

## Fact Sheet for Health Professionals: Early Puberty and Breast Cancer Risk

### **Windows of Susceptibility**

- Rapidly dividing cells are more vulnerable to the effects of environmental\* exposures than non-dividing cells.<sup>1</sup> These periods of rapid cellular growth are known as “windows of susceptibility.”
  - These “windows of susceptibility” – include perinatal, postnatal, pubertal, pregnancy, lactational, and menopausal stages of life.<sup>1-3</sup>
  - Alterations in breast development are most likely to occur when the timing of certain environmental exposures overlaps with periods of rapid cellular growth.<sup>1</sup>
- Researchers are focusing increasingly on the impact of early life exposures to environmental factors during the prepubertal and pubertal windows of susceptibility.
  - It is now becoming clearer that disease risk is the result of numerous exposures across the lifespan acting in concert with an individual’s own genetics.<sup>4-5</sup>

### **Early Pubertal Development and Breast Cancer Risk**

- Estrogen exposure over a long time may increase the risk of breast cancer. As estrogen levels are highest during the years a woman is menstruating, an early first period increases the number of years breast tissue is exposed to estrogen.<sup>6</sup>
- After reviewing multiple pubertal timing studies conducted since the mid-1900s, an expert panel concluded that, overall, girls’ bodies begin to show signs of entering puberty earlier now than in the recent past.<sup>7</sup>
- Initial results from the ongoing Breast Cancer and the Environment Research Program (BCERP) also show a trend towards earlier breast development.
  - Results showed 23% of Black girls, 15% of Hispanic girls, 10% of White girls, and 2% of Asian girls in the study started developing breasts by age 7.<sup>8</sup>
- Girls who enter puberty early may have a greater risk of developing breast cancer later in life.<sup>9</sup>
  - A young girl who is suspected of entering puberty unusually early should be evaluated by her family physician or pediatrician, who may refer her to a pediatric endocrinologist or other specialist for further evaluation.<sup>10</sup>

\* For the purposes of this fact sheet, “environmental factors” include the air we breathe, the food we eat, the water we drink, and things we touch and put on our skin.

## Fact Sheet for Health Professionals: Early Puberty and Breast Cancer Risk (page 2)

### **Possible Environmental Causes of Early Puberty**

- Studies of twins have confirmed that both genetics and environmental factors affect pubertal maturation.<sup>11 - 12</sup>
- A girl who is obese\* is more likely to develop breasts and get her period at an early age.<sup>13 - 15</sup>
- Studies conducted in laboratory animals suggest that high-fat diets can cause the subjects to mature earlier than animals fed a standard diet.<sup>16 - 17</sup>
  - Experimental animal studies using rodents play a vital role in advancing the understanding of the molecular biology of mammary gland development and tumorigenesis.
- Exposure to endocrine disruptors could affect the timing of the onset of puberty.<sup>18 - 19</sup>
  - Endocrine disruptors are chemicals that mimic estrogen and may interfere with the endocrine system, producing adverse effects in humans. The risk of this interference is thought to be greater during windows of susceptibility.
  - Endocrine disruptors produce harmful effects in laboratory animals, wildlife, and humans, and may interfere with the normal action of the body's hormones.
  - Scientists are paying particular attention to endocrine-disrupting compounds called phthalates<sup>20</sup> and bisphenol A (BPA).<sup>21</sup>
    - Animal studies have suggested that maternal exposure to phthalates may be related to less regulation of cell division in the mammary glands of female offspring.<sup>22</sup>
    - Animal studies have also shown that maternal exposure to BPA, while breastfeeding, can increase mammary cancer susceptibility of the female offspring.<sup>23</sup>
- Ongoing research by the Breast Cancer and the Environment Research Program is exploring relationships such as:
  - How endocrine disrupting chemicals (EDCs) affect the age at which girls enter puberty and the age at which they have their first period;
  - Whether certain types of dietary fat, when combined with exposure to EDCs, affect breast cancer risk later in life;

\* For the purposes of this fact sheet, "obesity" is defined as a BMI at or above the 95th percentile for children of the same age and sex on the Centers for Disease Control and Prevention (CDC) growth charts found at: <http://www.cdc.gov/obesity/childhood/basics.html>.

Fact Sheet for Health Professionals:

# Early Puberty and Breast Cancer Risk (page 3)

- How hormones affect normal mammary gland development;
- How exposures to phthalate/phenol at different time points in the life cycle affect gene expression in normal mammary tissue.

## Reducing Risk

- Both healthy eating and being active can help people maintain a healthy weight and body fat level, and may help to reduce the risk of developing breast cancer later in life.
- Pregnant and breastfeeding women may want to limit their exposure to phthalates and BPA when possible, since these substances may be passed *in utero* or through breast milk to their children.<sup>24</sup> Parents and caregivers can take steps to reduce girls' exposure to phthalates and BPA by:
  - Choosing to purchase personal care products such as nail polish, deodorant, hair care, body lotion, cosmetics, detergent, and soap that say "phthalate-free," "fragrance-free," or do not have the word phthalate anywhere in the ingredient list.
  - Avoiding the use of plastic food and drink containers and plastic or vinyl toys with the number 3 in the recycling triangle, as they contain phthalates.
  - Reducing the use of plastic food and beverage containers with the number 7 in the recycling triangle, as they often contain BPA.
  - Choosing fresh or frozen fruits and vegetables over canned. The cans used for food are often lined with material that contains BPA.



Cetyl Alcohol, Synthetic Beeswax,  
Stearyl Alcohol, Benzyl Alcohol,  
**DEP** (diethyl phthalate)  
Methylparaben, Propylparaben,  
Butylparaben, BHT, Sodium



**To learn more about environmental exposures and breast cancer risk, download a monograph for health professionals and/or patient education materials at [www.info.bcerp.org](http://www.info.bcerp.org).**

<sup>1</sup> Fenton, S. E., Beck, L. M., Borde, A. R., & Rayner, J. L. (2012). Developmental exposure to environmental endocrine disruptors and adverse effects on mammary gland development. In E. Diamanti-Kandarakis & A. C. Gore (Eds.), *Endocrine Disruptors and Puberty*. New York: Humana Press.

<sup>2</sup> Diamanti-Kandarakis, E., Bourguignon, J.-P., Giudice, L. C., Hauser, R., Prins, G. S., Soto, A. M., . . . Gore, A. C. (2009). Endocrine-disrupting chemicals: An Endocrine Society Scientific Statement. *Endocrine Reviews*, 30(4), 293-342 doi: 10.1210/er.2009-0002.

Fact Sheet for Health Professionals:

Early Puberty and Breast Cancer Risk (page 4)

- <sup>3</sup> Hiatt, R. A. (2011). Epidemiologic basis of the role of environmental endocrine disruptors in breast cancer. In J. Russo (Ed.), *Environment and Breast Cancer*. New York: Springer.
- <sup>4</sup> Barker, D. J. P. (2003). The developmental origins of adult disease. *Journal of European Epidemiology*, 18, 733-736.
- <sup>5</sup> Gluckman, P. D., Hanson, M. A., & Beedle, A. S. (2007). Early life events and their consequences for later disease: A life history and evolutionary perspective. *American Journal of Human Biology*, 19, 1-19. doi: 10.1002/ajhb
- <sup>6</sup> National Cancer Institute. (August 10, 2012). Estrogen (endogenous). In *Breast Cancer Prevention (PDQ®)*. Retrieved September 24, 2012, from <http://cancer.gov/cancertopics/pdq/prevention/breast/Patient/page3#Keypoint5>
- <sup>7</sup> Euling, S. Y., Herman-Giddens, M. E., Lee, P. A., Selevan, S. G., Juul, A., Sørensen, T. I. A., . . . Swan, S. H. (2008). Examination of US puberty-timing data from 1940 to 1994 for secular trends: Panel findings. *Pediatrics*, 121(Supplement 3), S172-S191. doi: 10.1542/peds.2007-1813D
- <sup>8</sup> Biro, F. M., Galvez, M. P., Greenspan, L. C., Succop, P. A., Vangeepuram, N., Pinney, S. M., . . . Wolff, M. S. (2010). Pubertal assessment methods and baseline characteristics in a mixed longitudinal study of girls. *Pediatrics*, 126(3), e583-e590. doi: 10.1542/peds.2009-3079
- <sup>9</sup> Claudio, L. (2007). Centered on Breast Cancer. *Environmental Health Perspectives*, 115 (3), A132-133.
- <sup>10</sup> Precocious Puberty. The Merck Manual for Health Care Professionals. (2009). Retrieved March 14, 2013 from [http://www.merckmanuals.com/professional/pediatrics/endocrine\\_disorders\\_in\\_children/precocious\\_puberty.html](http://www.merckmanuals.com/professional/pediatrics/endocrine_disorders_in_children/precocious_puberty.html).
- <sup>11</sup> Ge, X., Natsuaki, M. N., Neiderhiser, J. M., & Reiss, D. (2007). Genetic and environmental influences on pubertal timing: Results from two national sibling studies. *Journal of Research on Adolescence*, 17(4), 767-788. doi: 10.1111/j.1532-7795.2007.00546.x
- <sup>12</sup> Mustanski, B. D., Viken, R. J., Kaprio, J., Pulkkinen, L., & Rose, R. J. (2004). Genetic and environmental influences on pubertal development: Longitudinal data from twins at ages 11 and 14. *Developmental Psychology*, 40(6), 1188-1198. doi: 10.1037/0012-1649.40.6.1188
- <sup>13</sup> Adair, L. S., & Gordon-Larsen, P. (2001). Maturational timing and overweight prevalence in US adolescent girls. *Journal of Public Health*, 91(4), 642-644.
- <sup>14</sup> Biro, F. M., Khoury, P., & Morrison, J. A. (2006). Influence of obesity on timing of puberty. *International Journal of Andrology*, 29(1), 272-277. doi: DOI:10.1111/j.1365-2605.2005.00602.x
- <sup>15</sup> Kaplowitz, P. B. (2008). Link between body fat and the timing of puberty. *Pediatrics*, 121(Supplement 3), S208-S217. doi: 10.1542/peds.2007-1813F
- <sup>16</sup> Medvedovic, M., Gear, R., Freudenberg, J., Schneider, J., Bornschein, R., Yan, M., . . . Clegg, D. (2009). Influence of fatty acid diets on gene expression in rat mammary epithelial cells. *Physiological Genomics*, 38, 80-88. doi: 10.1152/physiolgenomics.00007.2009
- <sup>17</sup> Olson L.K., Tan Y., Zhao Y., Aupperlee M.D., & Haslam S.Z. (2010) Pubertal exposure to high fat diet causes mouse strain-dependent alterations in mammary gland development and estrogen responsiveness. *International Journal of Obesity*, 34(9), 1415-1426. doi: 10.1038/ijo.2010.51.
- <sup>18</sup> Euling S. Y., Selevan S. G., Pescovitz O. H., & Skakkebaek N. E. (2008). Role of environmental factors in the timing of puberty. *Pediatrics*, 121(Supplement 3), S167-S171. doi: 10.1542/peds.2007-1813C
- <sup>19</sup> Jacobson-Dickman, E., & Lee, M. M. (2009). The influence of endocrine disruptors on pubertal timing. *Current Opinion in Endocrinology, Diabetes & Obesity*, 16, 25-30. doi: 10.1097/MED.0b013e328320d560
- <sup>20</sup> Barlow, J., Brown, K., Johnson, J. P., & Scofield, L. (2007, November 7). *Fact Sheet on Phthalates*. Retrieved June 27, 2012, from the Breast Cancer and the Environment Research Program Web site: <http://www.bcerp.org/cotcpubs.htm>
- <sup>21</sup> Barlow, J., & Johnson, J. P. (2007, November 7). *Fact Sheet on Phenols*. Retrieved June 27, 2012, from the Breast Cancer and the Environment Research Program Web site: <http://www.bcerp.org/cotcpubs.htm>
- <sup>22</sup> Moral, R., Wang, R., Russo, I. H., Mailo, D. A., Lamartiniere, C. A., & Russo, J. (2007). The plasticizer butyl benzyl phthalate induces genomic changes in rat mammary gland after neonatal/prepubertal exposure. *BMC Genomics*, 8, 453.
- <sup>23</sup> Jenkins, S., Raghuraman, N., Eltoum, I., Carpenter, M., Russo, J., & Lamartiniere, C. A. (2009). Oral exposure to bisphenol A increases dimethylbenzanthracene-induced mammary cancer in rats. *Environmental Health Perspectives*, 117 (6), 910-915.
- <sup>24</sup> Lamartiniere, C. A., Jenkins, S., Betancourt, A. M., Wang, J., & Russo, J. (2011). Exposure to the endocrine disruptor bisphenol A alters susceptibility for mammary cancer. *Hormone Molecular Biology and Clinical Investigation*, 5(5), 45-52. doi: 10.1515/HMBCI.2010.075

Made possible by the Breast Cancer and the Environment Research Program (BCERP) grants U01 ES012770, U01 ES012771, U01 ES012800, U01 ES012801, U01 ES019453, U01 ES019435, U01 ES019454, U01 ES019457, U01 ES019471, U01 ES019466, U01 ES019434, U01 ES019480, U01 ES019482, U01 ES019459, U01 ES019472, and U01 ES019458 from the National Institute of Environmental Health Sciences (NIEHS) and the National Cancer Institute (NCI), NIH, DHHS.