Optimizing Potential for Fertility: Fertility Preservation Considerations for the Pediatric Endocrinologist

Peter A. Lee, MD, PhD[a,b,*], Alan Rogol, MD[b,c], Christopher P. Houk, MD[d]

KEY WORDS

• Cryopreservation • Sperm retrieval • Oocyte retrieval
• Infertility • Assisted fertility • Fertility preservation

Modern medicine now offers hope for many patients who would have been infertile in the past. Fertility preservation and assisted reproduction in adults has received considerable attention. In women, discussion of fertility preservation typically arises in patients with malignancies or nononcologic conditions that either require treatment with gonadotoxic drugs, ovariectomy,[1] or pelvic radiation. Among adult men, fertility preservation should be considered whenever testicular damage may result from medical/surgical therapy or from trauma. Fertility preservation is a consideration that should be discussed in those undergoing treatment for malignancy as well as those with genetic or other congenital conditions.

The dramatic success noted in the treatment for childhood cancers has resulted in a marked increase in survival rates creating many long-term cancer survivors with unique medical challenges. Preservation of fertility is one such challenge that has mandated the need to assess future reproduction among these individuals.[2] Topics related to fertility preservation in pediatric and adolescent patients being treated for

[a] Department of Pediatrics, Penn State College of Medicine, MC-H085, The Milton S. Hershey Medical Center, PO Box 850, 500 University Drive, Hershey, PA 17033-0850, USA
[b] Department of Pediatrics, Indiana University School of Medicine, Riley Hospital for Children, Indianapolis, IN 46202, USA
[c] Department of Pediatrics, University of Virginia, Charlottesville, VA 22908, USA
[d] Department of Pediatrics, Medical College of Georgia, Augusta, GA 31403, USA
* Corresponding author. Department of Pediatrics, MC-H085, The Milton S. Hershey Medical Center, PO Box 850, 500 University Drive, Hershey, PA 17033-0850.
E-mail address: plee@psu.edu (P. Lee).

Endocrinol Metab Clin N Am 38 (2009) 761–775
doi:10.1016/j.ecl.2009.08.003 **endo.theclinics.com**
0889-8529/09/$ – see front matter

cancers, including ethical considerations, have recently been summarized.[3] Given the recent improvements in fertility preservation, this issue must now become part of an overall care plan for such children and adolescents.

Awareness of current and developing techniques is appropriate for the pediatric endocrinologist because of the improved potential for fertility in children with malignancy who have undergone chemotherapy or radiation therapy as well as children and adolescents with other diagnoses, including endocrinopathy, who have long been considered to be infertile.

Efforts to address fertility preservation should be considered as soon as the risk is realized. This applies to those with gonadal failure previously considered to be incompatible with biologic parenthood such as Turner or Klinefelter syndromes. Parenthood may also be possible, albeit at considerable expense, for patients with hypogonadotropic hypogonadism, polycystic ovarian disease, or other ovulatory dysfunction. The potential for such therapies should be assessed at an early age.

ATTAINMENT OF FERTILITY POTENTIAL IN THE HUMAN

Although fertility potential is not normally attained until early or midpuberty, a low level of gonadal activity is present during childhood with limited follicular development and early stages of spermatogenesis. Even though mature sperm are not present until a mean age of 14 years, meiosis results in development of spermatids in the prepubertal testis.[4] Semen cryopreservation has been reported to be feasible in roughly two-thirds of boys aged 13.7 to 18.9 years.[5] Although sperm counts cannot accurately be predicted by hormone measurements, it is likely that an adequate sample for preservation could be obtained around midpuberty in those without chronic debilitating illness. Similar findings have also been noted in 14- to 17-year-old boys with malignancies.[6] Among females, there is no conclusive evidence of further oocyte production after birth and meiosis occurs during follicular maturation. There is potential for in vitro maturation of primordial oocytes into oogonia. Before ovarian failure, all females will produce mature follicles in response to gonadotropin stimulation. In fact most females are capable of ovulation by midpuberty.

ETHICAL CONSIDERATIONS FOR THE CHILD

Ethical and legal issues including risk-benefit determination, must be considered[7] before implementing fertility preservation procedures. These must be proposed to parents, and, in an age-appropriate way, to the patient. Investigational review boards require a pediatric counselor to discuss the proposed preservation with the child. Such discussion may be awkward for families who have recently been given a diagnosis of malignancy. In addition, the importance of future fertility may be difficult for the prepubertal child to assess; therefore, parents can and should play a role in decision making in this arena. Consent must be obtained from parents with appropriate assent from the child before attempting to obtain and cryopreserve germ cells or gonadal tissue. Any procedures should be presented to an appropriate ethical review board as experimental, as protocols to preserve fertility in children are only now being developed.

DIAGNOSES IN CHILDREN AND ADOLESCENTS FOR FERTILITY PRESERVATION CONSIDERATIONS

Procedures for adolescent women and prepubertal boys and girls being investigated[8] are listed in **Box 1**. Efficacy of these procedures must be verified in adults before they are used in children. Procedures applicable to children include oocyte banking,