

in 2 recent reports.<sup>1,2</sup> The authors of the current case report do not inform us whether the family in question gave consent to disclose the patient's diagnosis to at-risk extended family members. Regardless of whether they did or not, the "gender team" should be commended for delivering care to the family in a manner consistent with the recent Consensus Statement of Management of Intersex Disorders.<sup>3</sup> The process of disclosing all aspects of the DSD and its clinical care should be collaborative, on-going, and planned with the parents from the time of diagnosis. But, what if the family in this case refuses to allow disclosure to other, potentially affected family members? The 1983 President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research<sup>4</sup> provides some valuable guidance. For example, it states that when the patient refuses, a health care professional's disclosure to at-risk family members should take place only when: (1) reasonable efforts to elicit voluntary consent to disclosure have failed; (2) there is a high probability that harm will occur if the information is withheld, and the disclosed information will actually be used to avert harm; (3) the harm that would result to identifiable individuals

would be serious; and (4) appropriate precautions are taken to ensure that only the genetic information needed for diagnosis and/or treatment of the disease in question is disclosed. Approximately 10 years later, the Committee on Assessing Genetic Risks of the Institute of Medicine<sup>5</sup> added an additional criterion: that there is no other reasonable way to avert harm. Neither group implied that the clinician has a legal duty to inform relatives, instead arguing for an ethical duty and legal permission to inform in certain cases.

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## References

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## CAH Women: Sexual and Reproductive Outcomes

Gastaud et al performed a cross-sectional study using face to face interviews, written questionnaires, the Female Sexual Function Index (FSFI), a brief self-report measure of female sexual function, and a gynecological examination in 35 women aged 18 to 43 years with congenital adrenal hyperplasia (CAH), presenting Prader stages I-V at birth who had been treated from birth to adolescence in the same pediatric endocrine clinic. The objectives of the study were to obtain a detailed description of sexual and reproductive outcomes in adult women with CAH and to compare these outcomes among CAH subtypes and with non-CAH controls. Fourteen of the CAH patients had presented with severe masculinization of their external genitalia at birth (11 with Prader IV and 3 with Prader V stages).

None of the patients expressed doubts about their gender assignment. At gynecological examination cosmetic and anatomic outcomes were considered good by both the patients and the examiner, and 65% of the subjects presented with a satisfactory clitoris, introitus and vagina. However, 9 of 35 patients (26%) were diagnosed with vaginal stenosis, 6 of these belonging to the Prader IV-V group at birth. Seven subjects (20%) reported homosexual inclinations, compared with 5.7% in the control group and 6.6% in a large survey of age-matched women in France (ACSF) and these tendencies were present in 43% (6 of 14) of the Prader IV-V women. A decrease in sexual function was noted when the 35 CAH patients were compared with the 69 healthy controls utilizing the FSFI questionnaire, thus 37% (13 of 35) reported

never having sexual intercourse with vaginal penetration by their partners compared with 5% in the ACSF survey. Of these women, 8 attributed their lack of sexual intercourse to the anatomy of their genitalia, 2 believed intercourse would be painful and/or 7 had no partner; the 3 patients born Prader V were among this group. Some degree of pain during vaginal penetration was experienced by 56%, 9 of them presented with moderate or marked stenosis of their introitus. Eight patients cohabited with their partner or were married and 77% wished to be pregnant in the near future or at a later time. Eight subjects became pregnant, only one in the Prader IV-V group; however, only 17% (6 of 35) had children compared to 71% of French women in the ACSF survey. The authors concluded that despite the expert medical and surgical care received by these patients, women with CAH suffer major limitations in their sexual function and their reproductive life.

Gastaud F, Bouvattier L, Duranteau L, et al. Impaired sexual and reproductive outcomes in women with classical forms of congenital adrenal hyperplasia. *J Clin Endocrinol Metab*. 2007;92:1391-6.

**Editor's Comment:** *Female neonates with CAH may present with some degree of masculinization of their external genitalia at birth and those with severe virilization (Prader stages IV-V) may require extensive surgery to correct for different degrees of clitoral enlargement and labio-scrotal fusion. In addition, many may develop chronic masculinization as a consequence of being exposed to an excess of adrenal androgens postnatally, with the development of hirsutism, acne, muscle*

*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,<sup>1,2</sup> but while earlier studies suggested that they had mostly satisfactory sexual intercourse,<sup>3</sup> 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.<sup>4,5</sup> 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