Anthropogenic Chemicals: Pharmaceuticals and Personal Care Products

Joanne Parrott,
Science and Technology Branch,
Environment Canada, 867 Lakeshore Road,
Burlington, ON L7R 4A6

Why Worry about Pharmaceuticals?

- Pharmaceuticals are *designed* to have a therapeutic (=biological) effect
  - Effects on non-target organisms are mostly unknown
- Aquatic organisms are chronically exposed
- Potential for multigenerational exposure
- Little known about environmental persistence, fate

If pharmaceuticals are present at such low concentrations in surface water, then why are we concerned about them?

The main reason is because they are designed to have a biological effect and can be hormonally active, even at very low concentrations.

Since these compounds are present at such low concentrations, we aren't really concerned about acute toxicity, but rather effects that are the result of chronic exposure.

Since pharmaceuticals are entering streams on a regular basis through sewage treatment effluent, exposure is ongoing and would affect multiple generations of aquatic organisms.

Pharmaceuticals also have the potential to effect organisms at

Personal Care Products

Bath additives, shampoos, skin care products, hair sprays, oral hygiene, soaps, detergents

Fragrances

Preservatives

Disinfectants/Antiseptics

Sunscreen Agents

Daughton and Ternes (1999)

"Emerging Contaminants"

Our ability to detect them is emerging…

We can detect about 150 PPCPs…there are over 4,000 available on the market in Canada.

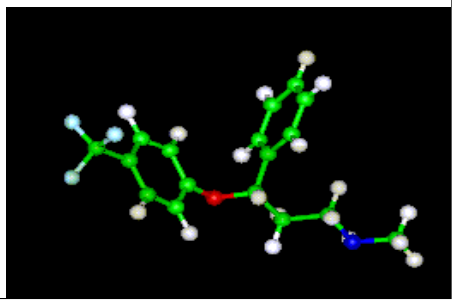
Pharmaceuticals and Personal Care Products (PPCPs) to Examine

Effects in lab organisms at low concentrations (low ug/L or below)… compare to levels in municipal wastewater effluents (MWWEs) and Great Lakes rivers and waters

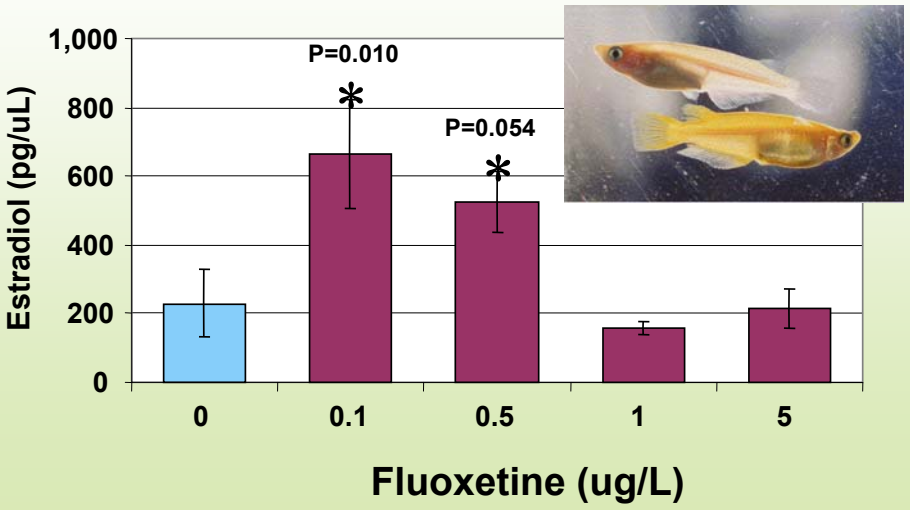
- **antidepressant - Fluoxetine, Fluvoxamine**
- **anti-inflammatory - Diclofenac**
- **heart drug - Propranolol**
- **fragrance - HHCB, Synthetic musk**
- **synthetic hormone - Ethinylestradiol**
- **complex effluent mixtures - MWWEs**

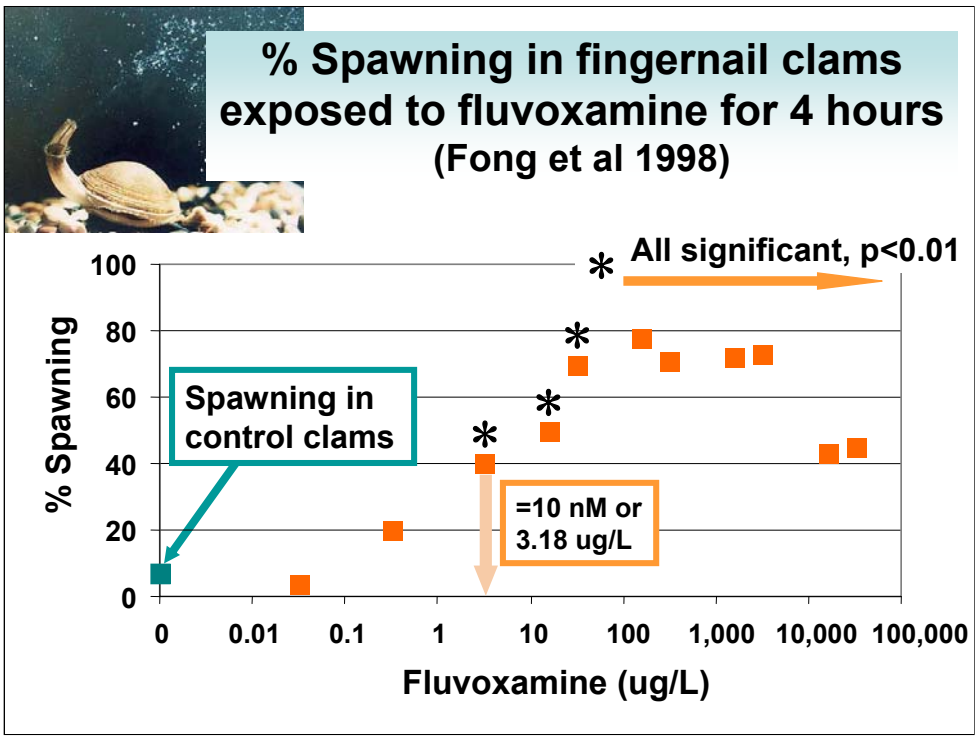
Fluoxetine

Antidepressant, anti-anxiety drug

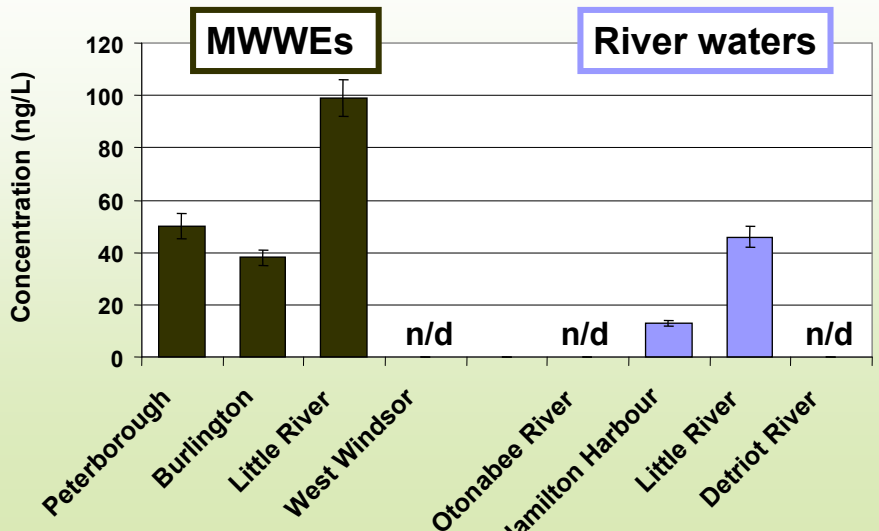


Plasma Estradiol in Female Medaka Exposed to Fluoxetine (Foran et al 2004)



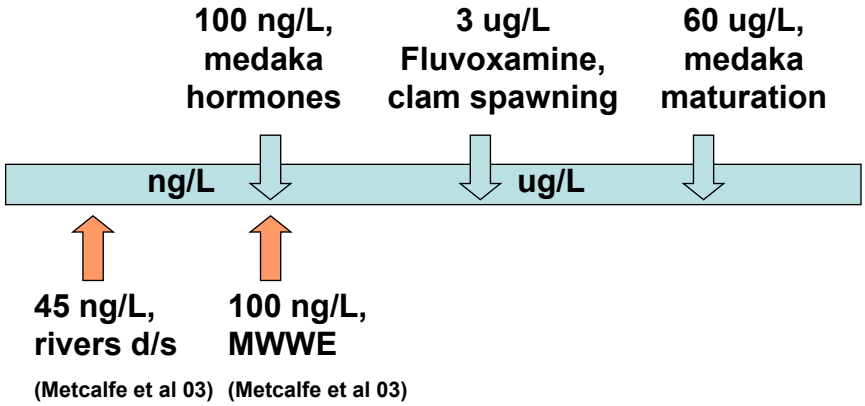


Concentrations of Fluoxetine in Great Lakes MWWEs and river waters (from Metcalfe et al 2003)



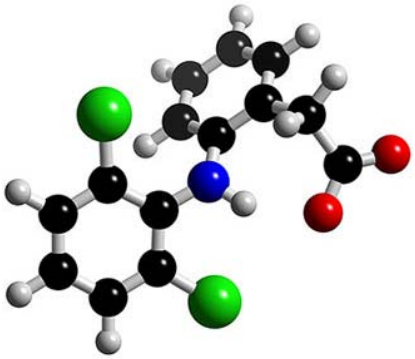
Fluoxetine

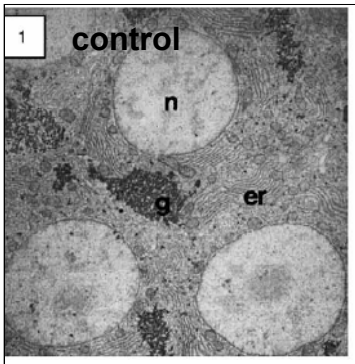
Antidepressant, anti-anxiety drug



Non-steroidal, Anti-inflammatory drug (NSAID)

Diclofenac



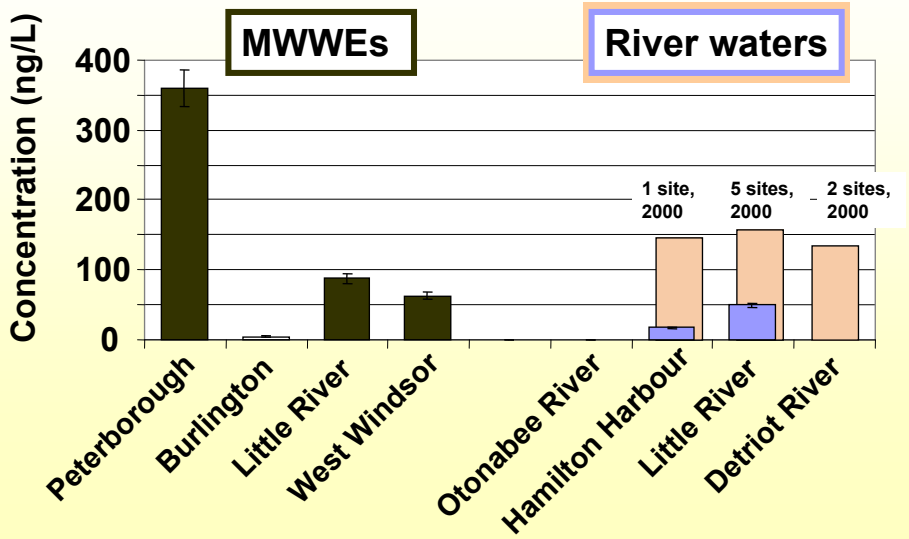


Liver - Hepatocytes - solvent control rainbow trout

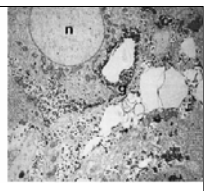
- **round nuclei (n)**
- **regularly arranged ER (er)**
- **glycogen storage areas (g)**

(magnification: 4200×).

Concentrations of Diclofenac in Great Lakes MWWEs and River Waters (from Metcalfe et al 2003)



Diclofenac



Non-steroidal, Anti-inflammatory drug (NSAID)

0.5 ug/L gill changes, 1 ug/L liver changes, rainbow trout

50-150 ng/L, rivers

(Metcalfe et al, 2003)

215 ng/L, MWWE, summer

(Lishman et al, 2005)

360 ng/L, max MWWE

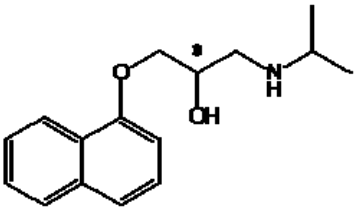
(Metcalfe et al, 2003)

430 ng/L, MWWE, fall

(Lishman et al 2005)

Propranolol

Heart Drug: *B*-blocker
decreases heart rate, blood pressure



Propranolol

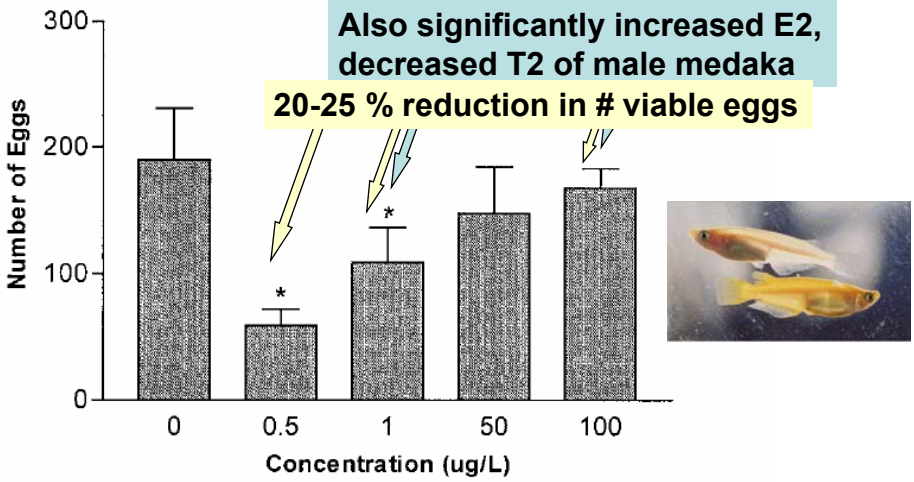
Daphnia magna
– crustacean invertebrate, water flea

	Lowest Observable Effect Concentrations (ug/L)
growth	440
fecundity	110
heart rate lowered	55

Dzialowski et al, 2006. Arch. Environ. Contam. Toxicol. 50, 503–510 (2006)

Propranolol

From Huggett et al, 2002



Decreased reproductive success of medaka after a 4-week exposure to propranolol. Average total number of eggs produced per medaka pair (n=6).

Mississippi and Texas… propranolol identified in all 34 of 34 MWWEs.

United States wastewater effluent samples

	$n > DL$ (%)[a]	Average	Median	Minimum	Maximum
		Concentrations, ug/L			
Propranolol	100	0.117±0.318	0.037	0.026	1.90

Huggett et al, 2003. Environmental Pollution 121:199–205.

Propranolol

Heart Drug: *B*-blocker
decreases heart rate, blood pressure

500 ng/L, egg prod'n, viable eggs, hormones in male medaka

55 ug/L, slower heart rate in *Daphnia*

ng/L ⟷ ug/L

117 ng/L, MWWE, average of 34

(Huggett et al 03)

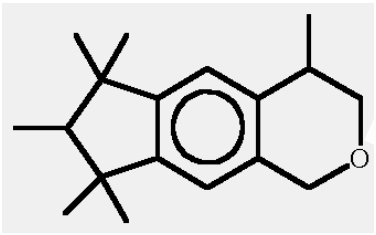
1.9 ug/L, MAX of 34 MWWEs

(Huggett et al 03)

Fragrances

Musks

HHCB = 1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexa-methylcyclopenta-[γ]-2-benzopyran

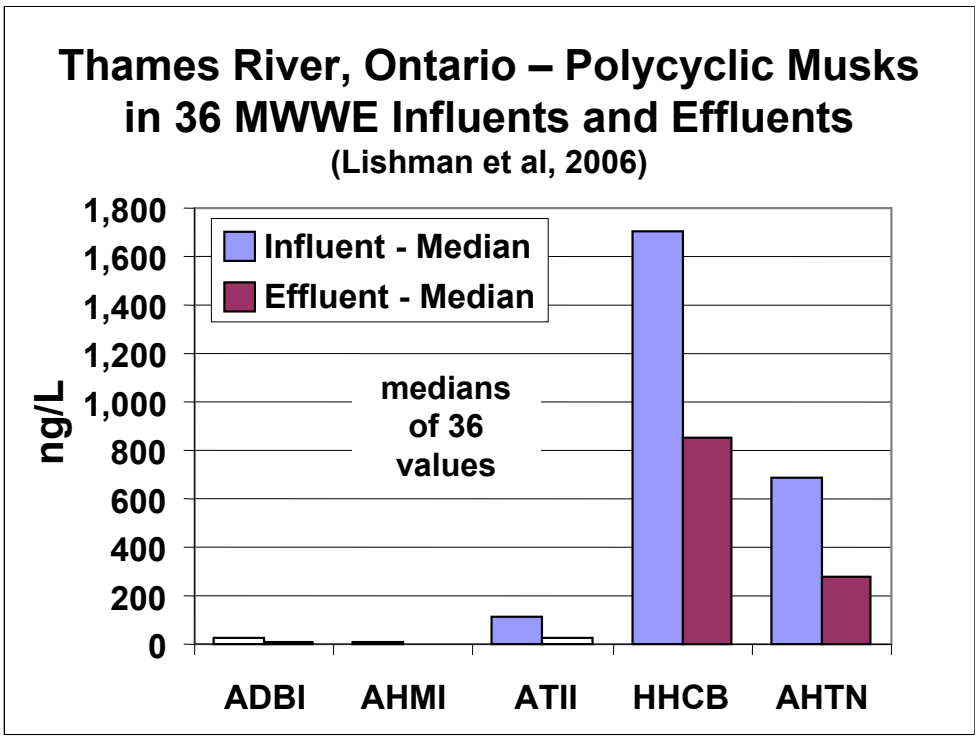


Bullfrog tadpole metamorphosis

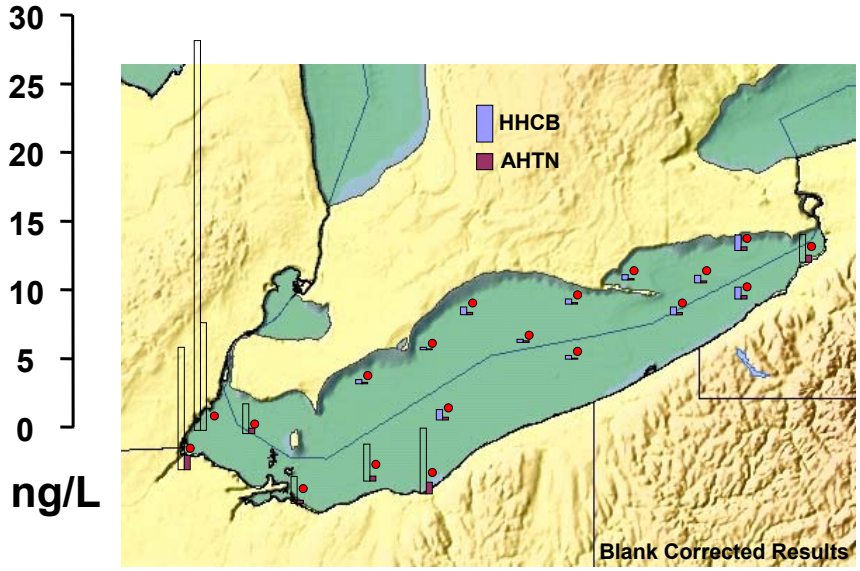
Preliminary data showed 0.1 ug/L HHCB musk

= delayed development in presence of thyroid hormone

Data from Caren Helbing, U Victoria and Graham VanAggelen, EC, Vancouver



HHCB Musk - Lake Erie Water

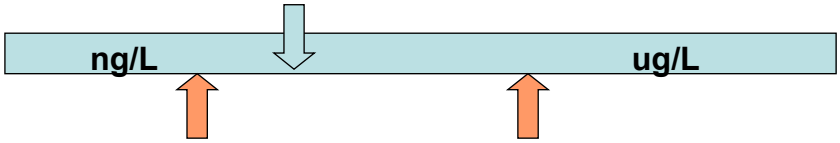


Data from Sean Backus, Science and Technology Branch

Environment Canada Environnement Canada

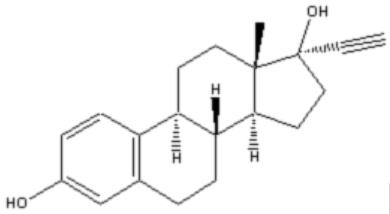
Polycyclic Musks, HHCB

100 ng/L, delayed metamorphosis, bullfrog tadpoles
(preliminary data from Helbing and VanAggelen)



Up to 28 ng/L, open water Lake Erie
(Backus et al, ms in prep)

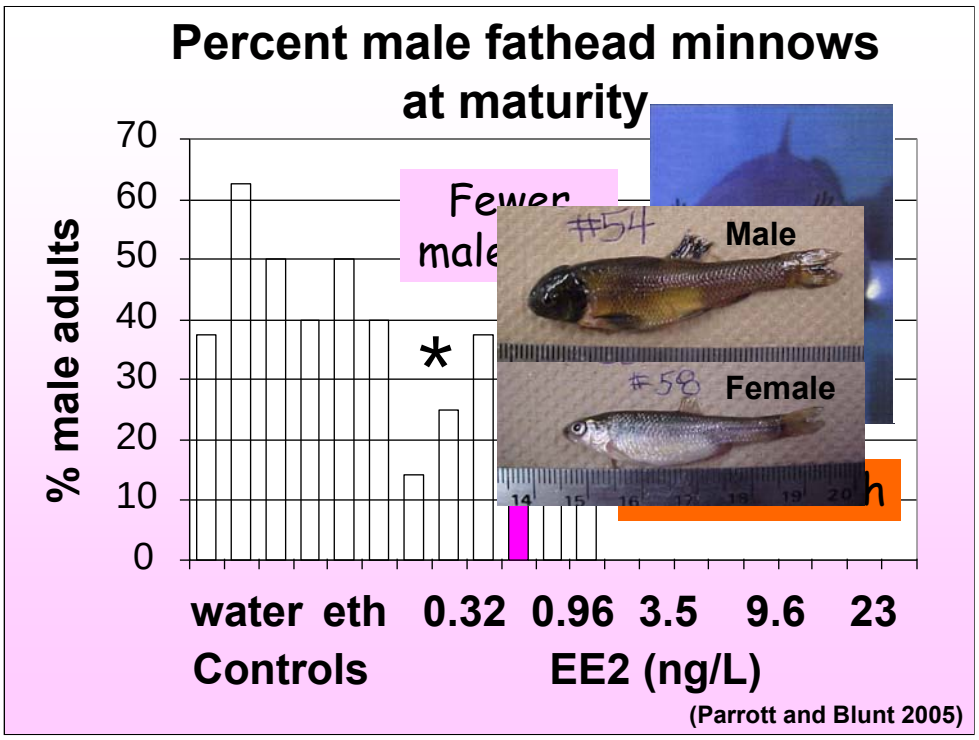
850 ng/L, MWWE, median of 36 values
(Lishman et al, 2006)

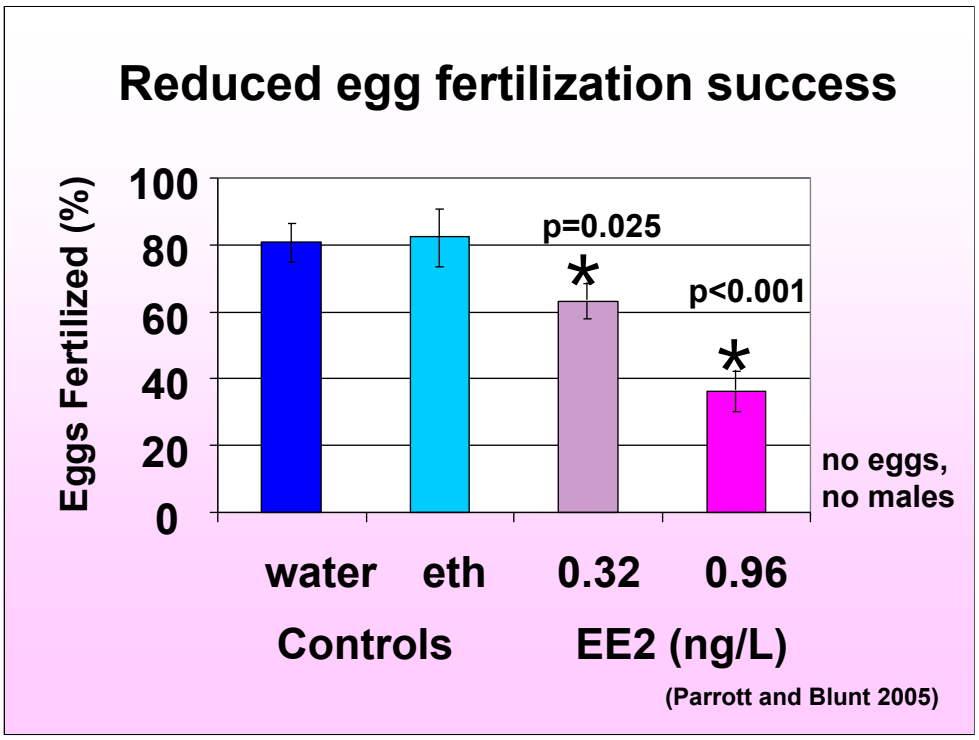


EE2

Ethinylestradiol

Synthetic estrogen in birth control pills





Ethinylestradiol

Synthetic estrogen in birth control pills

EE2 – effects 0.32 to 0.96 ng/L
(Parrott and Blunt 2005)

EE2 – effects on fish populations 5-6 ng/L
(Kidd et al 03)

ng/L ug/L

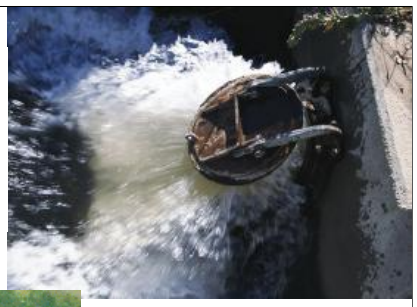
<1 ng/L
(Lee et al 04)

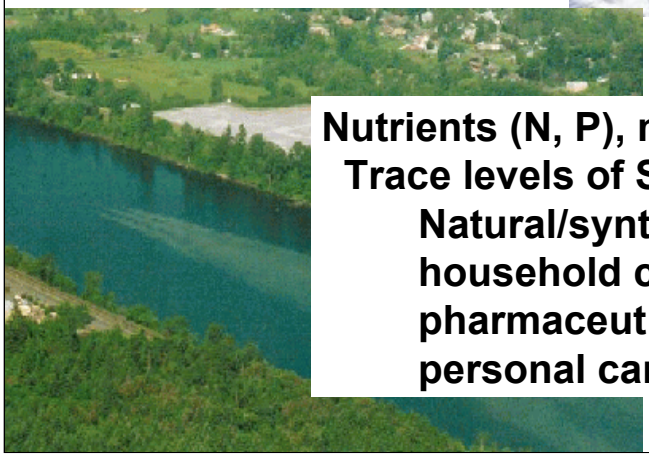
avg 9 ng/L
(Ternes et al 99)

max 273 ng/L in stream water
(Kolpin et al 02)

EE2 – concns in MWWE ND to 273 ng/L

What's in a Municipal Wastewater Effluent (MWWE)?

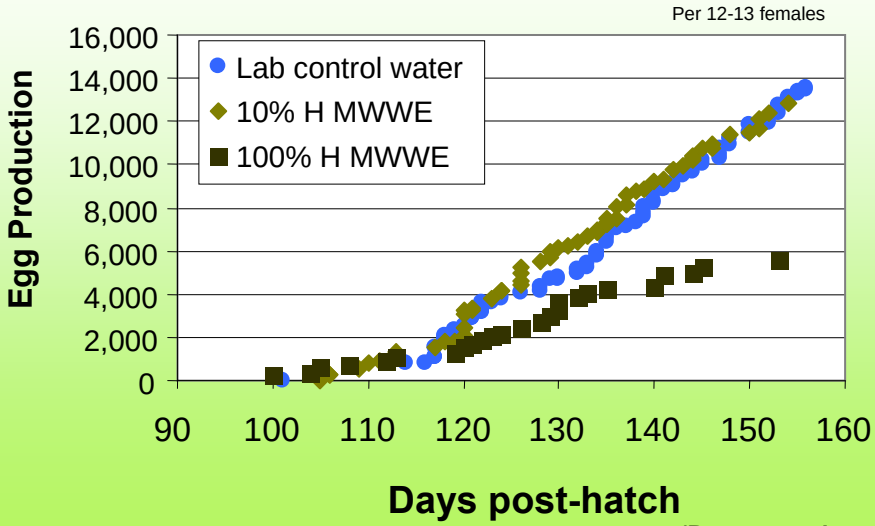




Nutrients (N, P), metals, oils,
Trace levels of SOME….
Natural/synthetic hormones,
household chemicals,
pharmaceutical drugs,
personal care products…

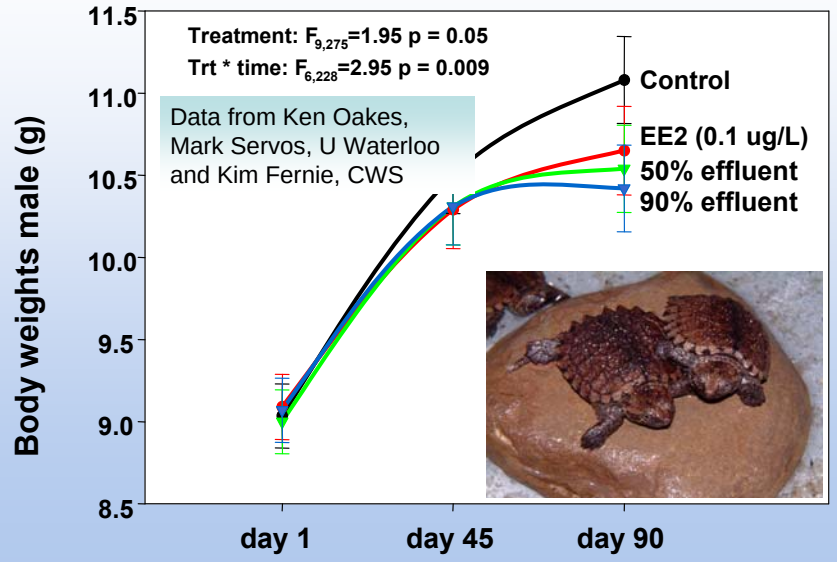
Pic of Victoria MWWE

Egg Production in Fathead minnows exposed to Municipal Wastewater Effluent



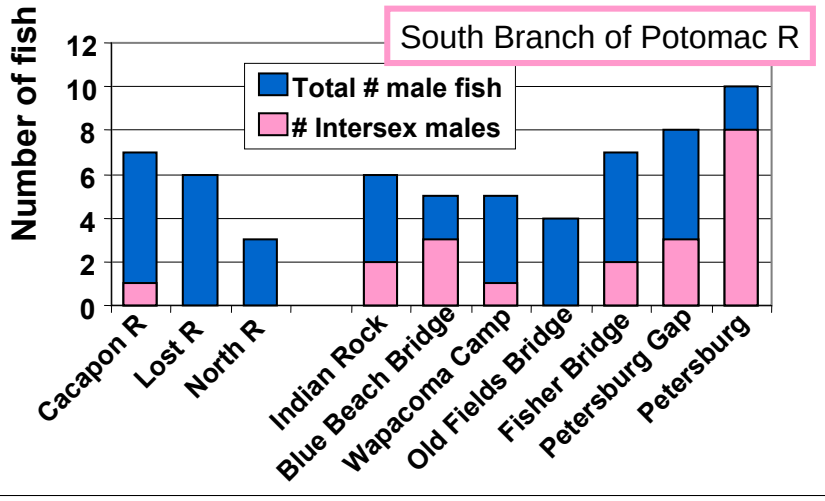
(Parrott, ms in prep)

Exposure to Doon MWWE and to EE2 reduced male snapping turtle body weight



Effects in wild fish????

Potomac River - Percentage of male smallmouth bass with intersex testes
(data from Jim Lazorchak, USEPA, Cincinnati)



Potomac flows to Chesapeake Bay, Maryland and Virginia, to Atlantic Ocean

EDCs in river??? Estradiol, estrone, ethinylestradiol, genistein (soy isoflavone)
EDCs phathalates, bisphenol A

Some PPCPs appear to cause effects in lab organisms at concns of low ng/L to low ug/L.

Some MWWEs in Great Lakes discharge PPCP concentrations in these ranges.

Thresholds for effects of synthetic estrogens very low (ng/L)…. Other PPCPs – higher thresholds (ug/L and above).

Some evidence of effects with fish and turtle exposure to MWWE in the lab.

What we don't know…

Assess effects in wild fish, frogs, turtles, etc., in Great Lakes rivers.

Are we looking at the right biological endpoints?