Long duration of function of ovarian grafts

S. Silber [1], E.Ernst [2], C. Andersen [3]

[1]St. Luke's Hospital, Infertility Center of St. Louis, St. Louis, Missouri, U.S.A. [2]Aarhus University Hospital, Dept of Gynecology and Obstetrics, Aarhus, Denmark. [3]University Hospital of Copenhagen, The Juliane Marie Centre for Women Children and Reproduction, Copenhagen, Denmark.

Introduction

We wished to determine the possible long-range duration of function of ovarian cortical tissue grafts.

Materials and Methods

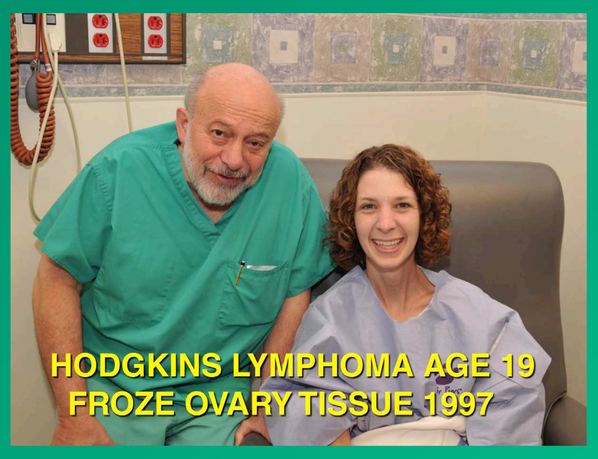
We reviewed the recipients of the longest lasting ovary cortical tissue grafts at a university fertility preservation program in Europe and a private practice program in the United States. One woman who underwent sterilizing cancer treatment and had frozen ovarian tissue replanted, and two women underwent fresh ovary tissue transplants either for premature ovarian failure or for ovarian failure caused by cancer treatment were the longest lasting ovarian grafts. In addition to frozen cortical ovary grafts, a total of 7 of 9 women with fresh ovary grafts had 14 pregnancies and 11 babies, and duration of function was reviewed.

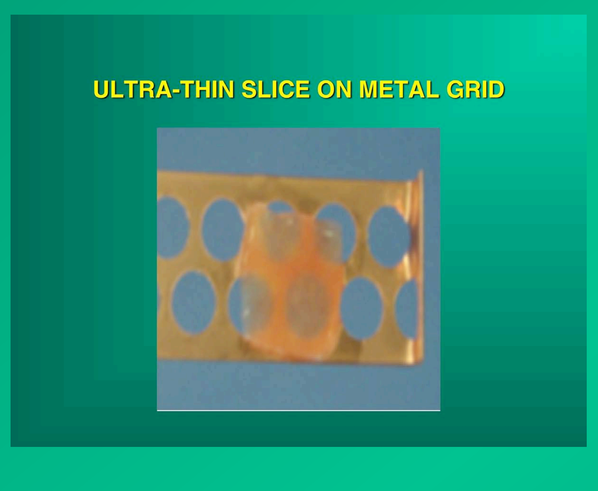
Results

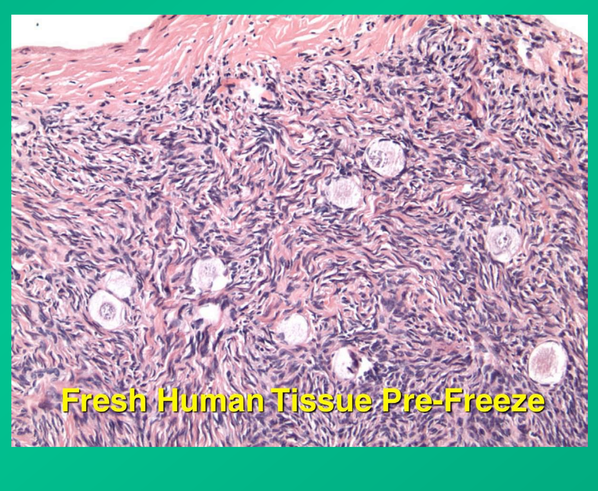
The longer lasting grafts had higher egg counts in the ovary tissue and antral follicle counts on pre-op ultrasound. Ovarian cortical strips have lasted for over seven years with eight healthy babies in three women from just one graft per patient. Seven of 9 fresh grafts lasted more than 4 years. Three lasted over 6 years.

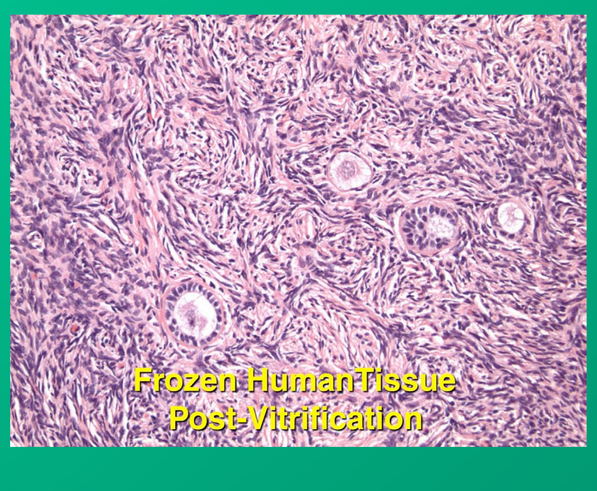
Conclusions

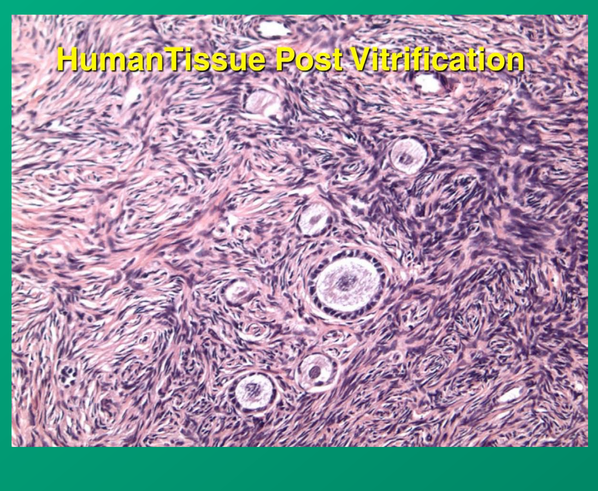
Three women have given birth to two or three healthy babies each (eight in all) following transplantation of a small amount of ovarian tissue. Thus far, the longest lasting graft is over 7 years and is still functioning. Transplanted cryopreserved or fresh ovarian tissue can robustly restore menstrual cycles and fertility, over prolonged periods of time and may even in the future be used to postpone the normal time of menopause or to alleviate its symptoms. Ovarian cortical graft ischemia must not be an impediment to long lasting cortical grafts, based on the robust results with fresh grafts and some frozen grafts.

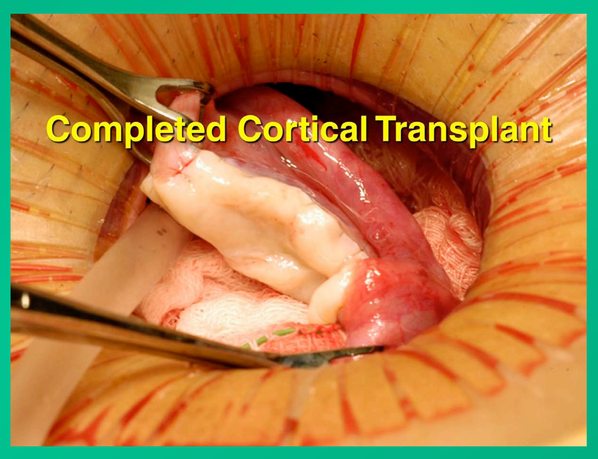


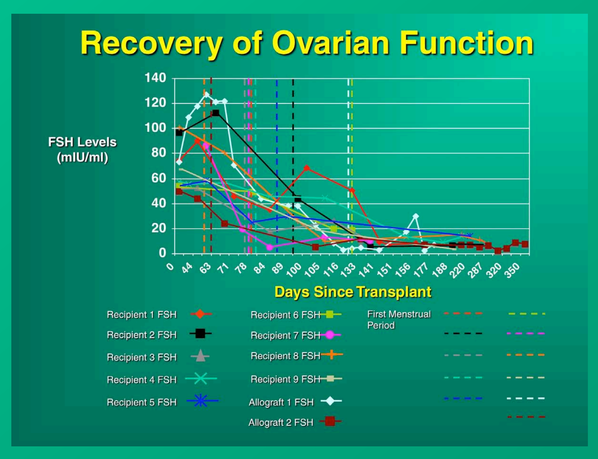












TIME TO CONCEPTION FOR HEALTHY PREGNANCIES:

- 0, 1, 2, 3, 5, 7, 8, 11, 16, 30, 53, 56, 72 cycles.
- three pregnancies required > 3 years.
- five pregnancies required > 1 year.
- two pregnancies (2nd and 3rd child) occured > 4 to > 6 years after the same transplant.

Duration of Function of Fresh Cortical Grafts

- The seven cases with AFC >10, and abundant primoridal follicles, have > 4 to > 8 years duration of function.
- The two cases with < 3 years of function had AFC < 5, and smaller number of primordial follicles.

Stimulated ovary post tissue transplantation: No apparent follicle loss from transplant.

MEIROW AND SILBER 2011

Ovarian Transplant Results

14 babies (11 from 9 fresh; 3 from 3 frozen)

Pt #	Age	Pre-OP FSH	Post-Op FSH	Initial Post-OP Menses intervals	Preg	Babies Delivered	Years of Graft Function
1	24	75	7.1	2nd baby: FROZEN	3	2	4
2	38	96	5.2	93, 42, 24, 27, 25…	3	3	>8
3	25	112	6.8	76, 23, 30, 26, 25, 26, 21, 24, 27, 34, 25, 27, 51, 30, 27, 26, 28, 19…	1	2	>8
4	34	58	9.4	81, 22, 47, 26, 21, 20, 27, 26…	2	1	4
5	40	60	6.8	86, 29, 38, 34, 28, 28, 31, 35, 34, 28, 33, 35, 30…	0	0	4
6	26	101	7.5	64, 20, 39, 40, 32, 26, 29, 26, 26, 41…	1	1	2
7	34	86	4.4	83, 22, 29, 29…	3	2	>6
8	37	86	7.4	100, 17, 39, 29, 27, 22, 23, 20, 34, 25, 26, 29…	1	1	>4
9	35	54	4.2	128, 42, 18, 25…	1	0	2
10	31	78	3.4	FROZEN	1	1	2
11	33	85	8.6	FROZEN	1	1	>1

**Note: each graft represents only 1/3 of one ovary or 1/6 of entire ovarian reserve.*

SUMMARY OF RESULTS: FRESH OR FROZEN OVARY TRANSPLANT

- 10 women with ovarian failure.
- 12 ovarian transplants: 9 fresh & 3 frozen.
- 8 cases were POF. 2 cases were cancer BMT.
- 16 pregnancies. 14 healthy babies.
- 11 babies: fresh transplant. 3 babies: frozen.
- 3 babies: recipient had pelvic irradiation.
- 4.5 months: return of normal ovulation.
- Usually > 4 years duration of function.
- No loss from transplant ischemia.
- With vitrification, no loss from freezing either.

Worldwide Frozen Ovarian Cortex Tissue Transplant Pregnancies

Case #	Diagnosis	Babies	Where
1	Hodgkins	1	Donnez
2	Neuro Tumor	1	Donnez
3	Non-Hodgkins	1	Meirow
4	Hodgkins	1	Demeestere
5	Ewings	3	Andersen
6	Hodgkins	1	Andersen
7	POF	1	Silber
8	Hodgkins	2	Silber
9	Polyangiitis	1	Piver
10	Breast Cancer	2	Pellicer
11	Sickle Cell	1	Piver
12	Hodgkins	2	Revel
Totals: 12 patients		17 Babies	8 Centers
Fresh + Frozen		29 Babies	Fresh: Silber, Donnez