Contraceptive pills cause sterile frogs

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Many animals are affected by humans, for example by the land and water exploitation and medicine consumption. We need to limit the growth of the human population to achieve a sustainability of natural resources, and contraceptives are a part of that process. The release of contraceptive substances into the environment causes difficulties for animals. Frogs can become unisex and sterile and this contributes to the catastrophic decline of amphibian species and populations all over the world. So far it is estimated that more than 100 frog species have become extinct. The decline started around 1980 and some scientists believe it to be the beginning of a sixth mass extinction, the fifth being the extinction of the dinosaurs. You probably know women who use contraceptives; it might be a friend, your sister, your girlfriend or even yourself. But how does everyday use of contraceptive hormones affect our amphibians?

How are the frogs affected?

Males can become females…
So-called endocrine disruptors can be chemical substances as well as natural or synthetic hormones. These substances disrupt the hormonal systems in humans and animals. Two examples of synthetic hormones in contraceptives that disrupt the hormone systems of frogs are ethinylestradiol and levonorgestrel. In a population of developing frog tadpoles, exposure to contraceptive hormones can cause a bigger proportion of females than males (figure 1). Males can develop both testicles and oviducts or only oviducts. The testicles often hold less sperm than normal and this lowers the fertility. After ethinylestradiol exposure of tadpoles, a larger amount of frogs than normal tend to die before they reach adulthood. This exposure also extends the time for a tadpole to reach metamorphosis, i.e., the transformation of the tadpole into a frog. This is a negative effect because tadpoles are more sensitive to predators than adult frogs.

Modified photo from Wikimedia commons.

… and females can become sterile!
After being exposed to contraceptive hormones, female tadpoles in some cases develop ovaries but no oviducts, and as a result of this they become sterile. Contraceptive hormones can cause the egg production to decrease so that the frogs end up laying fewer eggs. Additionally the eggs mature slower in the ovaries than what they normally would do. This trouble with the egg production, together with an unbalanced sex ratio and males' problems with the sperm production, lowers the fertility of frogs and can be devastating for a whole population.

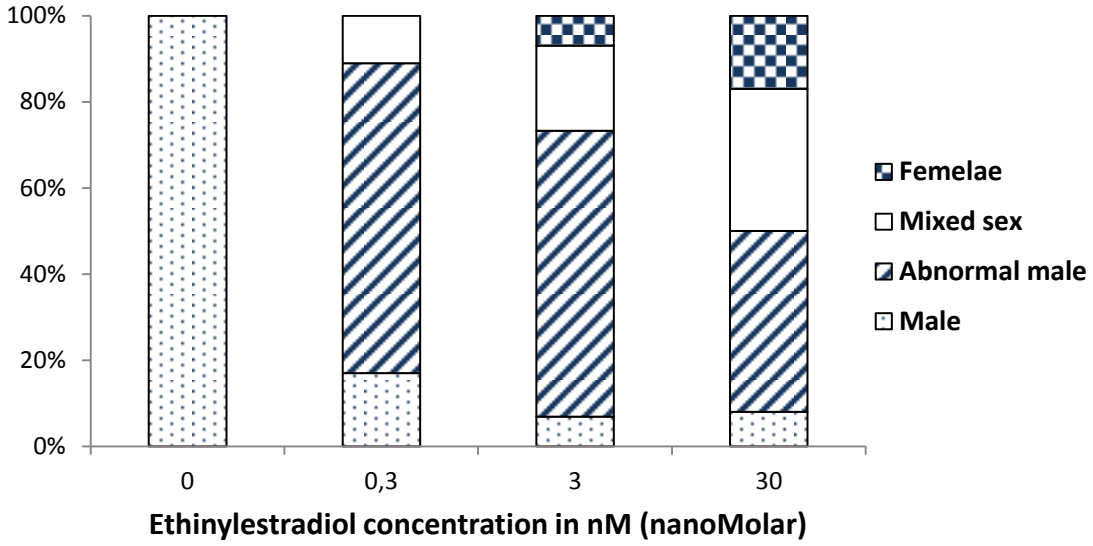

Figure 1. The figure shows that ethinylestradiol exposure in males can cause development of abnormal reproductive organs, mixed sex and complete conversion to females. The higher the hormone concentration, the higher the rate of mixed sex and females compared to normal males. The figure is modified from Tompsett with colleagues (2012), see Balck M (2013).

What about the hormones?

Endocrine substances are everywhere...
Endocrine disruptors are almost everywhere in our surroundings. These substances affect the development of humans and animals. Synthetic hormones are used in medical drugs, for example in contraceptives. About 400 000 women use contraceptive pills in Sweden and 100 million women use it worldwide. This causes large emissions of synthetic hormones into the environment. In human bodies, synthetic hormones break down slower than natural hormones. Unfortunately these hormones also break down slowly in the environment and in the bodies of animals. Common synthetic hormones in contraceptives are ethinylestradiol and levonorgestrel which both affect the reproduction of frogs.

...so the frogs in the world become fewer and fewer!
Frog species and populations have declined drastically since 1980 and it is believed that about 100 species have become extinct. Almost 2000 frog species are red listed, threatened by extinction, by the Union for Conservation of nature. In Sweden six out of eight species are red listed. Frogs are threatened by habitat fragmentation, overexploitation, a fungus disease, climate change and environmental contamination. Contaminants include hormones, and over the last 20 years a number of studies have been made about the effects that hormones have on frogs.

Habitat fragmentation = reduction in the total area of the habitat for a species population, often caused by humans

Overexploitation = human overuse of wildlife and plant species for food, clothing, pets, medicine and more

The two hormones
Both ethinylestradiol and levonorgestrel are released to aquatic systems through human urine and both hormones break down slowly in animals and nature. In Sweden, inland

waters contain low concentrations of these hormones but there can still be higher levels downstream of water purification plants. High concentrations have been recorded both in Europe and the rest of the world. This is especially the case near water purification plants and around factories producing contraceptives where unfiltered waste water leaks directly into the environment.

The model organisms

When studying the effects of hormones such as ethinylestradiol and levonorgestrel on amphibians, there are a couple of species of frogs that are commonly used. Two are the African and Western Clawed frog from the genus Xenopus and in some cases also a European species, the Common frog, is used. Xenopus is Latin for "strange foot", which is a physical characteristic for both the African and the Western species of clawed frog. Their feet are long and have a funny shape.

The African clawed frog has been used in studies since nearly a century ago, when it was discovered that the females ovulate shortly after an injection with urine from a pregnant woman. This became a common form of pregnancy test that was used for many years. Hospitals kept hundreds of frogs in their care for this reason. The fact that humans could regulate their ovulation made this species a suitable object of study. Also, the whole genome (total set of genes) has been mapped which is not the case for most frog species. The Western clawed frog also ovulates after a urine injection and both species have been used in studies about the effects of synthetic hormones.

Photo of the African clawed frog. Photo: Ben Rschr.

Photo on the Western clawed frog. Photo: Narbonne P, Simpson D and Gurdon J.

What about the future?

Contraceptives can make frogs sterile and create an unbalanced sex ratio. Put together with other factors contributing to the decline of frog species, like habitat fragmentation and over exploitation, we are lead to one conclusion. This conclusion is that the decline won't stop without human intervention and special efforts. It is important to study how chemicals and other substances affect not only humans, but also animals and nature. More studies are needed, especially to look at the so-called cocktail effect, i.e., the combined effect of different hormones. For example, both synthetic and natural estrogens bind to the same receptor, which leads to an increasing effect on the fertility of frogs. For this reason, it is important to know how concentrations that are higher than those that are environmentally relevant affect frog populations.

Areas near factories that produce synthetic hormones have high hormone concentrations present in the water. It would be interesting to make field studies there. Unfortunately very few field studies have been made. Most studies are performed in laboratories with the frogs residing in aquariums. Even though it is hard to make field studies scientifically accurate it is not impossible. The effects of endocrine disruptors are highly up-to-date, since the WHO and the UN recently finished a large report on the effects on organism and nature. Hopefully that report can inspire researchers to perform more field studies.

Human release of ethinylestradiol and levonorgestrel into the environment affects the populations of amphibians. We should start taking responsibility for the effects that we have on the environment and release less hormones and build better facilities for water purification. Now is the time to act, to create a sustainable future for this planet.

Curious to know more?

Balck M. 2013. Do contraceptives constitute a threat against viable frog populations? Independent project in Biology, Uppsala University.

Pettersson I, Berg C. 2007. Environmentally relevant concentrations of ethynylestradiol cause female-biased sex ratios in Xenopus tropicalis and Rana temporaria. Environmental Toxicology and Chemistry. **5**: 1005–1009.