



Recipharm
good for business

SCRIP

MAGAZINE

Pharmaceutical Issues
in Perspective

December 1998



WILL THE Hatch-Waxman Act have to be reopened?

Holes in the EC licensing system

The sham of Italy's cancer cure

Face to face with Erik Boggsch

talking points

Can drug companies rise to the environmental challenge?

by Lars Backsell

Attitudes of both consumers and pharmacists are forcing environmental issues onto the pharmaceutical industry agenda. According to market research company Euro Clip Information, two-thirds of people who use painkillers in Sweden would buy a green-labelled alternative if one was available. And when the same company asked 350 pharmacists to quantify the importance of environmental management on a scale from 0-5, the average score of around 4.7 suggested a similarly 'green' tendency.

This trend is supported by the findings from quarterly customer relations surveys carried out by Sweden's state-owned pharmacy monopoly, Apoteket. In these, the chain's more than 70,000 customers are questioned about various quality factors, the answers of which are compiled into what is called the Customer Satisfaction Index (CSI). Because these quality factors reflect areas of importance to the pharmacist, the index naturally differs from one pharmacy to another.

A pharmacist will normally try to concentrate on three or four quality factors at a time. How important these are to the customer is shown by the number of replies to questions about that particular factor. Reply percentages above 50% are viewed as high.

When the CSI interviews started in 1992, environmental questions hardly qualified for inclusion in the questionnaire. Today, more than half the pharmacists at the chain's 800 outlets consider it one of their quality factors and as many as 60% of the people interviewed



Although pharmacies and customers want 'green' products, industry appears to resist environmental change. Photograph by H.S. & P. von Holst/Science Photo Library.

have an opinion on the subject. No doubt this is an area where Apoteket, which may shortly lose its monopoly status, is trying to develop a strong profile. At product level, for example, it is written policy that the selection criteria for non-pharmaceuticals such as food supplements include ecological friendliness as well as efficacy and safety. And at shop level, more than 70% of customers believe its environmental management policies are better than the competition.

Doctors' interest in environmental issues also seems to be growing if the number of articles in professional journals is anything to go by. Moreover, the International Society of Doctors for the Environment, an organisation that started in July in 1990, now has more than 50,000 members. In the Stockholm area, over 5% of doctors are members. The aim of the organisation is to raise awareness about the effects of environmental degradation on human health and to propose solutions on how further damage can be limited.

In the Swedish hospital sector, new legislation on tenders means that the environmental impact of purchased products now has to be taken into account. The effects of this can be seen in the number of documents that carry environmental headings alerting people to, for example, hazardous materials, as well as in the fact that the content of a company's environmental programme, if one exists, must be filled in to take part in a tender.

On an authority level, the industry is in fact aware of the issue but has so far, it seems, not taken much action. In a study carried

out by Doctors for the Environment, 200 European companies were asked to reply to an environmental questionnaire. Only 63, or 32%, did. Whether this low response rate is an indication of the level of interest is hard to tell. It is equally hard to make sense of the fact that the majority of those who did respond had environmental policies and management training (80% had policies, 59% had had management training, and 68% had noticed increased environmental interest among their customers) but very few actually implemented them. Nevertheless, 93% of respondents claimed that environmental management considerations will be important for the pharmaceutical industry in the future.

The list of pharmaceutical environmental management policies can seem quite daunting, embracing as it does transportation, raw materials, packaging, process methods, waste management, sorting, printing materials, and product development – to mention just a few.

But guidance can be found by looking at other industries. There are many examples of companies going through environmental management certification processes such as ISO 14001, EMAS or BS7750. ISO 14001 is, in many ways, similar to the ISO 9000-9001 standard for good manufacturing practice.

A company can either certify single parts of its business or the



Recipharm
good for business



Lessons learned from adding “the pill” to a whole lake

Karen Kidd

Jarislowsky Chair in Environment and Health
Department of Biology & School of Geography and Earth Sciences
McMaster University, Hamilton, ON
Canada

Recipharm International Environmental Award Address
28 August 2018

The estrogen story

- Why put an estrogen into a whole lake?
- What happened after it was added?
 - **Chapter 1:** Direct effects on fish
 - **Chapter 2:** Indirect effects on other species
 - **Chapter 3:** Was there any recovery?
- What are the implications for wild fishes and aquatic food webs?

Rob Bajno, Chris Baron, Paul Blanchfield, Sandy Chalanchuk, Bob Evans, Dave Findlay, Brad Park, Vince Palace, Cheryl Podemski, Lianne Postma, Ken Mills, Kerry Wautier, and Julieta Werner, Fisheries and Oceans Canada, Manitoba

Mike Paterson and Mike Rennie, International Institute of Sustainable Development

Karsten Liber, University of Saskatchewan

Margaret Docker and Kathleen Londry, University of Manitoba

David Graham, University of Kansas

Mark McMaster, Environment Canada, Ontario

Jim Lazorchak and David Lattier, US EPA, Ohio





Urine and feces contain:

- drugs we use
- natural hormones we produce

Flushed into sewage system

Why did we do this study?



Male fish exposed to sewage effluents have:

- Smaller gonads
- Vitellogenin (egg yolk protein)
- Eggs (intersex)

100% of males in some rivers in U.K.



Environ. Sci. Technol. **1998**, 32, 2498–2506

Widespread Sexual Disruption in Wild Fish

SUSAN JOBLING,^{*,†} MONIQUE NOLAN,[‡]
CHARLES R. TYLER,[†]
GEOFF BRIGHTY,[§] AND
JOHN P. SUMPTER[†]

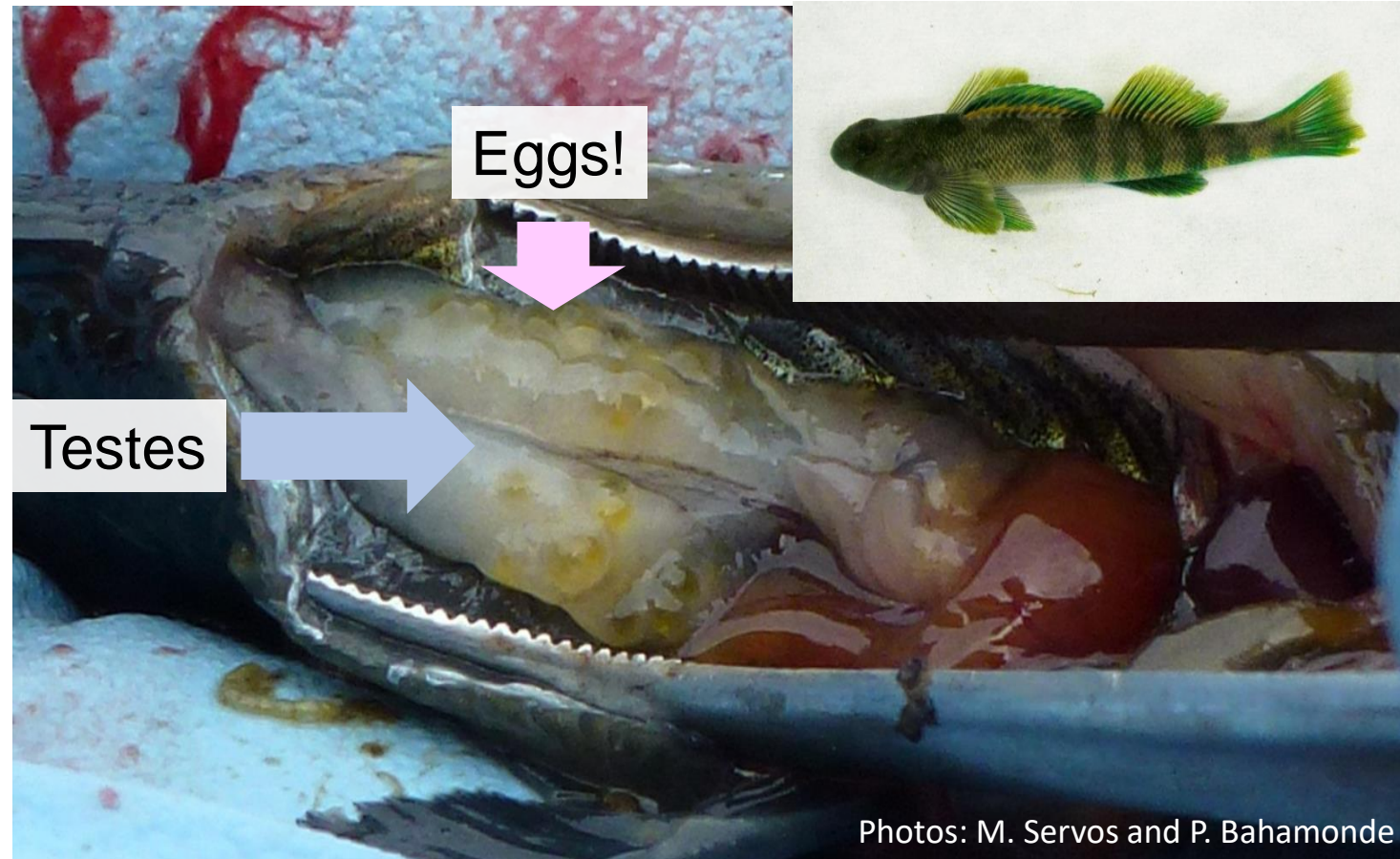
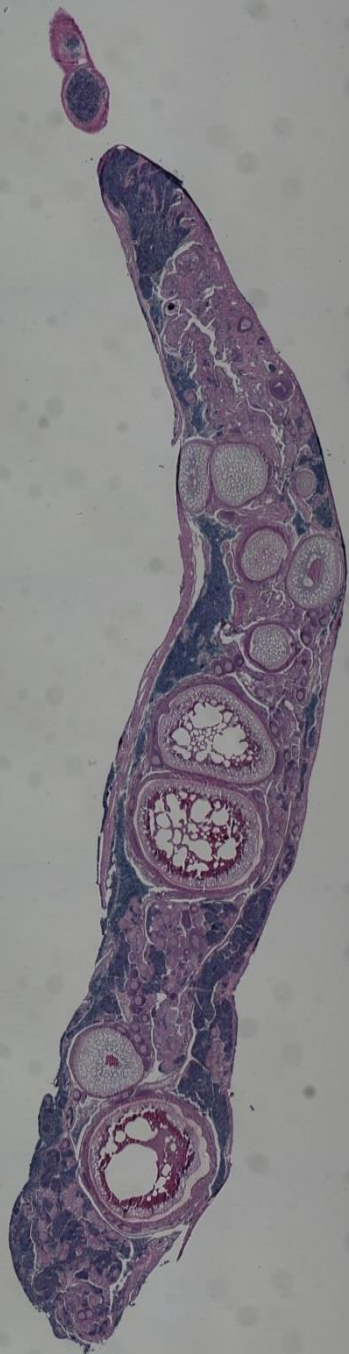
mented, but geographically (8–14). Most of the cherr many orders of magnitude li counterparts, and it therefc exposure will cause signific standing this, it is entirely pc of endocrine-modulating si present in the environmen even synergistic effects.

Caused by exposure

- Synthetic hormones
- Natural estrogens
- Anti-androgens

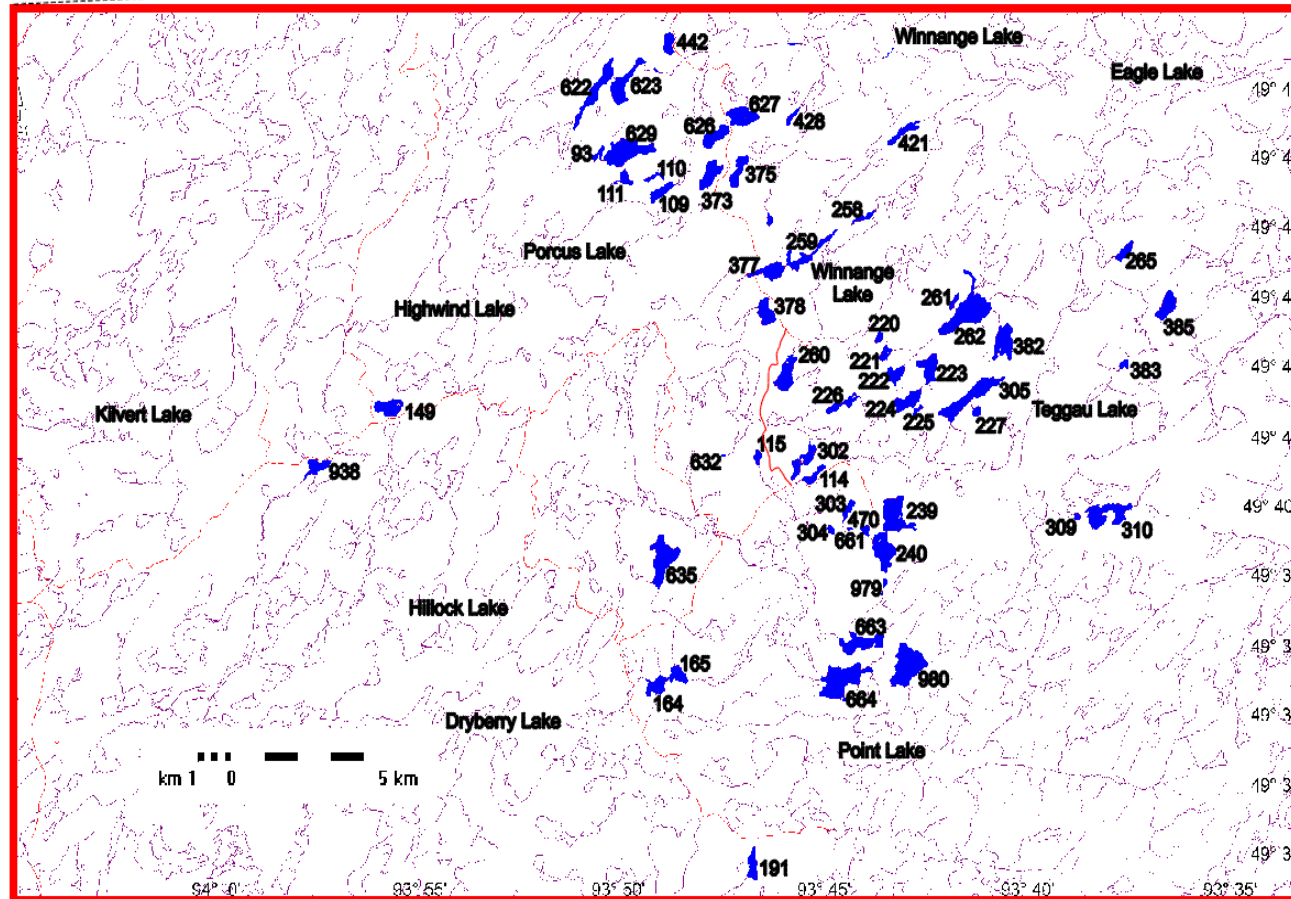


Intersex in wild fish in Canada



60% of male greenside darter downstream of sewage outfall (M. Servos et al., University of Waterloo)

58 Designated Research Lakes and their Watersheds Detailed Monitoring since 1969



Experimental Lakes Area

Designated Research Lakes shaded Blue

**Boreal
Shield of
northwestern
Ontario**

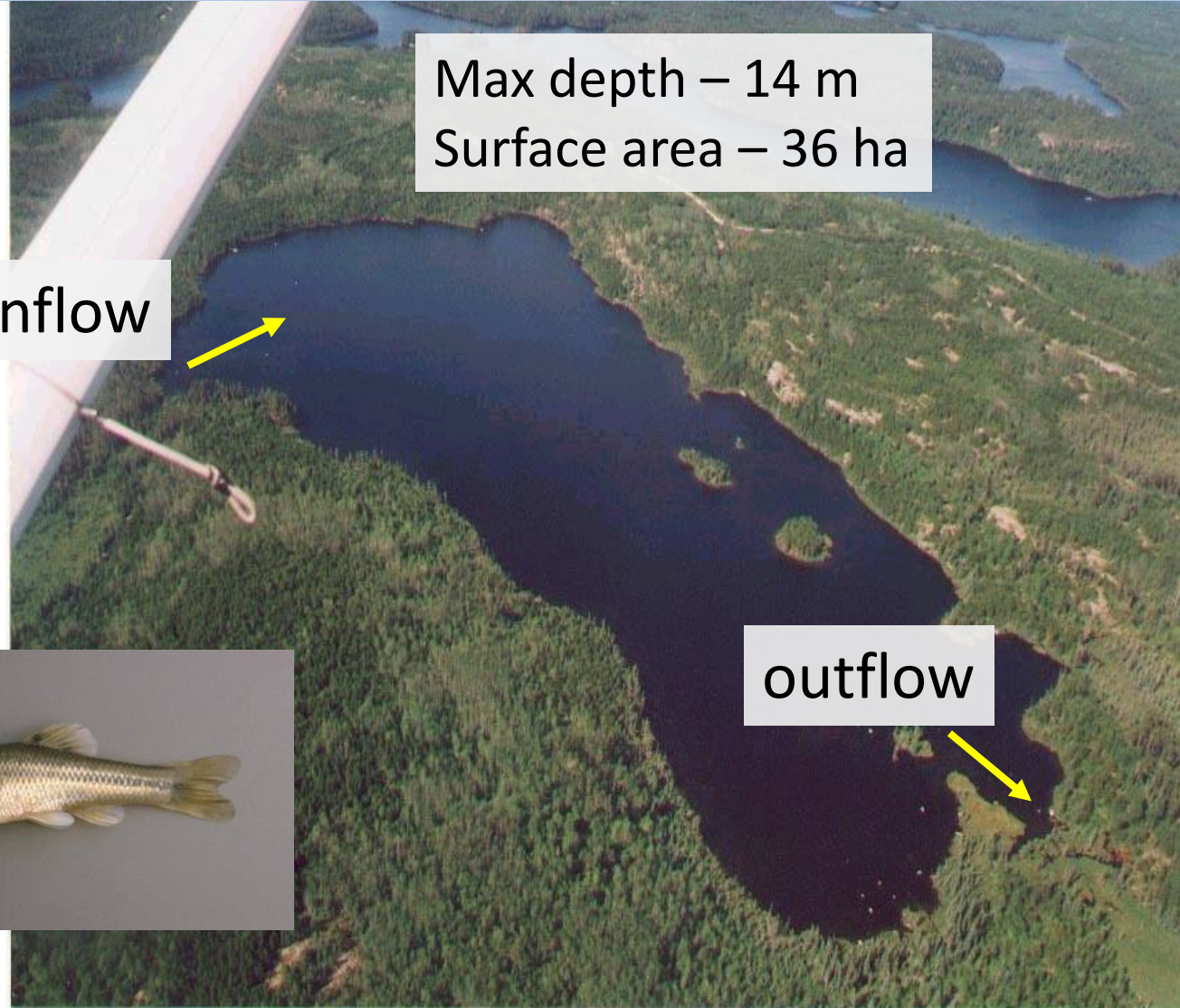
Lake 260 - Estrogen Addition Lake

Max depth – 14 m
Surface area – 36 ha

inflow



outflow



Study Design



baseline data



1999

2000

estrogen additions



2001

2002

2003

recovery?



effects on individuals & populations



2004

2005 thru 2010

reference lake data



How and how much of “the pill” did we add?

- One pill 30 μg EE2; added $\sim 10,500$ pills worth of EE2/day
- Dosed 3 times/week, 20-21 weeks



Measured EE2 in water column each week
Targeted and achieved 5 ng/L (parts per trillion)

Chapter 1: What happened to the main character?

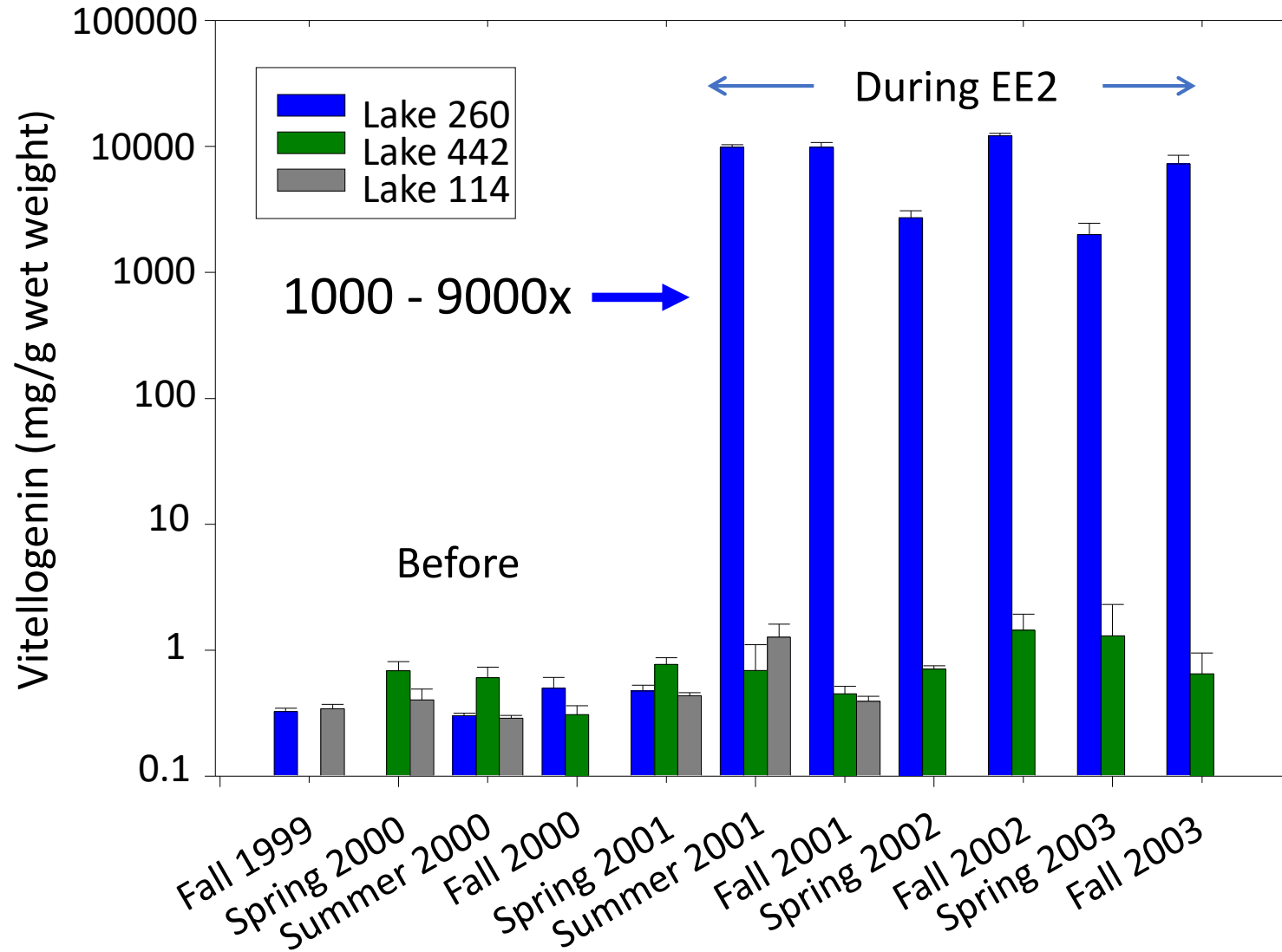


Photo credit: P. Blanchfield

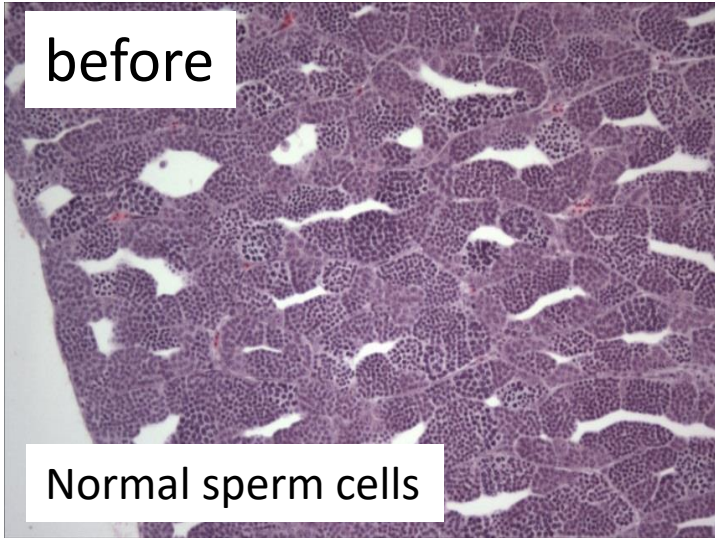
Fathead minnow

- mature at age 2, live 2-3 years
- spawn once mid-summer, then most die
- important prey for many sports fish

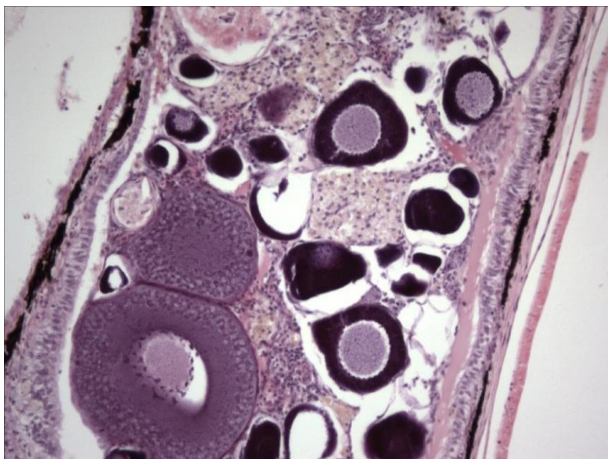
Vitellogenin in male fathead minnow



What happened to their ability to develop sperm?



spermatogonia \nrightarrow spermatocytes \rightarrow spermatozoa



100%

3 years of
EE2

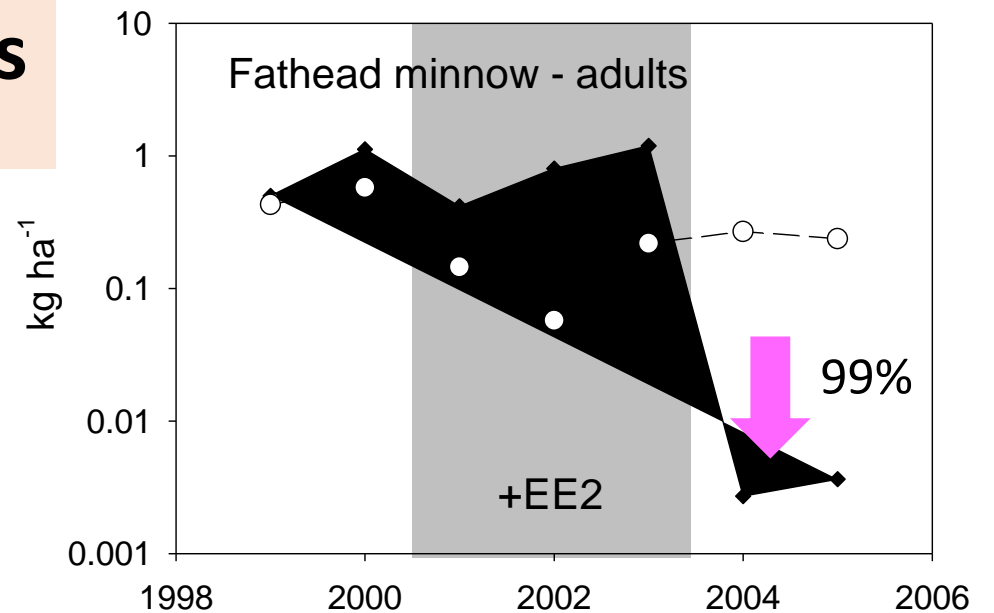
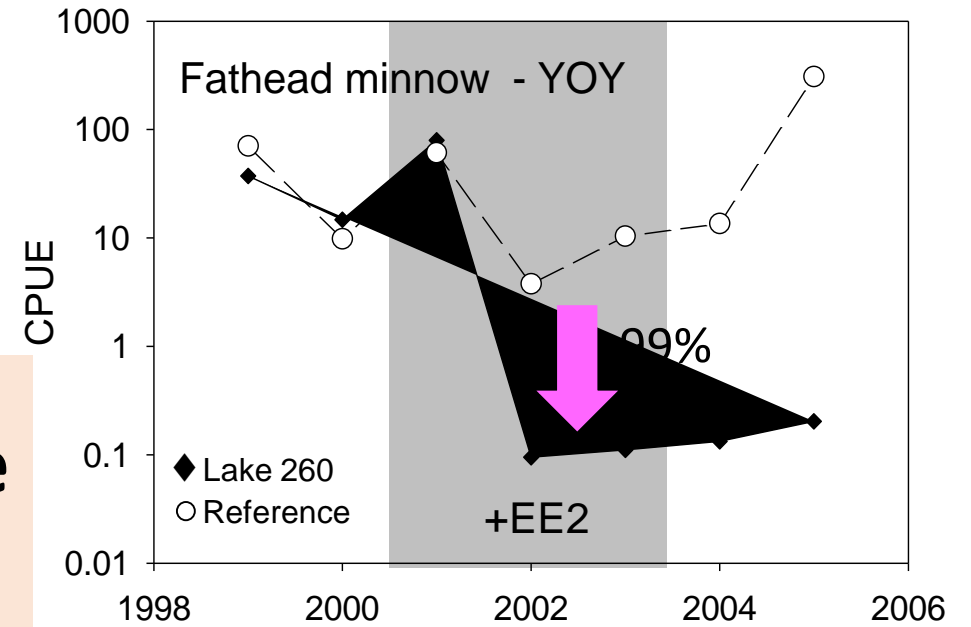


Effects of EE2 on the fathead minnow population of Lake 260 – spring catches



Kidd et al. Proc. Nat. Acad. Sci. 2007

Photo: infotrek.er.usgs.gov/wdnr_fishes/



Why was there a reproductive failure?

Likely combination of

- Delays in spermatocyte development
- Loss of secondary sex characteristics
- Smaller nests
- Changes in sexual behavior



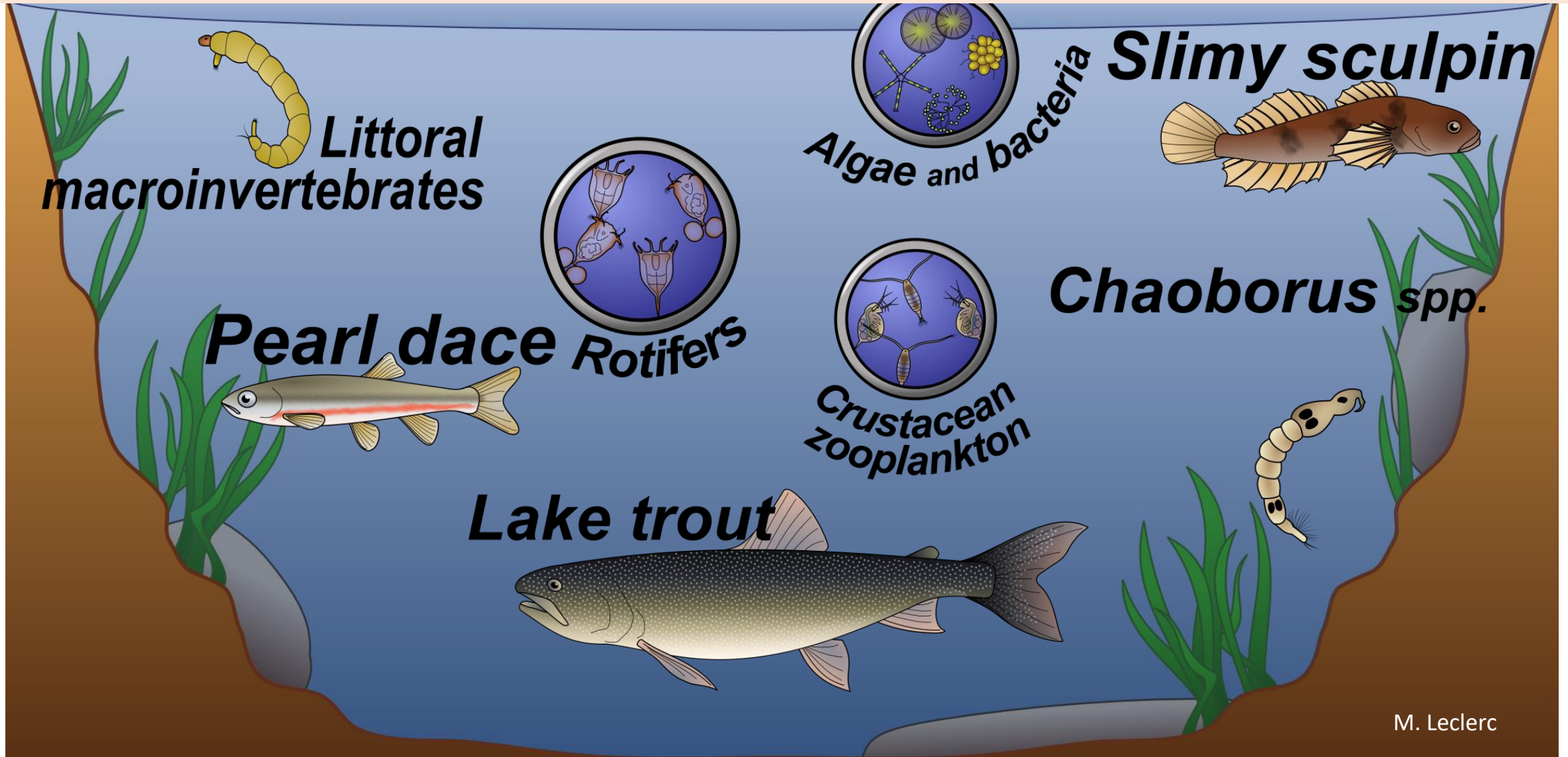
Male guarding nest

Photo: P. Blanchfield and D. Callaghan

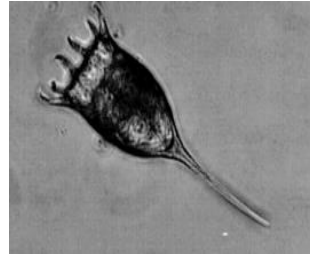


Photos: J. Parrott

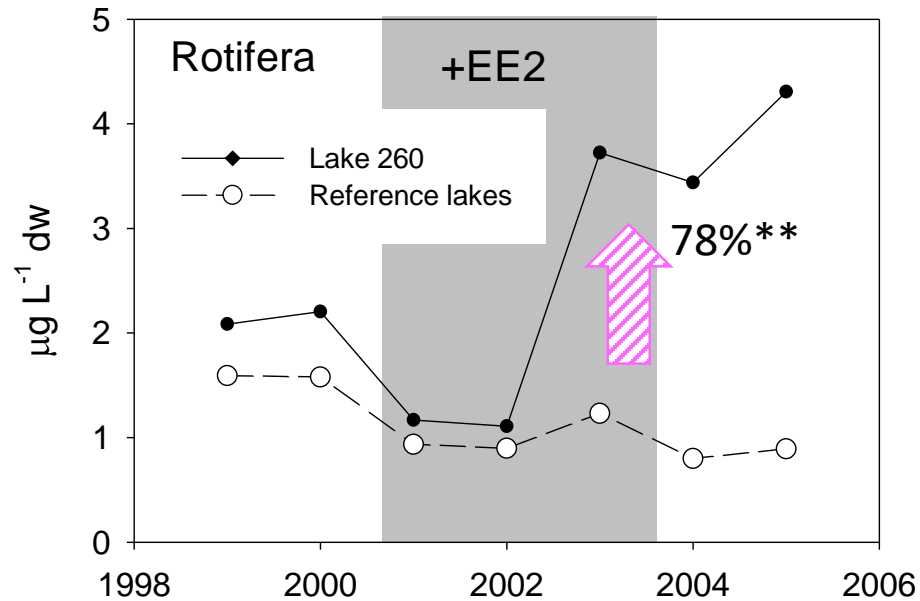
Chapter 2: What happened to the other taxa?



Any effects of EE2 on plankton and littoral macroinvertebrates?



- All increased from 41-89%
- Not because more food was available

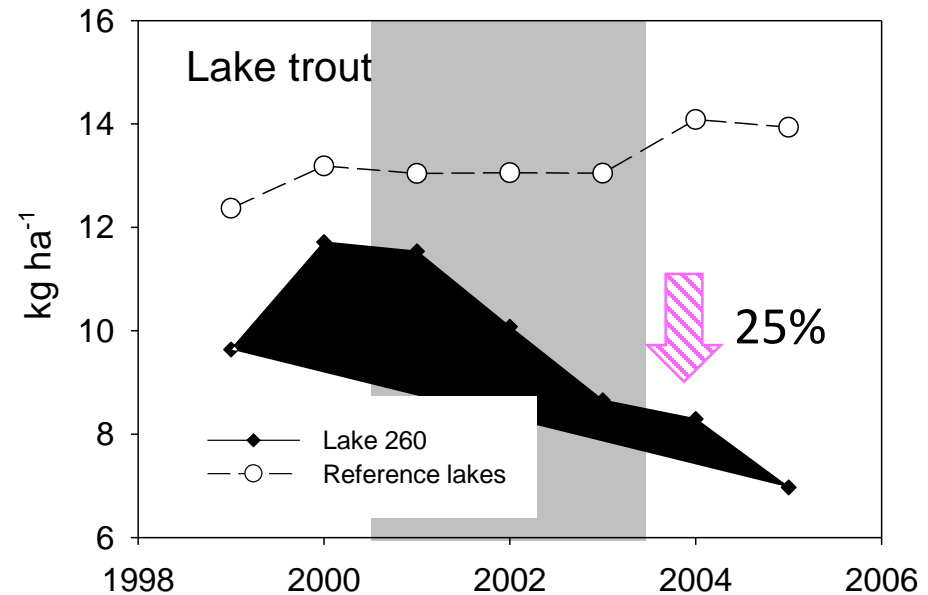


What about the lake's top predator?



Lake trout

- Elevated vitellogenin
- No effects on oocytes or spermatocytes



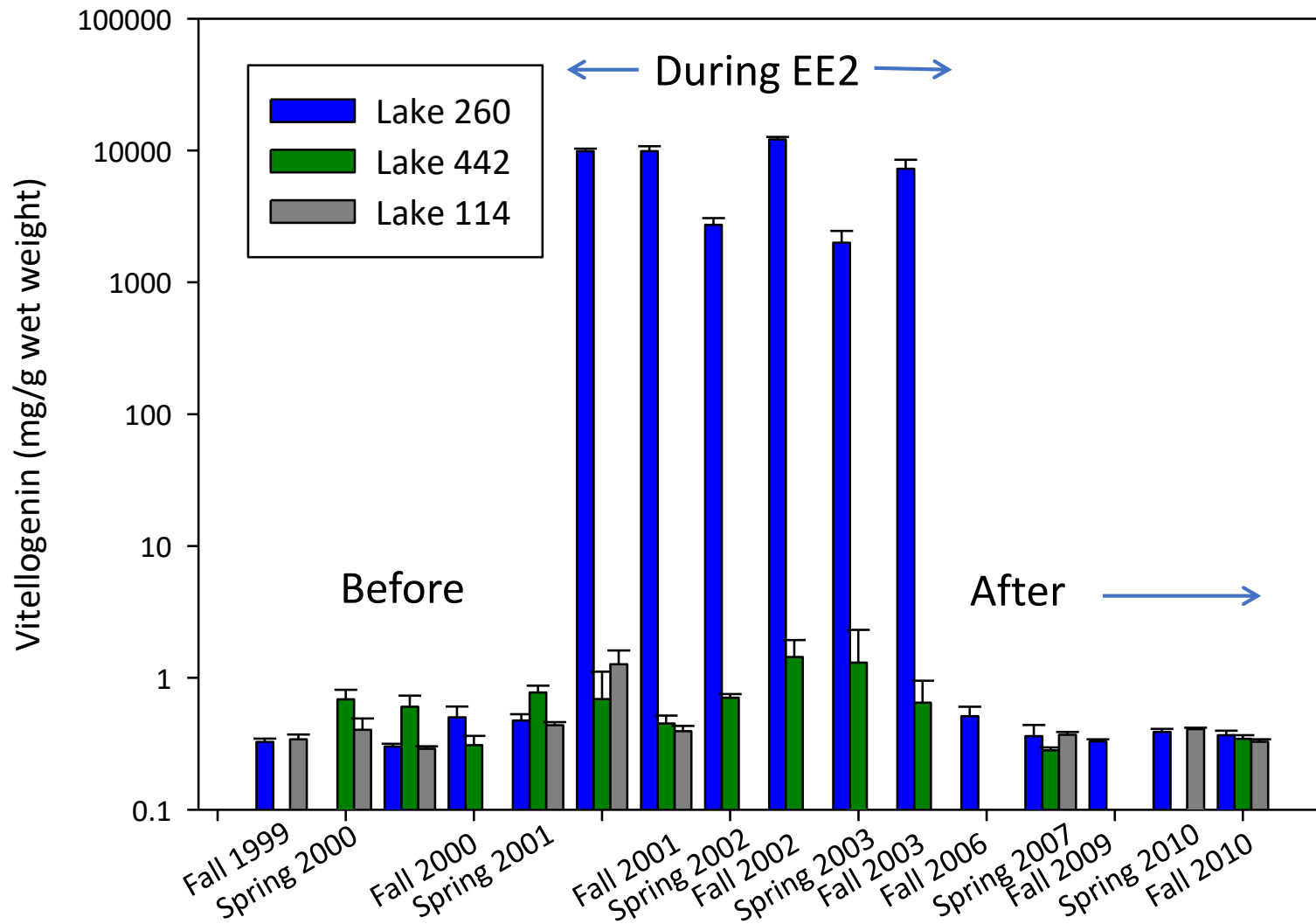
Decline in lake trout biomass from loss of prey – indirect effects

Chapter 3: Was there any recovery of the fathead minnow population?

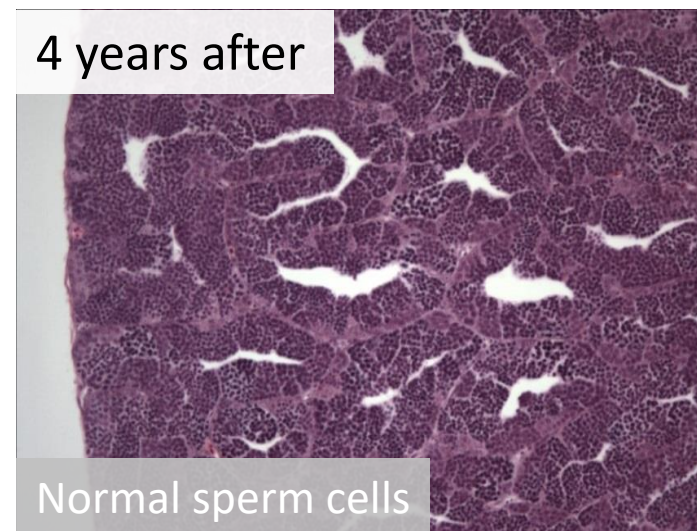
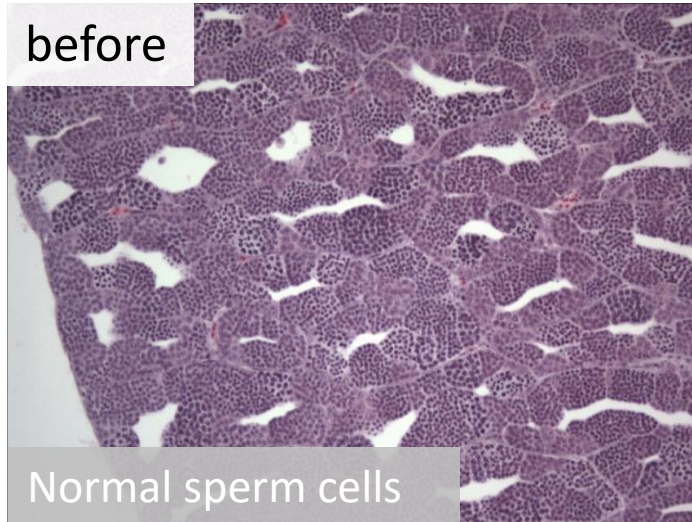


Photo credit: P. Blanchfield

Vitellogenin in male fathead minnow

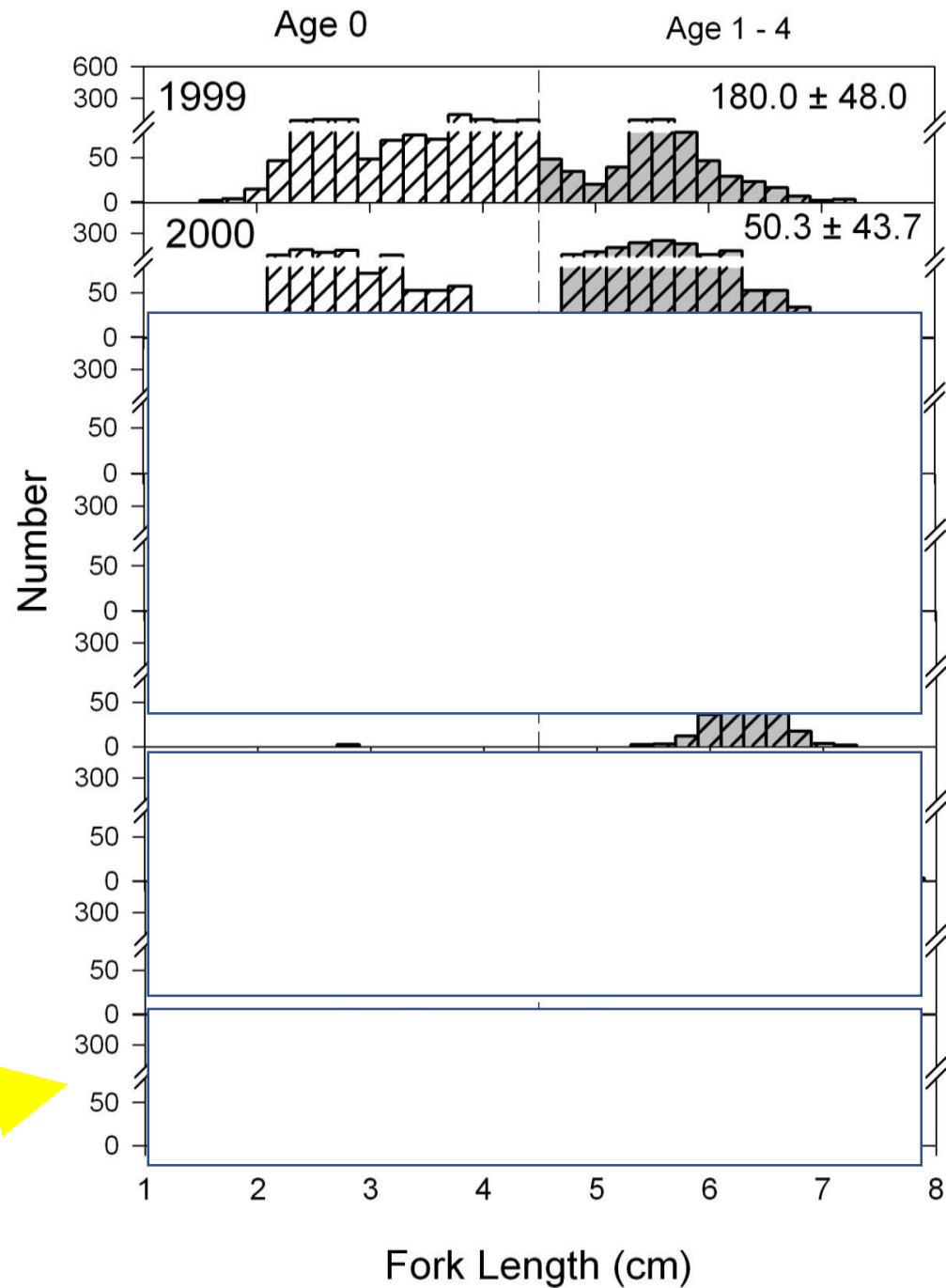


Did the males recover ability to develop sperm?



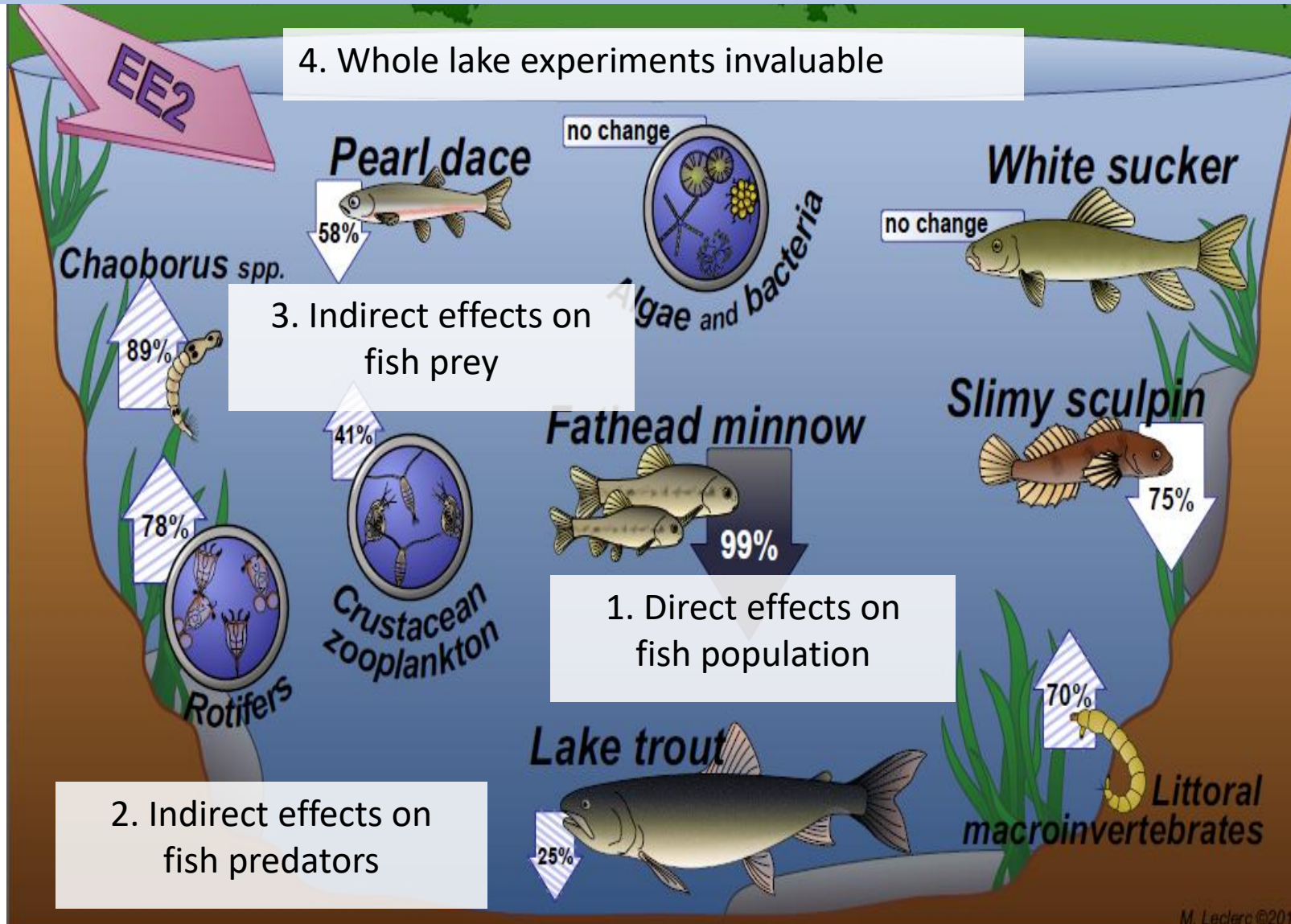
What about the population?

Lake 260



Awesome!!!

What did we learn from this study?



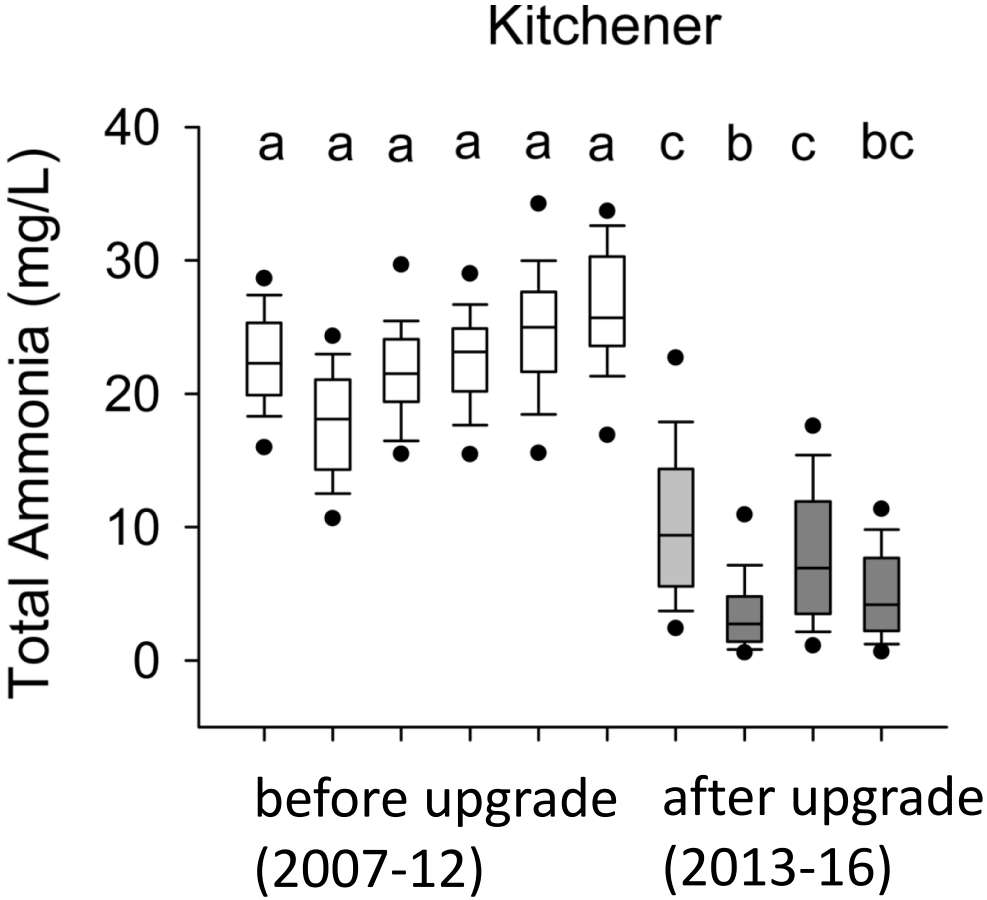
Does this mean that women should stop taking the birth control pill?



- No
- Answer is better wastewater treatment and management
- **Primary treatment**
 - Physical (~37%)
- **Secondary treatment**
 - Activated sludge (~33-85%)
- **Advanced treatment**
 - N and P removal (>90%)
 - Ozonation (>97%)



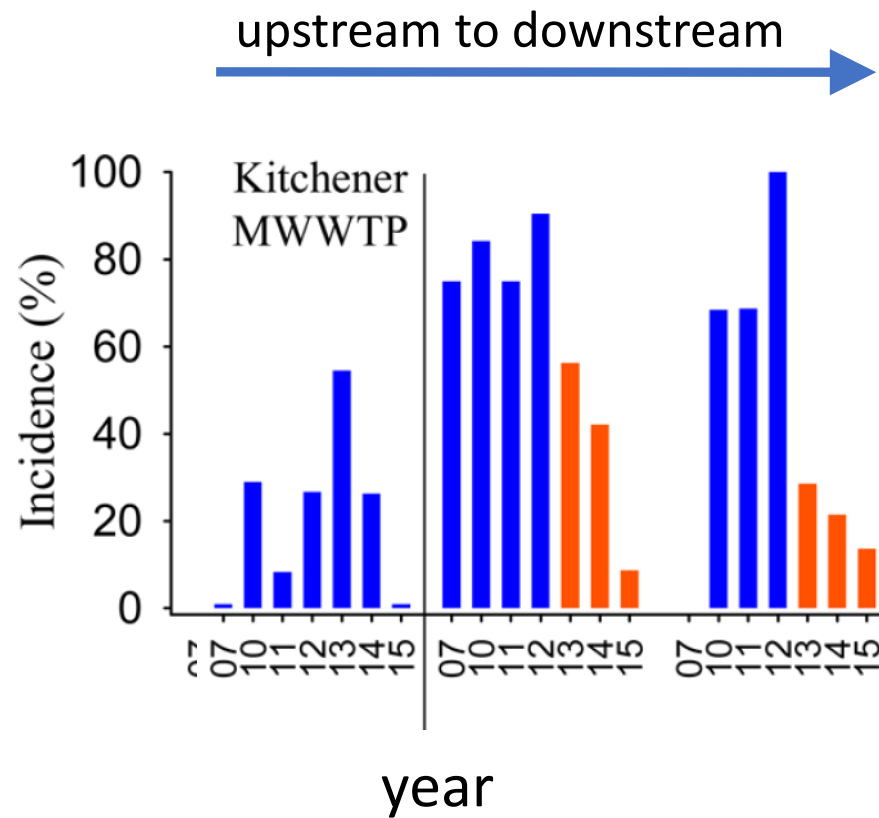
Wastewater treatment plant upgrades make a difference for effluent quality



Plant in southern Ontario upgraded to nitrifying system in 2012

Decreases in several pharmaceuticals and in estrogenicity of effluents

Municipal wastewater treatment plant upgrades make a difference for fish



Intersex in male darter declined within 3 years at downstream sites



What happens when you put fish on the pill?

Bad news

- Estrogens from municipal wastewater can affect sustainability of fish populations
- “The pill” is as effective for fathead minnow as for humans (~ 99%)
- Indirect, trophic cascades can also occur – not often considered



Good news

- Recovery of fish populations possible with removal of estrogens (upgrades have co-benefits)
- Move towards resource recovery from wastewaters likely also beneficial for pharmaceuticals



Support from

- Fisheries & Oceans Canada
- American Chemistry Council
- Canadian Toxic Substances Research Initiative
- Canadian Network of Toxicology Centres
- Canadian Water Network
- Bayer Schering Pharma AG
- Natural Sciences and Engineering Research Council



karenkidd@mcmaster.ca

Thank you! Tack!





Recipharm
good for business