



Critical Windows of Development Learning Module

Purpose: The purpose of this Learning Module is to use TEDX's Critical Windows of Development website to review research on the effects of prenatal exposure to endocrine disrupting chemicals in laboratory animals and to consider the potential implications for human health.

For this exercise, you will need to access the Critical Windows of Development website from The Endocrine Disruption Exchange (TEDX) <http://endocrinedisruption.org/interactive-tools/critical-windows-of-development/about-the-timeline>

Instructions: Read about the timeline on the webpage. For additional information, see *Methods* and *References* from the menu bar. To answer the questions below, click *View the Timeline*.

1: Normal Human Development

Learning Objective #1: to learn about events in normal human prenatal development.

1. The left column shows physiological systems. The top row shows trimesters and gestational weeks 1-38. The circled numbers in the gray bars indicate the number of developmental events during each week.
 - a. Which week has the most developmental events in the *Central Nervous System*?
 - b. If a woman found out she was pregnant four weeks after conceiving, how many events would have occurred in the endocrine system (including the fourth week)?
2. Click on *View Subsystems* on the left, just above the display. Under the *Endocrine System*, examine the events of thyroid development by clicking on the circled numbers.
 - a. At what week is the embryonic thyroid visible?
 - b. At what week does the fetus begin synthesizing its own thyroid hormone?
3. Choose another subsystem and explore development by clicking on circled numbers from left to right.
 - a. What subsystem did you choose?

- b. Discussion question: Which time period appears to be the most sensitive to disruption and why?

2: Chemical Effect Research

Learning Objective #2: To learn how prenatal exposure to endocrine disrupting chemicals is studied in laboratory animals.

4. Read the chemical descriptions by clicking on the name of each chemical in the *Low-Dose Chemical Research* box in the upper right.
 - a. Which chemical is a pesticide?
 - b. In what kinds of products would you expect to find bisphenol A and phthalates?
 - c. How are people exposed to dioxin?
 - d. What is the dose cut-off for inclusion of PFC studies in the timeline?
5. Click *All Chemicals* in the *Low Dose Chemical Research* box. Two new rows near the top show 'mouse days' and 'rat days' aligned with comparable weeks in human development. Colored rows represent chemical exposure research in laboratory rats and mice.
 - a. Exposure to PFCs during week three of comparable human development resulted in how many effects in the breast?
 - b. Exposure to dioxin during week six of comparable human development resulted in how many effects in the prostate?
 - c. Write a brief sentence summarizing how Dioxin affects the prostate.
6. In *Other Systems* examine *Adipose Tissue and Body Weight*. For phthalates, click on the circled number in week 1 of comparable human development.
 - a. What types of animals were studied?
 - b. How was the chemical given to the pregnant dams?
 - c. Did these studies include prenatal exposure, post-natal exposure or both?
 - d. Discussion question: How are the offspring exposed to the chemical?
7. In the *Endocrine system*, in the row for *Serum Hormones*, click on the circle in week 2 of the Bisphenol A row.
 - a. Which different hormones were affected by bisphenol A?
 - b. Which author found effects at some doses and not others?
 - c. Discussion question: Endocrine disrupting chemicals can exhibit non-linear dose-responses, for example, effects found at low doses and high

doses but not moderate doses. How is this type of dose-response different than those described in classical toxicology?

8. In the *Female Reproductive System*, in the row for *Ovaries and Eggs*, click on the circle week 2 of the bisphenol A row.
 - a. How did the effects on embryonic ovaries differ across the studies presented?
 - b. What differed in the study methods?
 - c. How many generations of animals were exposed to bisphenol A in these experiments?
 - d. Discussion question: If the same effects were measured in all the exposed generations, would you expect the effects to be different in the different generations? Why or why not?

3: Application to human health

Learning Objective #3: To consider the human health implications of laboratory research on endocrine disrupting chemicals.

9. Discussion question: What human disease outcomes might be implicated by the evidence presented in the timeline?
10. Discussion question: How is human exposure likely to differ from laboratory animal exposure with regards to dose concentrations, timing of exposure, and route of exposure?
11. Discussion question: Is the evidence from laboratory research on endocrine disrupting chemicals strong enough to cause concern for human health, despite the differences between human and laboratory animal exposure?