Effects of PPCPs on Wildlife: What do we really know?

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Potential Routes of Exposure
Sewage Effluent and Hermaphrodisism in Fish

- First Observed in Roach in the UK

- Germany, UK, US, Denmark, The Netherlands, Canada, South Africa, Spain and others

- Roach, white sucker, flounder, bass, sunfish, catfish, carp, salmon, perch, etc.

- 0-100% incidence intersex, often ~15-35%
Sewage Effluent and Hermaphroditism in Fish

• Other Effects
  – Vitellogenin induction in males (gold standard)
  – Abnormal spermatogenesis, gonadal ducts
  – Diminished secondary sexual characters
  – Effects in females include extended period of Vtg production, delayed oocyte maturation, atretic follicles

• Can intersex fish reproduce? May have fewer and less motile sperm as well as behavioral and/or morphological changes that confer disadvantage

• Population-level impacts?
Sewage Effluent and Hermaphrodisim in Fish

• 17α-ethynylestradiol most potent ED in effluent - LOEC 0.1-1.0 ng/L

• Kidd et al. dosed 34 ha lake with 17α-ethynylestradiol for 3 years (avg 4.8 to 6.1 ng/L)
  - examined fathead minnow population 7 years
  • Vtg in males 3 x reference
  • All males delayed spermatogenesis, fibrosis, malformed tubules
  • 44% intersex in year 2
  • High Vtg, delayed ovarian development, accelerated oocyte maturation, atretic follicles (rare in ref) in females
  • Population crashed, catch/effort from 180 before dosing to 0.1 in 5th year after start
  • Pearl dace
Toxic Effects of Sewage Effluent in Fish

• Liney et al. exposed juvenile roach to effluent at 0, 15, 35 and 79% levels.
  
  - Levels that produced intersex and Vtg induction also affected kidney development, immune function, and caused genotoxic damage.
  
  - These toxic effects occurred at effluent concentrations < those producing reproductive system effects.
SSRIs in Fish and Frogs

- Inhibit reuptake of serotonin (found in all animals), repeatedly stimulating postsynaptic receptors

- >33m prescriptions for Prozac alone in US in 2002

- Fluoxetine (Prozac) detected in effluents to 0.099 ppb (Metcalfe et al. 2003); Kolpin et al. one stream at 0.012 ppb

- Concentrations of fluoxetine and sertraline (Zoloft, Lustral) and 2 metabolites as high as 16 ng/g in 4 species of fish in municipal-effluent dominated stream in TX (Brooks et al.)
SSRIs in Fish and Frogs

- Marsha Black et al. University of Georgia
  - Fluoxetine caused behavioral changes in mosquitofish as low as 0.6 ppb; delayed maturity 6 ppb.
  - Delayed development and increased time to metamorphosis in *Xenopus* at 30 ppb (NOEC 2.95 ppb?)
  - Reduced mass and limb malformations a lowest treatment level- 0.059 ppb
  - No effects observed in gray tree frog
Triclosan and Thyroid Hormone-Associated Anuran Development

- Antibacterial agent in PCP, food handling, clothing, surgical supplies

- 0.01-0.65 g/L in effluent, 0.4-12 g/g in sludge; Kolpin et al. 55% of streams @ median of 0.14 g/L

- Detected in human breast milk, fish, shellfish

- Similar structure to TH and non-steroidal estrogens

- May be weakly androgenic
Triclosan and TH Associated Anuran Development

- Overt toxic effects in native anurans and fish at high concentrations demonstrated. Toxicity thresholds for fish well above conc. in effluent
- Veldhoen et al. – examined subtle effects on metamorphosis (TH mediated) in frogs
  - Environmentally-relevant concentrations as low as 0.15 μg/L disrupted thyroid hormone-associated gene expression and altered the rate of thyroid hormone-mediated postembryonic anuran development.
Synthetic Musks

- Detected in adipose tissue of humans (milk), fish, shellfish, crustaceans, marine mammals
- Found in the atmosphere along with receiving waters and sediments
- Inhibits efflux transporters in mussel gills—may affect organisms ability to rid of xenobiotics
- Weakly estrogenic and antiestrogenic in vitro and in vivo
- Otherwise very little known about possible health effects
- Importance to human and environmental health controversial.
Diclofenac and Vultures

• Dramatic declines (95%) in 3 species of vultures in India as well as Pakistan, Nepal, and others since 1990s. Critically endangered.

• Necropsies revealed acute gout

• Suspected disease, pesticides

• Birds with gout had high concentrations of NSAID diclofenac in kidneys
Diclofenac and Vultures

• Cheap, effective treatment of inflammation, pain and fever in livestock, used throughout SE Asia

• Dead cattle skinned and left to be scavenged; decline in vultures resulted in increased feral dogs

• Only 1 in 760 contaminated carcasses necessary to cause declines

• Diclofenac banned for general veterinary use in India, Nepal; meloxicam safer alternative
Research Needs

• Population-level studies, especially open systems

• Transfer from aquatic to terrestrial systems, e.g., fluoxetine in sunfish>herons, otters, etc.?

• Examine presence, fate and effects of:
  – antiestrogenic (tamoxifen), androgenic and antiandrogenic (flutamide) chemicals;
  – Proestrogens, e.g., soy isoflavone formononetin> equol
  – Metabolites of PPCP
  – Chemicals with demonstrated potential for environmental impacts beyond effluent plume e.g., musks

• Consider Possible Wildlife Exposure to Veterinary Drugs
COUNTERTHINK

Is it a boy or a girl?

Both, actually, thanks to all the chemicals in the water these days.

Fact: Pharmaceuticals destroy aquatic ecosystems.