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Abstract The field of wildlife toxicology can be traced to the late nineteenth and early twentieth centuries. Initial reports included unintentional poisoning of birds from ingestion of spent lead shot and predator control agents, alkali poisoning of waterbirds, and die-offs from maritime oil spills. With the advent of synthetic pesticides in the 1930s and 1940s, effects of DDT and other pesticides were investigated in free-ranging and captive wildlife. In response to research findings in the US and UK, and the publication of *Silent Spring* in 1962, public debate on the hazards of pollutants arose and national contaminant monitoring programs were initiated. Shortly thereafter, population-level effects of DDT on raptorial and fish-eating birds were documented, and effects on other species (e.g., bats) were suspected. Realization of the global nature of organochlorine pesticide contamination, and the discovery of PCBs in environmental samples, launched long-range studies in birds and mammals. With the birth of ecotoxicology in 1969 and the establishment of the Society of Environmental Toxicology and Chemistry in 1979, an international infrastructure began to emerge. In the 1980s, heavy metal pollution related to mining and smelting, agrichemical practices and non-target effects, selenium toxicosis, and disasters such as Chernobyl and the *Exxon Valdez* dominated the field. Biomarker development, endocrine disruption, population modeling, and studies with amphibians and reptiles were major issues of the 1990s. With the turn of the century, there was interest in new and emerging compounds (pharmaceuticals, flame retardants, surfactants), and potential population-level effects of some compounds. Based upon its history, wildlife toxicology is driven by chemical use and misuse, ecological disasters, and pollution-related events affecting humans. Current challenges include the need to more thoroughly estimate and predict exposure and effects of chemical-related anthropogenic activities on wildlife and their supporting habitat.

Keywords History · Environmental contaminants · Pollution · Wildlife

Introduction

Ecotoxicology is most broadly described as "the science of contaminants in the biosphere and their effects on constituents of the biosphere, including humans" (Newman 2001). Wildlife toxicology is a component of ecotoxicology, and from a phylogenic perspective it is focused on aquatic and terrestrial amphibians, reptiles, birds and mammals. It deals with a range of integrated activities (monitoring, hypothesis-driven research, forensics, exposure and effect assessment, risk assessment), biological scales (molecular through ecosystem levels of organization), research venues (laboratory, vivarium, mesocosm, field), and is multidisciplinary in nature (biochemistry, analytical chemistry, toxicology, ecology). Unlike some fields of science that mature through deliberate hypothesis testing, discovery, and accretion of basic knowledge, wildlife toxicology has been shaped by chemical use and misuse, ecological mishaps, catastrophic human poisonings, and research in the allied field of human toxicology.

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Its history can perhaps be traced to ancient times (Greek maxim "a bad crow lays a bad egg"), although reports of contaminant-related wildlife mortality events only appeared towards the end of the industrial revolution (Hoffman et al. 1990; Table 1). Incidents of lead poisoning from ingestion of spent shot by pheasants (*Phasianus colchicus*) in England (Calvert 1876) and waterfowl in the US (Grinell 1894), arsenic poisoning of fallow deer (*Dama dama*) at a silver foundry in Germany (1887 cited in Newman 1979), and alkali poisoning of ear grebes (*Podiceps nigricollis*) and shovelers (*Anas Spatula clypeata*) in the western US (Fisher 1893) made their way into the popular press and scientific literature.

Early twentieth century

At the turn of the century, several reports of lead poisoning from ingestion of spent shot by waterfowl appeared in the ornithological literature (Bowles 1908; McAtee 1908). Serious public concern over the effects of poisons on wildlife began when strychnine and thallium used for rodent and predator control were noted to affect non-target species like quail and song birds (Peterle 1991). Poisoning of waterfowl from lead mining wastes dumped into the Spring River in Kansas, and from the ingestion of phosphorus used in military munitions in the northern Chesapeake Bay of Maryland were both noted in 1923 (Phillips and Lincoln 1930). With expanded production and use of petroleum after World War I, maritime spills resulted in numerous waterbird die-offs along the coast of the US (Phillips and Lincoln 1930). Another early report (1926) described arsenic in liver tissue of dead deer following calcium arsenate application for forest insect control (cited by Keith 1996), and related controlled exposure and field studies followed (Whitehead 1934). Aerial application of pesticides fostered expanded use in the 1930s, and acknowledgement of their adverse effects was even discussed at the Third North American Wildlife Conference in 1938 (Strong 1938). During this era, about 30 pesticides were in use, including plant derivatives (e.g., pyrethrum, nicotine), inorganic compounds (e.g., calcium arsenate, lead), mercurial fungicides, and the synthetic weed killer dinitro-ortho-cresol (Sheail 1985).

Birth of the synthetic pesticide era

In 1939, Müller discovered the insecticidal properties of dichlorodiphenyltrichloroethane (DDT), and its use increased exponentially following World War II (Hayes 1991). Early "premonitions" on how DDT might inflict damage to wildlife were published in the Atlantic Monthly in 1945 (cited by Sheail 1985), and by 1948, DDT was detected in human tissues (cited in Loganathan and Kannan 1994). During this period, the insecticidal properties of other organochlorine compounds and rodenticides (e.g., sodium monofluoroacetate, a.k.a. Compound 1080) were realized, and their widespread use expanded after 1945. By the mid-1940s, laboratory and field trials by staff of the Patuxent Research Refuge of the US Fish and Wildlife Service (US FWS) investigated the effects of DDT on wildlife. Studies with captive game birds, passerines and small mammals documented its acute and chronic toxicity (Coburn and Treichler 1946). Some of the initial field studies with DDT revealed little or no effect on bird and small mammal populations at application rates of 2 pounds per acre (Stewart et al. 1946; Stickel 1946), but at greater concentrations effects on birds became apparent (Hotchkiss and Pough 1946; George and Stickel 1949; Robbins and Stewart 1949). Residues of DDT in bird tissues were eventually quantified in some studies (Barnett 1950; Mitchell et al. 1953). Laboratory and field trials demonstrated that DDT was far more acutely toxic to aquatic species (crayfish, crabs and fish) than to terrestrial vertebrates.

Between 1946 and 1950, seven farm workers died of dinitro-ortho-cresol poisoning in the UK (Sheail 1985). A "Working Party" of leading scientists chaired by Professor Solly Zuckerman was established by the Ministry of Agriculture to examine safety measures for pesticide applicators. Eventually they turned their attention to chemical effects on non-target wildlife.

By the 1950s, other insecticides and fungicides were in common use (e.g., aldrin, dieldrin, chlordane, heptachlor, toxaphene). Wildlife mortality was noted following pesticide use in agricultural and forest habitat (e.g., seed dressings for cereal crops, applications for spruce budworm control and Dutch Elm disease), and in grasshopper, mosquito and fire ant control programs (Peterle 1991). Use of organophosphorus compounds ensued, and a record number of wildlife poisonings (e.g., passerines, game birds, small mammals) were reported in 1952, possibly related to schradan use for control of aphids (Sheail 1985). At the same time, a report of parathion poisoning of geese attributed to spray drift appeared in the Journal of the American Veterinary Medical Association (Livingston 1952).

During this period, the relationships among quantities of chlorinated hydrocarbon ingested, toxic effects (reproduction and survival), and accumulation of residues in tissue of game birds were investigated in laboratory studies (DeWitt 1955, 1956; DeWitt et al. 1955). At the close of the decade, the Monks Wood Experimental Station was established in the UK, with the objective of describing toxic chemical effects on habitat, ecological change, and animals

Table 1 Timeline of select pollution events and wildlife toxicology activities

Years	Events
8000 BC	Rising sea levels
250 BC	Wildlife protection legislation in India
676 AD	Protection of birds in Northumberland, UK
1560	Use of coal and deforestation in England
1760	Beginnings of industrial revolution
1762	Ben Franklin leads committee to regulate water pollution
1820	World population reaches 1 billion
1866	Term ecology coined
1876	Lead poisoning of birds
	British River Pollution Control Act
1887	Arsenic poisoning of deer at silver foundry
1891	Alkali poisoning of waterbirds
1908	Arrhenius predicts greenhouse effect
1918	Lead gasoline introduced; Migratory Bird Treaty Act
	Great Lakes Water Quality report issued by IJC
1921	Observations following oil spill events
1923	Poisoning of waterfowl from lead mining wastes
1926	Arsenic poisoning of deer following application to forest
	PCBs first manufactured in US
	Field studies document effects of arsenic on wildlife
1930s	World population reaches 2 billion
	Aerial application of pesticides
	Bald eagle population diminishing in US
	Fish and Wildlife Coordination Act
	Insecticidal properties of DDT discovered by Müller
1945	Use of organochlorine pesticides and rodenticide expands
	Insecticides incorporated as seed-dressings
	Laboratory and field trials on DDT toxicity to wildlife
	Federal Insecticide, Fungicide, and Rodenticide Act in US
1950s	Studies on white phosphorus poisoning of waterfowl
	Expanded use of insecticides and fungicides
	Wildlife die-offs related to Shradan use
	Organochlorine pesticide accumulation studies in wildlife
	Wildlife mortality associated with seed-pesticide dressings
	Minamata Disease
	Publication of classic lead poisoning studies in wildlife
1960s	*Silent Spring* published; "Oil Slick is Shroud for Birds" (Washington Post)
	Poor reproduction in ranch mink fed Lake Michigan salmon
	International conferences on "wildlife toxicology"
	OC biomagnification, marine mammal studies, PCBs residues
	Diagnosis of OC poisoning based on brain residues
	Eggshell thinning of DDT in free-ranging raptors realized
	Torrey Canyon oil spill
	DDE-shell thinning relation established, "ecotoxicology" coined
1970s	Herring gull monitoring program established in Great Lakes
	U.S. EPA formed; NEPA, TSCA, and MMPA in US
	Endangered Species Preservation Act in US
	Biomarkers of OP/CB pesticide and Pb developed in birds
	Toxicity thresholds to methylmercury established in gamebirds
	Concerns about acid precipitation
	Reproductive studies illustrate sensitivity of mink to PCBs
	Petroleum oil studies with egg, young and adult waterbirds
	SETAC established; Conference on Estrogens in the Environment
1980s	CERCLA (Superfund) and NRDA legislation, NAPAP established
	Forensic investigations involving anticholinesterase pesticides
	Epidemic-like death/embryo deformity at Kesterson NWR
	Acid precipitation studies on wildlife and supporting habitat
	Ecological Risk Assessment and modeling
	Studies of indirect effects of pesticide (food, habitat) on wildlife
	Toxicity of Se, As and B examined in pen and field studies
	Poisoning of eagles consuming Pb shot crippled birds
	Lead shot phase-out for waterfowl hunting in North America
	Chernobyl nuclear disaster
	Exxon Valdez oil spill
1990s	Concern for declining amphibian populations
	Kuwait oil spill during war in Iraq
	Chemically Induced Alterations in Sexual Development: The Wildlife-Human Connection
	Great Lakes Embryo Mortality, Edema and Deformity Syndrome
	Expanded development of molecular biomarkers in wildlife
	Cyanide poisonings of wildlife related to micro-gold mining
	Toxicological significance of soil and sediment ingestion by wildlife
	Climate change warning

Table 1 continued

Years	Events
	Monocrotophos exposure linked to Swainson's hawk die-off
	Feminization of alligators in Lake Apopka
	Our Stolen Future
	Kyoto Protocol
	World population reaches 6 billion
2000s	Pharmaceuticals and surfactants detected in US rivers
	Perfluorinated compounds detected in wildlife worldwide
	PBDEs noted to be doubling in bird eggs at 3–5 year intervals
	Toxicity studies of PBDE initiated in wild birds and mammals
	NSAID diclofenac linked to decimation of *Gyps* vultures in India

Sources http://en.wikipedia.org/wiki/Timeline_of_environmental_events; www.runet.edu/~wkovarik/enhist/; Hoffman et al. 2003; Peterle 1991; Sheail 1985

CB carbamate, *CERCLA* Comprehensive Environmental Response, Compensation, and Liability Act, *IJC* International Joint Commission, *MPPA* Marine Pollution Protection Act, *NEPA* National Environmental Policy Act, *NRDA* Natural Resource Damage Assessment, *NAPAP* National Acid Precipitation Assessment Program, *NSAID* non-steroidal anti-inflammatory drug, *NWR* National Wildlife Refuge, *OC* orgaochlorine, *OP* organophosphorus, *Pb* lead, *PBDEs* polybrominated diphenyl ethers, *PCBs* polychlorinated bipehyls, *SETAC* Society of Environmental Toxicology and Chemistry, *TSCA* Toxic Substances Control Act

(sublethal responses, reproductive rates, mortality, and population effects; Sheail 1985). Pesticide seed-dressings were linked to die-offs of game birds and mammals (perhaps even secondary poisoning of foxes, *Vulpes vulpes*; Sheail 1985), and as early as 1962, some restrictions on the use of cyclodiene pesticides (e.g., aldrin, dieldrin) were imposed in the UK (Newton 1986).

Lead, munitions and mercury issues in the 1950s

During this era dominated by concern for pesticide toxicity, effects of other contaminants were also studied. The widespread hazard of spent lead shot was investigated in landmark studies of Bellrose (1959), and culminated in the classic monograph "Lead poisoning as a mortality factor in waterfowl populations". More formal diagnostic criteria of lead poisoning were developed, including measurement of lead tissue concentrations. It was estimated that greater than one-third of the continental population of waterfowl ingested one or more lead shot, and two to three percent of the population succumbed to lead poisoning annually. On a more localized scale, observations of phosphorescence and visible smoke from gizzard contents of poisoned waterfowl collected near a military site in Maryland continued; pathology and lethality data, and phosphorus tissue concentrations indicative of exposure were developed through a combination of dosing trials and field investigations (Coburn et al. 1950). Remarkably, some 40 years later, protracted investigations of waterfowl die-offs, and suspect secondary poisoning of bald eagles (*Haliaeetus leucocephalus*), were eventually linked to ingestion of white phosphorus particles at a military firing range in Eagle River Flats, Alaska (Sparling 2003).

Organomercurial compounds used as fungicidal seed dressings had substantial effects on some species of wildlife in Sweden during the late 1950s and early 1960s (Borg et al. 1969). Behavioral effects (staggering gait) and secondary poisoning of mammalian predators such as fox were observed, and some avian species (e.g., rook, *Corvus frugilegus*) may have been affected at the population level. In 1956, human poisonings (Minamata disease) related to the long-term discharge of methylmercury from chemical factories into Minamata Bay was officially described (Harada 1978), and subsequently dramatic effects on wildlife, including observations of "crows and grebes falling into to the sea while flying", were reported (Doi et al. 1984).

Dramatic discoveries in the 1960s

Carson's (1962) *Silent Spring* addressed many topics, including pesticide effects beyond target organisms, ecological imbalances, surface and ground water contamination, inadequate water treatment facilities, persistence and transfer of chlorinated hydrocarbons, use of natural products for biological control, human safety, and pesticide resistance. Many of these concepts, including the possibility that man was progressively poisoning the planet were new and provocative. Her account of pesticide effects across a broad scale catapulted what was known by environmentalists to the forefront of political, business, scientific and public sectors of society, and despite controversy, had a long-lasting impact (Briggs 1987; Sheail 2002).

By 1963, a long-term monitoring program examining pollutants in wildlife was initiated in the UK (Predatory Bird Monitoring Scheme 2007). In the US, collections of starlings (110 locations) and mallards (4 flyways) were initiated in the mid-1960s to track temporal changes in tissue residues of organochlorine pesticides, and subsequently incorporated measurement of polychlorinated biphenyls (PCBs) and metals (Jacknow et al. 1986). This effort continued over the next 20 years (Schmitt and Bunck 1995). Through the 1960s, governmental activities addressing environmental contaminant exposure and effects in wildlife began to

expand in the US, Canada, UK, and elsewhere. Initially research meetings were somewhat parochial, but in 1965, pesticide effects on wildlife were discussed at international meetings held at Monks Wood (addressed persistent organochlorine pesticides) and at the University of Wisconsin (focused on the peregrine falcon, *Falco peregrinus*; Sheail 1985). At this time, research documented the bioaccumulation of organochlorine pesticide residues in food chains, and the resultant mortality of fish-eating birds due to accumulation of lethal tissue residues (e.g., aldrin, dieldrin).

A classic paper by Ratcliffe (1967) was published in *Nature* that described decreases in eggshell thickness in peregrine falcons and Eurasian sparrowhawks (*Accipiter nisus*) in Britain following the use of DDT. Numerous papers appeared in journals such as *Science*, and *Nature*, over the next decade. For example, catastrophic declines in raptorial and fish-eating birds related to DDT were described in North America (Hickey and Anderson 1968), reproductive effects of dieldrin and DDT were demonstrated in feeding trials with sparrow hawks (*Falco sparverius*; Porter and Wiemeyer 1969), exposure studies with captive mallards (*Anas platyrhynchos*) showed that the metabolite *p*,*p*′-DDE caused eggshell thinning and lowered reproductive success (Heath et al. 1969), and a logarithmic relationship between *p*,*p*′-DDE residues and shell thinning was demonstrated in brown pelicans (*Pelencanus occidentalis*; Blus et al. 1972). Studies in various avian species replicated and extended these findings to establish dietary thresholds and concentrations of *p*,*p*′-DDE in eggs associated with shell thinning and impaired reproduction. Eggshell thinning was subsequently documented in 18 families of birds in North America, and was most pronounced in raptorial and fish-eating species (Blus 1996, 2003). Adverse population-level effects were described in the brown pelican (5 young hatched from about 1,300 nesting attempts at Anacapa Island, southern California in 1969; Blus 2003), sparrowhawk (near extinction in many agricultural areas in the 1950s and 1960s in Europe; Newton 1986), and many other avian species. Several groups of scientists focused on the biochemical and physiological events of shell thinning, although two decades elapsed before the complexity of the mechanism was fully realized (Lundholm 1997). Population-level effects of DDT and related organochlorine pesticides on other wildlife species were suspected to have occurred, a prime example being bats (Clark and Shore 2001). Other investigations began to focus on sublethal effects of DDT, including alterations in behavior and thyroid function.

In 1966, a Swedish scientist, Soren Jensen, reported several unknown peaks in a gas chromatogram that interfered with the quantification of DDT in environmental samples (Jensen 1966). These unknown peaks were subsequently identified as PCBs. Incidentally, some laboratories realized that previously reported DDT and metabolite values may have been falsely elevated by these interfering peaks. "Yusho" poisoning in man (1968), related to the ingestion of PCB-contaminated rice oil, elevated public awareness of the adverse effects of PCBs (Kuratsune et al. 1972). These discoveries ushered in an era of concern and investigation of the effects of PCBs and other industrial chemicals on wildlife. Numerous studies examined acute, chronic and reproductive toxicity of PCBs in birds and mammals. During the early 1960s, it was noted that ranch mink (*Mustela vison*) reproduced poorly when fed coho salmon (*Oncorhynchus kisutch*) from the Great Lakes, and it was eventually recognized that PCBs rather than DDT or dieldrin was the cause of reproductive failure (Aulerich and Ringer 1977). Reports describing the global distribution of DDT and PCBs in charismatic species of wildlife [e.g., white-tailed eagles (*Haliaeetus albicilla*), harbor seals (*Phoca vitulina*); George and Fear 1966; Jensen et al. 1969], even in remote regions like the Antarctic [e.g., adelie penguins (*Pygoscelis adeliae*), Weddell seal (*Leptonychotes weddelli*), Koeman and van Genderen 1966], raised further concern of the pervasive nature of pollution.

Widespread poisoning of birds and mammals by organomercury seed dressings and by mercury released at industrial sites (e.g., chlor-alkali plants, paper and pulp mills) was noted by the late 1960s. By the mid-1970s, dietary toxicity thresholds and adverse effects of methylmercury were described for game birds and mink, and considerable data on mercury concentrations in tissues of wildlife had been generated in field biomonitoring studies (Thompson 1996). Lead poisoning studies of various game bird species continued, and the oral toxicity of alternative materials (e.g., steel, copper, nickel, tin) for use as shot was investigated (Irby et al. 1967; Grandy et al. 1968). Massive chemical screening programs were initiated to examine the toxicity, repellency and hazard potential of chemicals to birds and mammals (Heath et al. 1972; Hill and Camardese 1986; Schafer and Bowles 1985; Schafer et al. 1983).

Scientific and technological advances in the 1970s

In 1969, Truhaut coined the term ecotoxicology as the logical extension of toxicology (i.e., the effects of poisons on individuals) to the ecological effects of pollutants (Truhaut 1977). Over the next decade, the size and diversity of research programs in government, academia and industry grew. Restrictions on the use of DDT and PCBs were instituted by many governments in North America and Europe by the early 1970s. Research continued on the hazards of chlorinated hydrocarbons, their declining concentrations in the environment and the recovery of affected

populations, including the sparrowhawk, brown pelican, and bald eagle (viz., "nature's great experiment").

Emphasis gradually shifted toward studies that addressed the toxicity of short half-life organophosphorus and carbamate pesticides that were presumed to be safer than organochlorine pesticides. Large scale field studies were launched examining anticholinesterase pesticide effects in birds and other non-target organisms (e.g., spruce budworm control in forest spray operations, grasshopper control on rangeland, mosquito abatement programs). These presumably "safer" insecticides were not without adverse effects on individuals, and perhaps even populations (reviewed in: Mineau 1991; Kendall and Lacher 1994; Grue et al. 1997; Hill 2003).

Indications that wildlife species were being adversely affected in the Great Lakes (particularly Lakes Erie and Ontario, and the upper St. Lawrence River; Gilbertson 1974) stimulated research and monitoring in that region. In the early 1970s, the Canadian Wildlife Service (CWS) initiated its herring gull (*Larus argentatus*) contaminant biomonitoring program (Burnett 1999; Hebert et al. 1999). This effort initially focused on organochlorine pesticides, PCBs and reproduction, and then expanded in scope to examine contemporary compounds and a wide array of biological and biochemical endpoints. The CWS had the foresight to establish a tissue bank which has proven to be an invaluable resource.

Research on contaminant exposure of marine mammals described elevated tissue concentrations of organochlorine compounds, cadmium, lead and mercury in numerous species of pinnipeds and cetaceans (reviewed in O'Shea and Tanabe 2003), and described detoxication mechanisms (metallothionein) to sequester cadmium (Olafson and Thompson 1974). Toxicological studies with captive seals (*Pusa hispida*) documented mercury excretion rates (Tillander et al. 1972), pathology and lethal tissue concentrations (O'Shea and Tanabe 2003). It was noted that females transferred contaminants to their young once they became reproductively active, and through observational science it became apparent that with increasing exposure, marine mammals progressed through stages of compensation, subtle effects, major disturbance, and eventually death (O'Shea and Tanabe 2003).

Oiling of birds and mammals following major petroleum spills (e.g., *Torrey Canyon* in 1967, Union Oil drilling platform in 1969, *Arrow* tanker in 1970) heightened public awareness of this environmental hazard, and by the mid-1970s studies of exposure pathways, and physiological and reproductive effects were undertaken (Albers 2003; Jessup and Leighton 1996). Observations that microliter quantities of crude oil on the shell of a bird egg could be embryotoxic were alarming. Towards the latter half of the 1970s, controlled exposure studies with game farm mallards, bobwhite (*Colinus virginianus*), and captive wild species of birds (e.g., American kestrel, *Falco sparverius*; black duck, *Anas rubripes*; black-crowned night heron, *Nycticorax nycticorax*; passerines) were initiated to determine sublethal responses to pesticides, petroleum crude oil and metals. Behavioral endpoints, physiological and endocrine function, reproduction, embryotoxicity and teratogenicity, histopathology, and biochemical indicators of exposure (e.g., activities of cholinesterase, delta-aminolevulinic acid dehydratase, and blood enzymes associated with cellular damage) were examined.

New infrastructure and large scale environmental problems in the 1980s

The establishment of the *Society of Environmental Toxicology and Chemistry* ushered in the 1980s. Graduate training programs in the area of ecotoxicology began to appear worldwide. The US FWS established a Division of Environmental Contaminants with a nationwide network of biologists that would go on to study contaminant issues both on and off National Wildlife Refuges. The US EPA built a new wildlife toxicology facility in Corvallis, Oregon. The Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (Superfund) and natural resource damage assessments fueled the environmental movement in the US. Wildlife research studies on hazardous waste sites and damage assessments gradually were initiated.

Studies of heavy metal pollution related to mining and smelting activities (Palmerton, Pennsylvania) examined effects at the level of the individual and population (Beyer and Storm 1995). Field monitoring and controlled exposure studies on PCBs in birds, and terrestrial and aquatic mammals continued, and by the close of the decade, potency estimates of individual PCB congeners and toxic equivalents began to be used for some wildlife species (Kubiak et al. 1989). Evidence supporting a Great Lakes Embryo Mortality, Edema, and Deformities Syndrome (GLEMEDS) in colonial fish-eating birds was compiled and described (Gilbertson et al. 1991). Interest in dioxins and dibenzofurans followed suit, and fortunately their effects on wildlife were much less widespread than suspected.

In the 1980s, epidemic-like death and embryo deformity in birds were observed at the Kesterson National Wildlife Refuge in California and were quickly linked to toxicity of the micronutrient selenium (Ohlendorf and Hothem 1994). Extensive monitoring and research on selenium and other elements in irrigation drainwater dominated much of the federal wildlife toxicology research effort through the 1980s. Forensic investigations of die-offs related to anti-

cholinesterase pesticides, rodenticides, and chlordane continued. Laboratory studies and field surveys of cyanide toxicity in wild birds were undertaken in response to death of wildlife at massive impoundments using new technologies for precious metal mining (Hill and Henry 1996). Field studies demonstrated that in addition to direct toxicity, insecticides, herbicides and agricultural practices were exerting dramatic effects on wildlife by altering habitat, vegetation and the insect prey base (reviewed in Sotherton and Holland 2003). Similarly, concerns related to acid precipitation documented that effects were principally indirect, related to alterations in habitat and changes in bioavailability of some metals. The meltdown of the Chernobyl nuclear reactor in 1986 fueled wildlife radiochemistry exposure and effects studies, and provided an opportunity to examine long-term population and genetic effects in many species (reviewed in Eisler 2003), especially small mammals (Chesser and Baker 2006).

After decades of research, the use of lead shot for hunting waterfowl and coots was phased out over a 5 year period in the US. Although it had been well-known that poisoning from the ingestion of lead shot accounted for the death of millions of wild birds annually (Pattee and Pain 2003), the driving factor for the lead shot ban was the realization that intoxicated or crippled waterfowl were causing secondary poisoning of the then endangered bald eagle (Pattee and Hennes 1983). In Canada, concern centered on findings that wings of first year waterfowl contained elevated concentrations of lead (Burnett 1999). At about the same time, the use of lead fishing sinkers was banned in the UK due to unintentional poisoning of mute swans (*Cygnus olor*; Pattee and Pain 2003). Toxicological testing and approval of "safe" alternatives to lead shot occurred by the early 1990s, although use of lead for hunting upland game birds and mammals continues, and has resulted in unintentional avian poisonings (Kendall et al. 1996; Pattee and Pain 2003). In the US, the Biomonitoring of Environmental Status and Trends program was established to systematically examine contaminant exposure and effects in fish and wildlife on a national scale (Zylstra 1994). Regrettably, the wildlife monitoring component stalled, and no large scale effort is currently in place for wildlife in the US.

The *Exxon Valdez* oil spill in Prince William Sound in 1989 was estimated to have caused the immediate death of 100,000–300,000 seabirds and 2,800–4,000 marine mammals (Albers 2003; Jessup and Leighton 1996). It resulted in the largest wildlife rehabilitation effort attempted to date, and made a long-lasting impression on the public and industry on legal aspects and compensation related to natural resource damage assessments. Fate and effects of petroleum related to the *Exxon Valdez* and Arabian Gulf War oil spills dominated the wildlife oil pollution literature through the 1990s, and included some population level assessments.

Biomarkers, endocrine disruption, amphibians and modeling in the 1990s

Symposia and research on bioindicators and biomarkers resulted in the development and application of many molecular assays (e.g., cytochrome P450, oxidative stress, genetic damage; McCarthy and Shugart 1990; Huggett et al. 1992) to assess contaminant exposure and effects, and some utilized nondestructive or minimally-invasive sample collection methods (Fossi and Leonzio 1994). Immunotoxic effects of contaminants were recognized as a factor contributing to numerous marine mammal die-offs (reviewed in O'Shea and Tanabe 2003). A major research effort identifying and testing wildlife sentinel species was initiated, yet field trials to assess potential effects of new pesticides on wildlife were phased out of the US EPA registration process for a variety of reasons (improvements in extrapolation, ecological risk assessments, and the need to streamline and expedite the registration process). Trans-boundary transport of contaminants in air and water, and international issues related to some highly toxic pesticides highlighted the global nature of pollution (e.g., monocrotophos used for grasshopper control caused a massive die-off of Swainson's hawk, *Buteo swainsoni*, in Argentina involving approximately 20,000 individuals; Hooper et al. 2003). Workshops on chemically-induced alterations of reproductive and endocrine function, along with the publication of *Our Stolen Future* (Colborn et al. 1996) launched a major effort to screen chemicals for endocrine-disrupting activity. Although much has been learned, and a few localized incidents have been described (e.g., feminization of alligators, *Alligator mississippiensis*, at Lake Apopka, Florida; Guillette et al. 1994), there is only moderate evidence for a causal linkage between endocrine-disrupting chemicals and effects in free-ranging wildlife (Hotchkiss et al. 2008).

Worldwide declines in amphibian populations resulted in new emphasis on laboratory and field studies of pesticides, metals and other pollutant effects in both amphibians and reptiles (Sparling et al. 2000). The Division of Environmental Quality (formerly the Division of Environmental Contaminants) of the US FWS initiated a nationwide survey of amphibian deformities on National Wildlife Refuges, including efforts to determine causation.

Effects of heavy metals released by mining activities were studied at numerous locations, and it was recognized that at some sites (Coeur d'Alene Basin in Idaho) free environmental lead (as opposed to lead shot) was resulting in the death of waterfowl and swans (Henny 2003). Concern over the hazard of lead artifacts (e.g., spent lead shot

and bullets at hunting sites and shooting ranges, lost lead fishing tackle) that were ingested by wildlife continued. Renewed interest and research on the hazard of mercury to wildlife occurred in response to recognition of its bioavailability near historic mining sites, its methylation to more toxic forms in freshwater systems, and widespread fish consumption advisories (Wiener et al. 2003).

Water quality guidelines were developed for DDT, PCBs, dioxin and mercury that specifically afforded protection to wildlife (US EPA 1995). Sophisticated techniques for assessing and modeling pollution effects on wildlife populations and communities were developed, although few empirical studies have examined large scale responses (Kendall and Lacher 1994; Albers et al. 2000). By the turn of the century, improvements and new techniques were developed for extrapolation of toxicant effects among species of vertebrates (body size scaling factors for birds, physiologically-based pharmacokinetic models, molecular basis for differential species sensitivity to dioxin-like compounds, toxicogenomics).

Emerging contaminant issues in the twenty-first century

Interest in brominated flame retardants occurred when it was found that concentrations in herring gull eggs from the Great Lakes had been doubling at 3–5 year intervals since the 1980s (Norstrom et al. 2002). Perfluoroalkyl substances were detected in wildlife on a global scale (Giesy and Kannan 2001), and work was initiated to generate toxic reference values for birds and mammals. The interconnections among wildlife toxicology, ecological integrity and human health received renewed emphasis, particularly in the area of risk assessment (Di Giulio and Benson 2002). Field exposure assessments began to quantify emerging contaminants including household and industrial surfactants, detergents, and pharmaceuticals. A remarkable forensic effort demonstrated secondary poisoning of *Gyps* vultures that fed upon carcasses of cattle treated with the non-steroidal anti-inflammatory drug diclofenac (Oaks et al. 2004). The vulture population in the Indian subcontinent was decimated, and this event constituted the first instance of a veterinary drug resulting in endangerment of a wildlife species. Recently, DDT use for the control of malaria has been initiated (World Health Organization 2005), although its indoor applications may not pose a serious threat to wildlife.

Perspective on wildlife toxicology

In some ways the field of wildlife toxicology seems to be at a crossroads. Over the years, scientific advances in analytical chemistry, biochemistry, ecology, population modeling and risk assessment have enhanced the stature of this field. However, as an applied discipline dealing with natural resources and their management, it continues to lag behind human-oriented toxicological research. Unexpected and unpredicted contaminant problems continue to drive the field of wildlife toxicology. In some instances, environmental contaminants could have resulted in extinction of species had not regulatory and remedial actions been undertaken. The actual cost of population recovery efforts for species such as the bald eagle, California condor (*Gymnogyps californianus*) and sparrowhawk has been astronomical. Our ability to predict hazard and prevent ecological mishaps remains limited. This can be attributed in part to logistical difficulties in studying wild animals, and the challenge of extrapolating data generated in vitro and in laboratory mammals to highly diverse free-ranging species. Some problems remain difficult to address (population consequences of molecular effects, the relative role of contaminants as one of many stressors affecting wildlife populations, screening the multitude of potentially toxic chemicals and extrapolating effects to highly diverse species). In many instances, human risk assessments do not adequately protect other biota, and for the most part wildlife toxicology continues to progress in response to exposure incidents and animal die-offs rather than proactive research. As a further challenge, interest, research funding and momentum in the field of wildlife toxicology has waned due to a shift in focus of environmental organizations and governments toward other looming issues such as global climate change and homeland security.

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