One Toxicology—Domestic & Wild Animals Are Sentinels for Humans (But Only When They Exist & are Carefully Observed)

Val Beasley DVM, PhD, Diplomate, American Board of Veterinary Toxicology Professor of Veterinary, Wildlife, & Ecological Toxicology Department of Veterinary & Biomedical Sciences

PennState

College of Agricultural Sciences

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Image: John Scott holding a canary cage used in coal mines rescue training at Cannock Chase, UK (Image courtesy of the Museum of Cannock Chase. Copyright unknown.)

Avian Respiratory Morphology & Physiology Bidirectional airflow through the trachea,..... but unidirectional airflow through the lungs....

....& birds have a very thin blood-gas barrier! → Absorb toxic gases faster than mammals! Historical 1890s-<u>1986</u>: Canaries in coal mines were sentinels of airborne toxicant exposures.



Data: https://en.wikipedia.org/wiki/John_Scott_Haldane

Image: Mining foreman, R. Thornburg, shows a small cage with a canary used for testing carbon monoxide gas in 1928. George McCaa, U.S. Bureau of Mines, <u>https://www.smithsonianmag.com/smart-news/story-real-canary-coal-mine-180961570/</u>

Today's World: The same airborne toxicants are important in homes – pet birds & families affected!

Methane, carbon monoxide.



from leaking gas lines or appliances.

from engines in garages & poorly-vented fossil-fuel heating systems.

Tangible. Immediate. Shared fate. Appreciated.





- Burning foods/overheating cooking oils, self-cleaning ovens.
- Fumes & particulates from overheated Teflon, Silverstone, & similar coatings, especially on drip pans.
- PAM spray.



- Second-hand tobacco smoke.
- Ammonia.
- Aerosol deodorants, perfumes, & hairsprays.

TODAY

- One Toxicology.
- Three Examples.
 - Outdoor Insecticides.
 - Local to Global Mercury.
 - Indoor Flame Retardants.
- Take Home Messages.

One Toxicology

If we consistently protected domestic & wild animals from environmental, food, & household contaminants, could we worry less about toxic impacts in humans?



Thyroid Adenoma in Cat

"Fireproof Killer Whales"

See: http://www.nrcresearchpress.com/doi/pdf/10.1139/f05-244

Environmental pollution is most extreme in developing nations,yet we do very little about it!

Images: Mr. Graeme Ellis, Dr. Mark E. Peterson, & Beasley Research Group. Data: Beasley 2009. http://www.instit/vet.italiana/2009/45.1/07.pdf



One Toxicology

The Lancet Commission on Pollution and Health (2017)

 If we consistently protected humans from environmental, food, & household contaminants, could we worry less about toxic impacts in domestic & wild animals?



Images: SuchichiO2 - Smog in Chaoyang, Beijing - https://commons.wikimedia.or./wiki/File/Smog_in_Chaoyang,_Beijinga

Impacts Depend on Genomes, Biochemical Receptors, Metabolism, Physiology, Lifestyles, Diets, Locations, & Human Choices (Exposures)

- All animals exposed to chemicals in their water, food, air, & soil.
- Domestic animals: Typically "stay home" & have "constant diets."
 - Pets:
 - Chemical exposures come from homes, yards & pet foods (e.g. melamine + cyanuric acid).
 - ----- Compressed lifespans relative to humans; but not enough are examined postmortem.
 - Farm animals:
 - Chemical exposures come from farm buildings, pastures, foodstuffs & water.
 - Meat-producing animals are killed & inspected when still young.
 - Dairy & breeding animals are killed & inspected when reproduction wains.
 - Wild animals: Diverse in form, function, habitats & exposures.
 - Game species (fish, birds, mammals) inspected by *people who fish & hunt*, & sometimes by *specialists* (e.g., deer at check stations examined by *veterinary pathologists*).
 - Wildlife veterinarians undertake field studies & sometimes examine road-kills.
 - Some = terrestrial; some = aquatic; & others = amphibious.
 - Mice range over a ~40 meter radius; Arctic terns & Swainson's hawks migrate >>20,000 miles each year.
 - Many eat plankton or plants... Many others are predators... & Some are top predators.



Daphnia live only 5-6 months; turkey vultures ~16 years; bowhead whales >200 years.







To Learn Enough to Protect Animals & People All At the Same Time

- Examine animals (alive & those that die) & their environments:
 - Clinical signs, physiological parameters, blood, urine, feces.
 - Gross postmortem & histopathology.
 - Food, water, sediments & soils, & air.
 - Appropriate specimens collected, packaged, labeled, shipped, & examined for infectious agents & toxic chemicals.
- <u>Undertake follow-up research</u> to establish <u>causation, mechanisms</u>, <u>impacts, diagnostic criteria</u>, & effective <u>therapies</u>.
 - In laboratories with the same species, surrogate species, & cultured tissues or cells.
 - In the field: studies of free-ranging animals.

Wild animals must be in peak condition to:

- Be effective in finding & competing for food.
 - Alertness, vision, smell, taste, coordination & strength, to find nutritious, "nontoxic" plants or to catch prey (milliseconds make a difference).
- Avoid becoming prey (milliseconds make a difference).
- **Compete for mates** (natural beauty, courtship behaviors).
- Breed & reproduce successfully.
- Protect & feed offspring.
- Survive extreme weather.
- **Resist infections** (without food handling training programs, hot water, detergents, disinfectants, refrigerators, stoves, facemasks, & vaccines).

Metals – Especially Mercury

Methylmercury (= MgHg = CH₃Hg⁺) Readily Biomagnified Up the Food Chain

(= in muscle of fish, crosses into the CNS & into developing young)

Plankton

Water

Humans Humans Humans Fish-eating fish Insect-eating fish Aquatic insects

Image: https://www.nps.gov/subjects/air/humanhealth-toxics.htm Data: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3139210/

mercury concentration

Mercury Then: Minamata, Japan

- In 1951, Chisso Chemical Company used mercury sulfate with a <u>new</u> <u>co-catalyst</u>* → Directly produced MeHg → Released to Minamata Bay.
- Soon, <u>dead fish</u> floated in the bay & catches by fishermen declined.
- In <u>1953</u>, <u>seabirds & crows</u> spiraled into the sea... & that same year...



http://www.med.or.jp/english/pdf/2006_03/112_118.pdf * Manganese dioxide changed to ferric sulfide. Fish-eating, mercury-poisoned cats were very unsteady, such that they sometimes held their limbs wide apart to maintain their balance.

Some of the cats knuckled over their hind paws.

<u>Some reports stated that affected cats "danced in</u> <u>circles</u>" (seizured) & they "<u>committed suicide</u>" (some fell into the bay & drowned).

Methylmercury

- In <u>1956</u>, <u>severe neurotoxicity</u> in <u>children</u> associated with <u>eating fish & shellfish of Minamata Bay</u>.
- In <u>1957</u>, poisoning was <u>reproduced in cats fed fish from</u> <u>the bay</u>.
- 11 years later, in <u>1968</u>, Chisso finally <u>stopped releasing</u> <u>MeHg</u>.
- By <u>2001</u>, <u>1,784 died</u> of <u>2,265 humans diagnosed</u> with MeHg poisoning; & ><u>10,000</u> were <u>compensated</u> after <u>lawsuits</u>.
- <u>Life-long effects in survivors!</u>

Mercury Now: Globally Important. Hotspots Important.



Image: US Fish & Wildlife Service - <u>https://usfwsnortheast.wordpress.com/2016/09/13/its-back-to-the-future-for-loons-in-massachusetts/</u> Data: <u>https://www.netl.doe.gov/File%20Library/Research/Coal/ewr/air-quality-research/Mercury-Soils-AQ-V.pdf</u>

Mercury Now: Globally Important. Hotspots Important.

- Australia, February 2018: MeHg mercury poisoning of dog & concerns for family members. → All were eating the same fish (seeking health benefits).
- History: "The dog was fed human-grade fish including Coles and Aldi branded Basa from Vietnam.
 - Basa (*Pangasius bocourti*) is a **commonly cultivated catfish in Vietnam**. It also goes by the names, "pangasius", "bocourti", "panga", "river cobbler", "cobbler", "swai", or any of these with "catfish".
- The dog had severe neurological signs with visual deficits, ataxia, tremors & mental dullness.
- Hair & blood analyses confirmed toxic concentrations of mercury.
- No other cause for the dog's neurologic signs were found based after MRI, CT, cerebral spinal fluid analysis, vit. B12 & thiamine analyses, & liver function testing. (Thiaminase in raw fish may cause illness → but, thiamine deficiency was ruled out).

- Historically: More Hg was sequestered in mineral deposits & coal.
- Human activity: Releases mercury & it circles the globe... deposition occurs in ~1 year.
- Coal burning was most important source, but now artisanal/small-scale gold = #1.



Data: Minamata Mercury Convention - http://www.mercuryconvention.org/Portals/11/documents/Awareness%20raising/FACT%20SHEETS/Minamata%20Convention%20on%20Mercury%20at%20a%20glance_COP1%202017.pdf, https://www.scientificamerican.com/article/new-catalyst-can-reduce-mercury-emissions/, http://www.wbcsdcement.org/pdf/MercuryReport%20Executive%20summary.pdf Image - UNEP = United Nations Environment Programme: http://wedocs.unep.org/bitstream/handle/20.500.11822/7984/-Global%20Assessment-201367.pdf?sequence=3&isAllowed=y



Power plants in Asia alone release 860T/yr.



Recent loadings of mercury in the environment are most bioavailable.

Data: https://www.nrdc.org/sites/default/files/potential-cobenefit-mercury-control-power-plants-china.pdf

Images: Pie Chart - Pacyna & Munth. Mercury Workshop in Brussels, Mar 29-30, 2004

Map – United Nations Environment Programme, Global Atmospheric Mercury. Assessment: Sources, Emissions and Transport, 2008, using 2005 data, as presented by the Arctic Monitoring and Assessment Programme Secretariat.

Mercury Concentrations in Fish: A Public Health Concern



Zebra Finch: Model for Avian Behavior

- We can't subject multiple species of wild animals to learning tests as they did with children of Faroe Island mothers who ate pilot whale meat.
- Captive zebra finches given a life-long diet with MeHg at 1.2 ppm (blood Hg ~8 to 25 ppm) → Ate less, lost weight, hyperactive, & impaired hearing & spatial memory, lower social hierarchy, hypersensitive to a predatory threat, delayed immunity & liver damage.

Data: Swaddle et al., 2017 - <u>http://jpswad.people.wm.edu/Swaddle%20et%20al%202017%20-%20Mercury%20and%20cognition.pdf</u>, Wolf et al., 2017 - <u>https://link.springer.com/article/10.1007/s10162-017-0619-7</u>, Kobiela et al., 2015 - <u>http://jpswad.people.wm.edu/Kobiela%20et%20al%202015.pdf</u> Also for loons & eagles, see Scheuhammer at al, 2008 - <u>https://link.springer.com/article/10.1007/s10646-007-0170-0</u>

Marilyn Spalding of the CVM of U Florida & Envirovet Students in 2010



MeHg Lethal to Great Egret Chicks

- Florida historically had low Hg emissions:



- Minor historical sources during droughts → Spontaneous oxidation of wetlands & Wildfires in wetlands.
- Florida incinerated medical wastes 1983-1991 → Emissions spiked+++.
 - Sphygmomanometers, bougies, thermometers, switches, thermostats, fluorescent tubes.
 - − In 1993, started autoclaving & landfilling medical wastes → Environmental Hg started downward.
 - Still, by 1998, largemouth bass contained Hg at ~2.5 ppm.
- In 2000, great egret chicks fed <u>fish</u> containing MeHg at 0.5 or 5 ppm:
 - Ate less & growth was slowed.
 - Most high-dose birds died by week 12.
 - Growing feathers (important excretory route) had highest Hg.
 - At 5 ppm in diet, <u>feathers (810 ppm)</u>, & <u>brain (35 ppm)</u>, <u>blood (93)</u>, & <u>liver (140)</u>.

Now: Because of the pollution controls, Hg in great egrets is markedly declining!

MeHg Endocrine Disruption in White Ibis.



- Reproduction has been low in Everglades crustacean- & fish-eating water birds, including white ibis.
- Nestling ibis collected from breeding colonies in Florida were placed in large aviary.
 - Starting at 90-days-old, fed pelletized <u>diet containing MeHg</u> at <u>concentrations</u> <u>found in wild (0.05, 0.1 or 0.3 ppm)</u> (the high dose = 0.28 ppm Hg).
 - Controls fed clean diet.
 - After they matured, ~<u>13% of the nests of birds fed Hg at any level had no</u>
 <u>offspring & at the high dose</u> → <u>35% fewer fledglings</u>.
 - <u>Low testosterone</u>.
 - Fewer offspring in heterosexual pairs.
 - <u>Male/male pairings</u> (55% of males at high dose).
 - High dose birds had mean blood Hg of ~4 ppm & mean feather Hg of ~37 ppm.
 - Low dose birds had mean blood Hg of ~0.7 ppm & mean feather Hg of ~7 ppm.

Image: US Fish & Wildlife Service - http://upload.wikimedia.org/wikipedia/commons/6/69/White_ibis_%289151955161%29.jpg Data: Frederick & Jayasena, 2011 - https://www.nps.gov/ever/learn/nature/upload/SecureWadingBirdReport2014.pdf. For more on effects of Hg on wildlife, see: http://www.nps.gov/ever/learn/nature/upload/SecureWadingBirdReport2014.pdf.

Arctic Ivory Gull Populations (Coastal Distribution) (Report from 2015)

- Feathers collected over 130 years were analyzed.
- Mercury increased almost 50-fold in that time.
- Current residues of MeHg feathers = 4.1 ppm.
- Ivory Gull populations in Canada decreased 80% since the 1980s.
- Authors concluded that MeHg may be playing a role in the decline.
- Mercury pollution at high latitudes is expected to continue increasing, in part, because of ongoing emissions & climate change.

Data: <u>http://rspb.royalsocietypublishing.org/content/282/1805/20150032</u> https://royalsociety.org/news/2015/03/mercury-pollution-danger-for-arctic-ivory-gulls/

Climate Change: Melting Permafrost as a Source of Hg Yukon River alone is releasing up to 5T of Hg/Year to Environment



Paul Schuster, of USGS:

- "What has happened in the past 30 yr is unprecedented."
- February 5, 2018: Schuster et al, in *Geophysical Research Letters*:
 - "Permafrost soils store nearly twice as much Hg as all other soils, the ocean, & the atmosphere combined, & this Hg is vulnerable to release as permafrost thaws...."
 - <u>30-99% of Arctic's near-surface permafrost is predicted to thaw by 2100</u>.

Images: National Park Service - https://www.nps.gov/scales/theparks/yuch/nationales/laure

Report US FWS:

 To protect sensitive species of birds that regularly consume fish & other aquatic organisms, <u>Hg in</u> <u>prey should not exceed 0.1</u> <u>ppm.</u>



How are we doing in Today's environment?

Image: Doug Racine, US Fish & Wildlife Service -

https://commons.wikimedia.org/wiki/File:Great_egret_eating_fish_at_Montezuma_National_Wildlife_Refuge. (8578390264).jpg Data: https://www.pwrc.usgs.gov/eisler/CHR_10_Mercury.pdf, Sørmo et al., 2011 - http://pubs.acs.org/doi/pdf/10.1021/es200478b, Cusack et al, 2017 - https://www.ncbi.nlm.nih.gov/pubmed/27928722



Data: FDA https://www.fda.gov/food/foodborneillnesscontaminants/metals/ucm115644.htm Image on right: Adapted from Biodiversity Research Institute. http://www.briloon.org/uploads/images/template/74/Fig7-LA-01-x980.jpg http://www.briloon.org/uploads/images/template/74/Fig7-LA-01-x980.jpg http://www.briloon.org/mercury-connections-landing-page/mercury-in-the-great-lakes-region

Some Regional Source of Mercury are "Fixable"



- In much of the US, the UK, & Sweden, concentrations peaked around 1960.
- Hg in paints in the USA was banned in 1990-1991.
- Hg being phased out in chloralkali plants.
- Current technologies for coal-burning power plants have reduced Hg emissions by ~90%.
- Artisanal gold: Methods are available to condense Hg in retorts; & better yet are concentration methods that capture heavy gold particles without Hg.

Images: Amanda Boyd/US Fish & Wildlife Service, US Fish & Wildlife Service - https://www.recreation.gov/recreationalAreaDetails.do?contractCode=NRSO&recAreald=1544

Data: https://www.recreation.gov/recreationalAreaDetails.do?contractCode=NRSO&recAreald=1544

Data: https://www.nps.gov/ever/learn/nature/upload/SecureWadingBirdReport2014.pdf, https://www.artisanalmining.org/casm/sites/artisanalmining.org/files/files/Pg53-89Ch5GoldAmalgamation.pdf, https://www.artisanalmining.org/casm/sites/artisanalmining.org/files/files/Pg53-89Ch5GoldAmalgamation.pdf, https://www.export.gov/article?id=European-Union-Marking-Labeling-and-Packaging-Overview https://www.export.gov/international-cooperation/artisanal-and-small-scale-gold-mining-without-mercurview.

Some Regional Source of Mercury are "Fixable"





 But, with A) current <u>high prices for gold</u> → prompting <u>artisanal gold</u> <u>mining</u>, B) <u>burning more coal</u> in <u>old & new-but-obsolete-technology</u> <u>power plants</u>, C) <u>improper disposal of wastes</u> (household, commercial, dental & medical), & D) <u>global climate change</u> →

People are still loading parts of the biosphere with Hg.

- A Way Forward: <u>STOP buying electricity & goods from producers who</u> foul the world with Hg.
- <u>Need universal ecolabeling & logos reflecting environmental</u> <u>stewardship (No Greenwashing).</u>

Images: US Fish & Wildlife Service - https://www.fws.gov/refuge/National_Key_Deer_Refuge/wildlife_and_habitat/birds/& https://training.fws.gov/resources/course-resources/es-slideshow/IMAGES.html Data: https://soils.ifas.ufl.edu/media/soilsifasufledu/sws-main-site/pdf/technical-papers/Howard-Nicole.pdf, https://www.artisanalmining.org/files/files/Pg53-89Ch5GoldAmalgamation.pdf, https://www.artisanalmining.org/files/files/Pg53-89Ch5GoldAmalgamation.pdf, https://www.export.gov/article?id=European-Union-Marking-Labeling-and-Packaging-Overview

Minamata Convention on Mercury

- = <u>A legally binding treaty</u>: The <u>US signed</u> on in 2013. Currently <u>86 nations</u>.
- Mercury uses & emissions must cover its life-cycle & be integrated into public health & environmental strategies at the local, regional, national & international levels as part of the overall pollution control agenda.
- <u>All sectors of society</u> must be involved with implementation, sharing the burden & benefiting from experience & expertise.
 - <u>No new mercury mines</u>, <u>close control</u> of mercury <u>exports</u>, <u>rapid phase-out</u> of mercury containing products.
 - <u>Expert guidance</u> on mercury handling, containment, disposal provided for energy & manufacturing sectors.
- Governments much reach out to their impacted communities.
 - <u>Legislation needed</u> to curtail illegal <u>traffic in Hg</u> (e.g. artisanal gold).
 - Artisanal gold mining communities need to know about, & be encouraged to use, alternatives.
- <u>Transparency</u> in national plans, sources, interim storage, disposal, & inventories of releases, & progress in reducing exposures.

Data: http://www.mercuryconvention.org/Portals/11/documents/meetings/cop1/KTM%20FINAL%202909.pdf,

http://www.mercuryconvention.org/Portals/11/documents/Awareness%20raising/UNEP%20PPT/Overview%20of%20the%20Minamata%20Convention%20on%20Mercury%20EN.pdf http://www.mercuryconvention.org/Portals/11/documents/Awareness%20raising/FACT%20SHEETS/Minamata%20Convention%20on%20Mercury%20at%20aglance_COP1%202017.pdf

Research Projects on Air Pollution, Birds (& Other Wildlife)

University of Turku in Finland – Research groups studying bats, birds, turtles, cell cultures due to exposures to <u>effluents from metal smelters</u>.
 Publications 2015-present:

- <u>Smelter workers</u> had increased numbers of <u>nasal, lung & stomach cancers</u>.
- Birds near the smelters—developed problems years before the people
 - They suffered from <u>direct toxicity & reduced food</u> availability
 - Pied flycatcher, Ficedula hypoleuca, had severe breeding & egg shell problems but they largely recovered over time after a ~99% decrease in the emissions of metal dusts from the smelter.
- Although wild birds are victims & sentinels for people, the <u>effects of air</u> <u>pollution on</u> wild or domestic <u>birds</u> are <u>rarely studied</u>.

Image: Ken Billington, https://commons.wkumed Data: https://www.utu.fi/en/units/sci/units/ende https://www.sciencedirect.com/science/ark/sci/sc https://www.researchgate.net/publics.hom/20972

/projects/birds_and_pollution/Pages/home.asny, http: 15001037, http://www.audubon.org/news/what-can-b r_incidence_among_conner_smelting_and_nickel_refir

can-birds-tell us-about-air-poll refining workers in Finland news/author/ken-bill article?id=10.1371/jou



r in Nickel Refinery Workers in Finland



Outdoor Insecticides

Image: U.S. Fish & Wildlife Service - https://www.fws.gov/mississippiES/images/mallard%20takeoff%20FWS%20image.JPG

- *Silent Spring* published **1962**, launched the environmental movement in the US.
- It described how animals & people were heavily exposed to pesticides, & documented links to serious illnesses & deaths.
- She was attacked by the chemical industry & some in government as an "alarmist" & "hysteric."
- Testifying before Congress in 1963, she called for new policies to protect human health & the environment.
- She **died in 1964** after a long battle with breast cancer.
- The US EPA was founded in 1970 & most of the laws that protect the environment today followed soon thereafter.





Insecticides Then: DDT

- Neurotoxic at Na⁺ & K⁺ channels.
- Inhibits calcification of eggshells.
- Estrogenic & anti-androgenic.

After WWII, massive amounts of DDT & other organochlorine insecticides used in agriculture, mosquito control & households.







Falco peregrinus Peregrine falcon





Haliaeetus leucocephalus Bald eagle





Images:

David Pereksta for US Fish & Wildlife Service - https://www.fws.gov/cno/newsroom/featured/2016/Brown Pelican Survey/; US Fish & Wildlife Service - https://www.fws.gov/midwest/eagle/; IS Fish & Wildlife Service - https://www.fws.gov/midwest/eagle/; IS Fish & Wildlife Service - <a hre

Pandion haliaetus Osprey Harmed by DDT



Image: Slightly modified from public domain - https://upload.wikimedia.org/wikipedia/commons/thumb/9/9f/Food_chain.png/160px-Food_chain.png

- Slow biodegradation/metabolism (crowded halogen atoms inhibit metabolism).
- Uncharged (neutral) molecules → cross blood-brain barrier & into developing offspring & mammary gland.
- When in an **anabolic** state → **Adipose (fat) depots**.
- But during catabolic states when animals mobilize lipids (e.g. migrating, egg laying, pregnant, & lactating). → Risk of toxicity in adults & *Firstborn young of top predators feeding in contaminated aquatic food webs are often massively exposed.*

After Publication of "Silent Spring"... ...DDT & many other chemicals that harmed wildlife populations & harmed or seriously threatened human health were banned from most or all uses!

Bald Eagle & Peregrine Falcon Recoveries after DDT was banned in 1972

(Listing & Delisting as Endangered Species in the US)



Bald Eagle Recovery in Pennsylvania

- History Commonly nested near Lake Erie but by 1973, only 3 pairs remained in PA.
- Shooting, disturbance, & habitat destruction, but DDT was most important in decline.
- 1983-1989: Pennsylvania released 92 Saskatchewan-born eaglets.
- By 2006, there were 106 nesting pairs in 31 of the state's 67 counties.



Breeding Bald Eagles in Pennsylvania: 1967-2006

Unique Exposures & Sensitivities of Birds

to Many Insecticides

• High metabolic rates:



• \rightarrow High intake of foodborne toxic chemicals.

- Rapidly lose body condition when feeding declines.
 Insecticides directly & indirectly affect feeding:
 - Direct: <u>Neurotoxicity</u> → <u>Stop eating</u> → <u>Malnutrition or starvation</u> (any spp.)
 - Indirect: <u>Kill organisms in foodweb</u> → <u>Malnutrition or starvation</u> (many spp.)
- ◆ Chronic Stress → Corticosterone → Immunosuppression → Infectious diseases.

Data: <u>http://eap.mcgill.ca/MagRack/JPR/JPR_14.htm</u> Image: US Fish & Wildlife Service - <u>https://www.fws.gov/refuge/Optima/contact.html</u>

Insecticides Now:

Fipronyl & Neonicotinoids

Fipronil = an ion channel blocker.

Clothianidin = a neonicotinoid.

Imidacloprid = a neonicotinoid.

Avian Toxicology: Fipronil



- Not as highly biomagnified as older organochlorines & more toxic to insects than birds, but <u>fipronil</u> is <u>not selective enough</u> to avoid direct avian toxicity.
- Neurotoxic (dropped wings, tremors, seizures) & thyrotoxic.
- Lethal poisoning from eating pre-treated seeds.
- Sublethal poisoning from treated seeds:
 - Reduced body condition, cellular immunity, carotenoid-based coloration, & steroid hormone levels, & especially reproduction.
 - Surviving offspring also have reduced cellular immunity.
- Toxic to insects, & potentially fish, lizards, & small mammals → Fewer of these prey → Malnutrition, stress, impaired reproduction in predatory species.
 - More research on impacts on predatory birds is needed.

Image: Marek Szczepanek, Creative Commons, <u>https://commons.wikimedia.org/wiki/File:Perdix_perdix_(Marek_Szczepanek).jpg</u> Data: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4284370/, http://pubs.acs.org/doi/full/10.1021/acs.est.5b03822?src=recsys,</u> <u>http://pubs.acs.org/doi/abs/10.1021/es0600678?prevSearch=fipronil&searchHistoryKey, http://www.sciencedirect.com/science/article/pii/S0045653510014621?via%3Dihub <u>https://link.springer.com/content/pdf/10.1007%2F978-1-4899-7283-5_1.pdf</u> In Reviews of Environmental Contamination and Toxicology 176, 2003. George Ware, Ed.</u>

Avian Toxicology: Neonicotinoids



- Neonicotinoids (e.g., Imidocloprid & Clothianidin) are the most important & fastest growing insecticides in the market.
- Although they are unlikely to biomagnify, & are less toxic to birds than insects, neonicotinoids are <u>not selective enough</u>.
- Direct exposure from spraying \rightarrow May kill sensitive spp. of birds.
- One to a few treated seeds \rightarrow May kill granivorous birds.
 - November 2016: Hundreds of red-winged blackbirds & other spp. died after eating imidacloprid-treated wheat seed that had been broadcast on a field in southern NJ.

Stimulation → Ataxia → Crash injuries (fractures, hemorrhages) & paresis, paralysis & apathy → vulnerable to predation.

Image: Walter Siegmund, Creative Commons - <u>https://commons.wikimedia.org/wiki/File:Agelaius_phoeniceus_0110_taxo.jpg</u> Data: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4284370/, http://biology-web.nmsu.edu/~houde/neonicotinoid%20insecticides.pdf</u>, Hallman et al Nature 2014: <u>https://www.nature.com/articles/nature13531</u> & Mineau & Palmer 2015: <u>https://abcbirds.org/wp-content/uploads/2015/05/Neonic_FINAL.pdf</u> <u>https://www.sciencedirect.com/science/article/pii/S0045653514013848</u>

Avian Toxicology: Neonicotinoids

- At well below lethal doses: Genotoxicity & reduced immunity, growth, & reproduction.
- Deplete invertebrate prey base needed by many spp. of birds.
- In the Netherlands, areas with high imidocloprid use are seeing average declines in insectivorous bird populations of 3.5%/year!



Image: Frebeck, Creative Commons - <u>https://commons.wikimedia.org/wiki/File:Wiesenschafstelze.JPG</u> Data: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4284370/, http://biology-web.nmsu.edu/~houde/neonicotinoid%20insecticides.pdf,</u> <u>http://www.sciencedirect.com/science/article/pii/S0045653510014621?via%3Dihub</u> & Hallman et al Nature 2014: <u>https://www.nature.com/articles/nature13531</u>

Protecting bees might also protect birds from these insecticides.

• *Neurotoxicity in bees* from fipronil & neonicotinoids:

(& bees seem to become addicted to neonicotinoids as people do to nicotine).

- Honey bees don't find way back to hives.
- Bumblebees are especially susceptible.
- Bees have fewer young.



- <u>Neonicotinoids & fipronil increase infectious diseases in bees</u>.
- 2009: USEPA banned fipronil corn seed treatments.
- 2013: Europe severely restricted neonicotinoids & fipronil.
- 2015: Montreal, Canada banned neonicotinoids.
- 2017: <u>Europe banned fipronil</u> in agriculture.



• 2018: US neonicotinoids being reviewed under current EPA Administrator.

Data: https://www.epa.gov/pollinator-protection/schedule-review-neonicotinoid-pesticides, https://www.nature.com/articles/srep24764, https://www.nature.com/articles/nature14414 https://pdfs.semanticscholar.org/1411/367f122c43218cca15d219025fac062b4367.pdf, http://onlinelibrary.wiley.com/doi/10.1002/ps.4489/full,

http://www.sciencedirect.com/science/article/pii/S2214574515000917, https://www.ncbi.nlm.nih.gov/pubmed/25703042,

https://ec.europa.eu/food/plant/pesticides/approval_active_substances/approval_renewal/neonicotinoids_en,

http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0091686,

http://heinonline.org/HOL/Page?handle=hein.journals/sjel7&div=5&g_sent=1&casa_token=&collection=journals

Image: Lance Gheung, USDA - https://nifa.usda.gov/national-monitoring-plan-native-bees-stakeholder-and-public-listening-session

Advocacy group (NRDC) summary: https://www.nrdc.org/experts/jennifer-sass/neonicotinoid-pesticides-still-bad-bees-two-studies-nature-journal-add

What if Fipronil & Available Neonicotinoids are Withdrawn?

- Other (*currently available, potentially more toxic*) organophosphorus insecticides may be used instead.
- Need more:
 - *Highly selective insecticides* (to target pest insects, not insects that prey on them, & not birds, bats, or other spp.).
 - Integrated pest management (IPM).
 - Integrated biodiversity management (to protect more species).
 - Crop rotation & better selection of crop varieties.
 - Companion plantings to support life cycles of more predatory insects.
 - Insect traps, pheromones, & economic spray thresholds.
- Scientists working, but an ongoing story & pressure + funding drive research, innovation, & protection....

Data: https://www.epa.gov/pollinator-protection/schedule-review-neonicotinoid-pesticides, https://www.nature.com/articles/srep24764, https://pdfs.semanticscholar.org/1411/367f122c43218cca15d219025fac062b4367.pdf, http://onlinelibrary.wiley.com/doi/10.1002/ps.4489/full, http://www.sciencedirect.com/science/article/pii/S2214574515000917, https://www.ncbi.nlm.nih.gov/pubmed/25703042, https://ec.europa.eu/food/plant/pesticides/approval_active_substances/approval_renewal/neonicotinoids_en, http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0091686, http://onlinelibrary.wiley.com/doi/10.1002/ps.4715/full http://heinonline.org/HOL/Page?handle=hein.journals/sjel7&div=5&g_sent=1&casa_token=&collection=journals Advocacy group (NRDC) summary: https://www.nrdc.org/experts/jennifer-sass/neonicotinoid-pesticides-still-bad-bees-two-studies-nature-journal-add

Halogenated Persistent Organic Pollutants (POPs)



PCBs & PBDEs





similar structures.

somewhat less

persistent than PCBs,

but biomagnification is

still a major concern.

PBDEs may be

- Humans, domestic animals, wildlife are exposed from development of gametes & fertilized ova through death.
- **Biomagnification** \rightarrow Food chain exposures important.
- Thyroid problems.
 - Weight loss.
- **Reproductive** problems.
- Cancers.
- **Developmental** disorders.
- Learning deficits.
- Behavioral problems.
- Nephrotoxicity.
- Hepatotoxicity.
- **Dermal** toxicity.

PCBs: A Slow Success Story in Progress: Trends in Concentrations US Great Lakes Fish

Great Lakes Fish Monitoring and Surveillance Program Mean Total PCB Concentration (ppb) in Lake Trout/Walleye from 1991 through 2009



PBDEs: A LESSON RELEARNED?





*Lanthanide Series	58	59	60	61	62	63	64	65	66	67	68	69	70	71
	Ce	Pr	Nd	Pm	Sm	EU	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu
	Cerium	Proseodymium	Neodymium	Prometificam	Samerium	Europium	Gedelinium	Terbium	Dysprosium	Halmium	Erbium	Thuliom	YBerbium	Lotetion
	Ido.115	140.9077	144.24	(1.4.5)	150.36	151 965	157.25	158.9254	162.50	164 9303	167-26	168 9342	173,04	174.967
[†] Actinide Series	90	91	92	93	94	95	96	97	98	99	100	101	102	103
	Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr
	Thorium	Protoctinium	Uranium	Neptusium	Fistoniam	Ame/icium	Carrum	Berkalium	Californium	Einsteinigere	farmium	Mendelevium	Nobelium	Lowrencum
	232.0381	231.0359	238.0289	237.048	[244]	[243]	(247]	(247)	[251]	(257)	[257]	(238)	1259	(260)

Image: Size of killer whale compared to a human. Credit: Chris Huh, Creative Commons By-SA 3.0

http://marinesciencetoday.com/2013/11/22/oceans-toughest-predators-great-white-shark-vs-killer-whale/

What are PBDEs? Polybrominated Diphenyl Ethers









A penta-BDE

An octa-BDE

Deca-BDE

Flame Retardants 209 Congeners 3 <u>Mixtures</u>: Penta, Octa, & Deca

Made by:

Dead Sea Bromine Group, Israel Albemarle Corporation, VA Great Lakes Chemical Corporation, West Lafayette, IN

Polybrominated Diphenyl Ethers (**PBDEs**): **Thyroid Adenomas** → Clinical **Hyperthyroidism** in **Cats**





Hyperthyroidism in cats became an important cause of morbidity & mortality.

Images of hyperthyroid cats: Dr. Mark E. Peterson, Veterinary Endocrinologist

Are Cats Sentinels for Human Exposures & Effects of PBDE? Are PBDEs a Cause of Feline Hyperthyroidism?



Structures of two common PBDE congeners compared to thyroid hormones (T3 & T4)

- Many house cats live indoors ~100% of the time, & sleep (a lot) on warm objects, like padded furniture & electronic equipment.
- PBDEs first commercially produced in 1970s.
- First case report of feline hyperthyroidism published in 1979.
 - Dye et al (2007) examined 11 hyperthyroid & 12 normal cats.
 - PBDE concentrations in cats were 20- to 100-fold those of U.S. adults.
 - Cat food (dry & canned) & house dust (esp. BDE47 & 99, likely from penta mixture) contributed to body burdens.
 - Cats *may be* sentinels of chronic human exposures & (perhaps) *adverse health effects from PBDEs.*



Cats in Homes with High PBDEs in Dust More Likely to Develop Hyperthyroidism Mensching et al (2012)



- Tested blood from 62 owned cats (with & without hyperthyroidism)
 & 10 feral cats.
- Obtained house dust (from vacuum bags).
- Feral cats had very low PBDE concentrations & T4s:
 - Their T4 values were ~1/2 of those of indoor euthyroid cats & ~1/4 of those of indoor hyperthyroid cats.
- Total PBDEs in canned cat food = 0.42-3.1 ppb, but <u>dust</u> from <u>homes</u> of <u>hyperthyroid cats</u> had <u>1,100-</u> <u>95,000 ppb</u>.

- One of the hyperthryoid cats had total PBDEs at 51,000 ppb in serum lipid (highest found in any species?).
- <u>PBDEs in dust</u> were <u>correlated</u> with abnormally <u>high T4</u> <u>levels</u>.
- Cats may be sensitive sentinels for PBDE exposures & risks of toxic nodular goiter in humans.

Hyperthyroid Cats Have Higher PBDE Burdens Guo et al (2012; 2016)

- 11 hyperthyroid & 11 normal cats.
- PBDE concentrations in cats were about 60-times higher than in humans.
- Concentrations of PBDEs in cats >> PCBs & DDE.

ng/g Lipid

- In addition to PBDEs from living indoors, thyroiddisrupting compounds in water & BPA in cat food may be involved.
- Fortunately PBDE concentrations have declined in some homes (small N).



Contaminants in Serum Lipid 2008-2010 vs. 2012-2013

Concentrations of PBDEs declined unlike PCBs & DDE.

Hyperthyroid Cats Have Higher PBDE Burdens

- Norrgran et al (2015): PBDE concentrations in cats were correlated with hyperthyroidism.
- Walter et al (2017): Hyperthyroid cats had higher concentrations of 4 PBDE congeners than normal cats.
 - Total **PBDE** concentrations **in cats** were **50x higher than** in **humans** of a similar area, whereas PCB concentrations in cats & people were similar.

OVERALL:

- Housecats = Sentinels for human exposure to PBDEs
 & possible thyroid disruption.
- Challenge of funding 15-year-long studies in cats.

Data: Norrgran et al. Environmental Science & Technology, 2015. <u>http://pubs.acs.org/doi/abs/10.1021/acs.est.5b00234</u> Walter, Lin, Kass, Puschner. 2017. BMC Veterinary Research. <u>https://www.ncbi.nlm.nih.gov/pubmed/28468659</u>

PBDEs in Outdoor Environments





Image: Orca & Pilot whale – NOAA Photo Library, Peregrine falcon – Barb Baldinger, MDNR volunteer in http://www.mlive.com/news/flint/index.ssf/2013/05/endangered_falcons_making_a_ho.html Data: http://www.noaanews.noaa.gov/stories2009/20090401 ecosystems.html, https://ehp.niehs.nih.gov/wp-content/uploads/2017/07/EHP2098.alt .pdf, https://www.ncbi.nlm.nih.gov/pubmed/19680967 & http://deohs.washington.edu/srp/sites/deohs.washington.edu.srp/files/images/D Rice Agency Seminar SBRP 3-08.pdf

PBDEs from household & industrial wastes → Surface waters → Fish & shellfish → Predators

Photodegradation is slow.

Aquatic environmental accumulation evident by ~1980.

PBDE Trends in Great Lakes Trout & Walleye (1980-2000)



From Zhu and Hites, Environ. Sci. Technol., 38 (10): 2779-84, 2004.

Species - PBDE Body Burdens

Chinook salmon (BC) 2.3 ppb w/w Buffalo River (NY) carp 13-23 ppb w/w Lake Superior smelt 150 ppb lipid Lake Michigan salmonids 80 ppb w/w Lake Huron trout 237 ppb lipid Lake Ontario smelt 240 ppb lipid Lake Ontario trout 545 ppb lipid Polar bear 7.6- ~70 ppb lipid Sperm whales (Dutch coast) ~100 ppb w/w White-beaked dolphin (Dutch coast) >700 ppb w/w Harbor seals (Dutch coast) >100 ppb w/w Beluga whales (Quebec) 20-~1000 ppb w/w Pilot whales (Faroe Islands) 843-3160 ppb lipid Orca/killer whale (Pacific NW) 8,560 ppb w/w Peregrine falcon eggs (Sweden) 39,000 ppb lipid

Are PBDE-induced Thyroid & Neurologic Diseases a Wildlife Concern?

- Increased susceptibility to hypothermia, infections, failed reproduction?
- Impaired brain development & capacity to learn?

1.44

- Increased risk of predation?
- Decreased energy & concentration for the hunt?



PBDEs On the Legal Front

Companies & governments moving away from PBDEs Stockholm Convention → Manufacture has fallen off. Products still in homes & being discarded.

- 1970s: First manufactured.
- 1989: Voluntary cessation, Germany.
- 1998: Penta banned, Sweden.
- 2004: Penta & Octa banned, EU.
- 2004: Voluntary cessation of Penta & Octa by Great Lakes Chemical Corp., US.
- 2006: California phase out of Penta & Octa.
- 2008: California phase out all but Deca.
- 2008: All PBDEs phased out in EU.
- 2013: No manufacture or import of Deca into US.

PBDEs in Products: What can we do now?

- Fix damaged upholstery.
- Place mattresses in covers designed to minimize exposures to allergens.
- **Vacuum** often & thoroughly, preferably with a high-efficiency particulate air (HEPA) filter.
- Purchase new furniture, fabrics, etc. that have no halogenated flame retardants.
- Note:
 - Disposing of PBDE-containing materials → Environmental contamination + Risks to workers in recycling facilities + Hand-off of contaminants to unsuspecting consumers (recycled carpet padding).
 - Workers in recycling facilities need **Personal Protective Equipment (PPE).**
 - **Burning** PBDEs at low temperatures can produce **dioxins & dibenzofurans** (higher toxicity).
 - Innovations are needed to develop safe disposal methods!
 - The US & Canadian governments are just getting underway in controlling emissions into the Great Lakes!

Data: <u>https://www.pharosproject.net/uploads/files/sources/1/e5ca3f715bb8c16764482235439a226273c140c0.pdf</u>, <u>http://ijc.org/files/publications/Polybrominated_Diphenyl_Ethers_Great_Lakes_EN.PDF &</u> <u>https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/polybrominated-diphenyl-ethers-pbdes</u>

Take Home Messages

- One Toxicology is central to One Health.
- Mercury is an important pollutant today.
- DDT devastated birds, but current insecticides can poison them & their foodwebs.
- Halogenated flame retardants will harm animals for decades to come.
- More diagnoses, more careful usage & disposal, & more green chemistry are essential.

Is This Fun or What?

1

Image: Beasley Lab Group

Image: Beasley Lab Group

Comparative Environmental Bioscience...



"The existence of groups would have been of simpler significance, if one group had been exclusively fitted to inhabit the land and another the water; one to feed on flesh, another on vegetable matter, and so on; but the case is widely different, for it is notorious how commonly members of even the same sub-group have different habits."

Charles Darwin Origin of Species