FERTILITY AND REPRODUCTION IN FEMALE CHILDHOOD CANCER SURVIVORS

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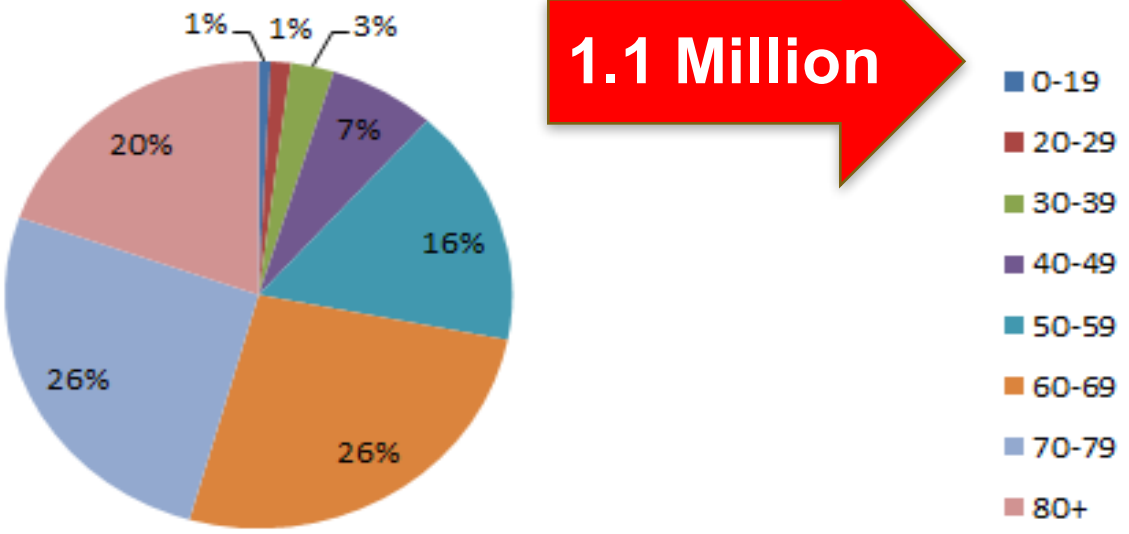
1% OF CANCER OCCURS IN CHILDREN

Estimated number of Persons Alive in the U.S. Who Were Diagnosed With Cancer, by Current Age – More Detail (as of January 1, 2014) (Invasive/1st Primary Cases Only, N = 14.5 M survivors)



[1] DeSantis C, Chunchieh L, Mariotto AB, et al. (2014). Cancer Treatment and Survivorship Statistics, 2014. CA: A Cancer Journal for Clinicians. In press.

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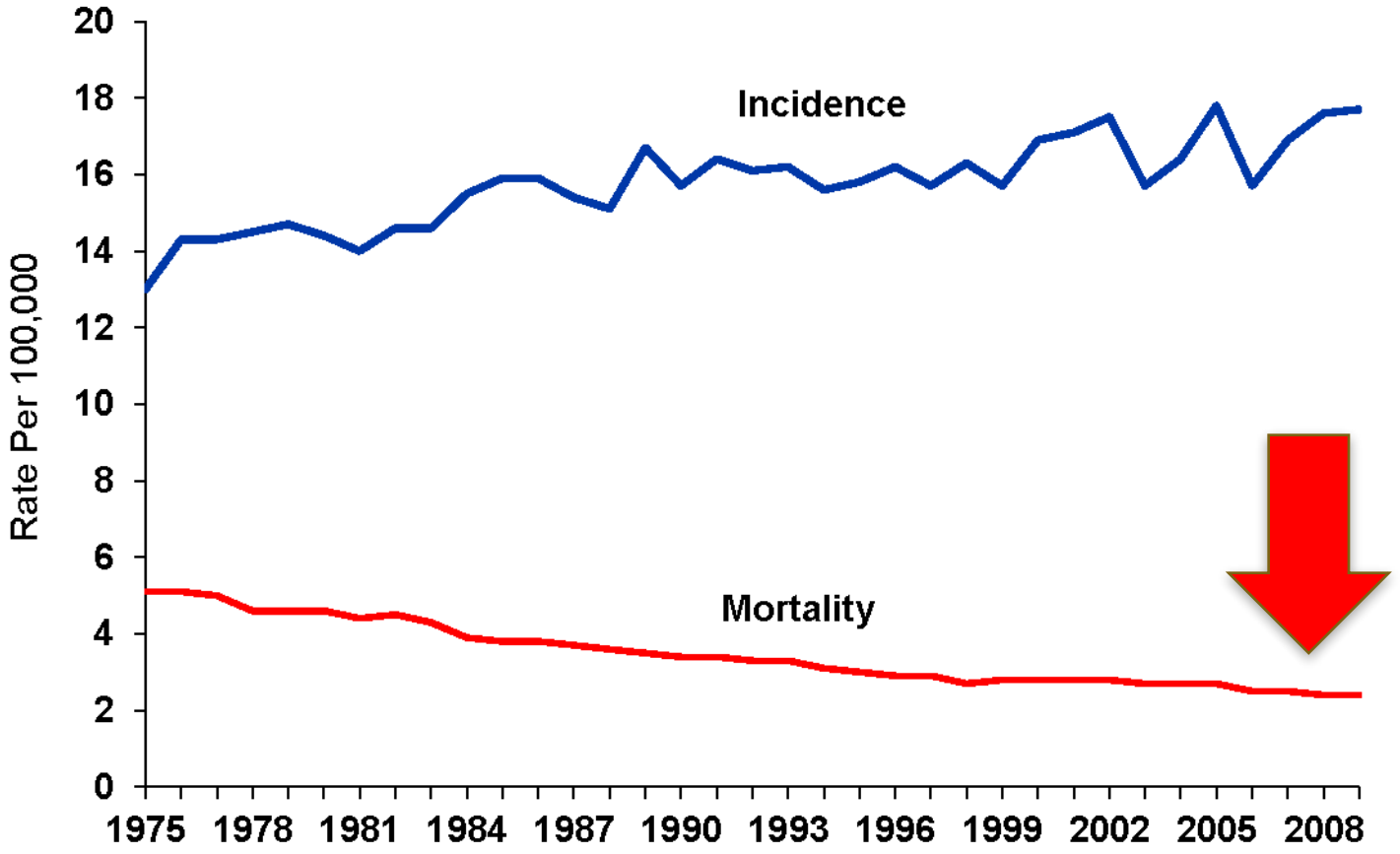
Cancer Incidence and Death Rates* in Children 0-19 Years, 1975-2009



*Age-adjusted to the 2000 Standard population.

Source: Incidence -Surveillance, Epidemiology, and End Results Program, Delay-adjusted Incidence database: SEER Incidence Delay-adjusted Rates, 9 Registries, 1975-2009, National Cancer Institute, 2012.
Mortality – National Center for Health Statistics, 2012.

BETTER TREATMENT=BETTER SURVIVAL

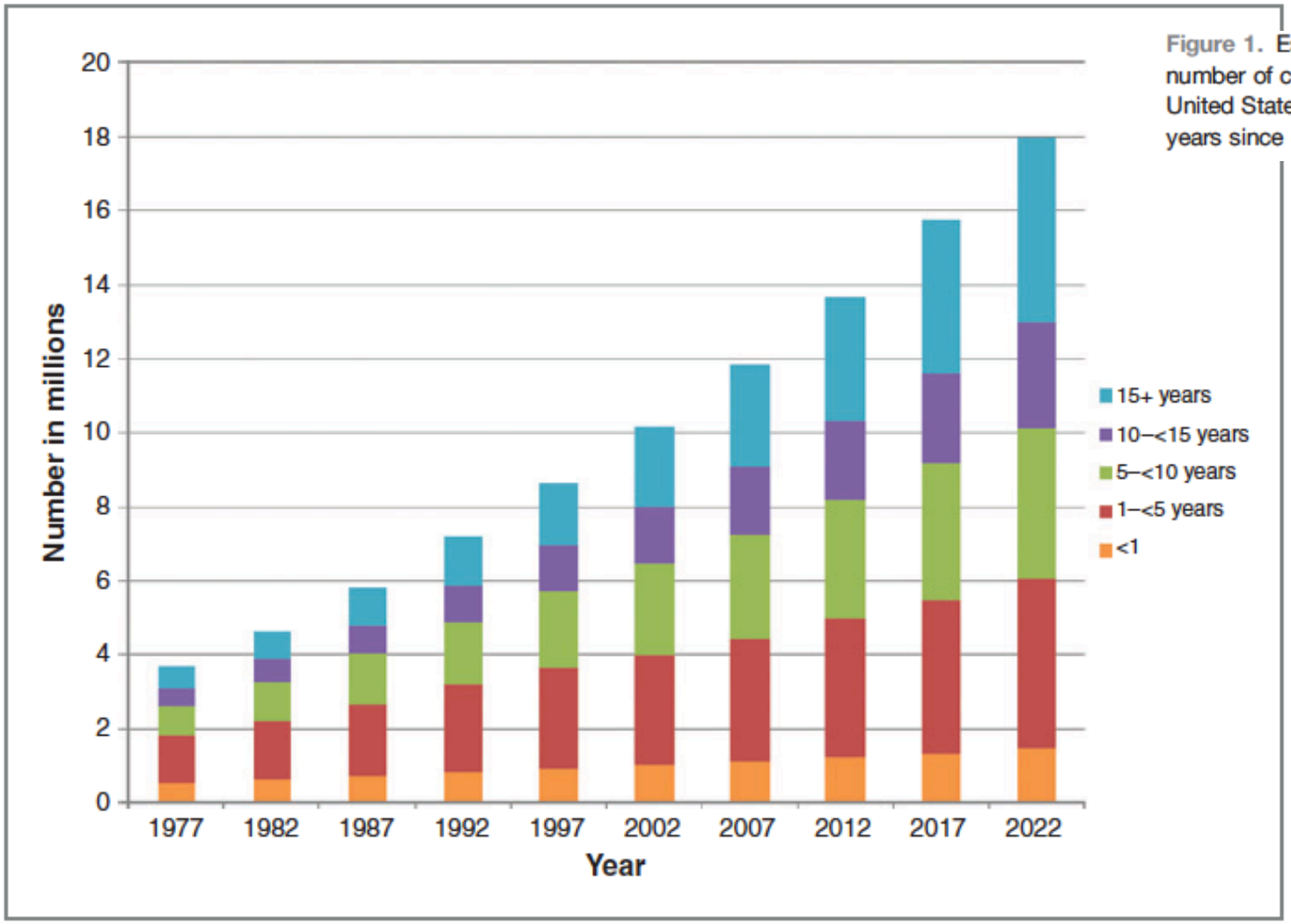


Figure 1. Estimated and projected number of cancer survivors in the United States from 1977 to 2022 by years since diagnosis.

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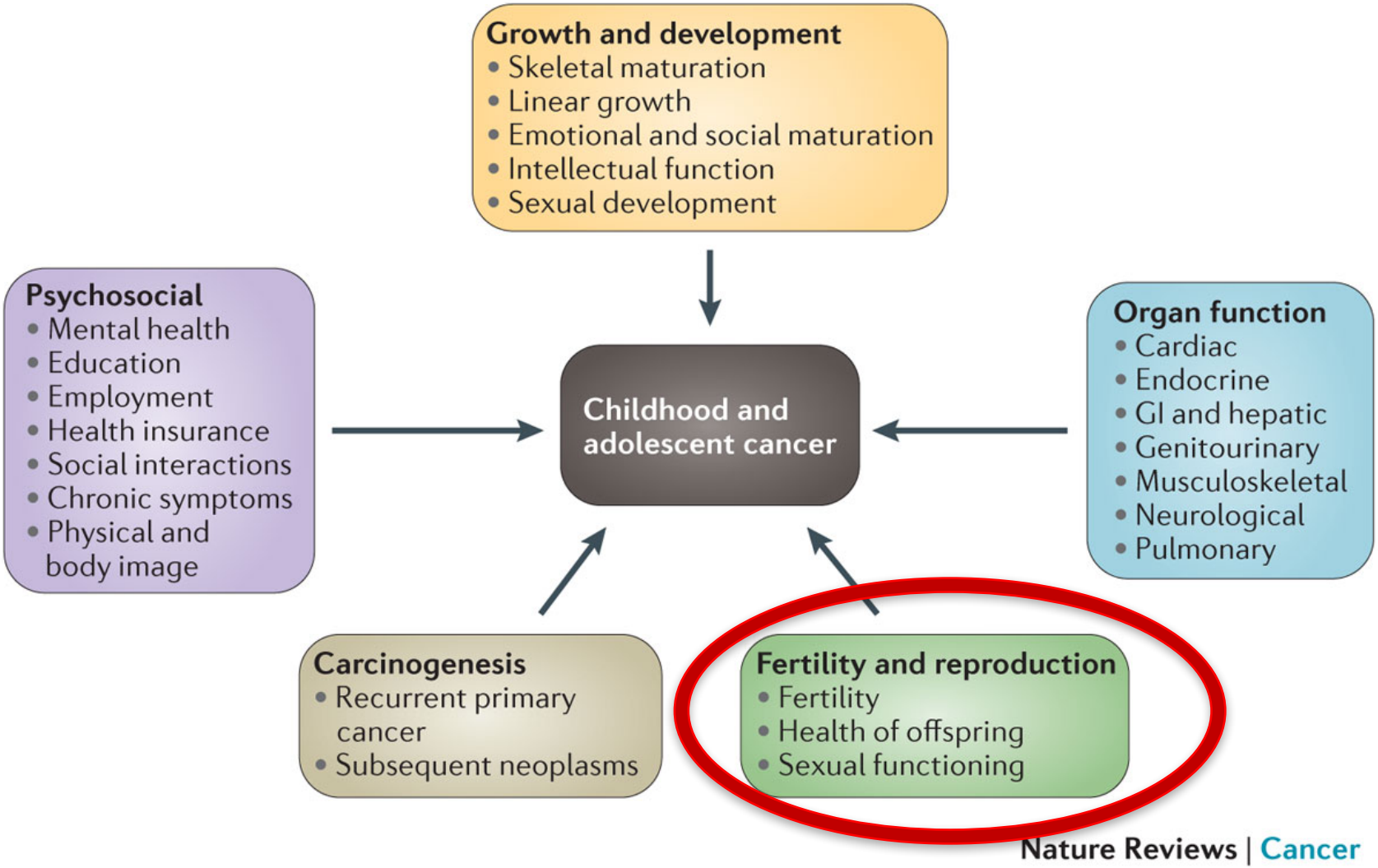
Cancer Epidemiol Biomarkers Prev 2013:22(4);561-70

MANY LONG-TERM HEALTH IMPACTS



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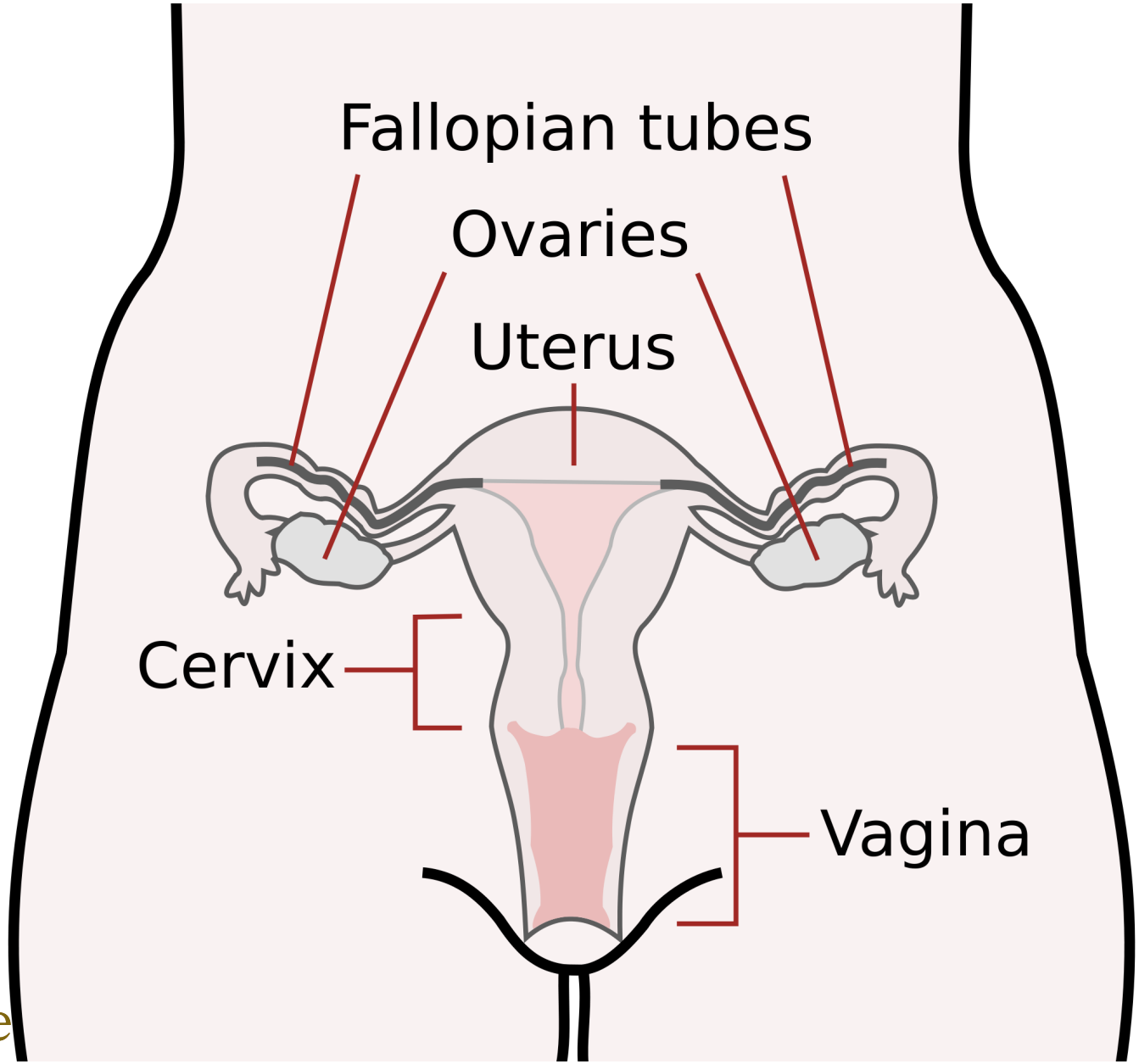
REPRODUCTIVE PHYSIOLOGY

FEMALE REPRODUCTIVE ORGANS



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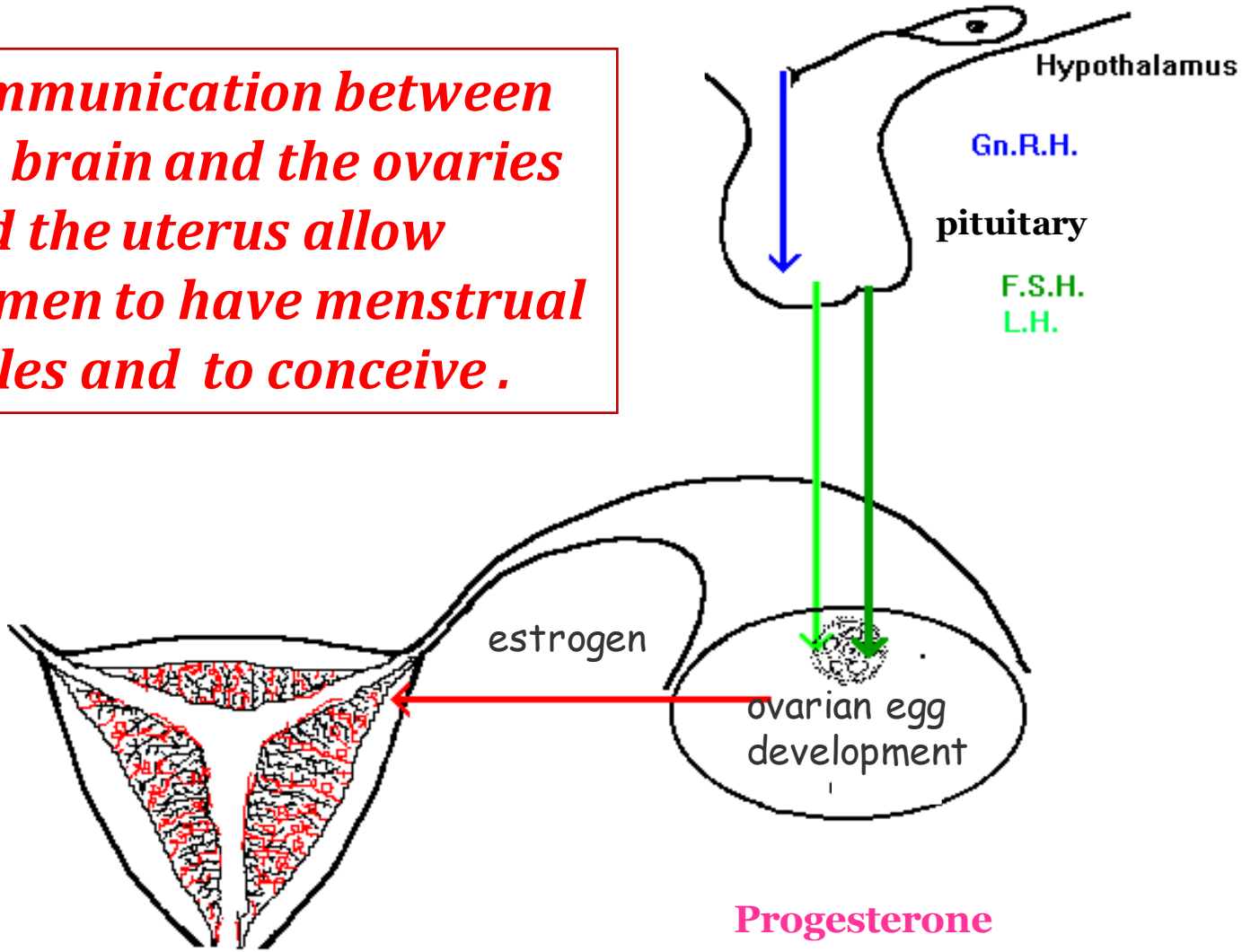
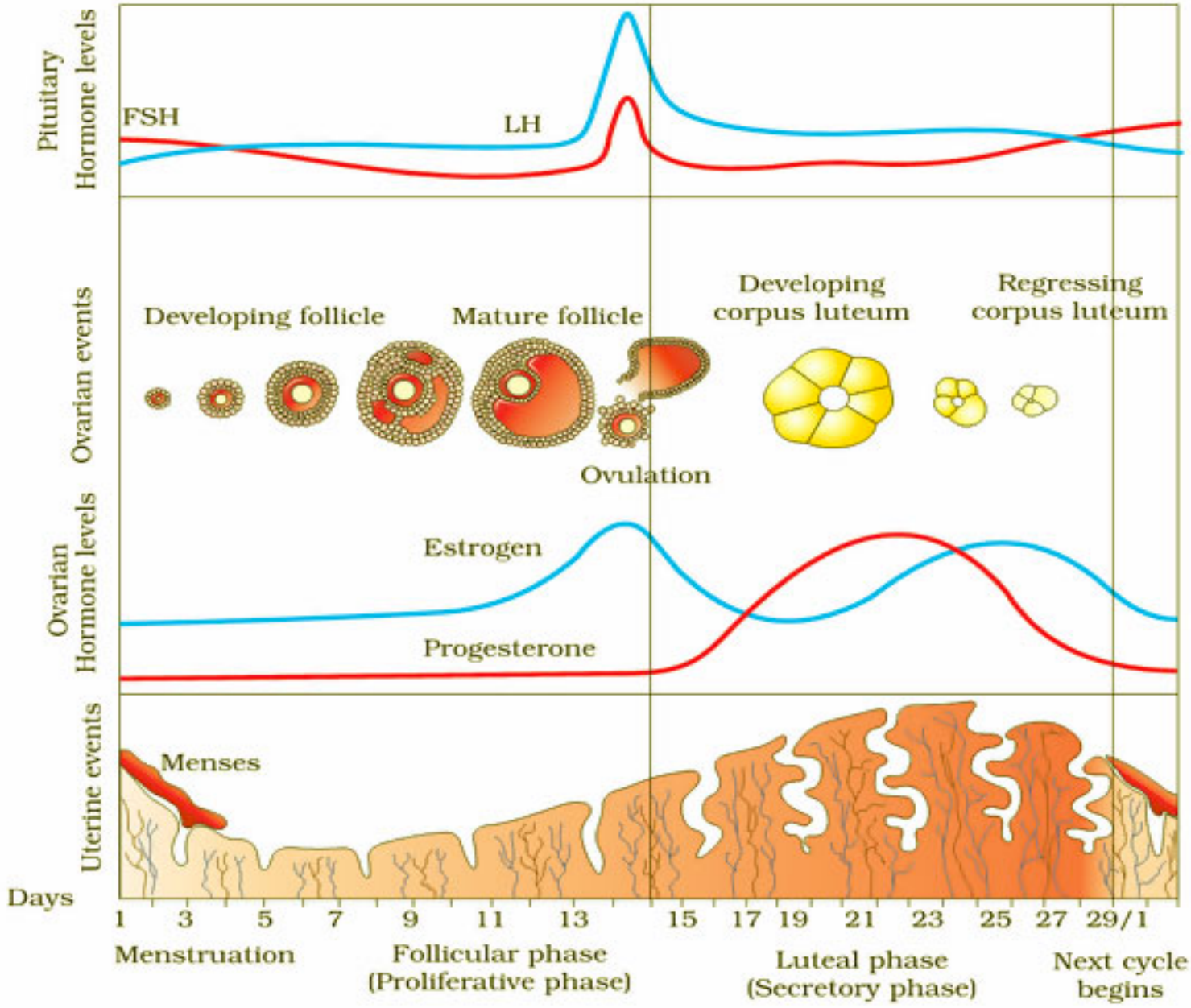
BRAIN, OVARY, UTERUS: KEY PLAYERS IN FEMALE REPRODUCTION

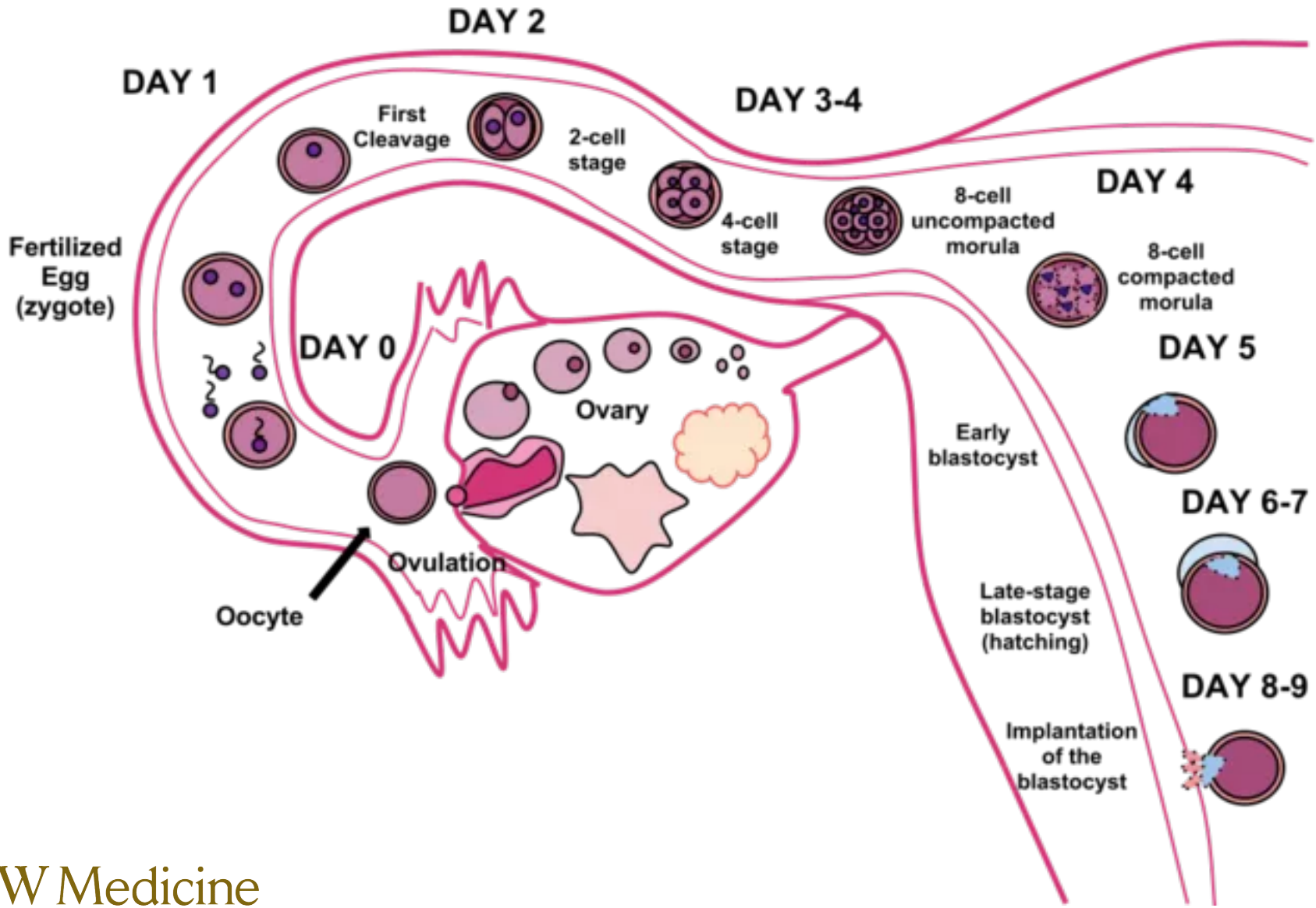
Communication between the brain and the ovaries and the uterus allow women to have menstrual cycles and to conceive .



MENSTRUAL CYCLE



BEGINNING OF A PREGNANCY



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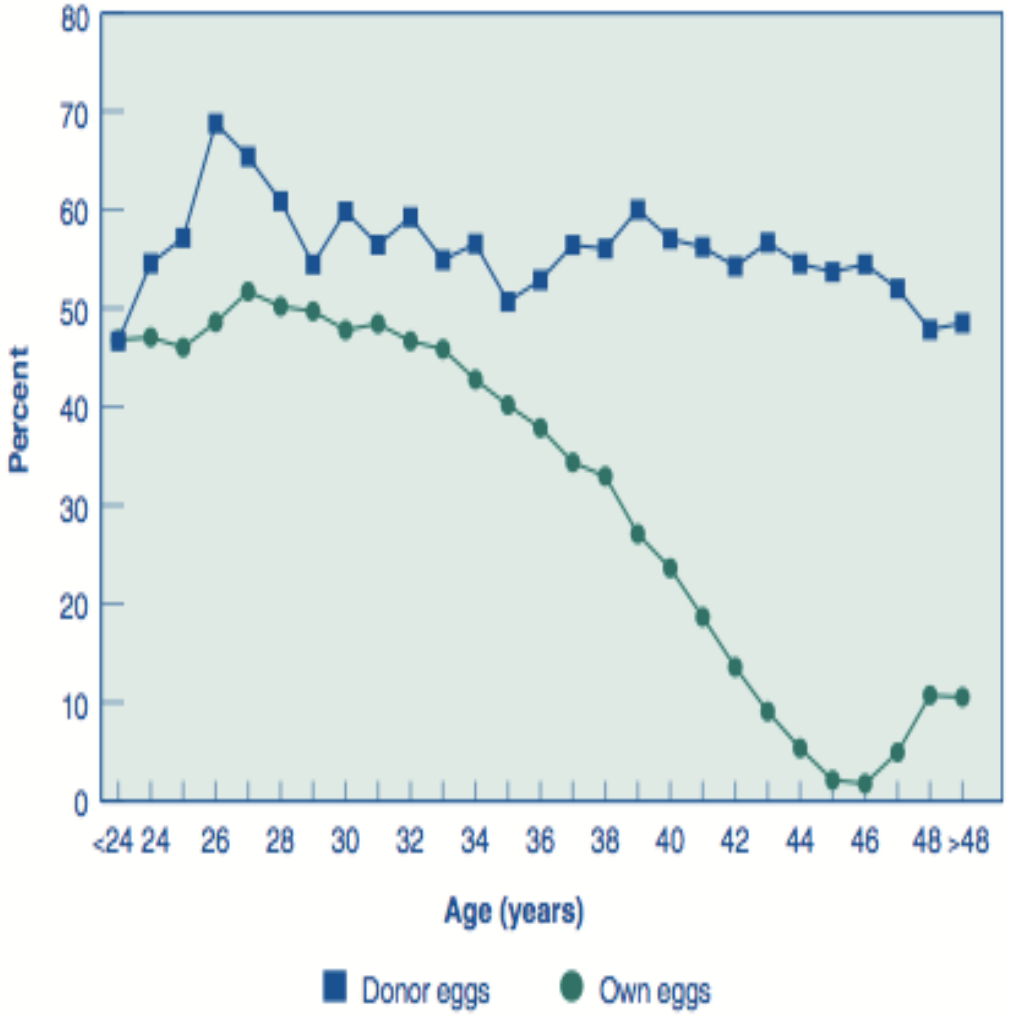
FEMALE FERTILITY DECLINES NATURALLY WITH AGE: DUE TO LOSS OF EGGS

- **Born with 1 million eggs → release 300-400 eggs over lifetime →1000 eggs remain at menopause**

- **Egg quantity and quality decrease with age→ fertility decline from 30s**



CDC, 2012

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REPRODUCTIVE CONCERNS OF FEMALE CHILDHOOD SURVIVORS

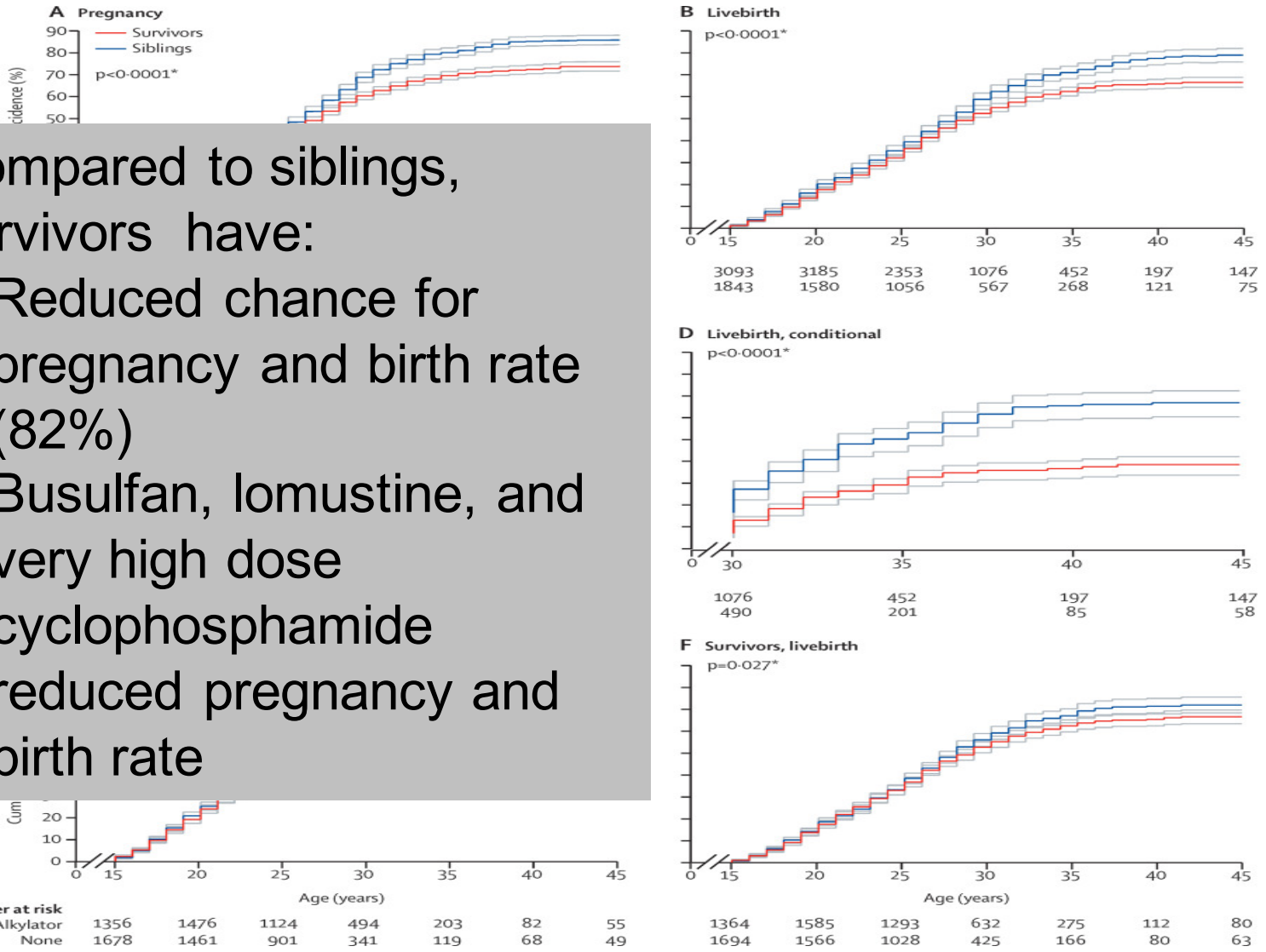
HOW DO CANCER TREATMENTS AFFECT FEMALE REPRODUCTION?

- **Many cancer treatments adversely affect:**
  - **egg quantity and quality**
  - **blood supply to the uterus**
  - **hypothalamus/pituitary function**

- **Many cancer surviors experience:**
  - **Decreased fertility**
  - **Premature menopause (premature ovarian failure)**
  - **Sexual dysfunction**
  - **Precocious or delayed puberty**

REDUCED FERTILITY

CHILDHOOD CANCER SURVIVORS: LOWER BIRTH RATES THAN SIBLINGS



Compared to siblings, survivors have:

- Reduced chance for pregnancy and birth rate (82%)
- Busulfan, lomustine, and very high dose cyclophosphamide reduced pregnancy and birth rate

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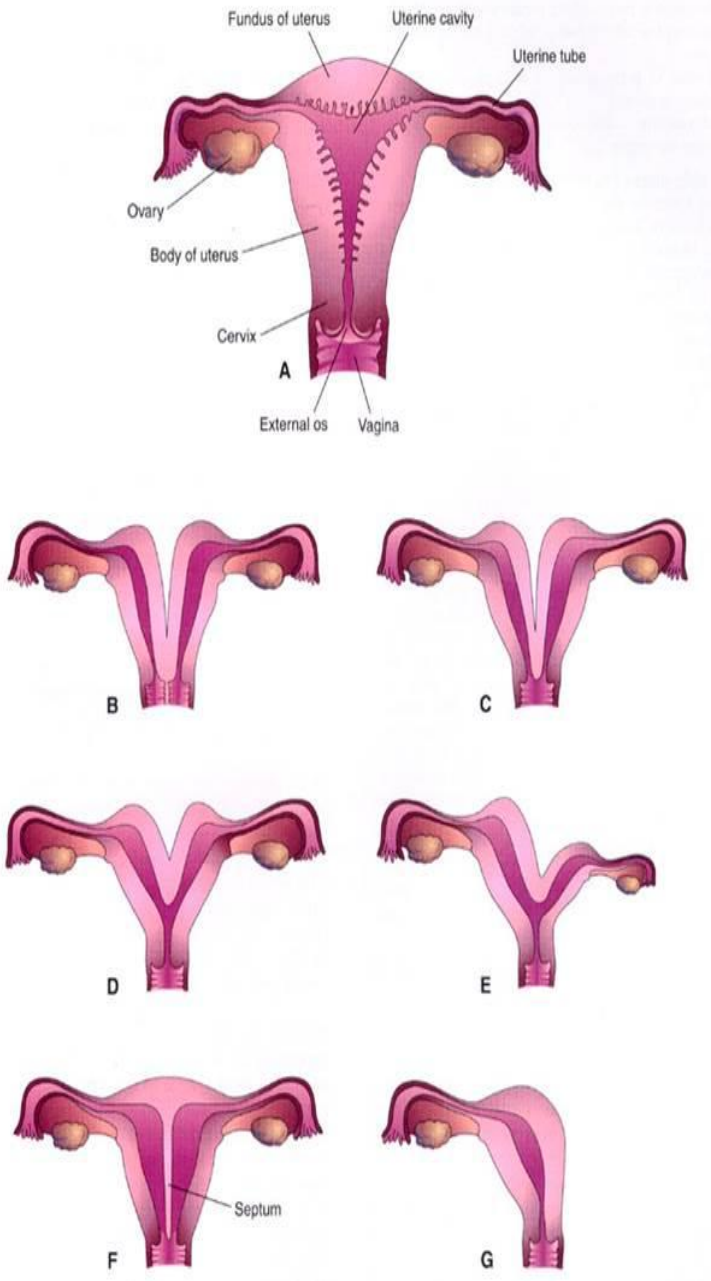
Chow EJ et al. Lancet Oncol. 2016 May;17(5):567-76.

DAMAGE TO UTERUS

- Pelvic radiation ≥ 30 Gy
  - Decrease uterine blood flow
- Wilm's tumor: 10% with abnormal uterus
  - Increased miscarriage, preterm birth, malpresentation, low birth weight
- Evaluation by REI: ultrasound, MRI



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IMPAIRED OVARIAN FUNCTION: RISK FACTORS

- **Primary: Direct damage to ovaries**
  - **Certain chemotherapy: alkylating agents (busulfan, cyclophosphamide)**
  - **Radiation: Abdomen, pelvis, spine, total body; especially after puberty**
  - **Removal of ovary**
- **Secondary or Central: Hypothalamic/pituitary damage**
  - **Brain radiation >30Gy**

IMPAIRED OVARIAN FUNCTION: PRESENTATIONS

- **Delayed or arrested puberty**
- **Acute ovarian failure:**
  - **Never had period, or stop period within 5 yrs after diagnosis**
- **Premature ovarian failure:**
  - **Menopause before 40yo**
- **Infertility**

IMPAIRED OVARIAN FUNCTION: WHAT TO DO?

- **Before or during Ca treatment:**
  - **Freeze eggs or ovarian tissue**
  - **Move ovaries out of radiation field**
  - **Lupron shots during chemo**

- **After Ca treatment:**
  - **Annual visit: follow puberty, periods, sexual function, pregnancy**
  - **Labs: baseline FSH, LH, Estrodiol, (AMH) at age 13, and if clinically indicated**
  - **Refer to GYN or REI as indicated**
  - **Freeze eggs if desires, before ovarian failure**
  - **Hormone replacement if ovarian failure**

EGG FREEZING (OOCYTE CRYOPRESERVATION)

Consultation

- Pre-Screening and Pre-Testing

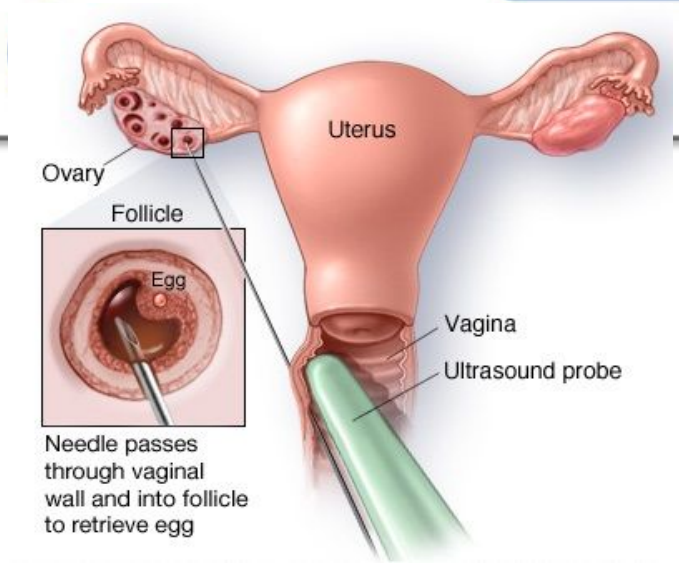
Hormone Injections

- Stimulate Ovaries to Ripen Multiple Eggs

Egg Retrieval under Sedation

- Ultrasound Guided Procedure to Retrieve Eggs

Freeze and store in liquid nitrogen



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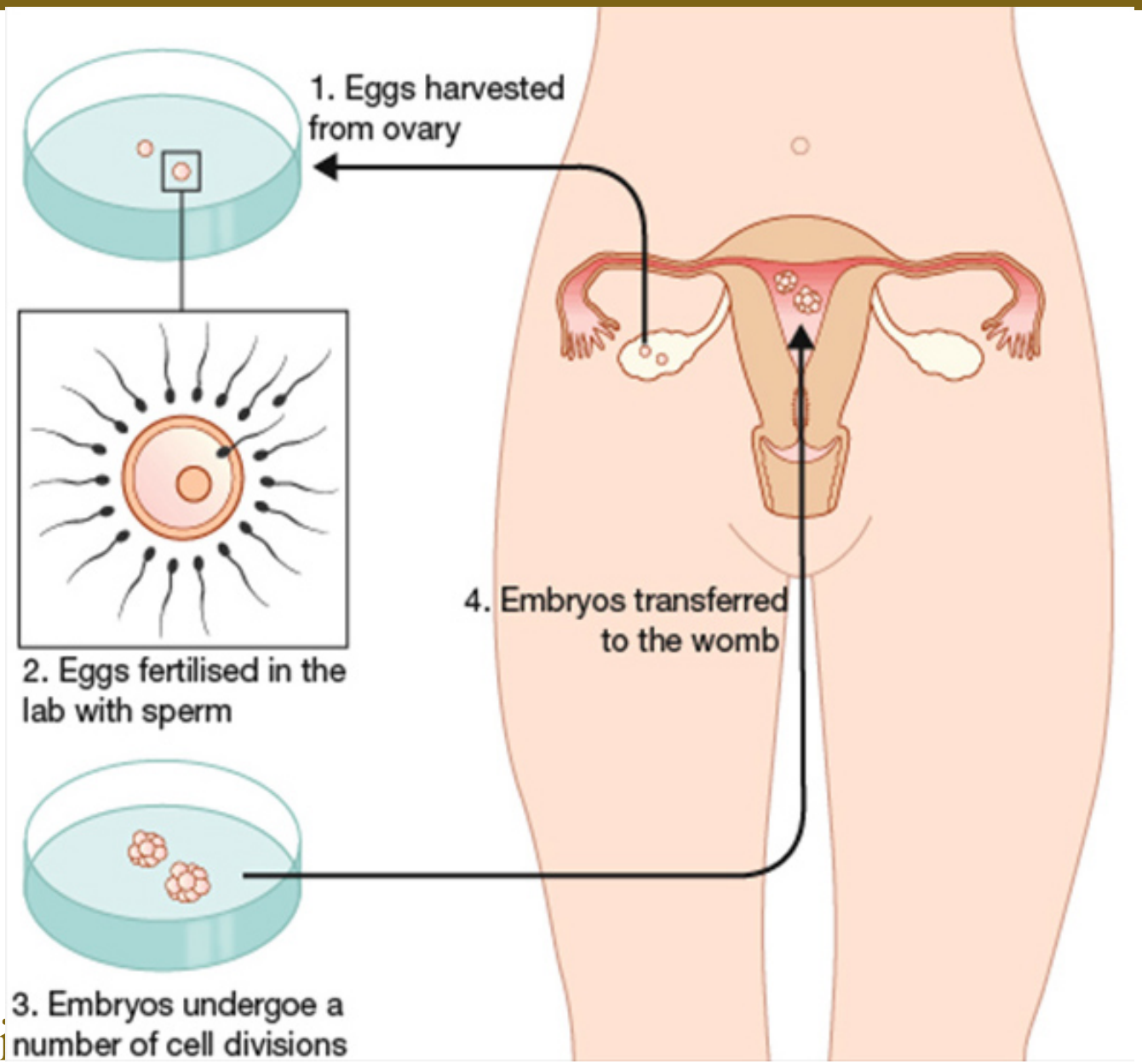
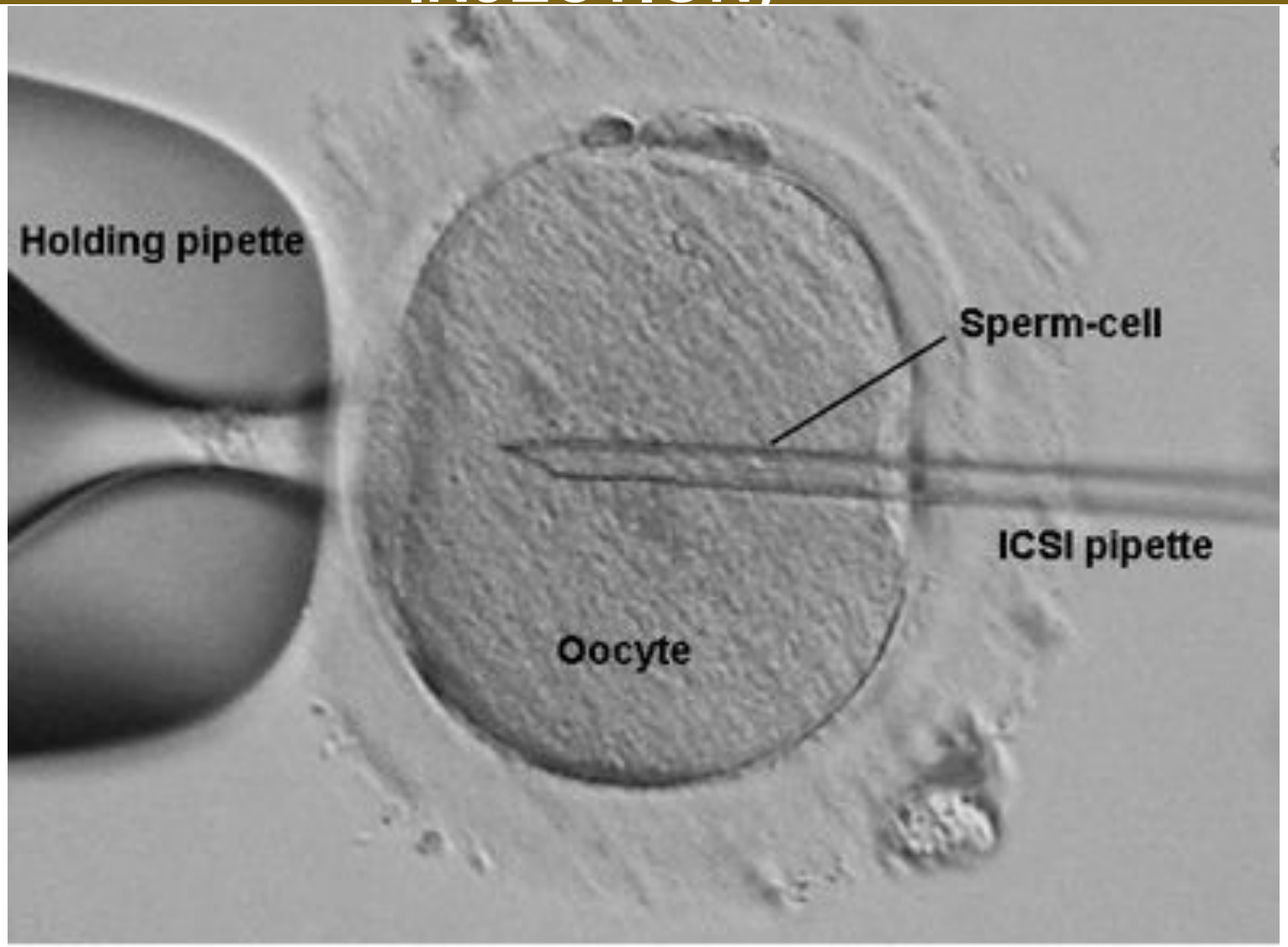
EMBRYO FREEZING



ICSI (INTRA CYTOPLASMA SPERM INJECTION)



ICSI

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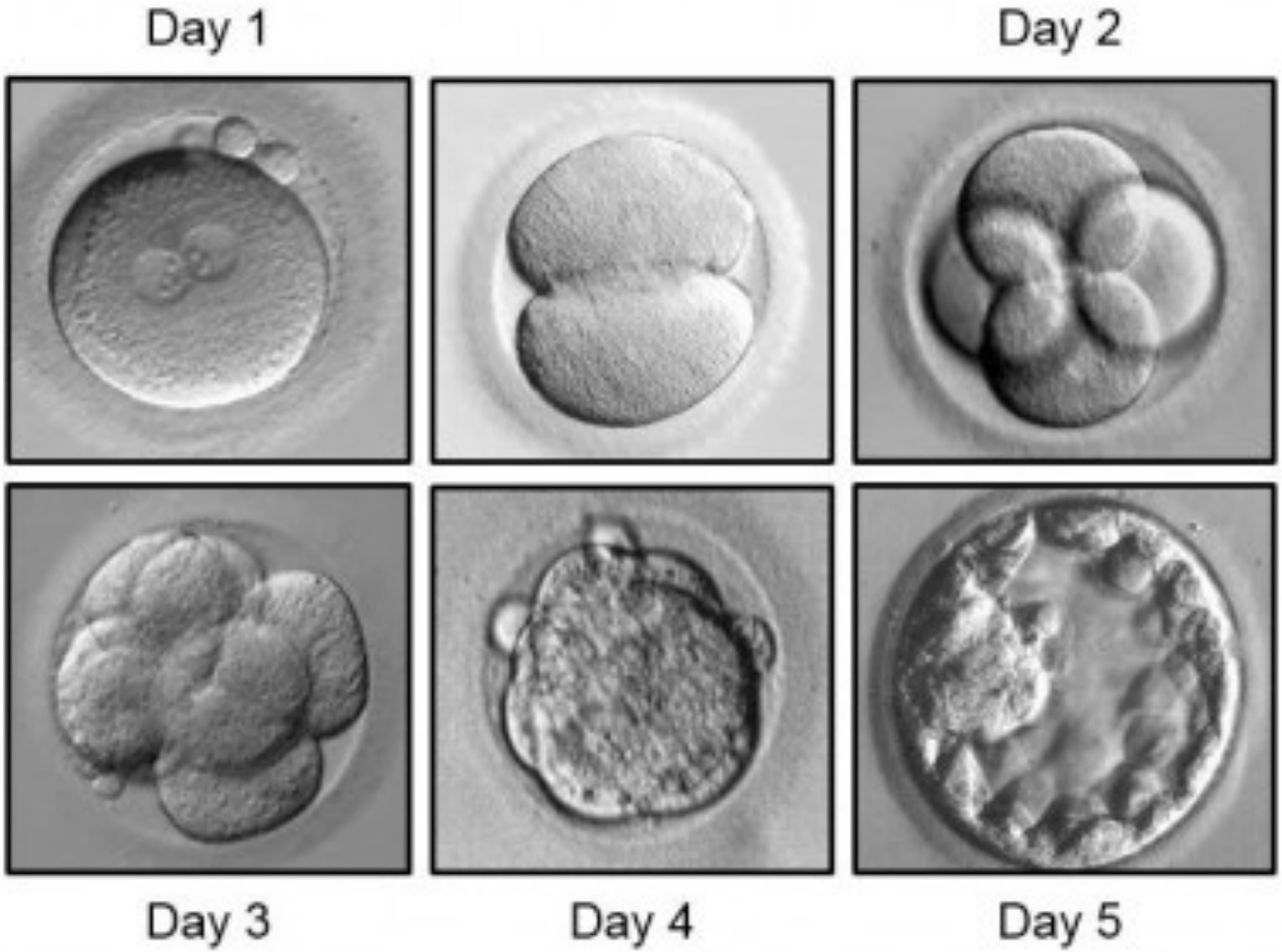
EMBRYO DEVELOPMENT BEFORE TRANSFER



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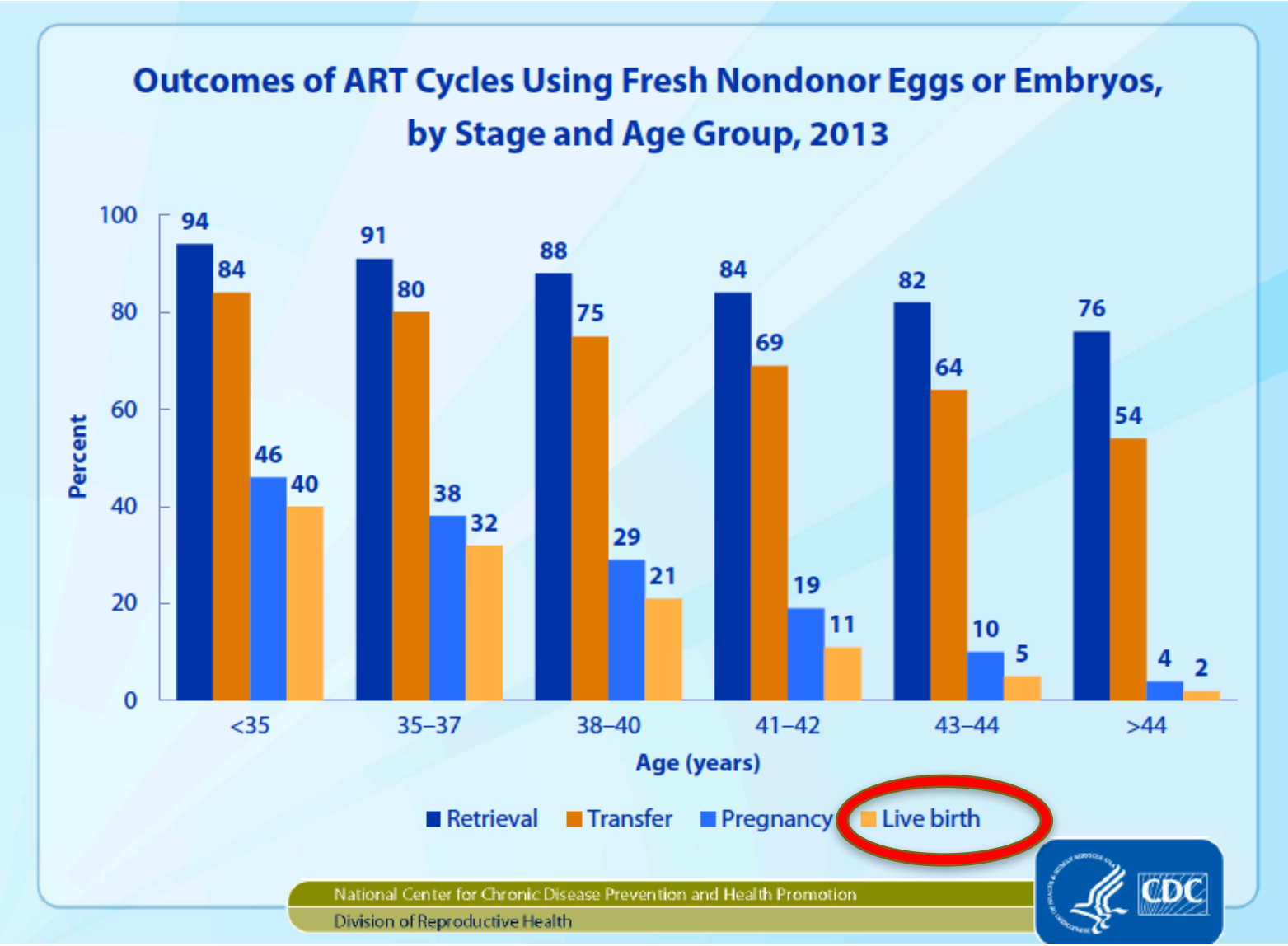
EARLY FERTILITY PRESERVATION IS KEY!

- Damage to ovaries is not reversible
- Normal periods ≠ normal fertility
- Fertility decline especially prominent after age 30-35
- Standard embryo or egg freezing takes ~ 4 to 6 weeks
- Success not guaranteed

IVF SUCCESS RATE IN NON-CA PATIENTS



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IVF SUCCESS RATE IN CA PATIENTS LOWER

Table III Likelihood of conception and live birth for women after ART by cancer diagnosis, limited to women who only used autologous oocytes.

Cancer diagnosis	*n*, women	Model	Live birth		Conception		Live birth given conception	
			OR/AOR	95% CI	OR/AOR	95% CI	OR/AOR	95% CI
No cancer	48 138		1.00	Reference	1.00	Reference	1.00	Reference
All cancers	393	Unadjusted	**0.36**	**0.29, 0.45**	**0.33**	**0.27, 0.41**	0.93	0.55, 1.58
		Adjusted[a]	**0.36**	**0.28, 0.46**	**0.34**	**0.27, 0.42**	1.21	0.69, 2.11
Endocrine	62	Unadjusted	**0.53**	**0.31, 0.90**	**0.52**	**0.31, 0.87**	0.77	0.26, 2.25
		Adjusted[a]	0.67	0.37, 1.18	0.65	0.38, 1.14	0.84	0.28, 2.56
Melanoma	43	Unadjusted	1.27	0.70, 2.32	1.14	0.62, 2.10	1.76	0.42, 7.45
		Adjusted[a]	1.59	0.83, 3.06	1.33	0.69, 2.56	3.07	0.69, 13.60
Breast	133	Unadjusted	**0.18**	**0.11, 0.30**	**0.19**	**0.12, 0.29**	0.49	0.19, 1.22
		Adjusted[a]	**0.19**	**0.11, 0.30**	**0.20**	**0.13, 0.32**	0.63	0.24, 1.64
Ovarian	12	Unadjusted	1.54	0.49, 4.86	1.15	0.37, 3.63	–	–
		Adjusted[a]	1.28	0.39, 4.16	0.98	0.30, 3.22	–	–
Cervical	24	Unadjusted	**0.37**	**0.15, 0.93**	**0.41**	**0.18, 0.96**	0.46	0.09, 2.29
		Adjusted[a]	**0.33**	**0.13, 0.84**	**0.36**	**0.15, 0.87**	0.70	0.11, 4.49
Uterine	15	Unadjusted	**0.28**	**0.08, 0.98**	**0.30**	**0.10, 0.94**	0.46	0.05, 4.43
		Adjusted[a]	0.30	0.08, 1.11	0.33	0.10, 1.05	0.38	0.04, 3.77
All female genital	53	Unadjusted	**0.48**	**0.27, 0.86**	**0.50**	**0.29, 0.87**	0.61	0.21, 1.83
		Adjusted[a]	**0.47**	**0.25, 0.86**	**0.49**	**0.27, 0.87**	0.79	0.23, 2.78

[a]Models adjusted for woman's age, parity, cumulative FSH dosage, infertility diagnosis and number of infertility diagnoses, number of ART cycles, State of residency and year of ART treatment. Bolded values are OR/AORs and 95% CIs which are significant.

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Luke B et al. Hum Reprod. 2016 Jan;31(1):183-9.

OTHER OPTIONS TO HAVE CHILDREN

- Ovarian tissue freezing: experimental, prepubertal girls
- Donor eggs
- Donor sperms
- Gestational carrier
- Adoption

OVARIAN FAILURE

PREMATURE OVARIAN FAILURE/INSUFFICIENCY

- Menopausal symptoms
  - Vasomotor symptoms
  - Sexual dysfunction
  - Atrophic vaginitis
- Long-term health after menopause
  - Bone
  - Metabolic
  - Cardiovascular

OVARIAN FAILURE: WHAT TO DO?

- Hormone replacement therapy
  - Before puberty: estrogen, monitored by pediatric endocrinologist or adolescent gynecologist
  - After menarche: estrogen and progesterone, follow up with GYN
- May occasionally ovulate → pregnancy
- Osteoporosis prevention
- Symptom relief

SEXUAL DYSFUNCTION

SEXUAL DYSFUNCTION: RISK FACTOR

- Chronic GVHD
- Low estrogen level: ovary, brain
- Spinal cord tumor or surgery
- Vaginal tumor or surgery
- Pelvic radiation
    - Prepubertal: ≥25 Gy
    - Postpubertal: ≥50 Gy

SEXUAL DYSFUNCTION: PRESENTATIONS

- Altered or diminished sensation
- Difficulty with tampon insertion
- Dyspareunia
- Vulvar pain
- Postcoital bleeding
- Vaginal fistula

SEXUAL DYSFUNCTION: TREATMENT

- Gynecologic consultation:
  - Lubrication
  - Vaginal dilators
  - Vaginal reconstructive surgery
  - Hormone replacement therapy
- Psychological consultation: for patients with emotional difficulties

OTHER GYN ISSUES

- Heavy periods during ca treatment due to low platelets
    - Lupron shot, birth control pills
- Routine GYN care, HPV vaccine, contraception

PRECOCIOUS PUBERTY

PRECOCIOUS PUBERTY

- Breast development before 8 years old
- Risk factor:
  - Head/neck radiation ≥18 Gy
  - younger age at time of irradiation
- Evaluation: Pediatric Endocrinologist
  - LH, FSH, estradiol, pelvic ultrasound, bone age
- Treatment:
  - GnRH agonist (Lurpon) until normal age of puberty

CONCLUSION

1) Improved and personalized cancer treatment plans have resulted in increased numbers of young cancer patients living long lives after cancer treatment.
2) Patients diagnosed with cancer want to live a full life and not just survive after cancer therapy.
3) Many reproductive aged patients identify normal reproductive function to be an important part of life.
4) Many treatment options are available to meet reproductive needs of survivors

UNIVERSITY REPRODUCTIVE CARE (URC)
UNIVERSITY OF WASHINGTON REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY DIVISION

Providers and Embryologists

Providers

1. Emalee Danforth, NP CNM
2. Rekha Matken, NP
3. Genevieve Neal-Perry, MD PhD
4. Diane Woodford, MD
5. Bo Yu, MD MS

Embryologists

1. Vahida Anchamparuthy, PhD
2. Michael Eagle, BA
3. Andy Dorfmann, PhD

Administrators

1. Rekha Matken (Nurse Manager)
2. Hannah Giese (Academic Practice Administrator)

Program Goals

To provide comprehensive and evidence based care to;

1) Assist with the management of endocrine and reproductive tract disorders that disrupt fertility

2) Assist with the management of endocrine disorders that disrupt baseline reproductive function

3) Assist with the management of reproductive function and family planning in the context of a cancer diagnosis

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SIGNATURE SERVICES

1. Infertility and family planning
2. Oncoreproductive health and oncofertility management
3. Reproductive health and nutrition
4. Reproductive health, menopause and hormones
5. Excellence in imaging studies focused on the evaluation of reproductive tract (i.e. HSG, SIS, pelvic ultrasounds)
6. Endocrine disorders and reproductive dysfunction
7. Recurrent pregnancy loss
8. Same sex and single partner fertility care
9. Donor gametes and reproduction
10. Gamete/embryo cryopreservation
11. Third party fertility management
12. Mullerian anomalies and reproductive management

URC IS DEDICATED TO PROVIDING THE HIGHEST QUALITY OF CARE

- Treatment protocols
  - Minimal stimulation IVF protocols
  - Oocyte and embryo cryopreservation
  - Oncoreproductive healthcare
  - Donor gamete services
    - Oocytes
    - Sperm
  - Preimplantation genetic diagnosis
  - Preimplantation genetic screening

****Oncofertility patient visits are prioritized and treatment is not dependent on IVF batching****

FOCUS ON SERVING THE PATIENT/FAMILY

1. Onsite social services with expertise in reproductive health
2. Onsite financial counselor

****Specially priced oncofertility packages****

3. Onsite male fertility specialist
4. Onsite pharmacy with significantly reduced cost for medications
5. Onsite laboratory facility
6. Onsite storage of gametes and embryos
7. Visits for patients diagnosed with cancer are prioritized
8. Personalized treatment plan
9. Patients have a wide range of services to select from

UNIVERSITY REPRODUCTIVE CENTER CONTACT INFORMATION

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ONLINE RESOURCES

- American Society of Reproductive Medicine: http://www.reproductivefacts.org/
- Fertile Hope/Livestrong Foundation: www.fertilehope.org
- Oncofertility Consortium: https://oncofertility.northwestern.edu/

- COG LTFU Guidelines: http://www.survivorshipguidelines.org/
- Childhood cancer survivor study: https://ccss.stjude.org/
- Coalition against childhood cancer (CAC2): https://cac2.org/

THANK YOU


Surviving cancer is not
The end of a gruesome story
It is the beginning
Of a beautiful one...
WishesMessages.com