

ECO-JOURNAL

March 2023

Bhavini Patel

Prenatal Exposure to Toxins and Delays in Brain Development

Prenatal growth is marked with multiple distinct and organized stages of brain and body development that exert an influence on the health of the child beyond the womb. The present scientific classification divides prenatal development into three phases: germinal, embryonic, and fetal. The germinal phase is the shortest as it is approximately 14 days in length and denotes the period during which the fertilized egg implants itself into the uterine lining. A successful implantation typically suggests the start of pregnancy and is

accompanied by the release of the human chorionic gonadotropin (hCG) hormone, i.e., the hormone that is detected by pregnancy tests (Gianfaldoni et al., 2020).

The embryonic phase of pregnancy lasts eight weeks and is relatively the most sensitive and critical part of development as this is when important bodily structures begin to form. Embryonic growth begins with the proliferation of stem cells which are genetically programmed to transform into specific body parts. Between the fourth and eighth week, multiple bodily systems are sculpted, including the heart, liver, pancreas, gall bladder, spleen, eyes, limbs (arms and legs), vascular system, lungs, and ears.

The last phase of prenatal growth is the fetal stage which represents the ultimate part of pregnancy, lasting up until birth. During this phase, the fetus begins to amass body weight as the organs continue their development to become more refined and functional for the external post-birth environment.

514-332-4320

bureau@aseq-ehaq.ca office@aseq-ehaq.ca

Exposure to Toxic Chemicals throughout Pregnancy

As can be observed from the graph above, specific hormones are released throughout pregnancy at varying levels as the gestation period progresses. One of the first hormones released is the human chorionic gonadotropin (hCG) hormone. Recent studies have shown that endocrine-disrupting chemicals (EDCs) – namely, bisphenol A and para-Nonylphenol (p-NP) – have deleterious effects on hCG production and could thereby influence whether or not the pregnancy is maintained, and if so, how the fetus will develop (Paulesu et al., 2018). Another study that looked at human cell lines also demonstrated that another EDC, dichlorodiphenyltrichloroethane (DDT), used as an insecticide in agriculture, inhibited hCG activity and progesterone secretion (Munier et al., 2021).

Progesterone levels progressively rise throughout pregnancy in an almost uninterrupted manner. The primary role of this hormone is to promote pregnancy and fetal growth, develop maternal breast tissue for later lactation, and strengthen pelvic muscles for labor (*Progesterone | You and Your Hormones from the Society for Endocrinology*, n.d.). Disruption in progesterone production during pregnancy is often linked with miscarriages (Ku et al., 2018), but in cases where the pregnancy is sustained, it can lead to altered fetal development, or what is coined "defective pregnancies" (Radwanska et al., 1978).

Estrogen is another interesting hormone whose levels also increase linearly during pregnancy. A group of EDCs are called "estrogen-like compounds" because they are known to resemble and mimic the effects of naturally produced estrogens. Since these compounds are foreign to the human body, they are called "xenoestrogens", and they are commonly found in plastics, personal and cleaning products, food (via pesticides), and tap water (Wise et al., 2011). Despite being similar to natural estrogens, xenoestrogens produce negative effects on embryonic and fetal development as they interfere with natural estrogenic activity (Watson et al., 2011). One study with pregnant Danish women found that exposure to perfluorinated alkyl acids (PFAAs) – a xenoestrogen – was linked with lower birth weight and size, an event that frequently infers the presence of developmental delays (Bjerregaard et al., n.d.). Animal studies have also supported the negative influence of xenoestrogens on pregnancy with evidence that has significance for human pregnancies and fetal growth (LaPlante et al., 2017; Witorsch, 2002).

What Happens to Child Brain Development?

So far, we have discussed how pregnancy hormones are affected by toxins and how these changes affect pregnancy maintenance and fetal development. In this section, we will dive deeper into the effects of toxic exposures on one specific system: the nervous system, which includes the body's nerves, spinal cord, and brain.

The nervous system first develops around the fifth week of pregnancy, but its true development is jumpstarted around the sixth or seventh week when the brain divides into its three rudimentary parts: the front brain, midbrain, and hindbrain (Konkel, n.d.). During the fetal stage of pregnancy, brain volume triples as the organ becomes more sophisticated, but this is also when the brain is most vulnerable to harmful factors such as EDCs.

(*Babies Born Early Can Have Brain Injury*, n.d.)

The Role of Progesterone. It has been demonstrated that progesterone has a neuroprotective effect on the fetal brain; thus, lowered progesterone levels (as discussed in the previous section) can render the brain susceptible to damage (Schumacher et al., 2020). Progesterone has also been found to be involved in the formation of neural circuits that control mood, memory, and learning in the child (González-Orozco & Camacho-Arroyo, 2019).

Xenoestrogenic Activity. The effect of xenoestrogens on fetal brain development have been extensively studied on various animal and human organoid¹ models given the recent

¹ Organoids are simplified versions of human organs (e.g., heart, brain, etc.) produced in vitro using human stem cells. They are used in many different types of scientific experiments as they create good models for studying the effects of various variables/factors/chemicals on humans without having to involve human participants.

Association pour la santé environnementale du Québec - Environmental Health Association of Québec (ASEQ-EHAQ)

findings about their toxicity. Primarily, xenoestrogens have been found to disturb the specialization of neural circuits (Fujiwara et al., 2018; Panzica et al., 2007), generating a multitude of problems for associated brain functions. Furthermore, many of these consequences have been found to be long-term, meaning that they affect the organism beyond their fetal years, and oftentimes, into adulthood.

Concrete Evidence on Observed Delays

By this point, it is clear that toxins negatively modulate brain circuits, but how does this precipitate in the child? The following points list some observations from human studies performed in the last two decades.

- \triangleright Exposure to phthalates a common ED during prenatal development correlate strongly with impaired social behaviour in children from a multiethnic population (Miodovnik et al., 2011).
- \triangleright In Swedish children (mean age = 7) exposed to endocrine disruptors prenatally, researchers found lower IQ scores, especially in boys (Tanner et al., 2020).
- ➢ Epidemiological studies have revealed that prenatal exposure to EDCs that disrupt thyroid function in the mother are often reflected by delays in language and psychomotor development when the child becomes school-aged (Ghassabian & Trasande, 2018).

Similar results have been replicated across many studies with the same conclusions being repeated: toxic exposures during prenatal development cause delays in brain development and behavioural growth in children.

Read More

Endocrine-disrupting chemicals (EDCs) are ubiquitous in the everyday environment, but there are ways to avoid them. Read our article on this subject [here.](https://aseq-ehaq.ca/wp-content/uploads/2021/03/4-EndocrineDisruptors-Part2-EN.pdf)

References

Babies Born Early Can Have Brain Injury. (n.d.). Frontiers for Young Minds. Retrieved April 14, 2022, from https://kids.frontiersin.org/articles/10.3389/frym.2018.00020

Bjerregaard, -Olesen Christian, Bach, C. C., Long, M., Wiels, øe M., Bech, B. H., Henriksen, T. B., Olsen, J., & Bonefeld, -Jørgensen Eva Cecilie. (n.d.). Associations of Fetal Growth Outcomes with Measures of the

Combined Xenoestrogenic Activity of Maternal Serum Perfluorinated Alkyl Acids in Danish Pregnant Women. *Environmental Health Perspectives*, *127*(1), 017006. https://doi.org/10.1289/EHP1884

Fujiwara, Y., Miyazaki, W., Koibuchi, N., & Katoh, T. (2018). The Effects of Low-Dose Bisphenol A and Bisphenol F on Neural Differentiation of a Fetal Brain-Derived Neural Progenitor Cell Line. *Frontiers in Endocrinology*, *9*. https://www.frontiersin.org/article/10.3389/fendo.2018.00024

Ghassabian, A., & Trasande, L. (2018). Disruption in Thyroid Signaling Pathway: A Mechanism for the Effect of Endocrine-Disrupting Chemicals on Child Neurodevelopment. *Frontiers in Endocrinology*, *9*. https://www.frontiersin.org/article/10.3389/fendo.2018.00204

Gianfaldoni, S., Tchernev, G., Tirant, M., Wollina, U., Castillo, D., & França, K. (2020). *Skin and Skin Disease Throughout Life* (pp. 1–24). https://doi.org/10.1007/978-3-319-45134-3_15-1

González-Orozco, J. C., & Camacho-Arroyo, I. (2019). Progesterone Actions During Central Nervous System Development. *Frontiers in Neuroscience*, *13*. https://www.frontiersin.org/article/10.3389/fnins.2019.00503

Konkel, L. (n.d.). The Brain before Birth: Using fMRI to Explore the Secrets of Fetal Neurodevelopment. *Environmental Health Perspectives*, *126*(11), 112001. https://doi.org/10.1289/EHP2268

Ku, C. W., Allen Jr, J. C., Lek, S. M., Chia, M. L., Tan, N. S., & Tan, T. C. (2018). Serum progesterone distribution in normal pregnancies compared to pregnancies complicated by threatened miscarriage from 5 to 13 weeks gestation: A prospective cohort study. *BMC Pregnancy and Childbirth*, *18*(1), 360. https://doi.org/10.1186/s12884-018-2002-z

LaPlante, C. D., Catanese, M. C., Bansal, R., & Vandenberg, L. N. (2017). Bisphenol S Alters the Lactating Mammary Gland and Nursing Behaviors in Mice Exposed During Pregnancy and Lactation. *Endocrinology*, *158*(10), 3448–3461. https://doi.org/10.1210/en.2017-00437

Miodovnik, A., Engel, S. M., Zhu, C., Ye, X., Soorya, L. V., Silva, M. J., Calafat, A. M., & Wolff, M. S. (2011). Endocrine disruptors and childhood social impairment. *NeuroToxicology*, *32*(2), 261–267. https://doi.org/10.1016/j.neuro.2010.12.009

Munier, M., Ayoub, M., Suteau, V., Gourdin, L., Henrion, D., Reiter, E., & Rodien, P. (2021). In vitro effects of the endocrine disruptor p,p′DDT on human choriogonadotropin/luteinizing hormone receptor signalling. *Archives of Toxicology*, *95*(5), 1671–1681. https://doi.org/10.1007/s00204-021-03007-1

Panzica, G. C., Viglietti-Panzica, C., Mura, E., Quinn, M. J., Lavoie, E., Palanza, P., & Ottinger, M. A. (2007). Effects of xenoestrogens on the differentiation of behaviorally-relevant neural circuits. *Frontiers in Neuroendocrinology*, *28*(4), 179–200. https://doi.org/10.1016/j.yfrne.2007.07.001

Paulesu, L., Rao, C. V., Ietta, F., Pietropolli, A., & Ticconi, C. (2018). HCG and Its Disruption by Environmental Contaminants during Human Pregnancy. *International Journal of Molecular Sciences*, *19*(3), 914. https://doi.org/10.3390/ijms19030914

Progesterone | You and Your Hormones from the Society for Endocrinology. (n.d.). Retrieved April 14, 2022, from https://www.yourhormones.info/hormones/progesterone/

Radwanska, E., Frankenberg, J., & Allen, E. I. (1978). Plasma Progesterone Levels in Normal and Abnormal Early Human Pregnancy**Presented at the Thirty-Fourth Annual Meeting of The American Fertility Society, March 29 to April 1, 1978, New Orleans, La. *Fertility and Sterility*, *30*(4), 398–402. https://doi.org/10.1016/S0015-0282(16)43571-5

Schumacher, M., Liere, P., & Ghoumari, A. (2020). Progesterone and fetal-neonatal neuroprotection. *Best Practice & Research Clinical Obstetrics & Gynaecology*, *69*, 50–61. https://doi.org/10.1016/j.bpobgyn.2020.09.001

Tanner, E. M., Hallerbäck, M. U., Wikström, S., Lindh, C., Kiviranta, H., Gennings, C., & Bornehag, C.-G. (2020). Early prenatal exposure to suspected endocrine disruptor mixtures is associated with lower IQ at age seven. *Environment International*, *134*, 105185. https://doi.org/10.1016/j.envint.2019.105185

Watson, C. S., Jeng, Y.-J., & Guptarak, J. (2011). Endocrine disruption via estrogen receptors that participate in nongenomic signaling pathways. *The Journal of Steroid Biochemistry and Molecular Biology*, *127*(1), 44–50. https://doi.org/10.1016/j.jsbmb.2011.01.015

Wise, A., O'Brien, K., & Woodruff, T. (2011). Are Oral Contraceptives a Significant Contributor to the Estrogenicity of Drinking Water? *Environmental Science & Technology*, *45*(1), 51–60. https://doi.org/10.1021/es1014482

Witorsch, R. J. (2002). Low-dose in utero effects of xenoestrogens in mice and their relevance to humans: An analytical review of the literature. *Food and Chemical Toxicology*, *40*(7), 905–912. https://doi.org/10.1016/S0278-6915(02)00069-8