A paper has just been released that will raise health concerns about Bisphenol A again. The paper, " Low-dose exposure to bisphenol A and replacement bisphenol S induces precocious hypothalamic neurogenesis in embryonic zebrafish " was published in the Proceedings of the National Academy of Sciences. This is a very interesting paper, but in terms of implications for human health everything hinges on what "low dose" means.

Bisphenol A (BPA) is a chemical widely used in the manufacture of plastics, is present as a developer in thermal printing paper and is present in trace amounts in the environment (I have written about BPA before here , here , here and here). Bisphenol S (BPS) is a replacement for BPA that is thought to be less estrogenic and more resistant to leaching into foods and the enviroment.

Because BPA has weak sex-hormone effects, being 1/10,000th as potent as estrogen, there has been concern that it may have adverse effects on human health. To date, no convincing evidence has been presented that the trace levels present in the environment represent a human health hazard.

The present paper looks in some detail at the ability of BPA to alter the brain development of zebra fish. Why zebra fish you ask? Zebra fish are a widely used model of vertebrate development that has been used in toxicological screening .

One of my friends and colleagues works extensively with them (I have two co-authored papers on zebra fish with him). They don't take long to grow from embryo to adult, have well established neuronal developmental pathways, they are easy to test behaviours on and their genes can be easily modified.

However, as with all models, you have to be careful about how you extrapolate your data to humans.

The paper finds evidence that there is an effect of BPA and BPS on zebra fish behaviour and

that nerve growth in specific brain regions are affected. The result that has drawn most attention is that fish embryos exposed to BPA become hyperactive as they develop (possibly due to the accelerated nerve growth).

Excitingly, the authors find that these effects are probably not due to an effect on estrogen receptors (or estrogen-like receptors) but may be working by affecting the levels of a key enzyme in steroid hormone synthesis (aromatase B).

However, despite these interesting results, this study is not applicable to human environmental exposures. There are two reasons, how much they were exposed to (relating to the “low” in low dose) and how and when they were exposed.

The concentrations of BPA in this study, while low, are still much higher than humans would be exposed to. It is a bit difficult to relate the exposures of the fish to those of humans, as humans typically do not swim immersed in solutions of BPA day in and day out, but let us look at it from a variety of perspectives.

The human exposure limit is between 25-50 microgram BPA per kilogram body weight per day (depending on which country you are in).

The fish were in water containing either 100 nanomole BPA per litre or 6.8 nanomole BPA per litre. Let’s take the lowest dose, 6.8 nanomole BPA per litre. This is 1.5 microgram per litre. This looks a lot less than the permitted human exposures, until you realise that a zebra fish embryo weighs on the order of 80 microgram. This means that their exposure is around 1,900 microgram BPA per kilogram per day (while the regulatory limit is 50 microgram per kilogram per day, humans typically consume less than 0.1 microgram per kilogram body weight per day).

Again, the fish are constantly soaking in the BPA laced water, so the BPA per kilogram body weight per day comparison may be misleading. What about looking at the intakes of the food we eat? Some canned soups will have on the order of 1.5 microgram BPA per litre (or even more), but you would have to be continuously drinking soup 24 hours a day to get the same exposure the zebra fish embryos had.

What about blood levels? Maybe that is a good comparison? The water contained 6.8 nanomole BPA per litre, human blood typically contains 0.0002 nanomole BPA per litre . Even newborns in intensive care units who are highly exposed to BPA through plastic tubing have around a thousand fold less BPA
in their blood.

So, even though the concentrations the zebra fish were exposed to were “low” they are still very much higher than human exposures (see also here).

Furthermore, the zebra fish embryos were directly exposed to the BPA and BPS at times when the major degradation pathway of BPA has not yet developed .

Human embryos at a similar developmental stage are protected by the placental barrier and the mother’s enzymes that remove BPA from the circulation. Human embryos would never be exposed to the kinds of BPA levels in this experiment.

While the ability of BPA and BPS to modulate changes in steroid hormone processing in zebra fish is intriguing, there is little evidence to suggest this pathway existing in mammals, let alone humans.

Finally, in the largest multigenerational study of exposure to low levels of BPA (from 2.5 micrograms per kilogram body weight per day and higher conducted in rats), no effects were seen until levels were achieved that could activate estrogen receptors (that is much more than seen in the zebra fish experiments.

Overall, a nicely done and very interesting paper, which identifies a new pathway that may be involved in embryonic neurogenesis. However, the concentrations used were many times what humans would be exposed to, and the fish were exposed at a time when the BPA degradation enzymes were not present. Thus it is of little relevance to human exposures and should be no cause for anxiety.

And, as always, the best way to avoid BPA is to eat plenty of fresh food, especially fresh fruit

and vegetables. This in itself has enormous health benefits beyond avoiding BPA.

Ian Musgrave does not work for, consult to, own shares in or receive funding from any company or organisation that would benefit from this article, and has no relevant affiliations.

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