

hypertrophy and stature, all of which may affect their sexuality and their physical attractiveness.

A number of studies have shown that 46,XX CAH women develop female gender identities,^{1,2} but while earlier studies suggested that they had mostly satisfactory sexual intercourse,³ more recent reports have suggested that they may present with an increased incidence of sexual dysfunction, which seems to be largely related to difficulties in vaginal penetration.^{4,5} This seems to be true mainly for those with the most virilized external genitalia at birth, whereas CAH women with a lesser degree of sexual ambiguity at birth seem to have nearly normal sexual outcomes.

While cosmetic and anatomic outcomes of surgery were generally satisfactory to most patients and medical examiners, CAH women, particularly those with Prader IV-V stages, expressed an increased homosexual orientation and a decreased frequency

of sexual intercourse. This report and previous studies seem to show that while a large percentage of women with CAH are satisfied with their physical and genital appearance, sexual dysfunction and impaired reproductive outcomes are frequent in this population and will require better medical and particularly surgical care, longer and more detailed follow up, and the transmission of more comprehensive information to parents and/or patients of the risks to sexual function following reconstructive surgery.

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Height in Survivors of Childhood Acute Lymphoblastic Leukemia

This paper describes adult height in a Childhood Cancer Survivor Study (CCSS) cohort of 2434 subjects who were at least 5-year survivors of acute lymphoblastic leukemia (ALL) and were diagnosed between 1970 and 1986. Their data were compared to that of 3009 siblings selected for being the closest in age to the proband. Only those over 18 years of age were included. Survivors were excluded from this analysis if they were diagnosed after 17 years of age or if they had a recurrence of their primary leukemia, a secondary malignant neoplasm, or underwent stem-cell transplant before 18 years of age. Cumulative chemotherapy doses were categorized into none, low, medium, or high based on tertiles from previously published end-cut points. For some of the agents dosage information was not available and exposure was recorded as yes or no. Central nervous system (CNS) radiotherapy doses were abstracted in 5-Gy increments. Of the survivors who received cranial radiotherapy, 95% were treated with doses of 15 to 29 Gy and as a result, radiotherapy was characterized into <20 Gy and >20 Gy. Height was expressed in absolute terms as well as SDS. Pubertal status was not always recorded, therefore this variable was dichotomized at age 8 for girls and 10 for boys.

The median age of the study cohort was 27 years, and 51% were female. Median age of the siblings was 31 and 52.7% were female. All survivor treatment groups, including those treated with chemotherapy alone, had decreased adult height and height SDS compared with siblings ($p < 0.001$). Effects of radiotherapy on adult height SDS differed between those who were prepubertal versus postpubertal at diagnosis. The height SDS was decreased at all doses of cranial and craniospinal radiotherapy in survivors diagnosed before puberty, compared with those treated with chemotherapy alone. Those survivors who had received >20 Gy of cranial radiotherapy were on average

shorter with height SDS scores on average 0.88 lower than those treated with cranial radiotherapy alone. Among survivors diagnosed after pubertal onset, significant negative impact on height SDS was not seen on any cranial radiotherapy dose as compared with chemotherapy alone. On average, the adult height SDS of survivors treated after pubertal onset remained shorter than their siblings. All survivor exposure groups were at significant greater risk of adult short stature (that is height SDS < -2) as compared with siblings. No chemotherapeutic agent analyzed had a consistent dose effect on adult height SDS analyzed individually or in combination. There was an increased proportion of female survivors with adult short stature (12.5%) as compared with male survivors (5.5%).

The authors stated that this report represents the largest cohort of adult ALL survivors evaluated for adult height to date. Significant differences in height outcomes between survivors treated with high doses of cranial radiotherapy as well as those treated with lower dose cranial radiotherapy versus chemotherapy alone were demonstrated. Survivors who received any spinal radiotherapy had the shortest adult heights.

Mechanisms by which cranial radiotherapy affects short stature remain uncertain. It is speculated that at higher doses of radiation there may have been some degree of growth hormone deficiency, especially as it relates to the pubertal growth spurt and peak growth velocity. The second possibility is that cranial radiotherapy exerts its effects on pubertal timing. It would appear that early puberty occurs, especially in females, when treated at an early age. A combination of growth hormone insufficiency and early puberty is certainly associated with short adult stature. Findings in the current study are consistent with this hypothesis, since the risk of adult short stature was greater in those diagnosed at a

younger age, and girls were more affected than boys. The authors pointed out that the limitations of the study included the use of self or proxy reported height data, lack of longitudinal growth information, and the specific time of documentation of pubertal status. However, the large size of the study and the use of sibling controls helped to validate the significance of the differences found. Finally, the authors stated that most patients with ALL were currently treated with chemotherapy alone. Therefore the relationship between chemotherapy agents and linear growth velocity should be available in the future.

Chow E, Friedman D, Yasui Y, et al. Decreased adult height in survivors of childhood acute lymphoblastic leukemia (ALL): A report from the Childhood Cancer Survivor Study. *J Pediatr.* 2007;150:370-5.

Editor's Comment: This paper is accompanied by a thoughtful editorial by Oberfield.¹ Her comments included a discussion of previous reports from the CCSS regarding morbidity among childhood cancer survivors

and specifically those who were survivors of childhood brain cancers and were subsequently treated with growth hormone. Oberfield points out shortcomings with regard to self reported or proxy reported height and the definition of prepubertal and pubertal based on age, but affirms the uniqueness of the study because of its large size and the fact that even with chemotherapy alone there was a greater than threefold increased risk of decreased stature.

The data in this study involved survivors of ALL who were treated with a treatment regimen which differs from that currently in use. It clearly demonstrated that previous treatment regimens were associated with reduced adult height. It is hoped that oncologists will continue to carefully record auxologic and pubertal data on their patients so that similar long-term outcomes can be examined from a different therapeutic era in the future.

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Reference

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Congenital Hypothyroidism—Outcome of Early Treatment

Previous research conducted by Kempers and colleagues, in a cohort born and screened in 1981-1982, demonstrated persistent cognitive and motor deficits associated with congenital hypothyroidism despite initiating T₄ replacement at a median age of 28 days after birth. In the present study, the same investigators examined potential benefits of commencing T₄ replacement at an earlier age (median = 20 days) for a cohort born in 1992 and 1993. During this time, Dutch pediatricians were advised to start with 6-8 µg T₄/kg/day with T₄ dose adjustments based on thyroid function labs obtained at regular outpatient follow-up visits.

Participants included 82 Dutch children (mean age 10.5 years, range 9.6 to 11.4 years) diagnosed with thyroidal congenital hypothyroidism (CH-T). An additional 5 participants were diagnosed with central congenital hypothyroidism (CH-C); results were

analyzed separately for these due to differing etiology, treatment regimen, and sequelae.

Intelligence was assessed with the Dutch version of the Wechsler Intelligence Scale for Children, third edition (WISC-III), except for the first 10 patients for whom the WISC-R was used (and recalculated into WISC-III scores according to recommended guidelines). Three IQ scores were derived for each participant: full-scale IQ (FSIQ), verbal IQ (VIQ), and performance IQ (PIQ). General population IQ scores for each domain have a mean of 100 (±15). Motor skills were assessed with the Movement Assessment Battery for Children (MABC), designed to identify motor function impairments in children aged 4-12 years, including subscales for manual dexterity, ball skills, and balance; higher scores indicating more motor problems. For the 1981-1982 cohort, motor skills were assessed using a

IQ scores of the CH-T group

	FSIQ	P (t)	Verbal IQ	P (t)	Performance	P (t)
Severe CH-T (n=41)	93.7(89.5-97.9) ^{1,3}	0.004(-3.0)	94.9(90.1-99.7) ²	0.039(-2.1)	93.9(90.9-97.8) ^{1,3}	0.003(-3.1)
Moderate CH-T (n=19)	96.2(88.9-103.5)	0.290(-1.1)	95.4(87.9-102.9)	0.210(-1.3)	98.0(91.1-104.9)	0.550(-0.6)
Mild CH-T (n=22)	105.0(99.5-110.4)	0.73(1.9)	103.6(98.2-109.1)	0.182(1.4)	105.3(99.3-111.3)	0.082(1.8)
Total (n=82)	97.3(94.2-100.4)	0.088(-1.7)	97.4(94.1-100.6)	0.113(-1.6)	97.9(94.8-100.9)	0.172(-1.4)
Range	57-129		65-138		58-134	

IQ scores, expressed as mean (confidence interval), are presented for the total CH-T group and the three severity subgroups.

P values (with t value in parentheses) refer to the comparison with the normative population.

¹ P < 0.01 compared to the population mean

² P < 0.05 compared to the population mean

³ P < 0.01 compared to mild CH-T

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