

Environmental estrogens affect early developmental activity in zebrafish

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Chemicals in the environment that mimic estrogen can strongly influence the development of humans and other animals. New research to be presented at the 2012 International Zebrafish Development and Genetics Conference, held June 20-24 in Madison, Wisconsin, reveals that these substances may act even earlier than previously realized, at the very beginning stages of embryonic development.

Estrogenic compounds in the environment are both naturally occurring, such as in food plants, and synthetic, such as bisphenol A (BPA), used in making hard plastic bottles, like baby bottles and metal-based food and [beverage cans](#), including those for baby formula. They are known to affect development of the [sex organs](#), but not much is known about other effects, including any at beginning embryonic development. "The timing of exposure is critical. Evidence from animals suggests that there are critical periods of development when endocrine disruptors could be more deleterious than exposure during adulthood," says Daniel Gorelick, Ph.D., a postdoctoral fellow at the Carnegie Institution for Science.

Working with Professor Marnie Halpern, Ph.D., Dr. Gorelick discovered a new and unexpected activity of estrogenic compounds during early stages of [embryonic development](#). He will present his findings at the conference on Sunday, June 24.

The researchers used zebrafish, which offer several advantages for studying this question. "People have used fish as environmental sentinels for aquatic pollution for decades," Dr. Gorelick says. Most studies,

however, have been limited to fairly crude effects such as death or large-scale changes in single genes.

The researchers took advantage of the [genetic tools](#) available for zebrafish to study where and when estrogen receptors are active throughout the body. They genetically developed fish whose cells make a [green fluorescent protein](#) when their estrogen receptors are activated and looked at the fish early in development, during formation of the major tissues and organ systems, including the heart, gut, and central nervous system. Because zebrafish embryos are optically transparent during early development, the researchers were able to see individual estrogen-responsive cells in living, growing embryos.

"We found some things that were expected, which was [estrogen receptor](#) activity in the liver and parts of the brain known to be estrogen-responsive," Dr. Gorelick says. "The big surprise was finding it in the heart, and specifically in heart valves, which to my knowledge had not been known to be sensitive to estrogens."

In fact, the heart appears to be even more sensitive than other organs to some estrogenic compounds, particularly genistein (a common dietary estrogen found in plants) and BPA.

That finding prompted the researchers to look for possible effects of environmental estrogens. In collaboration with the Fish Health Branch of the U.S. Geological Survey and the University of Maryland School of Medicine, they collected concentrated [water samples](#) from in and around the Chesapeake Bay and found that these water samples also activate the zebrafish estrogen receptors, with especially high activation in the heart valves.

Researchers don't yet know what role estrogen sensitivity in the heart may play, nor how the fish's development may be affected by such early

exposure to estrogenic compounds. As with many signaling molecules, it's likely that both the timing and the amount of exposure are critical.

"They can respond to estrogens in the lab, but also estrogens in the environment in samples from local rivers and streams," Dr. Gorelick says. "They're everywhere and they're unavoidable, but it's the dose that makes the poison."

Dr. Gorelick and his colleagues are now working to identify specific compounds from the water samples that activate the receptors, as well as to learn what physiological role estrogen receptor activity plays in heart development and function.

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