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Technical briefing on

Environmentally persistent pharmaceutical pollutants; effects on living organisms

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Origin of pharmaceuticals in the aquatic environment

Pharmaceuticals are chemicals

- **excreted from urine of patients under treatment with medicines**
- **discarded into toilets as unused or expired medicines**
- **released from manufacturers with improper internal sewage treatment**

Elimination of pharmaceuticals in sewage treatment plants

Action	Substance	sewage intake, ng/L	outlet to recipient, ng/L	elimination %
Cardiovasc.	Metoprolol	910	930	0
Tranquilizer	Oxazepam	420	430	0
Antibiotic	Erythromycin	290	270	7
Antidepr.	Citalopram	240	190	21
Diuretic	Hydroclortiazid	1600	1200	25
Diuretic	Furosemide	2400	1500	37
Cardiovasc.	Atenolol	1700	890	48
Pain killer	Diclofenak	460	220	52
Atiacetic	Ranitidin	270	120	56
Chemother	Sulfametoxazole	450	160	64
Cardiovasc.	Losartan	500	170	66
Chemother	Trimetoprim	390	100	74
Pain killer	Ketoprofen	1500	220	85
Pain killer	Codein	770	70	91
Pain killer	Naproxen	3300	190	94
Antibiotic	Ciprofloxacin	440	19	96
Sex horm	Oestriol	420	< 10	>97
Antibiotic	Tetracyklin	570	< 10	>98
Pain killer	Acetaminophen	130000	100	100
Pain killer	Ibuprofen	9700	4,4	100

Pharmaceuticals in 139 US streams 1999-2000

(*Kolpin et al. 2002*)

Action	Substance	maximum ng/L	average ng/L
Pain killer	Acetaminophen	10000	110
Pain killer	Ibuprofen	10000	200
Chemother.	Sulfametoxazole	1900	150
Antibiotic	Erythromycin	1700	100
Antibiotic	Oxytetracyklin	1200	340
Chemother.	Trimethoprim	710	150
Antibiotic	Norfloxacin	120	120
Antibiotic	Tetracycline	110	110
Cardiovascular	Enalapril	46	46
Antibiotic	Ciprofloxacin	30	20
Pain killer	Codein	19	12
Antibiotic	Fluoxetine	12	12
Acid prod. inh..	Ranitidin	10	10
Antiasthmatic	Salbutamol	ND	ND
Antikoagulant	Warfarin	ND	ND
Pain killer	Paroxetine metabolite	ND	ND

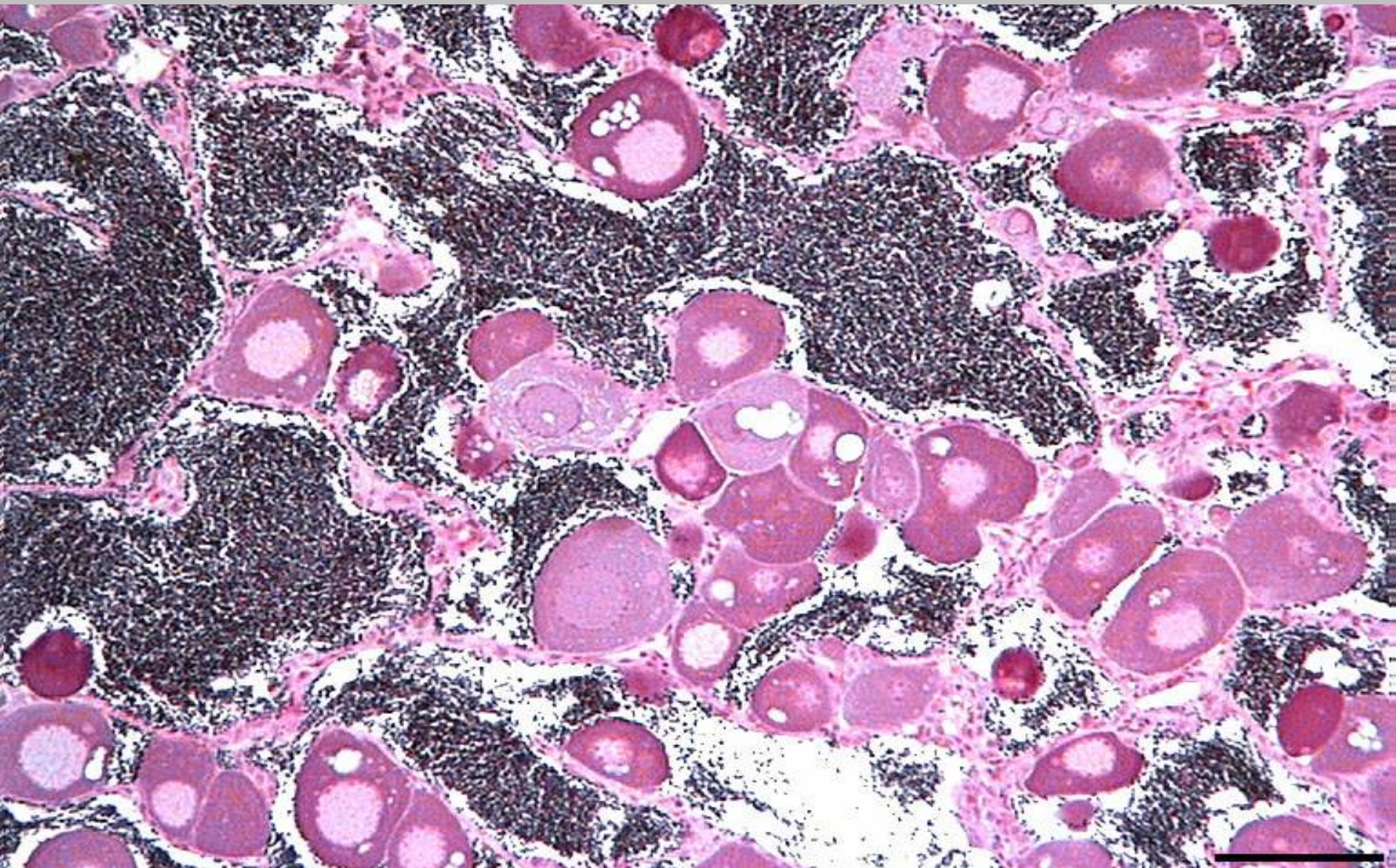
Global survey of persistent pharmacological pollutants in drinking water

Sampling position	Number of detected pharmaceuticals
Perth	14
Singapore	8
Paris	7
Beijing	6
Edinburgh	4
Hamburg, Johannesburg	3
Brussels, Helsingborg, HongKong, Copenhagen, Lyon, Sophia	2
Dubai, Düsseldorf, Hoorn (NL)	1
Manchester, New York, Shipol	0

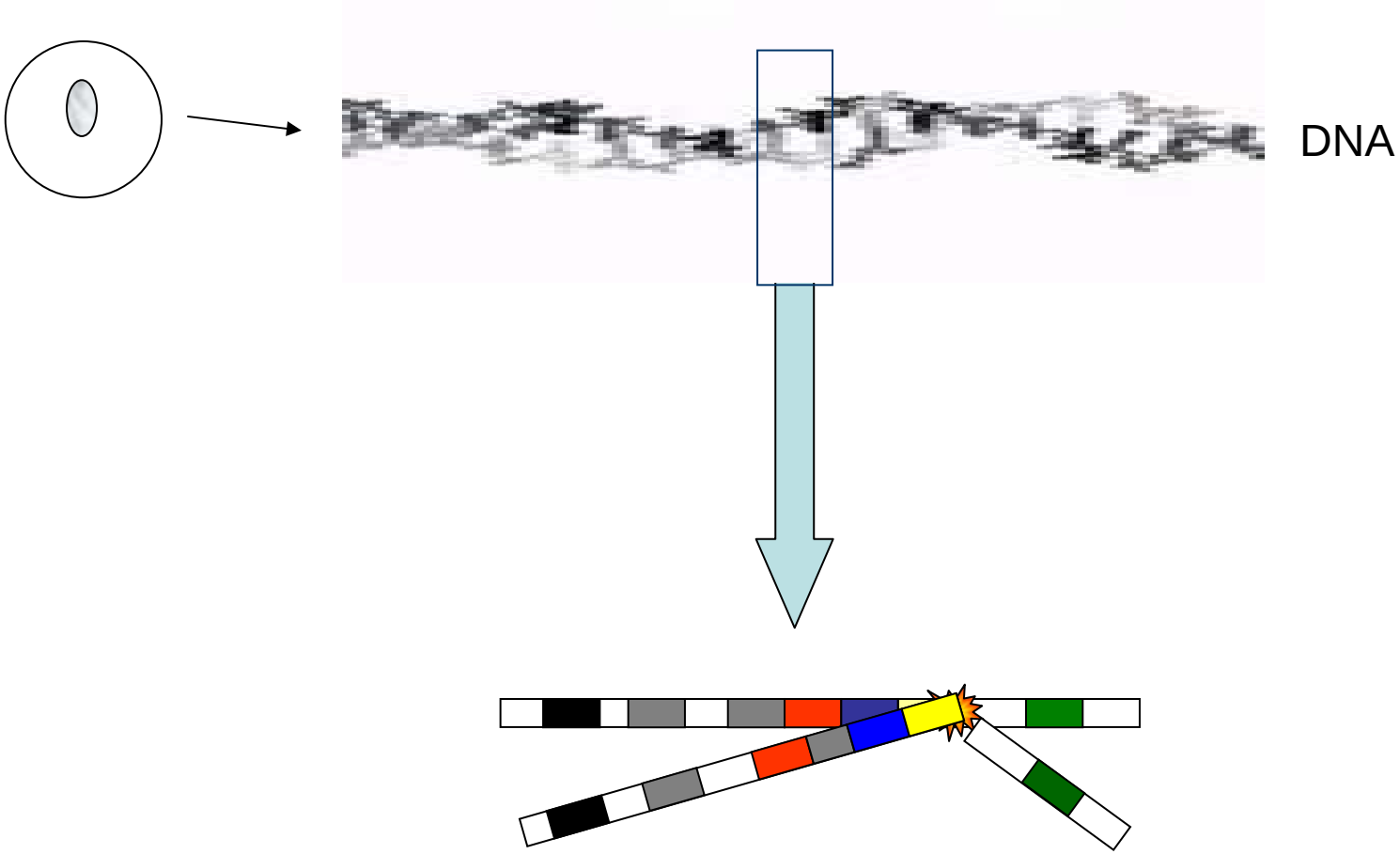
Drug residues in liver from perch caught in the Stockholm area

	Central Stockholm	30 km east	70 km east
Citalopram	0,1 µg/kg	<0,1 µg/kg	<0,1 µg/kg
Propoxyfen	0,25 µg/kg	0,16 µg/kg	<0,1 µg/kg

Testicular tissue from wild caught fish showing severe feminisation



Chemical pollutants and fetal development

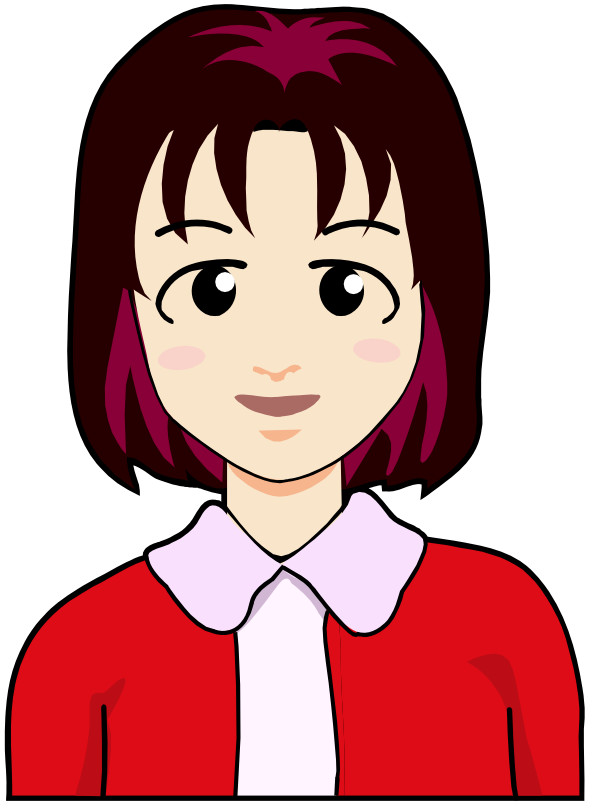


The new toxicology

toxicologi yesterday and today (after John Peterson Myers, PhD)

yesterday	today
High doses exceed the detoxification mechanisms of the human body	Low doses ínterfere with delicate differentiation- and development mechanisms
Focus on adult humans	Periods of rapid growth and development most sensitive to exposure
Immediate administration-effect relation	Long latency common, exposure during fetal life may cause symptoms after several decades
Suspected agents studied one by one	Multifactorial exposure may cause effects at much lower concentrations than those required by single substance exposure
Focus on traditional endpoints like mutagenesis, carcinogenesis och cell death	Many endpoints: immunodeficiency; neurological, cognitive, behavioural and reproductive disturbances, chronic disease

Water containing environmentally persistent pharmacological pollutants may threaten children's development and health



Environmental risk and hazard classification of chemicals of pharmaceutical origin

In Sweden an agreement was taken between health care providers, the medical products agency, pharmacy shops *and* the pharmaceutical producers to establish a classification system.

The international reference group for ”the Swedish initiative”

Risk assessment

for more than 50 % of the substances proper data for risk assessment were not available!!

Outcome of persistence assessment

	%
Persistence	
– degraded	11
– slowly degraded	37
– potentially persistent	52

Outcome of bioaccumulation assessment

	%
Bioaccumulation	
– no potential…..	79
– has potential……....	21

Policies taken by the European Union

The European Union has already taken action, by

- funding research on chemical pollution of water with pharmaceuticals for more than 10 years

- publishing a report from European Environmental Agency (EEA, report 01/2010) entitled ”Pharmaceuticals in the environment - Results of an EEA workshop” with strong action proposals

- stating the following in COM(2008)666

  ”*Pollution of waters and soils with pharmaceutical residues is an emerging environmental problem and also an emerging health concern. The Commission recognizing these concerns has funded several research projects to assess possible environmental and health impacts of pharmaceuticals. It is now necessary to focus on measures that could reduce the potentially harmful impact of pharmaceuticals on the environment and public health.”*

Conclusion

Pollution of surface waters with residues of persistent pharmacological residues in an emerging global threat to human and animal health