OBSTETRICS

Development of children born to mothers with cancer during pregnancy: comparing in utero chemotherapy-exposed children with nonexposed controls

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OBJECTIVE: Cancer is diagnosed in approximately 1 per 1000 pregnant women. Lifesaving cancer therapy given to the mother during pregnancy appears in conflict with the interest of the developing fetus. Often, termination of pregnancy is suggested but has not been proven in any type of cancer to improve maternal prognosis, while very few studies have documented the long-term effects of in utero chemotherapy exposure on child outcome. To counsel patients about the risk of continuing a pregnancy while undergoing cancer treatment, we performed developmental testing to provide more detailed follow-up on children exposed in utero to chemotherapy.

STUDY DESIGN: Mother-infant pairs, enrolled in the Cancer and Pregnancy Registry, were offered developmental testing for children who were ≥18 months of age. Based on age, the Bayley Scales of Infant Development—Third Edition, the Wechsler Preschool and Primary Scale of Intelligence-Revised, the Wechsler Intelligence Scale for Children, Third Edition, or the Wechsler Individual Achievement Test was administered. All parents or primary caregivers completed the Child Behavior Checklist, a parent questionnaire to assess behavior and emotional issues. Results of children exposed to chemotherapy before delivery were compared with children whose mothers were also diagnosed with cancer during pregnancy but did not receive chemotherapy before delivery.

RESULTS: No significant differences were noted in cognitive skills, academic achievement, or behavioral competence between the chemotherapy-exposed group and the unexposed children. Of children, 95% scored within normal limits on cognitive assessments; 71% and 79% of children demonstrated at or above age equivalency in mathematics and reading scores, respectively; and 79% of children scored within normal limits on measures of behavior. Older children had significantly higher rates of internalizing behavior problems.

CONCLUSION: We could not demonstrate a significant difference in cognitive ability, school performance, or behavioral competence for children exposed to chemotherapy in utero compared with nonexposed controls. The majority of these children scored within normal limits on all developmental measures. Premature birth was more prevalent in the chemotherapy-exposed group yet did not predict developmental outcome. Older children in the sample demonstrated higher rates of internalizing behavior problems.

Key words: cancer, chemotherapy, child development, pregnancy

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The diagnosis of cancer during pregnancy creates medical and moral dilemmas for physicians and patients. Pregnant women are hesitant to receive chemotherapy due to concerns about possible effects on the developing fetus, while physicians are hesitant to allow pregnant women to delay cancer treatment for the remainder of the pregnancy. Often, termination of the pregnancy is recommended. The Cancer and Pregnancy Registry, created in 1997 with approval of the Institutional Review Board at Cooper Medical School at Rowan University, follows up the pregnancies and long-term health of women diagnosed with cancer during pregnancy. Patients are enrolled at the time of cancer diagnosis, and the treatment during pregnancy is recorded. Several women were advised to terminate their pregnancies without information about receiving cancer treatment while pregnant. Absence of long-term follow-up data on children exposed to chemotherapy in utero influenced some patient and physician decisions regarding continuing a pregnancy complicated by cancer and/or cancer treatment during pregnancy.

A developmental psychologist performed standardized developmental testing for children born to mothers diagnosed with cancer during their pregnancies. The purpose of this study is

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to report developmental outcome for children exposed to chemotherapy in utero compared with a control group of unexposed children whose mothers were diagnosed with cancer while pregnant.

Approximately 1 in 1000 pregnancies is complicated by cancer.[1] The number of births in 2010 was 3,999,386 (National Vital Statistics Report). In the past, providers have recommended termination of pregnancy but are now recognizing that pregnant patients are able to receive chemotherapy. As the majority of women do not receive chemotherapy during organogenesis, the malformation rate is not higher than the general population.[2-6] The majority of organogenesis is completed by 12 weeks, yet the central nervous system continues to develop throughout gestation and after birth. A review summarized 340 fetal exposures to chemotherapy published to date and later expanded to 447 cases in 2008.[7,8] The literature at that time provided details of the cancer diagnosis, treatment, and general pregnancy outcomes, but long-term follow-up on the children was limited. Avilés and Neri[9] in 2001 reported long-term follow-up on 84 children born to mothers with hematological malignancies exposed in utero to chemotherapy, ranging in age from 6−29 years. All children were found to be normal physically and neurologically. School performances and standardized intelligence testing were within normal range and were not significantly different from controls (unrelated matched children and unexposed siblings).[9] Eleven years later, a prospective study on the neurodevelopmental outcomes of 70 children aged 18 months to 18 years exposed to cancer treatment in utero was conducted, assessing health status, cognitive performance, and behavioral competence. This study reported that the majority of these children were doing well, and those children showing delays in development were concentrated in the group delivered preterm.[10] This study lacked a control group of unexposed children and was unable to determine whether developmental delays were related to chemotherapy exposure or prematurity.

Documenting the long-term follow-up on children exposed to chemotherapy in utero could provide women and their physicians the information necessary to make informed decisions during diagnosis of cancer during pregnancy. In the present study, we report on cognitive and behavioral outcomes for children born to mothers with cancer diagnoses during pregnancy with comparisons of those children exposed in utero to chemotherapy with a control group of nonexposed children of mothers diagnosed during pregnancy.

Materials and Methods

Study sample

A cohort of women diagnosed with cancer during pregnancy was enrolled and followed up in the international Cancer and Pregnancy Registry. Establishment and conduction of follow-up for the registry was approved by the Institutional Review Board of Cooper Medical School at Rowan University. Since collecting cases in 1997, the registry is compiled of 338 pregnant women diagnosed with various types of cancer. Pregnant women, enrolled at the time of their cancer diagnosis, provide information, verified by medical records, of their diagnosis and treatment during pregnancy. Treatment course was determined by the oncologist caring for the patient based on stage of cancer and gestational age at diagnosis.

Women participating in ongoing data collection for the Cancer and Pregnancy Registry were offered standardized developmental testing if their child was at least 18 months of age. Letters were sent to 149 eligible participants regardless of cancer type or treatment during pregnancy. Patients were not paid for their participation, but travel expenses and parking were covered by grants from the Cooper Cancer Institute. Parents were allowed to be present during testing. In all, 53 women diagnosed with cancer during their pregnancy provided consent for their children to undergo developmental and behavioral assessments, and in 2 cases primary caregivers in families in which the mothers were deceased provided consent. Study participants were separated into 2 groups depending on type of cancer treatment (eg, chemotherapy vs nonchemotherapy) received before delivery. In the chemotherapy exposure group (n = 35),

TABLE 1
Demographic variables across chemotherapy exposure and controls

Variable	Exposure	n	Mean	SD	n (%)	*P* value
GA birth, wk	Chemo	35	36.7	±2.5		.04[a,b]
	Controls	22	38.2	±2.7		
Male sex	Chemo	35			24 (68.6)	.16[c]
	Controls	22			11 (50)	
Children with mother alive	Chemo	35			34 (97.1)	1.0[d]
	Controls	22			21 (95.5)	
Children with mother undergoing treatment for recurrence	Chemo	34			4 (11.8)	.46[d]
	Controls	21			4 (19.0)	
Age at evaluation, y	Chemo	35	4.5	±3.1		.59[a]
	Controls	22	4.9	±2.6		
GA at first chemo treatment, wk (range)		35	22.0 (11.7−31.3)	±4.9		

Chemo, chemotherapy; *GA*, gestational age.

[a] Independent *t* test; [b] Denotes significant value; [c] Pearson χ^2; [d] Fisher exact test.

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26 women were diagnosed with breast cancer during pregnancy. Other cancer types in this exposed group included ovarian (4), Hodgkin disease (4), and acute leukemia (1). The control group, those who did not receive chemotherapy during pregnancy (n = 22), included the following cancer types: breast (6); melanoma (6); 2 cases each of cervical, bladder, central nervous system, and Hodgkin disease; and 1 case each of rectal and parotid gland tumors.

Participants

Including 2 sets of twins, 57 children of 55 mothers diagnosed with cancer while pregnant served as the study subjects and were assessed on age-appropriate developmental tests. In all, 35 children exposed in utero to chemotherapy comprised the exposure group and 22 children of women diagnosed with cancer who did not undergo chemotherapy during pregnancy comprised the control group. During pregnancy women diagnosed with breast cancer received doxorubicin/cyclophosphamide (22), doxorubicin/cyclophosphamide with 5 fluorouracil (3), or doxorubicin/cyclophosphamide followed by paclitaxel (1). Patients diagnosed with ovarian cancer were treated with cisplatin/paclitaxel (2), etoposide/cisplatin/bleomycin (1), or carboplatin/paclitaxel (1). Four patients with Hodgkin disease received doxorubicin/bleomycin/vinblastine/dacarbazine. The sole participant diagnosed with acute leukemia received cyclophosphamide, daunorubicin, vincristine, L-asparaginase, cytarabine, 6-mercaptopurine, and intrathecal methotrexate. No one received chemotherapy until after 12 completed weeks of pregnancy. Women requiring chemotherapy postpartum were advised by their physicians not to breast-feed their infant.

The children undergoing developmental testing ranged in age from 18 months to 10.4 years. The psychologist performing the evaluations was blinded to the maternal treatment during pregnancy. Two women in the study were deceased. One child (exposed group) lost his mother at age 4.6 years and was tested at age 7 years, the other child (control group) lost her mother when she was 9 months old and underwent testing at age 4.2 years.

Measures

Cognitive assessment

Bayley Scales of Infant Development—Third Edition (BSID-III) was administered to the 29 children aged 18-42 months. The BSID-III assesses development across 5 domains, with 3 used for the present study. Composite scores were generated for cognitive, language, and motor abilities (mean, 100; SD, 15). Scores <85 were considered abnormal.

The Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R) was administered to the 19 children aged 3-7 years. This battery of tests assesses intellectual functioning and provides composite scores that represent cognitive functioning in verbal (verbal intelligence quotient [VIQ]) and performance (performance intelligence quotient [PIQ]) domains, as well as a composite score (full-scale intelligence quotient [FSIQ]) reflective of a child's overall intellectual ability (mean, 100; SD, 15). Scores <85 were considered abnormal.

The Wechsler Intelligence Scale for Children, Third Edition (WISC-III) was administered to the 9 children aged ≥7 years. Similar to the WPPSI-R, it provides composite scores of cognitive functioning (VIQ, PIQ, FSIQ) for the

TABLE 2
Cognitive ability, school performance, and behavioral competence by chemotherapy exposure

Assessment	Exposure (n)	n (%WNL)	*P* value	Mean ±	SD	*P* value
Cognitive		n (%WNL)				
WNL						
54/57	Chemo (35)	34 (97)	.55[a]			
(95%)	Controls (22)	20 (91)				
School performance math						
WNL	Chemo (8)	6 (75)	1.0[a]	99.1	27	.30[b]
10/14	Controls (6)	4 (67)				
(71%)				113.8	22.3	
School performance reading						
WNL	Chemo (8)	6 (75)	1.0[a]	101.1	26.1	.93[b]
11/14	Controls (6)	5 (83)				
(79%)				102.2	17.3	
Behavior						
WNL						
45/57	Chemo (35)	27 (77)	.75[c]			
(79%)	Controls (22)	18 (82)				
Internalizing behaviors	Chemo (35)			46.7	8.7	.32[b]
	Controls (22)			44.1	10.4	
Externalizing behaviors	Chemo (35)			45.4	10	.88[b]
	Controls (22)			44.9	11.5	
Total problem behaviors	Chemo (35)			46.3	10	.68[b]
	Controls (22)			45.1	11.8	

Chemo, chemotherapy; *WNL*, within normal limits.

[a] Fisher exact test; [b] Independent *t* test; [c] Pearson χ^2.

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older children in the sample (mean, 100; SD, 15). Scores <85 were considered abnormal.

School performance

Wechsler Individual Achievement Test was administered to the 14 school-aged children ≥7 years of age. This provides a comprehensive test of reading, writing, language, and mathematics. For the present study, only scores for reading and mathematics were considered (mean, 100; SD, 15). Standard scores <25th percentile (<90), were below age and/or grade expectancy and considered abnormal.

Behavioral competence

The Child Behavior Checklist (CBCL) is a parent-report questionnaire on which the child is rated on various behavioral and emotional problems. The CBCL assesses internalizing (ie, anxious, depressive, and overcontrolled) and externalizing (ie, aggressive, hyperactive, noncompliant, and undercontrolled) behaviors. Scales are age-specific and generate internalizing scores, externalizing scores, and total-problem behavior scores. The CBCL ranks children's behavior according to severity compared with other children of the same age. The CBCL scores are categorized by established clinical cutoffs to represent behavior problems according to risk level. Borderline clinical scores (T ≥65) were considered abnormal for this report. Similar questions are grouped into a number of syndrome scales (ie, attention, somatic symptoms) to produce a score for each syndrome. In all, 55 respondents (53 mothers, 1 father from a deceased mother family, and 1 grandmother from the other deceased mother family) completed the 118-item questionnaire for the 57 children.

TABLE 3
Cognitive scores by cohort across chemotherapy exposure

Cognitive scale	Exposure	n	Mean	SD	*P* value
BSID-III, n = 29					
Cognitive					.23
	Chemo	21	111.43	10.97	
	Controls	8	118.13	18.11	
Language					.15
	Chemo	21	105.43	10.86	
	Controls	8	112.63	13.50	
WPPSI-R/WISC-III, n = 28					
VIQ					.94
	Chemo	14	113.00	18.50	
	Controls	14	113.57	20.70	
PIQ					.66
	Chemo	14	107.43	17.99	
	Controls	14	110.57	19.14	
FSIQ					.92
	Chemo	14	111.71	17.56	
	Controls	14	112.43	20.85	

Independent *t* test used.

BSID-III, Bayley Scales of Infant Development—Third Edition; *Chemo*, chemotherapy; *FSIQ*, full-scale intelligence quotient; *PIQ*, performance intelligence quotient; *VIQ*, verbal intelligence quotient; *WISC-III*, Wechsler Intelligence Scale for Children, Third Edition; *WPPSI-R*, Wechsler Preschool and Primary Scale of Intelligence-Revised.

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Results

Demographic comparisons

Comparisons of the demographic variables can be found in Table 1. Only mean gestational age at birth was significantly different between the 2 groups (36.7 vs 38.2 weeks; $P = .04$) with the chemotherapy-exposed group demonstrating higher levels of prematurity. Although the mean gestational age was significantly earlier in the chemotherapy-exposed group, the incidence of premature birth <36.9 weeks was not statistically different between the 2 groups (51.4% vs 38.1%; $P = .33$). One child in this cohort weighed within the <10% percentile at birth and was in the exposed group. Two children in the exposed group were diagnosed with congenital anomalies, each resolved by the time of developmental testing. One child was born with plagiocephaly, corrected with a helmet, and the other child was born with syndactyly of 2 fingers on 1 hand, surgically corrected soon after birth. The mean age at developmental evaluation was 4.5 ± 3.1 years in the exposed group and 4.9 ± 2.6 years in the control group ($P = .59$).

Cognitive assessment

Across the entire sample, 54 of 57 children (95%) scored within normal limits on age-appropriate cognitive assessments (Table 2). Only 1 child of 35 children exposed to chemotherapy in utero had abnormal cognitive test results compared with 2 children (of 22) in the control group who tested abnormally. This difference between groups scoring within normal limits on assessments of cognitive ability was not statistically significant ($P = .55$).

Analysis of group differences of cognitive ability across age cohorts showed similar results. No significant differences were noted in cognitive skills for the younger cohort on the BSID-III

(cognitive, language scores) or for the older cohort on the WPPSI-R/WISC-III (VIQ, PIQ, or FSIQ scores) between exposed and nonexposed groups (Table 3).

School performance

On tests of academic achievement for all children, 71% demonstrated mathematic ability at or above age equivalency, with 79% demonstrating at or above age expectancy in reading levels (Table 2). Two children (25%) in the chemotherapy-exposed group and 2 children (33%) in the nonexposed group showed academic deficits in mathematics, and 2 children (25%) in the chemotherapy-exposed group and 1 child (17%) in the control group showed deficits in reading levels. Academic achievement scores did not differ between groups (for math, $P = .30$; for reading, $P = .93$).

Behavioral competence

For the entire sample, 79% of children scored in the normal range on maternal reports of problem behaviors (Table 2). Twelve of the 57 children (21%) scored in the borderline clinical range on the maternal-reported behavior scales. Eight children in the exposed group (23%), demonstrated behavior problems in the clinical range, compared with 4 children (18%) in the control group showing similar behavioral issues ($P = .75$). Mean scores were not statistically different for chemotherapy-exposed vs control children on measures of internalizing ($P = .32$), externalizing ($P = .88$), or total behavior problem ($P = .68$) scales (Table 2).

Demographic predictors of developmental outcome

Cognitive ability

Cognitive ability did not appear to be influenced by demographic variables (Table 4). Mean gestational age at birth did not differ for children with normal (37.2 ± 2.6 weeks) and abnormal (37.0 ± 4.1 weeks) test results ($P = .87$) and sex was not statistically different between these 2 groups ($P = .28$). However, all 3 children scoring in the abnormal category

TABLE 4
Demographic variables and cognitive outcome

Variable	Cognitive category	Mean	SD	Percent	*P* value
GA birth, wk (n = 57)	WNL (54)	37.2	2.6		
	Abnormal (3)	37.0	4.1		.87[a]
Male sex (n = 35)	WNL (32)			59.3	
	Abnormal (3)			100	.28[b]
BSID-III, n = 29					
Cognitive					
Male (n = 18)		109.2	10.2		
Female (n = 11)		120.0	15.5		.03
Language					
Male (n = 18)		103.2	11.4		.01
Female (n = 11)		114.4	9.2		
WPPSI-R/WISC-III, n = 28					
VIQ					
Male (n = 17)		115.5	22.5		
Female (n = 11)		109.8	13.0		.45
PIQ					
Male (n = 17)		106.8	20.5		
Female (n = 11)		112.4	14.5		.44
FSIQ					
Male (n = 17)		112	21.9		
Female (n = 11)		112.2	14.1		.98
Mother alive (n = 55)	WNL (52)				
	Abnormal (3)			94.5	
Mother deceased (n = 2)	WNL (2)			100	1.0[b]
	Abnormal (0)				
Mother undergoing treatment (n = 8)	WNL (7)			87.5	
	Abnormal (1)				
					.27[b]
Mother cancer free (n = 47)	WNL (45)			95.7	
	Abnormal (2)				
Age at evaluation, y (n = 57)	WNL (54)				.08
	Abnormal (3)	4.5			
		7.5			
GA at first chemotherapy, wk (n = 35)	WNL (34)				
	Abnormal (1)	21.9 ± 5.2			
		23.3[c]			

BSID-III, Bayley Scales of Infant Development—Third Edition; *FSIQ*, full-scale intelligence quotient; *GA*, gestational age; *PIQ*, performance intelligence quotient; *VIQ*, verbal intelligence quotient; *WISC-III*, Wechsler Intelligence Scale for Children, Third Edition; *WNL*, within normal limits; *WPPSI-R*, Wechsler Preschool and Primary Scale of Intelligence-Revised.

[a] Independent *t* test; [b] Fisher exact test; [c] No *P* value could be calculated due to lack of SD in 1 group.

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TABLE 5
Demographic variables and behavioral competence

Demographic	Behavior category (n)	Mean	SD	*P* value	Percent	*P* value
GA birth, wk (n = 57)	WNL (45)	37.4	2.7			
	Abnormal (12)	36.9	2.6	.61[a]		
Male sex (n =35)	WNL (27)				27/45 (60%)	
	Abnormal (8)				8/12 (66.7%)	.75[b]
	CBCL					
	Internalizing					
	Male (n = 35)	46.	9.9			
	Female (n = 22)	45.2	8.8	.89[a]		
	Externalizing					
	Male (n = 35)	47	10.7	.21[a]		
	Female (n = 22)	43.1	9.9			
	Total problems					
	Male (n = 35)	48.	10.7	.10[a]		
	Female (n = 22)	43	10.5			
Mother alive (n = 55)	WNL (44)				80	
	Abnormal (11)					.38[b]
Mother deceased (n = 2)	WNL (1)				50	
	Abnormal (1)					
Mother undergoing treatment (n = 8)	WNL (7)					
	Abnormal (1)				87.5	
						1.0[b]
Mother cancer free (n = 47)	WNL (37)				.79	
	Abnormal (10)					
Age at evaluation, y (n = 57)	WNL (45)	4.7 + 2.9				
	Abnormal (12)	4.6 + 2.9		.94		
	Internalizing			.02[c]		
	Externalizing			.94[c]		
	Total problems			.37[c]		
GA at first chemotherapy, wk (n = 35)	WNL (27)	22.7	5.0			
	Abnormal (8)	19.2	3.9			
				.07[a]		

CBCL, Child Behavior Checklist; *GA*, gestational age; *WNL*, within normal limits.

[a] Independent *t* test; [b] Fisher exact test; [c] Pearson χ^2.

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for cognitive ability were male. On the BSID-III, males scored statistically lower than females on both the cognitive scales ($P = .031$) and on the language scales ($P = .011$). These significant sex differences were not found in the older children on the WPPSI-R/WISC-III.

Cognitive results were not statistically different for children whose mothers were deceased compared with children whose mothers were alive at the time of testing, and children's cognitive score category did not differ by maternal recurrence at the time of assessment, although this sample size was very small.

There was no significant difference in age at evaluation between the children with normal and abnormal development ($P = .82$). Gestational age at first chemotherapy exposure was 21.9 weeks in the group testing within the normal range, and 23.3 weeks in the 1 child in the exposed group who tested below normal.

Behavioral competence

Demographic variables were generally not predictive of overall behavioral problems in this sample (Table 5). The mean gestational age at birth was 37.4 ± 2.7 weeks in children with normal behavioral assessment scores and 36.9 ± 2.6 weeks in the 12 children with clinical behavioral scores ($P = .61$).

Behavioral scores were not significantly affected by maternal survival ($P = .38$), by mother's health status at time of evaluation ($P = 1.0$), by child sex ($P = .75$), or by child age at evaluation ($P = .94$). Further analyses, however, showed that older children had significantly higher rates of internalizing behavior problems than younger children ($P = .02$). The mean gestational age at first chemotherapy treatment was 22.7 ± 5 weeks in the behaviorally normal group and 19.2 ± 3.9 weeks in the clinically abnormal group, a nonsignificant difference ($P = .07$).

Comment

The effect, if any, on fetal maturation of the central nervous system in terms of long-term neurological follow-up is understudied for children of women diagnosed with cancer while pregnant. This is a major concern of pregnant women considering undergoing cancer treatment. In this report, and the few previous publications, the majority of children born to mothers diagnosed with cancer while pregnant had normal test results on age-appropriate developmental assessments.[2]

Reassuringly, we could not demonstrate a significant difference in cognitive ability, school performance, or behavioral competence for children exposed to chemotherapy in utero compared with their nonexposed controls. This was true despite a statistically significant earlier gestational age at birth for the chemotherapy-exposed group. Amant et al[10] reported a high incidence of prematurity in their sample of children exposed in utero, with the greatest delays in development found in the group delivered preterm. In our study, the mean age at birth was significantly earlier in the 35 children exposed to chemotherapy in utero compared with the 22 unexposed children, yet no developmental outcome differences were observed with regard to gestational age.

The youngest children (≤3 years) showed significant sex differences on measures of cognition and language, a difference not seen in the older children. This could possibly be attributed to the passage of time and less proximity to the family's ordeal of a cancer diagnosis during pregnancy. Conversely, age at evaluation was significantly related to internalizing behavior scores, with older children showing increased reports of behavior problems such as somatic symptoms, anxiety/depression, and social/withdrawal issues. Older children may have a better understanding of their mothers' medical condition.

Although no difference was noted with regard to behavioral assessment between exposed and nonexposed children, there was a high incidence of borderline clinical behavior scores reported overall in this population of children born to mothers diagnosed with cancer during their pregnancy. Syndrome behavior problems most frequently reported by mothers were problems of attention, aggression, and somatic complaints. Such findings are consistent with other studies of emotional and behavioral problems found among school-aged children of cancer patients and in mice exposed in utero.[11-14]

Few children in this sample had abnormal scores on measures of cognition or borderline clinical range scores on measures of behavior (8 of 35 chemotherapy-exposed and 4 of 22 in the control group). Interestingly, one child exposed to chemotherapy was significantly delayed on both cognitive and school performance measures and scored clinically on 4 behavioral syndrome scales. However, his fraternal twin scored within normal limits on cognitive and behavioral scales and was mildly delayed on the math portion of the school performance assessment. In another set of twins, also in the chemotherapy-exposed group, each performed well on cognitive testing yet 1 twin demonstrated clinical scores of aggressiveness and hyperactivity. A similar finding of neurodevelopmental delay in 2 children, each members of a twin pregnancy, was reported in a prior study.[10]

The majority of children exposed prenatally to chemotherapy fared well on cognitive and behavioral testing. Further, post-first-trimester gestational age at first chemotherapy treatment was not predictive of developmental outcome. We were unable to find significant developmental outcome differences comparing exposed children with a control group also experiencing a maternal cancer diagnosis during pregnancy but without chemotherapy treatment in utero.

Finally, as in prior studies[11-13] there was an increased maternal reporting of clinical behavior problems found in this population of children regardless of exposure status. A high frequency of somatic complaints, anxiety/depression, attention problems, and social/withdrawal issues requires further study with an additional focus on maternal/familial well-being in this at-risk population. A limitation of this study is the small sample size. Definitive conclusions from this sample are difficult, yet the findings are promising. Continued follow-up of this cohort, with retesting of the younger children as they reach school age, and growth of the sample size, is planned. Prospective collection of additional mother-infant pairs diagnosed with cancer during pregnancy is ongoing. ■

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