 10 to 15 times as many infections as children from southern Quebec (Dewailly et al. 1989, 1994).

It appears that the difference in methodology involved in estimating the concentrations of PCB in these studies affected the results, making comparisons among studies difficult. As methodologies shift, the range of values in studies will shift. In this case, the ratio between the subjects and the controls provided a benchmark for comparison. However, if one were to apply these diverse methodologies to cetaceans without a benchmark population or species, the differences among populations would be interpreted as geographic variation, trophic feeding level differences, and metabolism.

Cetacean exposure, like that of humans (Jensen and Slorach 1990), is widespread and reflects low levels of PCBs and DDT in their food resources. Stress on obligate breast feeders such as cetaceans, as the result of reduced lactation, could compromise the growth and survival of their calves.

C. Effects Associated with Exposure to Organochlorines

In recent years, technology has increased the sensitivity of analytical equipment so that chemicals can be tracked in living tissue at 10^{-9} g (ppb) and 10^{-12} g (ppt). Scientists have correlated this quantitative information with the intensity of observable effects in wildlife at the cellular, tissue, organism, and population levels of biological organization and demonstrated associations that heretofore were impossible (see *Specificity*). This ap-

proach cannot currently be used in the case of cetaceans because of the lack of information on effects from the cellular to the population level in these species. However, it is possible to use the data on the concentrations of organochlorines in cetaceans to determine possible risk from exposure by using estimated TCDD-TEQs for the same chemicals and comparing the results with effects in other species.

D. Effects Associated with Enzyme Activity Reported as TCDD-TEQs

The wood duck (*Aix sponsa*) appears to be one of the species most sensitive to contaminants that bind to the Ah receptor (White and Seginak 1994). A measurable but not significant reduction in egg hatchability was reported at 5 pg/g (ppt) TEQs, and a significant reduction in fledgling numbers was reported at greater than 20–50 pg/g (ppt) TEQs (Table 9). In the wood duck study, it was determined that the Ah-induced enzyme activity was primarily from dioxin and a small fraction from furans. In contrast, a median level of 2175 pg/g (ppt) TEQs was reported in eggs from a colony of Forster's terns at Green Bay, Lake Michigan, U.S., in 1983 that showed massive reproductive failure (Kubiak et al. 1989). This population was compared

Table 9. TCDD-TEQ (pg/g) in egg samples from aquatic avian species (wet weight) and harbor seals (lipid adjusted, serum).

Species	Parts per trillion (ppt)	Effects	Source
Wood duck (*Aix sponsa*)	5[a] >20–50[a]	egg hatchability reduced number fledgling*	White and Seginak 1994
Forster's tern (1983) (*Sterna forsteri*)	2175[b]	egg hatchability* wasting* reduced fledgling*	Kubiak et al. 1989
(1988)	913[b]	wasting onset day–17	
Double-crested cormorant (*Phalacrocorax auritus*)	85[c]	egg mortality	Tillett et al. 1992
Harbor seal (*Phoca vitulina*)	61.8[d] 208.7[d]	normal immune suppression	Ross et al. 1995

Superscript letters represent methods used to determine TEQs: [a]TCDD-TEQ furans and dioxins (pg/g); [b]Dioxin and seven congeners of PCB TCDD-EQ (pg/g) H4IIE assay; [c]direct *in vitro* H4IIE assay (pg/g); [d]lipid adjusted, serum, based on dioxin, furans, PCBs; *, significant difference, $p < 0.05$.

with an inland colony of Forster's terns that was not dependent on food from the Great Lakes. The Green Bay eggs took longer to incubate, 37% of the eggs hatched compared with 75% inland, wasting was visible at hatching, and by day 17 only a few of the chicks that hatched were alive. In 1988, the median level of TEQs dropped to 913 pg/g (ppt), and incubation and egg hatchability were similar to that of the inland colony. Everything appeared normal until day 17, when wasting struck the chicks. By day 31, mortality was the same as observed in 1983 (Harris 1990). These sequential studies demonstrate the insidious nature of the delayed effects of chemicals. As concentrations in the eggs decreased, some effects were no longer observed and others were delayed; however, mortality did not change.

Mortality ranging from 8% to 39% in eggs collected from 11 Great Lakes double-crested cormorant colonies (*Phalacrocorax auritis*) between 1986 and 1988 was measurable at approximately 85 pg/g (ppt) TEQs (Tillitt et al. 1992) and increased in a dose–response manner ($r^2 = 0.703$, $p < 0.0003$). A weaker association with ΣPCB was found ($r^2 = 0.319$, $p < 0.045$). Extracts from eggs were tested in the H4IIE assay, and the results were compared with PCB technical standards. The residues in the eggs were three to four times more potent in the bioassay than that of the standards, revealing the conservative nature of the more toxic congeners in the environment. This enrichment phenomenon was seen among all the colonies throughout the Lakes. Enrichment has been reported by others, suggesting that this is a pervasive situation throughout the world (Kannan et al. 1989). This study may also explain why adverse health effects in Great Lakes birds are persisting today even though concentrations of ΣPCB have declined since the late 1970s. In this double-crested cormorant study and the Forster's tern study, it was determined that approximately 90% of the Ah activity was from two coplanar PCBs, 3% from 2,3,7,8-TCDD (dioxin), and the balance from other organochlorine chemicals (Kubiak et al. 1989; Tillitt et al. 1992).

E. Cetaceans

Only limited data are available on the concentrations of coplanar PCB congeners, dioxins, and furans in whales (see Tables 6 and 7). The TEQ estimates for whales in Table 7 are based solely on four PCB congeners (118, 138, 153, 180) and therefore are very conservative. PCB 118 contributed 22%–77% of the total Ah activity of the four congeners in these animals. The large whale species carry a range of TEQs from 0 to 506 pg/g (ppt) TCDD compared with humans in the U.S. (Atlanta, GA), who carry 81.6 pg/g (ppt) TEQs adjusted on a fat basis from serum for the same four congeners (Patterson et al. 1994). Congener 118 contributed 91% of the TEQ for the four congeners in the Atlanta cohort.

Patterson estimated that the Atlanta population carries a total of 126.1 TEQs pg/g (ppt), the sum of all of the planar PCBs, dioxins, and furans in the serum. Patterson and co-workers (1994) estimated that human breast

milk from Sweden adjusted on a fat basis held 32 TEQs from the four congeners, of which 79% was contributed by congener 118. Data are not available to estimate the TEQs from dioxins and furans in whales. Ono and co-workers (1987) reported finding no dioxin in killer whales (*Orca orcinus*) but did find 480 ppt Σfurans in a pregnant female, 380 ppt in a nonpregnant female, and 300 ppt in a mature male.

Using the available ΣPCB data on baleen whales to estimate congener loading, it appears that the fin (0–15), bowhead (5), sei (2–6), right (3–11), minke (0–13), humpback (17), and gray whales (2–19 TEQs) carry a lower TEQ burden than humans (Table 10). The highest values are found in the St. Lawrence beluga whales (863–1593 TEQs) and the Faroe Island long-finned pilot whales (198–560 TEQs). The Arctic belugas are within the range of humans. Where comparisons were made between male and female whales, the females were less contaminated, presumably through transfer of contaminants to their young during pregnancy and through lactation. Most important, even using a very conservative approach, some whale species are within the range of enzyme-induced TEQs at which effects have been associated with adverse health effects in other aquatic species.

A full spectrum of analysis of organochlorines that includes dioxins, furans, and PCB congeners in baleen whales is necessary to determine the baleen whale susceptibility to enzyme induction, which is only one mechanism that leads to functional damage.

VIII. Coherence

The logic that has prompted the drafting of this review embraces a number of arguments that contribute to the tenet of coherence. The timing of the sequence of marine mammal die-offs, the pathways of exposure, the evi-

Table 10. TEQs determined from serum and breast milk of humans and estimated from ΣPCB in cetaceans.

Species	TEQs (ppt)	ΣPCB (ppm)	Source
Human: U.S., serum	86[a]	1.1	Patterson et al.
Sweden, breast milk	32[a]	1.1	1994
Minke whale	0–313[b]	0.005–27	See Table 7
Fin whale	0–15[b]	0.01–1.26	
Bowhead whale	5[b]	0.44	
Sei whale	2–6[b]	0.18–0.46	
Right whale	3–11[b]	0.20–0.90	
Humpback whale	17–506[b]	1.4–44	
Gray whale	1–19[b]	0.08–1.60	
Long-finned pilot whale	198–560[b]	16.95–48.81	

[a]Lipid adjusted, serum, based on PCB congeners 118, 138, 153, 180.
[b]Lipid adjusted, blubber, based on PCB congeners 118, 138, 153, 180.

dence of contamination in the animals, and the relevant research on lowered fertility and decreased reproductive success among humans and wildlife all contribute to the hypothesis that organochlorines may be hazardous to cetaceans. The biological plausibility of the evidence supports this hypothesis as well.

A. Conservative Nature of the Endocrine System

Scientists have long recognized similarities in the development and functioning of the endocrine system among various vertebrate species (Bern 1990). For example, steroid hormones (e.g., estradiol, testosterone) are essential for the development of the reproductive duct system in all vertebrates studied to date, and these hormones play a fundamental role in the maturation and function of the reproductive system once sexual maturity is achieved. Estrogens are responsible for uterine growth and secretory activity, progesterone for the maintenance of pregnancy in most species, and androgens for stimulation of male duct growth and male secondary sexual characters (Martin 1985). Beyond the hormones themselves, recent studies have shown that the cytoplasmic receptors for these hormones are highly conserved, as are their responsive elements associated with specific genes (McLachlan et al. 1992).

It should be noted that differences in functioning of a given hormone can occur among species, but it is more likely that these differences exist at a specific or generic level rather than that of the class or order. For example, a given species of a teleost fish may use the steroid hormone cortisol to adapt to freshwater, whereas a related species uses the same hormone to adapt to saltwater (Bern 1990). The important point, however, is that in both cases the hormone is functioning in salt and water balance, although the actions may be opposite between the species. This conservatism in the types and functioning of hormones has allowed comparative endocrinologists to develop insight into the evolution of the vertebrate endocrine system. This conservatism has also been suggested as an important tool for comparing wildlife and human responses to environmental toxicants that affect the endocrine system (Colborn and Clement 1992). Therefore, the argument that the associations between adverse health effects and organochlorines documented in other vertebrates do not apply, or occur in baleen whales solely because they occupy a different phylogenetic clade, is not based on sound scientific data.

B. Maternal Transfer

Breast-feeding is by far the period of highest exposure to organochlorines for humans as well as marine mammals. The amount of transfer reflects the mother's lifetime burden, which ultimately establishes the background burden in the offspring. This legacy of contamination is then passed on to the next generation and so on.

The process of maternal transfer of contaminants to offspring has been studied in pinnipeds. Addison and Stobo (1993) estimated that transfer through breast milk accounted for 98% of the contaminant burden in grey seal (*Halichoerus grypus*) pups and was the primary source of these contaminants for the pups during their first year of life. Similar to humans, transplacental transfer appears to be low, with about 1% in grey seals (Donkin et al. 1981) and 2% in Weddell seals (*Leptonychotes weddelli*) (Hidaka et al. 1983). However, the amount of contaminant reaching the embryo under these conditions may still be enough to have an effect. The embryo is particularly sensitive to exogenous chemicals that can induce long-term changes in the endocrine, nervous, and immune systems and the reproductive tract at doses that have no effect on an adult.

The major contaminant pathways of exposure for cetaceans are similar to pinnipeds and humans: through food and embryonic, fetal, and neonatal exposure (Addison et al. 1973; Aguilar et al. 1993; Borrell and Aguilar 1993; Cockcroft et al. 1989; Martineau et al. 1987; Tanabe et al. 1986). As with pinnipeds and humans, transplacental transfer is low, in striped dolphins from 4% to 9% of the mother's contaminant burden passing to the embryo (Tanabe et al. 1982). Barring accidental exposure, lactational exposure is by far the most significant pathway of exposure for cetaceans throughout their lives, as it is for humans.

The concentrations of contaminants in immature males and females increase with age, and it is only when the females reach sexual maturity that they do not continue to show an increase in body burden at the same rate as seen in males (Martineau et al. 1987). This same pattern of contaminant accumulation is reported in humans (Holleman and Hammons 1980). Female burdens may even decrease during their reproductive years. The decreases reflect the transfer of organochlorines from the female to her offspring (Tanabe et al. 1981a). The striped dolphin's first calf may get as much as 80% of the mother's burden (Cockcroft et al. 1989), which can be as high as four times the amount that succeeding calves will get (Fukushima and Kawai 1981).

Dolphins, porpoises, and whales produce the most lipid-rich milk reported in mammals. For example, gray whale milk is as much as 53% fat (Rice and Wolman 1971), beluga milk is 45%, and that of dolphins ranges from 30% to 35% fat (Tanabe et al. 1988).

A nursing bottlenose dolphin calf that was consuming about 4 L of milk/d was estimated to acquire 10.8 mg/d ΣPCB, 9 mg/d ΣDDT, and 6.4 mg/d dieldrin (Cockcroft et al. 1989). Whole milk from a beluga held 1.72 μg/g (ppm) ΣPCB, 2.04 μg/g (ppm) ΣDDT, and 45% fat, which is equivalent to 3.8 ppm ΣPCB and 4.18 ppm ΣDDT/g milk fat (Masse et al. 1986).

Killer whales (Ono et al. 1987), minke (Tanabe et al. 1984, 1986), Northern right (Woodley et al. 1991), and fin whales (Aguilar and Borrell 1994) have all shown substantial transfer of organochlorines to their nursing young. Fin whales were estimated to deliver as much as 1.0 g ΣDDT and 1.5

g ΣPCB to the calf over the course of lactation, which is 6–7 months (Klinowska 1991). Concentrations of ΣDDT and ΣPCB in minke whales were considerably higher in young animals than adults, signaling the magnitude of maternal transfer (Tanabe et al. 1984).

The latter part of the fasting interval in baleen whales coincides with the onset of nursing of the newborn calf. Prolonged fasting would lead to the mobilization of contaminants, as maternal fat is metabolized for energy, and elevation of contaminant levels in blood and milk that is passed on to the calf. The effects of the higher concentration of contaminants both in the milk and in the calf may have a profound effect on the developing tissues and organ systems of the newborn.

C. Transgenerational Effects on Development and Reproduction

A number of laboratory studies have provided evidence of risk to the fertility of mammals, including cetaceans and humans, when exposed to ubiquitous synthetic chemicals. For example, in repeated trials it was demonstrated that the sperm of mature male rats that were exposed to PCBs postnatally through contaminated breast milk have difficulty penetrating the ova or maintaining a viable zygote (Sager et al. 1987). In this case, only breast-feeding exposure, not prenatal PCB exposure, affected sperm function.

In another study, pregnant rats fed one meal of dioxin at 0.064, 0.16, 0.4, and 1.0 μg/kg (ppt) (bw) on day 15 of gestation, the approximate day that sexual differentiation commences in rats, gave birth to male offspring who were demasculinized and feminized (Peterson et al. 1992). Rats whose mothers were exposed to the lowest dose, 0.064 μg/kg (bw) or approximately 25 ng dioxin, experienced significant changes in sexual behavior as they matured, along with a 75% reduction in sperm production and a 60% decrease in ventral prostate weight (Mably et al. 1991). Many of the effects were not measurable until the pups reached sexual maturity. The researchers pointed out that although sperm production in the rat was reduced significantly, standard testing protocols for reproductive success would not have revealed this fact because rats produce ten times more sperm than is needed for impregnation.

In a similar study using one dose of 1.0 μg/kg (bw) dioxin, female rat pups exhibited morphological changes in external genitalia at birth as well as a sequela of adverse effects in the vagina and uterus reported in mice and humans exposed *in utero* to diethylstilbestrol (DES) (Birnbaum and Gray, personal communication). The effects discovered in these studies are irreversible and under most conditions would not be expressed until the animals attempted to reproduce when they reached adulthood. The studies also emphasized the importance of a "single hit" by a developmental contaminant at a critical stage of development. The long-term delayed effects in the Peterson and Mably studies raise concerns about chemicals that are not as

persistent as the organochlorines but are frequently disposed of in coastal waters.

D. Vitamin A

Vitamin A plays an essential role in normal growth, reproductive success, and resistance to infections. Retinoic acid, a form of vitamin A, appears to be critical to cellular differentiation during development; therefore, disruption of retinoid metabolism may lead to abnormal embryonic development (Spear et al. 1988). Vitamin A deficiency has been associated with reproductive impairment, embryonic mortality, growth retardation, and decreased resistance to infections.

Exposure to DDT, dioxin, and PCBs can lead to depletion of vitamin A storage forms in the liver and in the plasma. Exposure of laboratory animals to PCB congeners causes a decrease of both plasma vitamin A and thyroid hormone levels. This appears to result from interference by a PCB metabolite with the plasma transport protein for both vitamin A and thyroid molecules (transthyretin) (Brouwer and van den Berg 1986; Brouwer et al. 1988). DDT exposure decreases the total amount and concentration of vitamin A in rats (Phillips 1963). Likewise, dioxin has been shown to deplete the storage form of vitamin A in the liver of rats (Poland and Knutson 1982).

The association between exposure to organochlorines and decreases in vitamin A reported in the laboratory has also been documented in wildlife populations under natural exposure conditions. Liver retinoid depletion in Great Lakes herring gulls is inversely proportional to Ah-induced activity, which is associated with the presence of dioxins, furans, and certain PCB congeners (Spear et al. 1986). Vitamin A levels in herring gulls from a relatively uncontaminated North Atlantic coastal colony were significantly higher than vitamin A levels in Great Lakes herring gulls (Anonymous 1991). The Great Lakes herring gull colonies have experienced high rates of reproductive failure and embryonic abnormalities (Gilbertson et al. 1991).

White suckers (*Catostomus commersoni*) from the vicinity of Montreal Island, Canada, a contaminated site, had high prevalence of reproductive failure and 2.75 times the risk of embryonic malformations compared with suckers from a reference site (Branchaud et al. 1995). The vitamin A storage forms in the liver of suckers from the polluted site were significantly reduced compared to fish from the less polluted area.

The association between organochlorines and reduced vitamin A has also been documented in marine mammals. Common seals fed a diet of fish from the Wadden Sea, which was heavily contaminated with PCBs, showed a drastic reduction in plasma vitamin A compared to seals fed relatively uncontaminated fish from the North Atlantic (Brouwer et al. 1989). A significant reduction in thyroid hormone levels was also found in this study. Furthermore, the seals fed the contaminated fish had significantly reduced reproductive success.

Data on the relationship between vitamin A levels and organochlorine chemicals in cetaceans are lacking. However, as the previous studies have demonstrated, PCBs, DDT, and dioxins are known to deplete vitamin A in a wide variety of species under both natural and experimental conditions. In fact, reductions in vitamin A and thyroid hormone seem to be among the more sensitive biological effects of exposure to these organochlorine contaminants. Because of the central role that vitamin A plays in normal reproduction, growth, development, and resistance to infectious disease, contaminant-induced depletion of vitamin A levels could potentially have a profound impact on the health and reproductive success of cetaceans.

E. New Discoveries Regarding Mechanisms of Action of Synthetics

For years, DDE has been considered an estrogen-like compound because of its feminizing and demasculinizing effects on male animals. Male chicks exposed to DDT/DDE early in development, either in the egg or posthatching, did not reach sexual maturity and developed oviductal tissue (Burlington and Lindeman 1950; Fry and Toone 1981). *o,p'*-DDT and *p,p'*-DDE have a weak affinity for the estrogen receptor, and it was hypothesized that this was the mechanism driving these effects. However, two new mechanisms of action of *p,p'*-DDE have been reported. Haake and co-workers (1987) reported that *p,p'*-DDE induces male rat hepatic 16a- and 16b-testosterone hydroxylases and androstenedione hydroxylase, thus enhancing the excretion of endogenously produced male hormones. In addition, *p,p'*-DDE has now been demonstrated to have a strong affinity for the androgen (male hormone) receptor, competing with testosterone and dihydrotestosterone for the receptor and blocking it (Kelce et al. 1995a,b). Female rats fed the antiandrogen vinclozolin, a fungicide, give birth to male pups with no penises, vaginal sacs, undescended testicles, and nipples. All of the estrogen-binding compounds tested in the androgen receptor assay thus far have had an affinity for the androgen receptor and block it as well (Earl Gray, personal communication). These new findings concerning the mechanism of action of *p,p'*-DDE provide an explanation for effects that were never clearly understood in the past, such as the significant inverse association with testosterone blood levels of Dall's porpoises (Subramanian et al. 1987). However, these results also raise concern about the effects these antiandrogens are having on breast-fed offspring during a period of growth when testosterone is critical for normal neonatal development of the testes and the male reproductive tract, and how the antiandrogens are affecting directly exposed adults.

F. Effects of Plastics on the Endocrine and Reproductive Systems

Recent findings suggest that the risks to marine mammals from contaminant exposure are not confined to the chlorinated compounds already discussed. A number of nonchlorinated compounds produced in large quanti-

ties have penetrated the aquatic environment, although they may not be as persistent as the organochlorines. Sterility in fish has been reported below sewage outfalls in rivers in the United Kingdom (Jobling and Sumpter 1994; Purdom et al. 1994). The effects were traced to octa- and nonyl-phenols, breakdown products of alkyl phenol polyethoxylates, which are found in detergents, plastics, pesticides, and gasoline additives (Soto et al. 1992). Bisphenol A, a monomer used to make polycarbonate plastic, has an affinity for the estrogen receptor, as do the alkyl phenols (Krishnan et al. 1993).

Phthalates, used as plasticizers in polyvinyl chloride (PVC), degrade slowly under anaerobic conditions and have become ubiquitous (Wams 1987). When tested at high doses, phthalates caused testicular damage (Heindel and Chapin 1989). Peakall (1975) reported phthalates in marine fish and seal pups. Large quantities of these compounds have become components of products used in commerce worldwide and now litter the oceans. Significantly more plastic debris, which had been picked up from the surface of the North Pacific by adult Laysan albatrosses, was found in chicks dead in the nest than in chicks that died accidentally (Aumann 1994). The possible endocrine disruption effect of chemicals leaching from these products in the chicks is under investigation.

IX. Predictive Performance

Little research has been directed toward making direct causal links between contaminants and the health status of marine mammals. The extreme difficulty of working with large animals that live in marine systems is an obstacle that may never be overcome. Further, in some cases the animals of concern are protected legally, making access impossible. In this respect, whales are in the same predicament as humans, for whom scientific manipulation is unethical. Consequently, as in the case of humans, researchers will be forced to use alternative species and *in vitro* assays as models for determining risks to cetaceans from exposure to chemicals.

Applying this protocol to cetaceans, the papers cited in this review concerning colonial nesting birds, harbor seals, and white croakers, in which scientists measured concentrations in the tissues of wild animals and, subsequently, under controlled conditions, were able to induce the same effects in the same or similar species with the same chemical, provide the tenet of predictive performance. The testing protocols established in the Great Lakes colonial nesting bird studies have been taken to other regions of the world to examine other vertebrate species, including other birds.

The study undertaken by Ross and co-workers to determine the role of contaminants on the functional status of the harbor seal immune system provides an excellent approach for future studies. This was an international, collaborative, multidisciplinary study involving experts from the field and the laboratory. Ross and his group monitored contamination in the food of the seals and also in the seals' tissues, and were able to make

links between a food source, body burden, and loss of function. Studies such as these provide models for future cetacean and other marine mammal research. Taking all these studies into consideration, they also provide evidence that the functional capacity for cetaceans to survive may be at stake.

Closer scrutiny of cetaceans could identify effects that may appear as changes in external morphology (penis length, anogenital distance, variation in sexually dimorphic characters), immune system (composition or activity of lymphocytes, granulocytes, immunogloblins), endogenous hormone or vitamin A concentrations, Sertoli cell numbers or sperm counts and motility, or histopathology of endocrine glands and other internal organs.

X. Conclusions

There may continue to be no reason to suspect that exposure to organochlorines has been directly lethal to baleen whales (O'Shea and Brownell 1994). However, there is sufficient evidence to suspect that organochlorines may be altering the reproductive potential and health of all cetaceans, including the baleen whales. Knowlton and co-workers (1994) reported that mean calving interval in a North Atlantic population of right whales was significantly longer than the calving interval in a South African population. Brown and co-workers (1994) reported that the population growth rate of a right whale population in the North Atlantic is 33% of that in the South Atlantic. The proportion of reproductive females in this population is 38% compared to 54% in the South Atlantic population.

Over a period of 11 years, 13 females of reproductive age in the North Atlantic population were never seen with calves. Knowlton and co-workers suggested that sublethal effects of toxic chemicals may be involved, and Brown and co-workers suggested that the lack of recovery in this right whale population may be the result of fewer reproductively capable females, and that among those in the population that can reproduce, the intervals are longer between calvings. The evidence presented in this review's epidemiological analysis provides the mechanisms that could underlie the conclusions of the Knowlton and Brown studies.

In addition, the epidemiological analysis in this review would predict such population instability in mammals chronically exposed to organochlorines. The geographic variation of effect in right whales reported over vast oceanic regions, from the southern to the northern Atlantic Ocean, again supports the hypothesis that environmental contamination is affecting the reproductive success of baleen whales.

Across all species that have signaled problems at the population level since the 1950s, the specific chemical cause and the specific effect often remain obscure (Aguilar and Borrell 1994). However, the evidence shows consistently that the effects are the consequence of more than one mechanism, are in many cases transgenerational and/or associated with changes

in functionality, affecting fecundity, and are also associated with chronic exposure to organochlorine chemicals. Unfortunately, there are few individuals among humans and wildlife that have not been exposed to synthetic chemicals during embryonic development.

Because of the widespread dispersal of these chemicals in the environment, it is too late to find unexposed populations for comparison. The cetaceans in some cases have been more exposed than humans, and over time the exposure will extend longer than that of humans because the oceans are the ultimate sink for persistent chemicals.

The growing number of reports about the decline in number, quality, and motility of sperm and increases in other reproductive tract problems in human males contribute to the uneasiness about the status of cetaceans. Although the data on contaminant burdens in cetaceans are sparse and are not comparable statistically, there is enough evidence to suggest that whale embryos, fetuses, and suckling calves are exposed to concentrations of organochlorines within the range of human exposure and, in some cases, exposed to much higher concentrations than those reported for humans. Current contamination in cetaceans has reached concentrations in a number of geographic regions at which there are known sublethal effects sufficient to impair populations of other species.

Population size alone is not sufficient to determine the status and viability of a population. The presence of breeding-age adults and what appear to be healthy young does not necessarily reflect a healthy population. Detailed information on population age structure is needed to determine whether offspring have the functional capacity to survive to adulthood and to reproduce.

Little is known about the kinetics and metabolism of persistent chemicals in cetaceans. Evidence to date identifies a complex process of uptake, metabolism, and storage of the congeners of PCBs, dioxins, and furans. In the absence of such information, one must rely on other mammalian models. Small odontocetes can serve as useful models for all cetaceans, even though they may have different life histories, feeding habits, behaviors, and levels of contamination when compared to other cetaceans, because of the commonality of the underlying physiological and developmental processes that all mammals share.

The long latency period between exposure in the womb or during early development and expression of the functional deficits may result in the absence of a statistical correlation with contaminant burdens in the animal in various stages of its life. This lack of a statistical correlation does not necessarily discount a chemical(s) as a causal agent, especially if the effect was instigated during development or postnatally.

The effects discussed in this review are the result of disrupted gene expression and not damage to genes. Chemical contaminants can have multiple effects depending on levels and duration of exposure, timing, and stages of development. In general, the damage incurred in early stages of

development is irreversible, whereas alterations later in life may be reversible.

Pelagic cetaceans, which may carry lower body burdens than other species, are not necessarily unaffected by their exposure; instead, they should be viewed as animals with low-dose chronic exposure. Likewise, geographic regions that have been categorized as "pristine" or "contaminated" should instead be thought of as "low-dose" or "high-dose" regions.

Summary

Information is provided to test the hypothesis that organochlorines introduced into the environment since the early 1940s could threaten the reproductive potential of baleen whales and other cetaceans. Comparisons are made using data on the role of organochlorines in a model system, the Great Lakes region of North America, and in model animals, including humans, pinnipeds, and other wildlife. DDT and PCB are used as model organochlorines with the caveat that there may be thousands of other chemicals in the environment also involved. Improved sensitivity in analytical quantification of synthetic chemicals in biological tissue has been accompanied by an increase in knowledge about biochemical processes that control development and function.

The effects described in this review are the result of disrupted gene expression, not damage to the gene. The mechanisms of action of the organochlorines reveal their ability to affect developing organisms at very low concentrations during critical life stages: embryonic, fetal, and early postnatal. Exposure during early development can disrupt the organization of the endocrine, reproductive, immune and nervous systems, effecting irreversible damage that may not be expressed until the individuals reach adulthood.

The recent discovery that human sperm count is declining worldwide at a rate of 1×10^6 sperm/(mL·yr) suggests common exposure to estrogen-like chemicals during prenatal and early postnatal development. This raises concern for other top predator species that also share the same exposure. Periods of intense feeding followed by long periods of fasting are common among species of baleen whales. This unique strategy places the embryonic and nursing calves in vulnerable positions, because under both situations maternal blood levels are elevated as a result of absorption from food intake or as a result of mobilization as fat is metabolized.

Estimates of Toxic Equivalents (TEQs) based on the occurrence of four PCB congeners (118, 183, 153, 180) in ΣPCB reported in whales are highest for St. Lawrence belugas and Faroe Island long-finned pilot whales. This conservative approach reveals that some whale species are within the range of enzyme-induced TEQs at which effects have been associated with adverse health effects in other aquatic species.

The epidemiological approach was used for analysis because it was devel-

oped to handle multiple exposure scenarios in which direct causal links are virtually impossible to isolate. The analysis includes the tenets of time-order, strength of association, specificity of cause and effect, consistency, coherence, and predictive performance.

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