The complete androgen insensitivity syndrome (CAIS) is due to inactivating mutations or deletions in the androgen receptor gene, completely abolishing the androgenic effects on target tissues before and after birth [Hughes et al., 2012]. These individuals present with a female phenotype, but a male karyotype and hormonal active testes [Hughes et al., 2012]. Diagnosis may be suspected in a prepubertal girl presenting with inguinal hernia containing male gonads or in an adolescent with a female habitus and normal breast development but absent or scanty growth of pubic and axillary hair, and primary amenorrhea [Audi et al., 2010; Hughes et al., 2012]. Today, a mismatch between the genital appearance at birth and the prenatal karyotype can be an additional feature for diagnosis [Audi et al., 2010]. In females with CAIS, the androgens produced by the testes are converted into estrogens with the action of aromatase. In the absence of androgen action, this mechanism permits the development of female secondary sexual characteristics and all the other estrogen actions [Audi et al., 2010; Hughes et al., 2012], including the effects on bone maturation and mineralization [Almeida et al., 2017].

CAIS was clinically characterized in the 1950s [Morris, 1953]. From then on, a long-lasting debate regarding the need and the timing of gonadal removal in these women started. The debate aroused mainly because an increased risk of testicular malignancy has been reported in adulthood and seldom also before puberty [Hughes et al., 2012; Achus and Quint, 2015]. Obviously, adequate hormone replacement therapy must be started from adolescence onward in the girls operated on before puberty to assure the development of secondary sexual characteristics as well as in females who undergo gonadectomy during or after adolescence to complete or maintain female phenotypic features [Bertelloni et al., 2011], while intact gonads permit well-being from endogenous hormones and avoid lifelong medical therapy.

Recommendations for gonadal removal in women living with CAIS vary in literature. The “Consensus statement on management of intersex disorders” stated that “the testes in patients with CAIS ….. should be removed to prevent malignancy in adulthood. The availability of oestrogen replacement therapy allows for the option of early removal at the time of diagnosis which also takes care of the associated hernia, psychological problems with the presence of testes and the malignancy risk” [Hughes et al., 2006]. Indeed, literature indications range from “the testes should be removed as soon as they are discovered” [Donahoue, 2016] to “support leaving the testes in until after puberty has been completed and then either removing them ….. or instituting a careful monitoring process for the early detection of seminoma”
In this issue of *Sexual Development*, a special series of 3 articles is enclosed, addressing the issues of tumor risk in CAIS and the problems related to gonadectomy. Cools and Looijenga (this debate) updated the mechanisms underlying testicular germ cell tumor (TGCT) development in CAIS, the data regarding the incidence of TGCT in adults with CAIS, and provided an overview of existing and novel screening tools for in situ and invasive neoplastic lesions. Bertelloni et al. (this debate) revised the issue of bone health in women living with CAIS, showing that better bone mineral density (BMD) is present in those with intact gonads in comparison to patients with removed gonads. Hormone replacement therapy may improve BMD, but it seems that it does not normalize it.

Recently, King et al. [2017] confirmed in a large series ($n = 129$) that mean BMD was reduced in women living with CAIS. However, they found no relationship between the age of gonadectomy and BMD; no drop in BMD in individuals followed up after gonadectomy was also reported, suggesting that different factors may be operative on bone status in CAIS. Döhnert et al. (this debate) showed that because the tumor risk before puberty is very low, the timing of gonadectomy in CAIS can be postponed to allow spontaneous puberty and to involve the patients in important decisions affecting their body and health. They also reported that gonadectomy after puberty still is subject to controversy and that endogenous hormone profiles show very specific features, which, for example, influence bone health and psychosocial well-being.

We are sure that the data from these 3 articles will give relevant indications for practice, regarding a better approach to the decision-making process on the gonadal management of girls/women living with CAIS. We are very well aware that the information given here does not cover all aspects of this topic. Thus, we hope that this debate will turn out to be “a stone thrown in the pond,” encouraging other authors to share their point of view (e.g., physical, legal, and psychosocial) contributing to highlight this still unresolved topic.

### References