Published in final edited form as:
J Pediatr Adolesc Gynecol. 2009 February ; 22(1): 3–6. doi:10.1016/j.jpag.2008.12.003.

Impact of yesterday's genes and today's diet and chemicals on tomorrow's women

Frank M Biro, MD,
Division of Adolescent Medicine, Cincinnati Children's Hospital Medical Center, Cincinnati OH

Mary S Wolff, PhD, and
Mount Sinai School of Medicine, Division of Environmental Health Sciences, New York NY

Lawrence H Kushi, ScD
Division of Research, Kaiser Permanente, Oakland CA

A previous editorial in this journal (Puberty - Whither goest?) discussed whether pubertal maturation was occurring earlier in U.S. girls, and the potential causes of those changes.[1] Several original manuscripts, review papers, and convened consensus groups have discussed these topics, and most of the published works have accepted that 1) there is a decrease in the age of onset of puberty, as defined by breast development, and 2) there is a more modest decrease in the age of menarche (reviewed by Kaplowitz).[2] Black women experience menarche approximately six months earlier than white women, whereas their breast development appears to be up to one year earlier than white women. When examining the potential causes of the continued decrease in age of onset of puberty in girls, many have noted that there has been a coincident epidemic in rates and degrees of obesity. They concluded that increased body mass index (BMI) accounts for much of the change in age of onset of puberty in girls; the changes in pubertal onset, and association with increased BMI, are not as clear in boys.

The relationship between onset of breast development and age of menarche appears to have changed over the past 50 years, however. For example, the correlation between onset of breast development and menarche was 0.86, as reported by Reynolds and Wines in women born in the 1930s, [3] contrasted to 0.37 in women born in the late 1970s. [4] This changing relationship suggests that other factors could be contributing differentially to earlier onset of breast development, when contrasted to decrease in age of menarche; these factors could include, in addition to increased BMI, exposure to endocrine disrupting chemicals (EDCs), or hyperinsulinism and/or insulin resistance.[5] There has been a growing body of scientific literature regarding the impact of purported EDCs. These include the effect of certain environmental exposures on body composition (phthalates and increased central obesity[6]; phytoestrogens and reduced adiposity[7]); onset of earlier puberty (phthalates and early thelarche[8]; polybrominated biphenyls [PBBs]) and early thelarche[9]; DDE and precocious puberty[10]; and DDE and earlier menarche).[11–12] Other exposures have been observed to delay pubertal maturation (lead and menarche).[13–15] However, some studies have not shown a relationship between these same chemicals with changes in pubertal milestones (for example, Denham 2002).[13] The impact of endocrine disruptors on breast development and on pubertal

Corresponding Author: Frank M. Biro, M.D., Division of Adolescent Medicine, Cincinnati Children's Hospital Medical Center, 3333 Burnet Avenue, Cincinnati OH 45229. Cincinnati OH. Phone: 513 636-8602. Fax: 513 636-1129. Email: frank.biro@cchmc.org.

maturation has been reviewed recently.[14–18] The relationship of EDCs and puberty may be very complex, with interactions between timing of exposure, exposure levels, body composition, and genetics. For example, in a cross sectional study, phytoestrogen biomarker concentrations were lower among girls with breast development, but the effect was seen in those with lower BMI.[19] These studies are limited by small numbers or cross-sectional design, but find stronger support in the animal literature.

Studies have suggested that there has been a selective advantage in lower age of maturation, yielding more progeny over a period of several decades. Genetic variation has been estimated to account for 57–100% variation of pubertal timing,[20] with the remainder of the variability accounted by environmental influences. The trait of earlier maturation is conserved,[21–23] and the timing of reproductive functioning sensitive to environmental cues to maximize reproductive success.[24] However, the advantage conferred to the human species in the past may provide a disadvantage in the contemporary setting. Cultural changes proceed faster than genetic accommodations, which Eaton has described as the mismatch of “Stone Age” genes with “Space Age” circumstances.[25] For example, the contemporary milieu has eliminated programmed biochemical cycles from feast-famine and physical activity-rest cycles, which would be experienced by hunter-gatherer societies, and provides food abundance with physical inactivity, which has led to biochemical changes and obesity, with subsequent insulin resistance.[26] Thus, the “thrifty phenotype” conferred a survival advantage to the hunter-gatherer, but it has become a risky phenotype for obesity and diabetes, as observed in contemporary Native American populations who adapted sedentary occupations over recent generations.[27] Regular physical activity has decreased dramatically when contrasted to earlier times (see Table).[28] In contemporary adolescent girls, higher BMI has been shown to be associated with greater declines in physical activity.[29] Additionally, in a young adult population followed since adolescence, the faction of selected adverse health outcomes attributed to watching television for more than two hours a day included 17% of that group’s overweight status, 15% of the elevation noted in cholesterol levels, 17% of tobacco smoking, as well as 15% of poor fitness in that group.[30] In brief, earlier pubertal maturation with an earlier ability to reproduce would have provided a selective advantage, especially 5,000 or more years ago. If the biologic price was an increase in hormone-dependent and/or reproductive tract factors in the fifth decade, that trait would be selected and preserved.

The costs to earlier maturation in 21st century girls are many. Girls who mature earlier have lower self-esteem during adolescence and lower levels of body satisfaction,[31] greater likelihood of depression[32] and eating disorders[33], greater perceived stress,[34–35] greater vulnerability to peer pressures,[34] younger ages of sexual initiation,[36–37] and smoking and drug use.[38–39] As adults, early maturing girls exhibit poorer adjustment[40] and lower life-long academic achievement[41]. They also have greater weight and BMI,[42] as well as insulin resistance and cardiovascular disease[43]; additionally, women with breast cancer are noted to have young age of menarche.[44–48] Of note, when age at peak growth is included in the analysis, the age of menarche is not associated with risk of breast cancer; menarche, as well as age of peak growth, may reflect age at onset of puberty.[49] With earlier age of menarche, and later age at first birth, there is a longer interval from menarche to first birth; this lengthened period potentially leads to a longer period of susceptibility of breast tissue to carcinogens.[50] Additionally, contemporary women have a greater number of ovulatory cycles, contrasted to women from several centuries ago,[51] again increasing the risk for hormone-dependent tumors (Table).[28]

In short, the fertility goddess of the Bronze Age 2000 BC would have had children at a younger age, and more children. The goddess of the year AD 2009 would have insulin resistance and be more likely to develop breast cancer. It is food for thought that much of this difference could be preventable.

Acknowledgments

Funded, in part, by U01-ES 12770, 012771, 012800, 012801.

References

1. Biro FM. Puberty - Whither goest? J Pediatr Adolesc Gynecol 2006;19:163–5. [PubMed: 16731407]
2. Kaplowitz PB. Link between body fat and timing of puberty. Pediatrics 2008;121 Suppl 3:S208–17. [PubMed: 18245513]
3. Reynolds EL, Wines JV. Individual differences in physical changes associated with adolescence in girls. Am J Dis Child 1948;75:329–50. [PubMed: 18882060]
4. Biro FM, Huang B, Crawford RB, et al. Pubertal correlates in black and white girls. J Pediatr 2006;148:234–40. [PubMed: 16492435]
5. Euling SY, Selevan SG, Pescovitz OH, et al. Role of environmental factors in the timing of puberty. Pediatrics 2008;121 Suppl 3:S167–71. [PubMed: 18245510]
6. Stalhut RW, van Wijngaarden E, Dye TD, et al. Concentrations of urinary phthalate metabolites are associated with increased waist circumference and insulin resistance in adult US males. Environ Health Perspect 2007;115:876–82. [PubMed: 17589594]
7. Cederroth CR, Vinciguerra M, Kühne F, et al. A phytoestrogen-rich diet increases energy expenditure and decreases adiposity in mice. Environ Health Perspect 2007;115:1467–73. [PubMed: 17938737]
8. Colon I, Caro D, Bourdony CJ, et al. Identification of phthalate esters in the serum of young Puerto Rican girls with premature breast development. Environ Health Perspect 2000;108:895–900. [PubMed: 11017896]
9. Blanck HM, Marcus M, Tolbert PE, et al. Age at menarche and tanner stage in girls exposed in utero and postnatally to polybrominated biphenyl. Epidemiology 2000;11:641–7. [PubMed: 11055623]
10. Krstevska-Konstantinova M, Charlier C, Craen M, et al. Sexual precocity after immigration from developing countries to Belgium: Evidence of previous exposure to organochlorine pesticides. Hum Reprod 2001;16:1020–6. [PubMed: 11331654]
11. Vasiliu O, Muttineni J, Karmaus W. In utero exposure to organochlorines and age at menarche. Hum Reprod 2004;19:1506–12. [PubMed: 15131079]
12. Ouyang F, Perry MJ, Venners SA, et al. Serum DDT, age at menarche, and abnormal menstrual cycle length. Occup Environ Med 2005;62:878–84. [PubMed: 16299097]
13. Selevan SG, Rice DC, Hogan KA, et al. Blood lead concentration and delayed puberty in girls. N Engl J Med 2003;348:1515–6. [PubMed: 12700370]
14. Wu T, Buck GM, Mendola P. Blood lead levels and sexual maturation in US girls: The Third National Health and Nutrition Examination Survey, 1988–1994. Environ Health Perspect 2003;111:737–41. [PubMed: 12727603]
15. Denham M, Schell LM, Deane G, et al. Relationship of lead, mercury, mirex, dichlorodiphenyldichloroethylene, hexachlorobenzene, and polychlorinated biphenyls to timing of menarche among Akwesasne Mohawk girls. Pediatrics 2002;115:e127–34. [PubMed: 15653789]
16. Den Hond E, Schoeters G. Endocrine disruptors and human puberty. Int J Androl 2006;29(1):264–71. [PubMed: 16466548]
17. Fenton SE. Endocrine-disrupting compounds and mammary gland development: Early exposure and later life consequences. Endocrinology 2006;147:S18–24. [PubMed: 16690811]
18. Rasier G, Toppari J, Parent AS, et al. Female sexual maturation and reproduction after prepubertal exposure to estrogens and endocrine disrupting chemicals: A review of rodent and human data. Mol Cell Endocrinol 2006;254–255:187–201.
19. Nebesio, TD.; Pescovitz, OH. The role of endocrine disruptors in pubertal development. In: Pescovitz, OH.; Walvoord, EC., editors. When Puberty is Precocious: Scientific and Clinical Aspects. Vol. 1. Totowa NJ: Humana Press; 2007.
20. Buck, Louis GM.; Gray, LE.; Marcus, M., et al. Environmental factors and puberty timing: Expert panel research needs. Pediatrics 2008;121 Supple 3:S192–207. [PubMed: 18245512]
21. Wolff MS, Britton JA, Boguski L, et al. Environmental exposures and puberty in inner-city girls. Environ Res 2008;107:393–400. [PubMed: 18479682]

22. Wehkalampi K, Silventoinen K, Kaprio J, et al. Genetic and environmental influences on pubertal timing assessed by height growth. Am J Hum Biol 2008:417–23. [PubMed: 18293372]
23. Treloar SA, Martin NG. Age at menarche as a fitness trait: Nonadditive genetic variance detected in a large twin sample. Am J Hum Genet 1990;47:337–48.
24. Kaprio J, Rimpela A, Winter T, et al. Common genetic influences on BMI and age of menarche. Hum Biol 1995;67:739–53. [PubMed: 8543288]
25. Kirk KM, Blomberg SP, Duffy DL, et al. Natural selection and quantitative genetics of life-history traits in Western women: A twin study. Evolution 2001;55:423–35. [PubMed: 11308097]
26. Mustanski BS, Viken RJ, Kaprio J, et al. Genetic and environmental influences on pubertal development: Longitudinal data from Finnish twins at ages 11 and 14. Dev Psychol 2004;6:1188–98. [PubMed: 15535766]
27. Eaton SB, Strassman BI, Neese RM, et al. Evolutionary Health Promotion. Prev Med 2002;34:109–18. [PubMed: 11817903]
28. Chakravarthy MV, Booth FW. Eating, exercise, and “thrifty” genotypes: Connecting the dots toward an evolutionary understanding of modern chronic disease. J Appl Physiol 2004;96:3–10. [PubMed: 14660491]
29. Pavkov ME, Bennett PH, Hanson RL, et al. Changing patterns of type 2 diabetes incidence among Pima Indians. Diabetes Care 2007;30:1758–63. [PubMed: 17468358]
30. Cordain L, Gotshall RW, Eaton SV, et al. Physical activity, energy expenditure and fitness: An evolutionary perspective. Int J Sports Med 1998;19:1–8. [PubMed: 9506791]
31. Kimm SYS, Glynn NW, Kriska AM, et al. Decline in physical activity in black girls and white girls during adolescence. N Engl J Med 2002;347:709–15. [PubMed: 12213941]
32. Hancox RJ, Milne BJ, Poulton R. Association between child and adolescent television viewing and adult health: A longitudinal birth cohort study. Lancet 2004;364:257–62. [PubMed: 15262103]
33. Striegel-Moore RH, McMahon RP, Biro FM, et al. Exploring the relationship between timing of menarche and eating disorder symptoms in black and white adolescent girls. Int J Eat Disord 2001;30:421–33. [PubMed: 11746303]
34. Angold A, Worthman CW. Puberty onset of gender differences in rates of depression: A developmental, epidemiologic and neuroendocrine perspective. J Affect Disord 1993;29:145–58. [PubMed: 8300975]
35. Kalttiala-Heino R, Rimpela M, Rissanen A, et al. Early puberty and early sexual activity are associated with bulimic-type eating pathology in middle adolescence. J Adolesc Health 2001;28:346–52. [PubMed: 11287254]
36. Ge X, Conger RD, Elder GH. Coming of age too early: Pubertal influences on girls’ vulnerability to psychological distress. Child Dev 1996;67:3386–400. [PubMed: 9071784]
37. Van Jaarsveld CH, Fidler JA, Simon AE, et al. Persistent impact of pubertal timing on trends in smoking, food choice, activity, and stress in adolescence. Psychosom Med 2007;69:798–806. [PubMed: 17942841]
38. French DC, Dishion TJ. Predictors of early initiation of sexual intercourse among high-risk adolescents. J Early Adolesc 2003;23:295–315.
39. Rosenthal SL, Von Ranson KM, Cotton S, et al. Sexual initiation: Predictors and developmental trends. Sex Transm Dis 2001;28:527–32. [PubMed: 11518870]
40. Lanza ST, Collins LM. Pubertal timing and the onset of substance use in females during early adolescence. Prev Sci 2002;3:69–82. [PubMed: 12002560]
41. Patton GC, McMorris BJ, Toumbourou JW, et al. Puberty and the onset of substance use and abuse. Pediatrics 2004;114:e300–6. [PubMed: 15342890]
42. Graber JA, Seeley JR, Brooks-Gunn J, et al. Is pubertal timing associated with psychopathology in young adulthood? J Am Acad Child Adolesc Psychiatry 2004;43:718–46. [PubMed: 15167088]
43. Johansson T, Ritzen EM. Very long-term follow-up of girls with early and late menarche. Endocr Dev 2005;8:26–36.
44. Biro FM, McMahon RP, Striegel-Moore R, et al. Impact of timing of pubertal maturation on growth in black and white female adolescents: The National Heart, Lung, and Blood Institute Growth and Health Study. J Pediatr 2001;13:636–43. [PubMed: 11343036]

45. Morrison JA, Sprecher DL, Barton BA, et al. Overweight, fat patterning, and cardiovascular disease risk factors in black and white girls: The National Heart, Lung, and Blood Institute Growth and Health Study. J Pediatr 1999;135:458–64. [PubMed: 10518079]

46. Kelsey JL, Gammon MD, John EM. Reproductive factors and breast cancer. Epidemiol Rev 1993;15:36–47. [PubMed: 8405211]

47. Peeters PH, Verbeek AL, Krol A, et al. Age at menarche and breast cancer risk in nulliparous women. Breast Cancer Res Treat 1995;33:55–61. [PubMed: 7749133]

48. Petridou E, Syrigou E, Toupadaki N, et al. Determinants of age at menarche as early life predictors of breast cancer risk. Int J Cancer 1996;68:193–8. [PubMed: 8900427]

49. Clavel-Chapelon F. Differential effects of reproductive factors on the risk of pre- and postmenopausal breast cancer. Results from a large cohort of French women. Br J Cancer 2002;86:723–7. [PubMed: 11875733]

50. Okasha M, McCarron P, Gunnell D, et al. Exposures in childhood, adolescence, and early adulthood and breast cancer risk: A systematic review of the literature. Breast Cancer Res Treat 2003;78:223–76. [PubMed: 12725422]

51. Ahlgren M, Melbye M, Wohlfahrt J, et al. Growth patterns and the risk of breast cancer in women. Int J Gynecol Cancer 2006;16 (Suppl 2):569–575. [PubMed: 17010075]

52. Russo J, Tay LK, Russo IM. Differentiation of the mammary gland and susceptibility to carcinogenesis. Breast Cancer Res Treat 1982;2:5–73. [PubMed: 6216933]

53. Strassman BI. The viology of menstruation in Homo sapiens: Total lifetime menses, fecundity, and nonsynchrony in a natural fertility population. Curr Anthropol 1997;38:123–9.

Table

It's Greek to me, but the Goddesses of Yesteryear lived well, though not long, and Today live longer but…

	Greece of 2000 BC	United States of 2000 AD
Age of menarche	17	12
Interval menarche to first birth (years)	3 years	12 years
Number of children	6	1.8
Duration of breast feeding	3 years	0–6 months
Daily energy expenditure	20 kcal/kg/day	< 5 kcal/kg/day
Age at death	40 years	75 years
Risk of breast cancer	Unknown (minimal)	1 in 8