



Pharmaceuticals and Antibiotics in Water— The Emerging Controversies

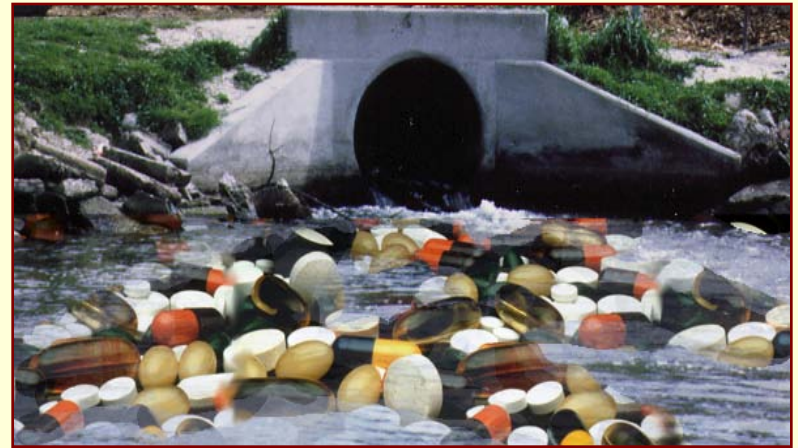


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Drugs in the Water

- Pharmaceuticals have been detected in
 - Treated municipal wastewater that is discharged to the environment
 - Surface waters
 - Rivers
 - Lakes
 - Drinking water
- USGS study (2002) found pharmaceuticals, hormones, and other organic contaminants in 80 percent of streams sampled





What's been found?

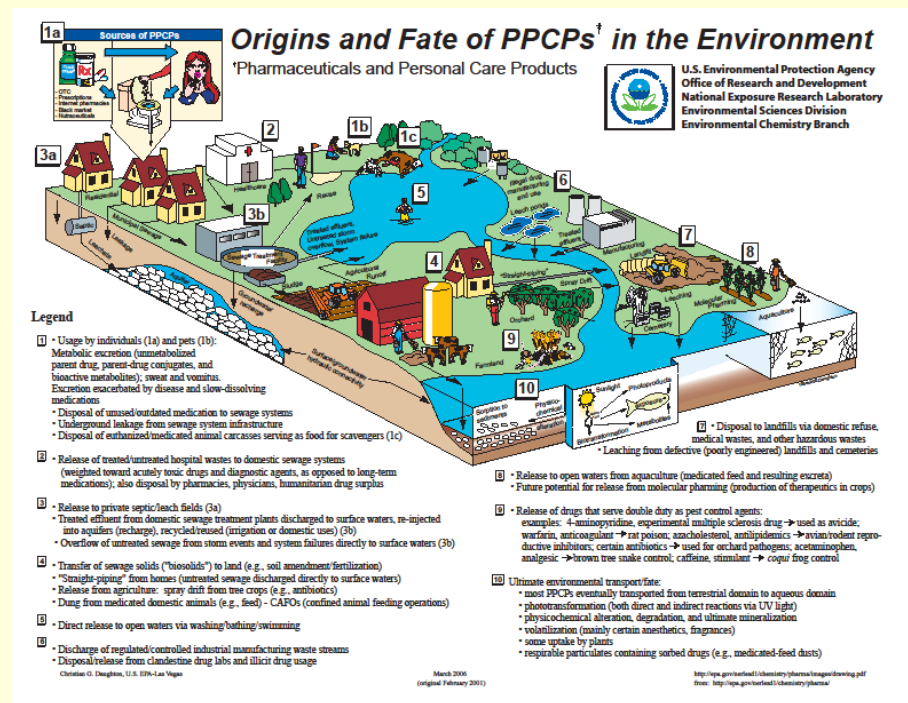


- **Compounds include**
 - Antibiotics
 - Sulfamethoxazole
 - Beta-blockers
 - Atenolol
 - Anti depressants
 - Fluoxetine aka Prozac
 - Anticonvulsants
 - Carbamazepine
 - Anti anxiety
 - Meprobamate



What are the sources?

- Human usage
 - Excretion
 - Disposal into the toilet, sink, or trash
- Animal feeding operations
- Aquaculture
- Agriculture
- Landfill leachate
- Leaking septic systems
- Wastewater from hospitals and production facilities

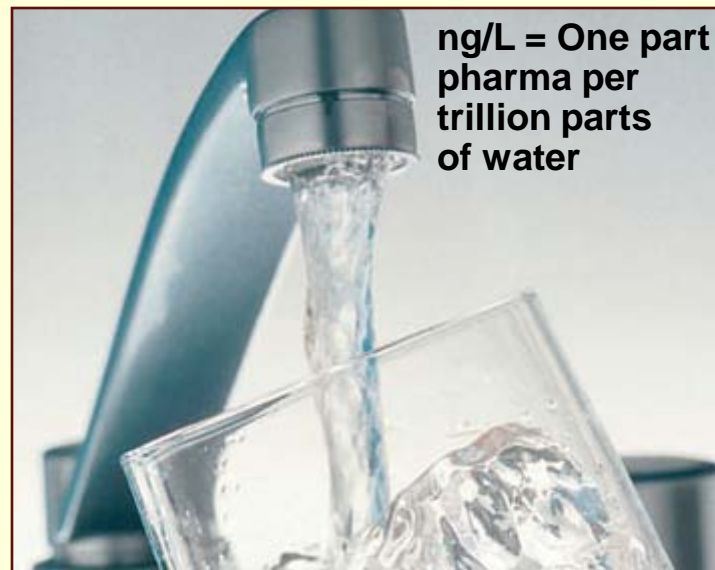


Source: U.S. EPA (2006)



Pharmaceuticals in Drinking Water

- Benotti et al. (2009)
 - Tested drinking water for 28 million people
 - 19 U.S. water utilities
 - Median concentration of detected compounds < 10 ng/L
 - Most frequently found drugs
 - Meprobamate (antianxiety)
 - Phenytoin (antipsychotic)
- Massachusetts and Illinois have tested and found extremely **low to undetectable** levels in drinking water (< 5 ng/L)



ng/L = One part
pharma per
trillion parts
of water

Source: www.cookstown.gov.uk



Ecological Exposure and Effects

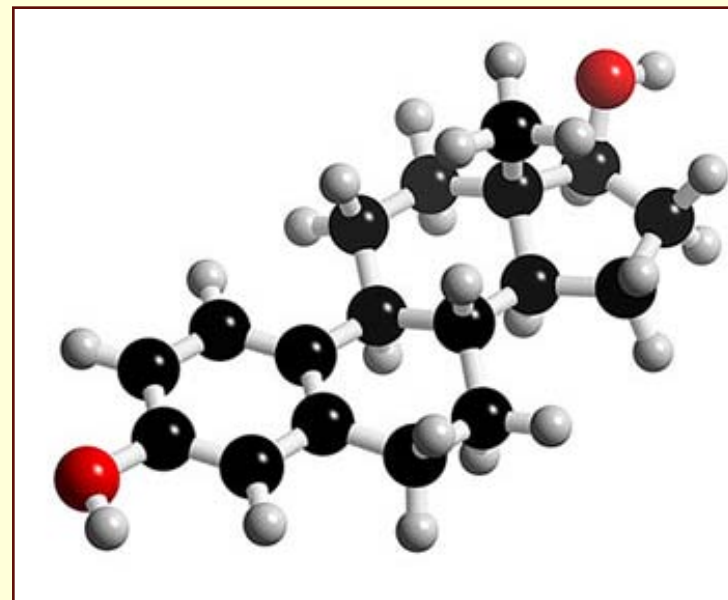
- **Continuous inputs of pharmaceuticals**
 - Exposures are chronic and multi-generational
- **Mixture effects**
 - Antagonistic or synergistic?
- **Aquatic toxicity data**
 - Available only for a few species
- **Metabolites and transformation products**
 - Possible effects





Toxicity/Endocrine Disruption

- Endocrine disruptors
 - Substances that affect the production, actions, or elimination of hormones in the body
- Hormones affect
 - Growth
 - Reproduction
 - Behavior
 - Mating
 - Migration
 - Metamorphosis
 - Frogs and salamanders



Source: www.3dchem.com



Endocrine Disruption

- Feminization of male fish
 - Exposure to estrogenic compounds in wastewater
 - Birth control pills
 - Develop ovaries; produce vitellogenin
- Changes in sex ratios of *Daphnia* exposed to mixtures of antibiotics
- Implications for population-level effects





Antibiotic Effects

- Aquatic bacteria, microalgae, and blue-green algae are most sensitive
- Brine shrimp and water flea reproduction also affected at low concentrations
- Fish not affected
- Microbial resistance development





Other Aquatic Effects

- Prozac (fluoxetine)
 - Delayed development of fish and frogs exposed to the antidepressant
- Mixture of fluoxetine and clofibric acid (a cholesterol reducer)
 - Mortality and deformities in *Daphnia*





Human Health—EPA Messages

- “To date, scientists have found no evidence of adverse human health effects from PPCPs in the environment.”
- “PPCPs have probably been present in water and the environment for as long as humans have been using them.”





Human Health—EWG Messages

- Immediate release: Monday, March 10, 2008
Contact: EWG Public Affairs (202) 667-6982
 - Washington: A wide range of pharmaceuticals, including antibiotics, sex hormones, and drugs for epilepsy and depression, contaminate drinking water supplies of at least 41 million Americans...





Testing the Drinking Water

- EPA estimates that more than 100 individual pharmaceuticals and personal care products (PPCPs) have been **identified** in drinking water
 - In addition to antibiotics and steroids
- EPA sampling for PPCPs
 - Fish and surface water
 - Part of the National Rivers and Stream Assessment
 - Sampling 150 randomly selected sites nationwide
 - August 2008–2011



Pharmaceuticals, Risk Assessment, and Risk Management

- Hazard and dose response
- Exposure assessment
- Risk characterization
- Regulatory action and communication

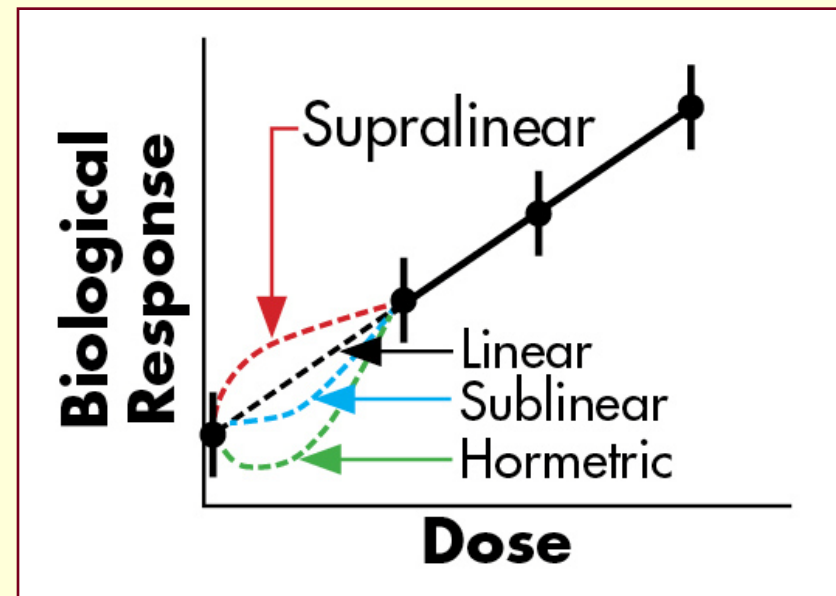


TABLE 2. CHEMICALS DETECTED IN RAW AND FINISHED DRINKING WATER SCREENING LEVELS, AND HAZARD INDICES

CHEMICAL	DETECTED AMOUNT (ng/L, ppt)		SCREENING LEVEL (ng/L, ppt)	HAZARD INDEX FINISHED
	RAW	FINISHED		
Chicago				
Cotinine	4.0	2.0	2,000	0.001
Monensin	3.6	<0.1	100,000	0.000000
Nicotine	8.0	<5.9	NA	----
Gentibrozil	9.9	0.6	120,000	0.000005
Elgin				
Carbamazepine	8.0	2.0	20,000	0.0001
Cotinine	5.0	6.0	2,000	0.003
DEET	16	12	1,000,000	0.00012
Diltiazem	2.0	<1.9	12,000	0.000008
Lincomycin	9.5	<0.1	10,000,000	<0.000000

TABLE 2, continued

CHEMICAL	DETECTED AMOUNT (ng/L, ppt)		SCREENING LEVEL (ng/L, ppt)	HAZARD INDEX, FINISHED
E St Louis				
Carbamazepine	8.0	7.0	20,000	0.00035
Cotinine	4.0	4.0	2,000	0.002
DEET	12	8.0	1,000,000	0.000008
Fluoxetine	2.0	1.0	2,000	0.0005
Lincomycin	8.5	<0.1	10,000,000	<0.00000001
Monensin	1.4	2.8	100,000	0.000028
Nicotine	11	11	NA	----
Paraxanthine	6.0	14	NA	----
Total Sulfa	20	<13	100,000, Total Sulfa ⁽¹⁾	<0.000013

TABLE 2, continued

CHEMICAL	DETECTED AMOUNT (ng/L, ppt)		SCREENING LEVEL (ng/L, ppt)	HAZARD INDEX FINISHED
E St Louis				
Carbamazepine	4.0	4.0	2,000	0.002
Cotinine	4.0	4.0	2,000	0.002
DEET	12	8.0	1,000,000	0.000008
Fluoxetine	2.0	1.0	2,000	0.0005
Lincomycin	8.5	0.1	10,000,000	<0.00000001
Monensin	1.4	2.8	100,000	0.000028
Nicotine	11	11	NA	----
Paraxanthine	6.0	14	NA	----
Total Sulfa	20	13	100,000, Total Sulfa ⁽¹⁾	<0.000013
Rock Island				
Sulfadimethoxine	9.5	0.1	10,000,000	<0.00000001
Method 1220	11	7.0		
Method 1221	11	7.0		
Sulfamethazine	1.0	1.0		
Sulfamethoxazole	8.0	5.0		
Method 1220	8.0	5.0		
Method 1221	2.0	2.0		
Gentibrozil	13.5	10.6	120,000	0.000088
Naproxen	4.0	3.0	44,000	0.000068
Calcine	<0.05	0.05	NA	----
Rock Island				
Carbamazepine	6.0	4.0	20,000	0.0002
Cotinine	2.0	3.0	2,000	0.0015
Lincomycin	5.2	0.1	10,000,000	<0.00000001
Monensin	1.3	2.6	100,000	0.000026
Nicotine	7.0	5.0	100,000	0.00005
Total Sulfa	9.4	<5.1	100,000, Total Sulfa ⁽¹⁾	<0.000051
Rock Island				
Sulfadimethoxine	9.4	0.1	10,000,000	<0.00000001
Sulfamethoxazole	9.0	5.0		
Method 1220	2.0	2.0		
Method 1221	2.0	2.0		
Imoxicepim	1.0	1.0	20,000	0.00005
Certrifoxim	17.4	7.5	120,000	0.0000625

(1) The screening level pertains to the sum of all sulfa drugs.



Conclusions and Challenges

- Low levels of pharmaceuticals and antibiotics are found in water, including drinking water
- Risk is determined by dose, response, and exposure
 - Is it available?
 - Is it absorbed?
 - Is the dose sufficient to cause harm to fish or people?
- Who is responsible for keeping PPCPs and antibiotics out of our water?
 - Pharma industry?
 - Water treatment plants?
 - Agriculture/aquaculture?
 - Hospitals?
 - The public?

