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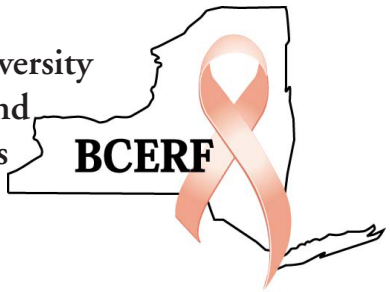
A Newsletter of the Cornell University Program on Breast Cancer and Environmental Risk Factors in New York State (BCERF)



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Premature Thelarche in Puerto Rico: Natural Phenomenon, Man-made Health Catastrophe or Both?

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Puberty/Breast Development: When is Premature?

In humans, the onset of puberty is primarily assessed by the physical changes that occur in the genitalia of both sexes. In females, the physical signs associated with the onset of puberty are enlargement of the breasts, ovaries, and uterus, as well as the growth of pubic and axillary (armpit) hair with apocrine secretion (sweat with odor). The process by which puberty occurs is primarily regulated by the endocrine system through its chemical messengers, specifically the sexual hormones (Liwnicz, B.H. and R.G. Liwnicz, 1989). The onset of pubertal changes at an earlier age than expected may occur secondary to a varied group of disorders. When the cause of premature sexual development is unknown, the condition is considered idiopathic (having no known cause). Premature sexual development in the human female is presently defined as the appearance of any physical change characteristic of puberty with onset before eight years of age (Sippell, 1994; Stanhope, 2000).

Hyperplasia (increased but non-cancerous growth) of breast tissue in newborns may be present during the first six months of life as a result of placental passage of maternal estrogenic hormones. When this condition persists beyond this period or occurs before eight years of age in females, it is known as premature or precocious thelarche (figure 1). The majority of cases occur before two years of age. Girls diagnosed with premature thelarche have one or both breasts enlarged without any other physical signs of the onset of puberty (Kulin and Muller, 1996; Stanhope, 2000).

Premature Thelarche in Puerto Rico

Since 1979, pediatric endocrinologists in Puerto Rico have detected an alarming increase in the number of patients with premature thelarche (Pérez, 1982; Bongiovanni, 1983). Among the hypotheses proposed to explain the observed premature sexual development in this US Caribbean island territory, the most controversial theory associated thelarche with the subject's diet. Sáenz et al. (1985) suggested that dairy and meat products were contaminated with anabolic estrogenic chemicals, which are used for increasing muscle mass in cattle and poultry. In 1985, studies conducted by the US Department of

Agriculture, in conjunction with a scientific commission from the Puerto Rico Department of Health, led to the conclusion that no abnormal levels of the suspected chemicals were present in the approximately 800 samples of meat and dairy products that were analyzed (Montgomery, unpublished data). Other theories are still under consideration, such as the association with ovarian cysts, premature endogenous production of sexual hormones, and environmental contamination by pharmaceutical waste products. These theories do not establish a strong association with the majority of the cases reported (Freni-Titulaer, et al., 1986). Also, a genetic predisposition of Puerto Rican girls for the study of premature sexual development in a human population. The objectives of this surveillance system are to define the epidemiologic, clinical, and etiologic aspects of the different manifestations of premature sexual development on the island. Although the registry was established in 1988, retrospective data to 1969 and prospective data to 2001 have been collected. In this time period, approximately 7,600 cases of premature sexual development have been registered, of which 70% are premature thelarche cases. Based on the data accumulated by the registry, the estimated annual average incidence rate of premature thelarche in Puerto Rican girls 6-24 months of age is eight cases per 1,000

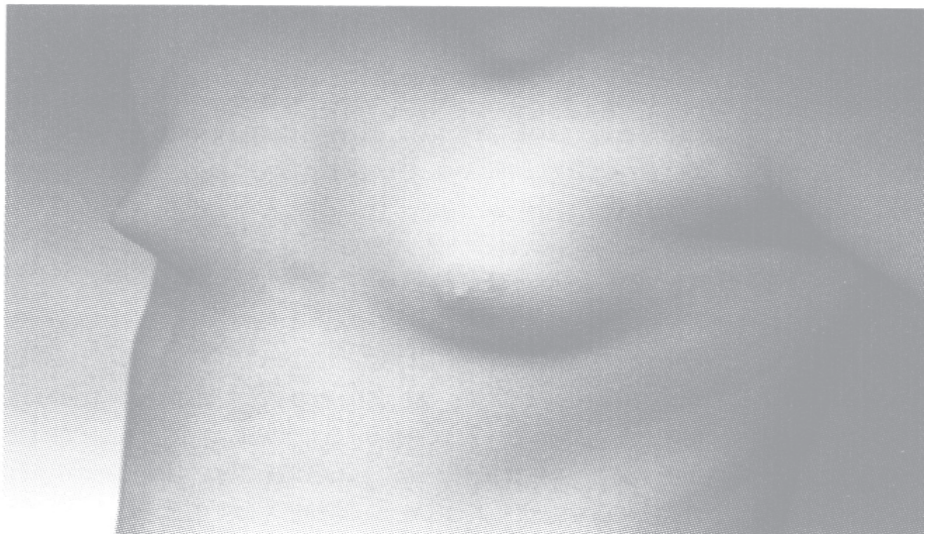

Figure 1. Twenty-four month old Puerto Rican female with precocious breast development (thelarche). Photo courtesy of Dr. Carlos Bourdony.

developing premature thelarche is unlikely. Investigation of this ethnic group in the Philadelphia area did not reveal a similar pattern of early sexual development (Freni-Titulaer, et al., 1986). Moreover, other ethnic groups living in Puerto Rico are also affected by the condition (Freni-Titulaer, et al., 1986).

In 1987, the Puerto Rico Department of Health created by law the Premature Thelarche and Early Sexual Development (PTESD) Registry in response to the observed increase in cases (Commonwealth of Puerto Rico, 1989). This is the only world registry created for live female births from 1984 to 1993 (Bourdony, 1998). This incidence is, to our knowledge, the highest ever reported. Compared to a study conducted in Minnesota (Van Winter, et al., 1990), this estimated incidence of premature thelarche in the Puerto Rican female population is 18.5 times higher. The actual incidence is much higher since only the cases diagnosed by some of the pediatric endocrinologists practicing in the island are being recorded by the Registry. The other 30% of registered cases consist of premature sexual hair, strong (apocrine) odor in both sexes, vaginal bleeding in females and prepubertal enlarged breasts (gynecomastia)

in males. No studies have been conducted to define the clinical, epidemiologic, etiologic or prognostic characteristics of these conditions.

Exploring an Environmental Connection

In the last decade, there has been a growing interest and concern for the study of the impact of man-made chemicals on wildlife and humans. These studies have suggested that synthetic and naturally occurring substances in the environment may affect the normal function of the endocrine system. These substances are also referred to as endocrine disrupting chemicals (EDCs). In wildlife, alterations in sexual reproductive behavior have been observed in areas of contamination with EDCs. For example, malformations in the sexual organs of alligators have been reported in Lake Apopka, Florida, where high concentrations of DDT and its degradation products have been detected (Guillette, et al., 1994; Vonier, et al., 1996). Feminization of male trout in the Great Lakes has been associated with the high levels of polychlorinated biphenyls (PCBs) in water samples (Colborn, et al., 1993). Other studies have indicated that many chemicals, including phthalate esters, may affect development and reproduction, including germ cells, sperm motility, chryptorchidism, and hypospadias in laboratory animals (Siddiqui and Srivastava, 1992; Fredricsson et al., 1993; Imajima, et al., 1997; Poon, et al., 1997; Arcadia, et al., 1998). The specific mechanisms by which these chemicals may affect human health are mostly unknown. Extrapolations to humans of the effect of these substances on wildlife are difficult. A limited number of reports (Mocarelli, et al., 1996; Weisglas-Kuperus, et al., 1995; Sattin, et al., 1984) in the scientific literature describe the accidental exposure of humans to chemicals such as lindane and other organochlorine pesticides, dioxins, and PCBs with known endocrine disrupting properties. The study of these exposures has led to the conclusion that these compounds can alter the female-to-male ratio in offspring (Mocarelli, et al., 1996) and cause learning disabilities, behavioral problems, suppression of the immune system, and gynecomastia (abnormal enlargement of the male mammary glands) in the exposed subjects (Weisglas-Kuperus, et al., 1995; Sattin, et al., 1984).

At present, the cause of the observed high incidence of premature sexual development in Puerto Rico is unknown, and the long-term consequences of the aberrant premature sexual development in this population are also unknown. Many of the chemicals that are classified as EDCs have been imported or produced in high quantities in Puerto Rico. Until 1988, a total of 450 million pounds of chlorinated pesticides were imported to the island (Quiñones, 1992). Although many of these pesticides are currently banned for use in US territories, these pesticides are known to bioaccumulate and to persist in the environment. Also, many of these substances such as phthalate esters, alkyl phenols, and surfactants are present in commercial products commonly used for packaging, storing, and preserving food (Ross, 1994). The environmental load of plasticizers in Puerto Rico is unknown, but is assumed to be significant because of the high level of consumption of dietary products in plastic containers imported to the island. Based on the high exposure to these substances in the general population in Puerto Rico and the fact that exposure of human fetuses, newborns, and young girls to exogenous estrogenic chemicals may lead to adverse effects in their sexual development, in 1997 we designed a study to search for known EDCs in the serum of Puerto Rican girls with premature thelarche and controls (Colón, et al., 2000). Significant high levels of phthalates [dimethyl, diethyl, dibutyl, and di-(2-ethylhexyl) and its major metabolite mono-(2-ethylhexyl) phthalate] were identified in 28 (68%) samples from thelarche patients. Of the control samples analyzed, only one showed significant levels of di-isooctyl phthalate. The phthalates that we identified have been classified as endocrine disruptors. This study suggests a possible association between plasticizers with known estrogenic and antiandrogenic activity, and the cause of premature breast development in a human female population.

Among the observations that may arise to explain the results that we have obtained in our study is the possible contamination during collection or analysis of the patient samples. It is well known that phthalates are ubiquitous in the environment and such contamination can occur unless particular care is observed to avoid it. With this possibility in mind, the experimental procedures were designed to assure that all the control samples were obtained, stored, handled and analyzed in exactly the same conditions as the patient samples. The presence of EDC phthalates were not observed in the control samples. Had the source of the EDC phthalates in the patient samples been due to contamination, these too would have been detected in the controls. In addition, synthetic serum matrix samples, known commercially as Monitrol, were used as blanks to monitor the overall procedure. No

contamination was observed in these blanks. In addition to the evidence from the controls and the blanks previously described, to further discard possible contamination, metabolites of the phthalates were also analyzed and detected in the study samples. Had contamination of the samples been the source, the metabolites would not be detected since the metabolites are formed when phthalates esters are internalized in the patient.

Where Do We Go From Here?

The findings of this study cannot be interpreted as the specific cause of premature thelarche in Puerto Rican girls. It may well be that the etiology of the various manifestations of premature sexual development (including thelarche) on this island is multifactorial. Further research should be performed to clarify if phthalate esters by themselves, or in association with other endogenous or exogenous estrogenic compounds, are capable of inducing precocious sexual development in animals and humans.

In the last century, the average age of menarche in the US and Europe has decreased by two to three months per decade, probably as a result of improved nutrition and living conditions (Marshall and Tanner, 1989). In a study conducted by the American Academy of Pediatrics in 1997 that included 17,077 girls, Herman-Giddens et al. (Herman-Giddens, et al., 1997) reported that girls in the United States are developing pubertal characteristics at younger ages than previously reported, but the age of menarche was not significantly reduced. These authors concluded that "the possibility that the increasing use of certain plastics and insecticides that degrade into substances that have estrogen-related physiological effects on living things should be investigated in relation to the earliest onset of puberty". Is the observation of premature sexual development in Puerto Rico a more prominent manifestation of a wider US or world phenomenon? The answer to this important hypothesis awaits confirmation by future research.

There is growing concern that premature thelarche may not be the homogeneous or benign medical condition that it was once considered (Stanhope, 2000). A descriptive analysis of 1,196 cases from Puerto Rico revealed that 73% of the girls (under two years of age) had "classical" thelarche as compared to the rest (two to eight years of age) which conformed more to an atypical variant as classified by Stanhope (Stanhope, 2000; Larriuz, 1998). This study also revealed that in Puerto Rico, girls under two years of age with premature thelarche have a hormonal profile characterized by increased LH (luteinizing hormone) and estradiol (one of the naturally-occurring estrogens) levels. This finding suggests some degree of endogenous activation of the mechanisms of puberty in this cohort, in the absence of all the physical characteristics of complete sexual development. The possible association of early exposure to estrogens in young girls and development of breast cancer later in life is currently under scientific scrutiny. The long-term sequelae of premature thelarche have not been adequately studied and defined. Preliminary data suggest several possible complications like progression to central precocious puberty, ovarian cyst formation, and development of benign or malignant tumors of the breast (Stanhope, 2000). The possible associations of other physical or psychological sequelae to thelarche cases in Puerto Rico have not been adequately studied. Unfortunately, the problem of premature sexual development in Puerto Rican children is not a priority health issue for the island's health authorities, pediatric professional associations and health research centers. This may explain why, although this important public health observation has been known for more than two decades, its etiology, long term consequences, and prevention still await elucidation. Is the increased occurrence of premature sexual development in Puerto Rico (and in particular premature thelarche) a natural phenomenon, a public health catastrophe induced by environmental man-made toxicants, or a combination of these two factors? The elucidation of this biologic enigma should prove to be of important scientific and public health value for improving the health care of children in Puerto Rico, but also for further understanding the future of sexual development in humans.

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Premature Thelarche: Clinical Follow-up and Indication for Treatment

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Journal of Pediatric Endocrinology & Metabolism, 13 (2000):827-830.

Abstract

Not only is the diagnosis of isolated premature thelarche difficult to distinguish from other variants of premature sexual maturation, but within the subgroups of isolated premature thelarche, there are probably at least two subgroups: "classical" and "atypical". We do not appreciate how potential treatment could affect each group, although it seems likely that those in the "classical" group would not have an indication for treatment. The longer-term follow-up of large numbers of patients is essential if we are to understand the long-term sequelae of this condition.

NOTE: Due to space restrictions, *The Ribbon* was not able to reproduce this article in full. We encourage interested readers to obtain the full article.

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When Little Girls Become Women: Early Onset of Puberty in Girls

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There are new guidelines for pediatricians that are guaranteed to shock: girls who start to develop breasts and pubic hair at age six or seven are not necessarily "abnormal" (Kaplowitz, et al., 1999). In fact, by their ninth birthday, 48% of African American girls and 15% of white girls are showing clear signs of puberty.

The new guidelines, developed by the Lawson Wilkins Pediatric Endocrine Society and published in the journal of the American Academy of Pediatrics, *Pediatrics*, are based primarily on a study of more than 17,000 girls between the ages of three and 12 who were patients in more than 200 pediatricians' offices across the country (Herman-Giddens, et al., 1997). The study, by Marcia Herman-Giddens, DrPH, and her colleagues at University of North Carolina School of Public Health, is unique, making it difficult to know exactly how the age of breast and pubic hair development has changed over time. Previous standards of "normal puberty" were set more than 30 years ago, based on a study of less than 200 girls in a British orphanage in the 1960s (Marshall and Tanner 1969).

Based on the new pediatric guidelines, pediatricians are less likely to prescribe monthly hormone shots to slow down puberty for these young girls. Although evaluation and treatment remains important for very young girls showing signs of puberty, the new criteria have redefined what is considered normal and abnormal. The pediatricians decided that these hormone shots are usually not necessary, since girls who start puberty early will develop normally – that is to say, they will grow to their full height. But the implications for parents, teachers, and others who work with children are equally important: many young girls in early elementary school are developing breasts and pubic hair at a time when they are still playing with dolls and Junior Monopoly, and are too young to understand the emotional mood swings and

other symptoms of adolescence. In addition, the long-term health implications for cancer and other diseases are unknown, but there is reason to be concerned.

Before we can examine the likely psychological impact or long-term health implications, we need to understand the data. They were gathered from a cross-sectional study conducted in pediatric practices that participate in the American Academy of Pediatrics' Practice-Based Research Network. Practices were recruited from the network which had 632 self-selected clinicians in 155 practices located in 34 states and Puerto Rico. Sixty-five practices participated in the study. Ninety percent of the girls studied were white, and most of the others were African American.

Pediatricians, nurse practitioners, and physician assistants examined three- to 12-year-old girls between July 1992 and September 1993. Girls were recruited who came for a well-child visit, or for a problem that would routinely require a complete physical.

Results found that in their seventh year, 27% of African-American girls and 7% of white girls had begun breast development and/or had pubic hair. Between ages eight and nine, those numbers had increased to 48% of African-American girls and 15% of white girls. Also at age eight, 17% of African-American girls and 2% of white girls had axillary hair.

Menarche occurred in the girls' eleventh year for 28% of African-American girls and 13% of white girls. At age 12, 62% of African-American girls and 35% of white girls had begun menstruating. For white girls in the US, the age of first menstruation has remained stable over the past 45 years. In African-American girls, age at menarche has declined by about six months in the past 20 to 30 years. The authors felt that the change in age at menarche in African-American girls may be due to their coming closer to achieving optimal nutritional and health status.

Girls in this study were taller and heavier than in the first and second National Health and Nutrition Examination Surveys (NHANES, which occurred more than 20 years ago), especially the older girls. Girls in the study who had one or more secondary sexual characteristic were larger and heavier than girls who had not begun puberty. A 1994 report on the National Growth and Health Study found a similar increase in the height and weight of nine and 10-year-old African-American and white girls compared to results from previous NHANES studies.

The mean onset age for breast development was 8.9 years for African-American girls and 10.0 for white girls. Pubic hair onset began at age 8.8 for African-American girls and 10.5 for white girls. Axillary hair appeared at the average age of 10.1 in African-American girls and 11.8 in white girls. All of the characteristics emerged significantly earlier in African-American girls both with and without controlling for height and weight.

Although there are few other sources of data to compare these new findings to, the authors state that white girls in their study appear to be developing six months to one year earlier than girls in earlier studies. There are no data available to determine whether African-American girls are developing breast and pubic hair earlier than in past years, although the data indicating earlier menarche suggest that this is likely.

We don't know what causes the disparity between white and African-American girls. A number of previous studies in the US have noticed earlier development and larger pre-pubertal size of African-American girls compared to white girls. Several studies in the 1970s and 80s found African-American girls to be taller, heavier, and maturing earlier than white girls their age.

In addition to their differing size, another hypothesis about the racial discrepancy is that hair products used by African-Americans that contain estrogen or placenta may be increasing the prevalence of early puberty.

The Herman-Giddens study has received a great deal of attention, and some have questioned whether it represents all girls in the US. The pediatric practices and the girls selected were not a random sample, and it is possible that girls with evidence of early pubertal development were more likely to be brought in for a doctor's visit because their parents were concerned. Of course, parents might also be likely to bring in older girls who had not yet shown pubertal development, and that would have balanced that selection bias. There is no evidence that these kinds of selection biases occurred. On the contrary, in my experience, many physicians and many mothers have commented on their observation that girls seem to be maturing much earlier than they did 30 to 40 years ago. And, the pediatric endocrinologists changed their guidelines because they believe the findings from the Herman-Giddens study.

If girls are starting puberty earlier, it is important to determine the potential causes and consequences. Many scientists believe that earlier puberty is caused, in part, by the widespread exposure to pesticides and other

chemicals that have qualities like estrogen. There are a number of studies showing that chemicals that disrupt the endocrine system can affect pubertal development or sexual behavior in animals (Guillette, et al., 1994; Howdeshell, et al., 1999; Yamomoto et al., 1996). Those studies, and many others implicating the effects of endocrine-disrupting chemicals on reproductive function, were described in the seminal work, *Our Stolen Future* by Coburn, Dumanoski, and Myers (Coburn, et al., 1996). In addition, there are studies in people that show a correlation between exposure to endocrine-disrupting chemicals and changes in pubertal development. One of the most provocative studies shows that Puerto Rican girls who have premature breast development have higher blood levels of a particular type of chemical called phthalates, used in many cosmetics, toys, and plastic food containers (Colon, et al., 2000). A recent study by the Centers for Disease Control and Prevention showed that women of childbearing age have the highest levels of phthalates in their blood, perhaps putting their future children at risk of early puberty or other reproductive problems (Blount, et al., 2000).

Dr. Paul Kaplowitz from the Medical College of Virginia, co-chair of the panel that wrote the new pediatric guidelines, believes that "at least part of the explanation is overweight" since a certain amount of body fat is required for normal reproductive function. Fat cells manufacture leptin, a hormone that might be involved in triggering puberty. If girls get to a higher level of body fat and secrete enough leptin a few years earlier than they did in the past, it is possible that the first signs of puberty could emerge earlier. However, since puberty often causes weight gain, it is difficult to determine whether obesity causes early puberty or vice versa.

The long-term health risks of early puberty also deserve attention. It has already been demonstrated that girls who begin menstruating at a very young age have an increased risk of developing breast cancer as adults, so it is certainly possible that earlier onset of puberty may also put girls at greater risk of breast cancer. Since most girls who experience early signs of puberty do not necessarily have earlier menarche, further study is needed to determine whether they will have an increased breast cancer risk.

There is research evidence that early puberty may put young girls at risk for emotional and social problems that could be devastating. Maturing young girls will have to cope with their own confusing sexual feelings as well as the impact that their maturing appearance has on boys and men. Research indicates that girls with early menarche face consequences as young girls and as teenagers. Studies of young girls indicate that those who develop early are more likely to be depressed, aggressive, socially withdrawn, and moody (Sonis, et al., 1985). Studies of teens indicate that girls who developed early are more likely to be sexually active, have more problems in school, and are more likely to smoke and use alcohol and drugs (Phinney, et al., 1990; Ge, et al., 1996; Graber, et al., 1997).

As a think tank concerned about the health and well-being of women and families, the National Center for Policy Research for Women & Families is examining the causes and consequences of early puberty, and identifying policies that can help to reverse the trend. CPR is also partnering with other experts and organizations to help girls and their families who already must cope with this problem. Additional information is available on CPR's website at www.center4policy.org

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Research Commentary

Identification of Phthalate Esters in the Serum of Young Puerto Rican Girls with Premature Breast Development

Colon, I., D. Caro, C.J. Bourdony, and O. Rosario. Environmental Health Perspectives 108 (2000):895-900.

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This study examines serum concentrations of a group of phthalate compounds in girls with premature breast development and compares these values to those obtained from an age-matched group of girls with no premature breast development. In Puerto Rico, over approximately the last 20 years, clusters of young girls (eight years old and below) have experienced early thelarche. The author's report that the incidence rate in Puerto Rico is approximately 18.5 fold greater than an incidence reported in a study in the US. An Early Thelarche Registry has been established in Puerto Rico since 1987. Girls were taken from this registry for this study. Girls selected had no other signs of puberty, such as early menarche or pubic hair growth. Using a combination of gas chromatography and mass spectroscopy (GC/MS), the authors looked for pesticides or phthalates in the serum of selected girls, and compared these values to a control group; the hypothesis being that perhaps there was a difference between the groups in environmental chemical exposures leading to early thelarche. No chlorinated pesticides were detected in the serum samples. However, phthalate diesters and monoesters were detected in 28 out of 41 samples from girls with early thelarche and one out of 35 samples of the controls. The monoester metabolite of DEHP, MEHP, was detected in five out of 41 of the experimental and none of the control samples. It is suggested by the authors that a possible association exists between phthalate exposure and premature female breast development.

Phthalate diesters, also known as phthalates, are a class of chemicals used to soften vinyl plastic, hence, are also called 'plasticizers'. Phthalates are ubiquitous in the modern environment, because they are not chemically bound to the plastic polymer and can readily leach out of the plastic. Phthalates are small, fat-soluble chemicals found in PVC-type and other plastics, but not in polyethylene. Some examples of materials that contain phthalates are food products, perfumes, hair sprays, nail polish, garden hoses, car interiors, lotions, and vinyl flooring. Food products are the most common products where humans are exposed to phthalates, because phthalates leach into the food from contact with plastics containing the chemical. Phthalates are poorly absorbed through the skin.

After oral ingestion, phthalates are hydrolyzed from the diester to monoester form by lipases present in saliva, stomach and small intestine. Lipases are also present in breast milk. The monoester form is very rapidly absorbed by the gut. Upon absorption, the chemical is conjugated by the liver and excreted in the urine as a conjugated monoester phthalate. Evidence of oral phthalate exposure would therefore be indicated by the presence of the monoester in the serum or urine. However, if exposure

to phthalate diesters is through intravenous tubing, then the diester form would be present in the serum. Based upon this information, it is likely that the serum levels of phthalate diesters reported in this study are assay contaminants and not the result of ingestion of the chemicals. However, in this study, the DEHP monoester, MEHP, was reported in five of the test samples, indicating an oral exposure in these individuals. No other monoester phthalates were reported. More information would be needed from the authors to determine whether other phthalate monoesters were assessed. Exposure data could be estimated from the serum values obtained for the monoester metabolites.

Recently, monoester phthalate levels were measured from spot urine samples taken from the NHANES III study sponsored by the Center for Disease Control (*Environmental Health Perspectives*, 108 (2000):979-982). Samples from 289 adults were extracted and analyzed by GC/MS. Specifically labeled phthalate monoester internal standards and extensive quality control measures were used. Estimates of actual exposures to several phthalates were calculated based upon these monoester values (*ibid.* A440-A442).

Investigations have shown that some phthalates can act as "endocrine disrupters".[1] The research demonstrated that exposures of rodents to some phthalates (at high doses) prior to development of the reproductive tract affected reproductive tract maturation and fertility. In rodent reproductive studies, some phthalates, when given to the dams during gestation, were found to disrupt sexual development of male mice. Effects on female development were also observed, but at higher chemical doses. The exact pathogenesis of this process has not been elucidated, but is believed to involve a drop in testosterone levels leading to an "antiandrogenic" effect. No evidence of an estrogenic effect from phthalate exposure has been reported in animal studies. Toxicology studies on phthalates have shown that some are carcinogenic in rodents, but only at very high concentrations. In long-term exposure studies, no tumors have been described in the mammary gland nor has there been any reported evidence of abnormal mammary gland development although tumors at other sites, such as the liver and testis, did occur. Therefore, it seems very unlikely that phthalates would affect early development of mammary glands.

If early thelarche is due to an increase in ductal development, then the question arises as to what hormone or hormone-mimic could cause an effect independent of other signs of puberty? Substances that promote prolactin levels in the serum are possible candidates. Because of these concerns, it would have been informative if this study could have examined serum hormone levels such as estradiol, prolactin, testosterone, progesterone, thyroid hormone, growth hormone, cortisol, and insulin in both control and experimental groups.

In spite of analytical doubts concerning the exposures of the experimental group in this study, there is a valid concern for determining the causative factor leading to early thelarche. Breast enlargement due to documented ductal development and carefully age and weight matched controls are needed. A detailed epidemiology study documenting lifestyle, family history, and diet is necessary to help determine a cause for early thelarche.

[1] *In July, 2000, the NTP-Center for the Evaluation of Risks to Human Reproduction Phthalate Expert Panel completed evaluations on seven phthalates for developmental and reproductive effects. These reports are available on the CERHR website at: http://cerhr.niehs.nih.gov*

Breast Cancer Survivors Needed as Lay Reviewers for the 2001 Grant Competition of the NYS Health Research Science Board (HRSB)

New York State breast cancer survivors are needed as part of the panel reviewing research and education proposals submitted for funding to the HRSB. Candidates need to apply by April 30, 2001. Previous experience is not required, as the Board seeks a balance of experienced and new reviewers. For an application please contact:

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Phone: 518.474.8543
Email: HRSB@wadsworth.org

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Feasibility Being Explored for a New York State Companion Animal Tumor Registry

The Comparative Cancer Program at Cornell University is interested in determining the feasibility of a New York State companion animal tumor registry. Such a registry would support current efforts in New York to enhance cancer detection in humans and provide essential information regarding cancer control in companion animals.

Until now, the role of animals in public health has focused on zoonotic diseases and food safety. It is now recognized that cancer in companion animals provides a vastly underutilized resource for cancer risk assessment in humans. Naturally occurring cancers in pets have similar histopathological features and biologic behavior to tumors in man but often progress more rapidly. Furthermore, in contrast to human cancer studies, cancer development in companion animals is not subject to confounding risks, such as smoking and alcohol consumption. Finally tumor tissue and serum or urine samples can be readily collected and analyzed in animal patients allowing characterization of exposure history to tumor development.

Significant logistic issues have limited development of animal cancer registries in the past. No census data currently exists for pets and cancer is not a reportable disease in companion animals. In addition, standards and guidelines for reporting, collecting, coding and archiving data also need to be established that would complement data collection in humans. However, with sufficient resources and expertise, these problems may be overcome. It is our goal to more fully characterize the obstacles confronting development of an animal tumor registry and to define the resources needed to support this important resource for human and animal health. We are planning a workshop on the subject April 28 in NYC. This will bring together veterinarians and epidemiologists and anyone else that has an interest in an animal tumor registry to discuss strategies to over come some of the hurdles. Anyone that is interested should contact Dr. Susan Ettinger: se19@cornell.edu.

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