LEARNING OBJECTIVES

At the conclusion of this presentation, participants should be able to:

1. Explain the impact of chemotherapy and radiation treatments on fertility
2. Discuss the unique fertility preservation challenges in children
3. Discuss standard and experimental options to preserve fertility
4. Describe experimental stem cell therapies for treating infertility

DISCLOSURE

- I have nothing to disclose
Fertility after Cancer

- Chemotherapy and radiation treatments for cancer or other conditions can cause permanent infertility.
- Adult women and men can cryopreserve eggs, sperm or embryos, which can be used in the future to achieve pregnancy.
- These options are not available to preadolescent boys and girls who are not producing mature eggs or sperm.
- The five-year survival rate for preadolescent cancer patients is 85% (SEER).
- Prepubertal boys have spermatogonial stem cells in their testes that are poised to initiate sperm production at puberty.
- Centers worldwide are preserving testicular tissue for boys and ovarian tissues for girls in anticipation that new reproductive technologies will be available for them in the future.

Fertility Preservation for Boys with Cancer


Monkey model of cancer survivorship

- Hermann et al., Stem Cells, 2007

- Bony Hermann, PhD
Spermatogenic deficits

Hermann et al., Stem Cells, 2007

Autologous SSC Transplantation

- Biopsy
- Chemotherapy
- Cryogenic Preservation
- Auto Transplant
- Mark donor cells with GFP

Ultrasound-guided rete testis injection
Regeneration of Spermatogenesis

Hermann et al., Cell Stem Cell, 2012

SSC Transplantation appears technically feasible in higher primates

Ultrasound images courtesy of Richard Yu, Children’s Hospital of Boston

SSC Transplantation is Ready for the Clinic

- SSC transplantation is ready for the clinic now
  - The technology is mature – proven in mice, rats, hamsters, dogs, cats, goats, sheep, pigs and monkeys
  - We have the patients – more than 1000 so far worldwide (201 at Magee & affiliates)
- SSC transplantation in humans already happened
  - Testicular cells suspensions frozen for 12 Hodgkin’s patients (Radford et al., 1999)
  - Transplant later performed on 7 of those patients (Brooke et al., 2001, Radford et al., 2003)
  - Technology was in early stages in those days and had not been performed in any large animal species
- Optimal patient to transplant/Optimal age to transplant
  - Patients receiving bone marrow transplant for benign disease
  - Best time to transplant: during puberty
Fertility Preservation for Boys with Cancer

Autologous Grafting of Prepubertal Testis Tissue

Adetunj Fayomi, PhD
Karen Peters, RN

Pre-Graft Histology—Prepubertal Rhesus Testis

Fayomi et al., In Press
Fresh Frozen Matrigel

Recipient
- Chemotherapy treated
- Castrated

Grafts
- 4 tissues per site
- 6 sites on back
- 2 sites in scrotum

Experiments
- Fresh vs. Frozen
- Back vs. Scrotum
- Matrigel vs. Not

Fayomi et al., In Press

Testosterone

Autologous Grafting

Fayomi et al., In Press

Graft growth and appearance

Little Testes

Little Testicles

Fayomi et al., In Press
Recovered Graft
(8-13 months post-graft)

Complete spermatogenesis from autologous grafts

Preimplantation embryo development after ICSI
- ICSI: 11/10/2017
- Embryo transfer: 11/17/2017
- Preg. Confirmed: 12/25/2017

Jon Hennebold & Colleagues – ART Core, Oregon National Primate Research Center
Grady
Graft-derived baby

Born April 16, 2018 by c-section

World's first baby born from autologously grafted, frozen and thawed testicular tissue

Fayomi et al., In Press

Future Directions

- Developmental assessments of Grady
- Assess Grady's fertility and health of her progeny
- Repeat experiment in animals with testes to model the prepubertal cancer survivor
- Repeat with human tissues
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