

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



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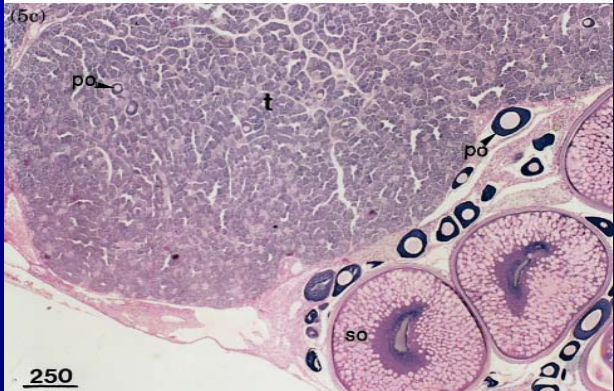
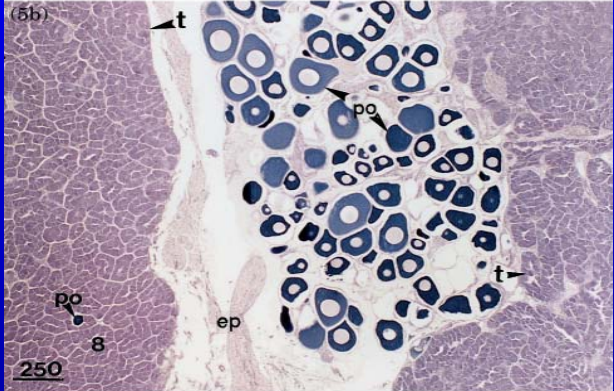
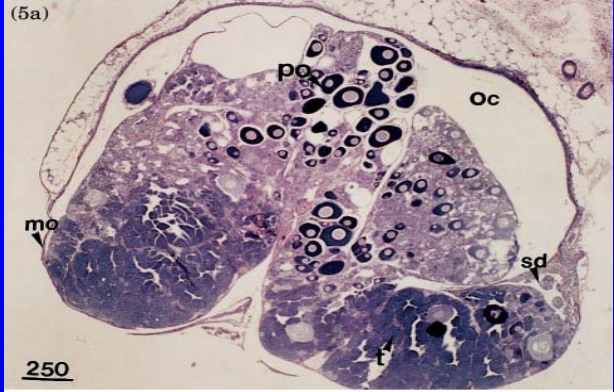
Potential Routes of Exposure



Sewage Effluent and Hermaphroditism 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 Hermaphroditism in Fish

- 17 α -ethynylestradiol most potent ED in effluent - LOEC 0.1-1.0 ng/L
- Kidd et al. dosed 34 ha lake with 17 α -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 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

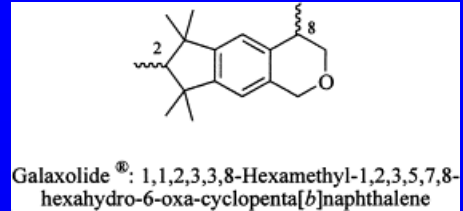
- **Antibacterial agent in PCP, food handling, clothing, surgical supplies**
- **0.01-0.65 $\mu\text{g/L}$ in effluent, 0.4-12 $\mu\text{g/g}$ in sludge; Kolpin et al. 55% of streams @ median of 0.14 $\mu\text{g/L}$**
- **Detected in human breast milk, fish, shellfish**
- **Similar structure to TH and 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 μ g/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

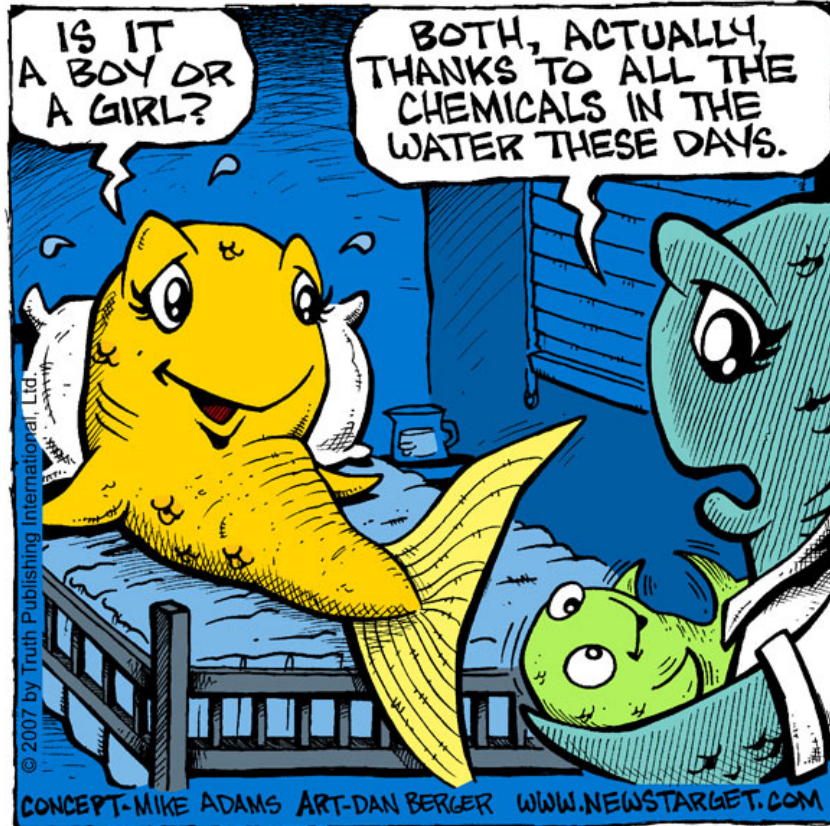
- **Cheap, effective treatment of inflammation, pain and fever in livestock, used throughout Se Asia**
- **Dead cattle skinned and left to be scavenged; decline in vultures resulted in increased feral dogs**
- **Only 1 in 760 contaminated carcasses necessary to cause declines**
- **Diclofenac banned 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



**FACT: PHARMACEUTICALS DESTROY
AQUATIC ECOSYSTEMS.**