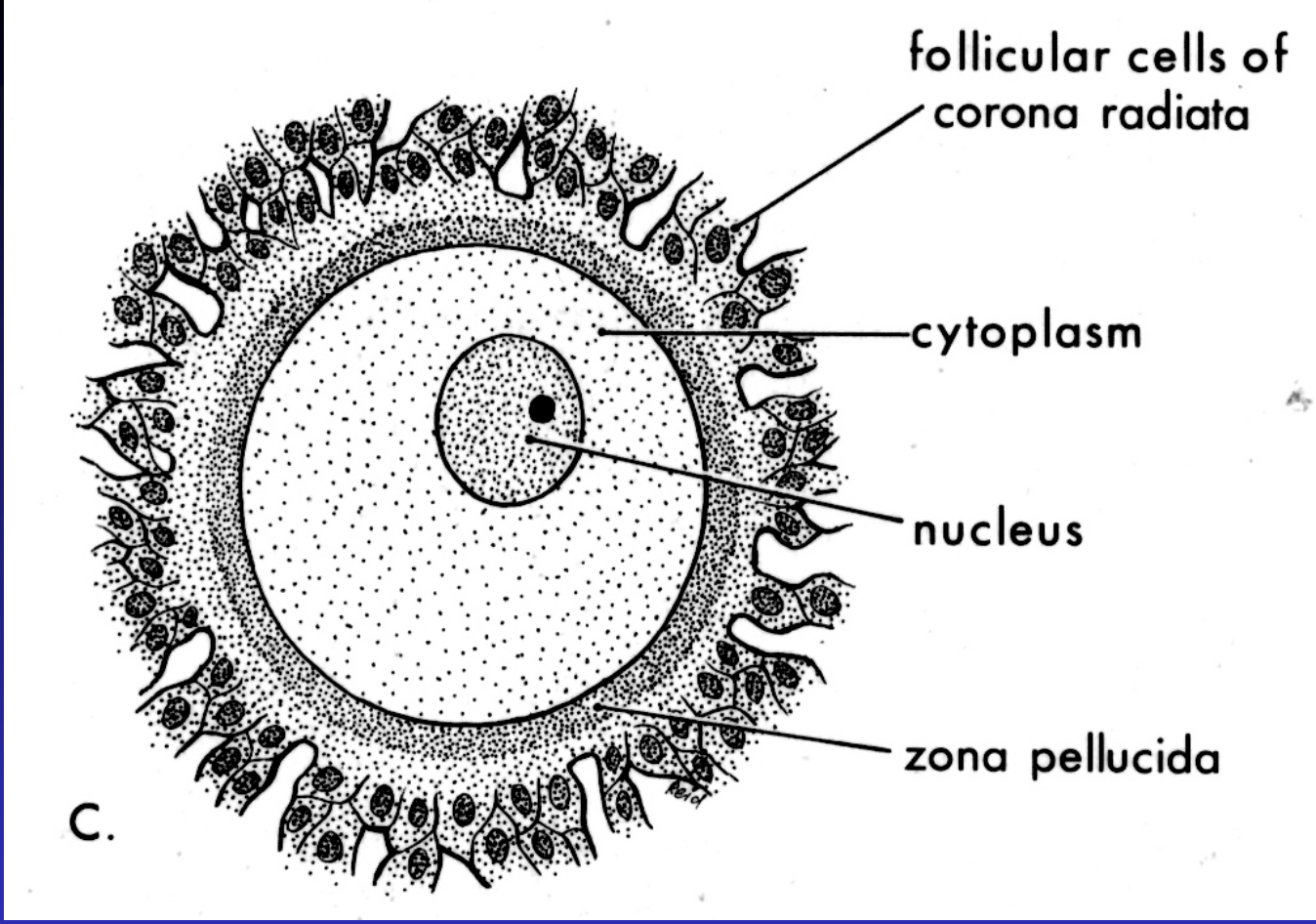
Outline

- Fertilization
  - Gametes
- Germ Cells
  - Meiosis
- Male Reproductive Tract
  - Spermatogenesis
- Female Reproductive Tract
  - Oogenesis
- Menstrual Cycle
  - Hormones

Fertilization

Gametes – Oocyte, Sperm
Acrosomal reaction
Cell Fusion
Cortical reaction
Completion of Meiosis – 2^{nd} polar body released
Pronuclear fusion
Zygote = fertilized egg

Oocyte



Corona radiata, follicle cells
Zona pellucida, acellular – 3 primary glycoproteins (ZP1, 2, 3)
Cortical Granules – vesicles, hydrolytic enzymes, polysaccharides
Female pronucleus

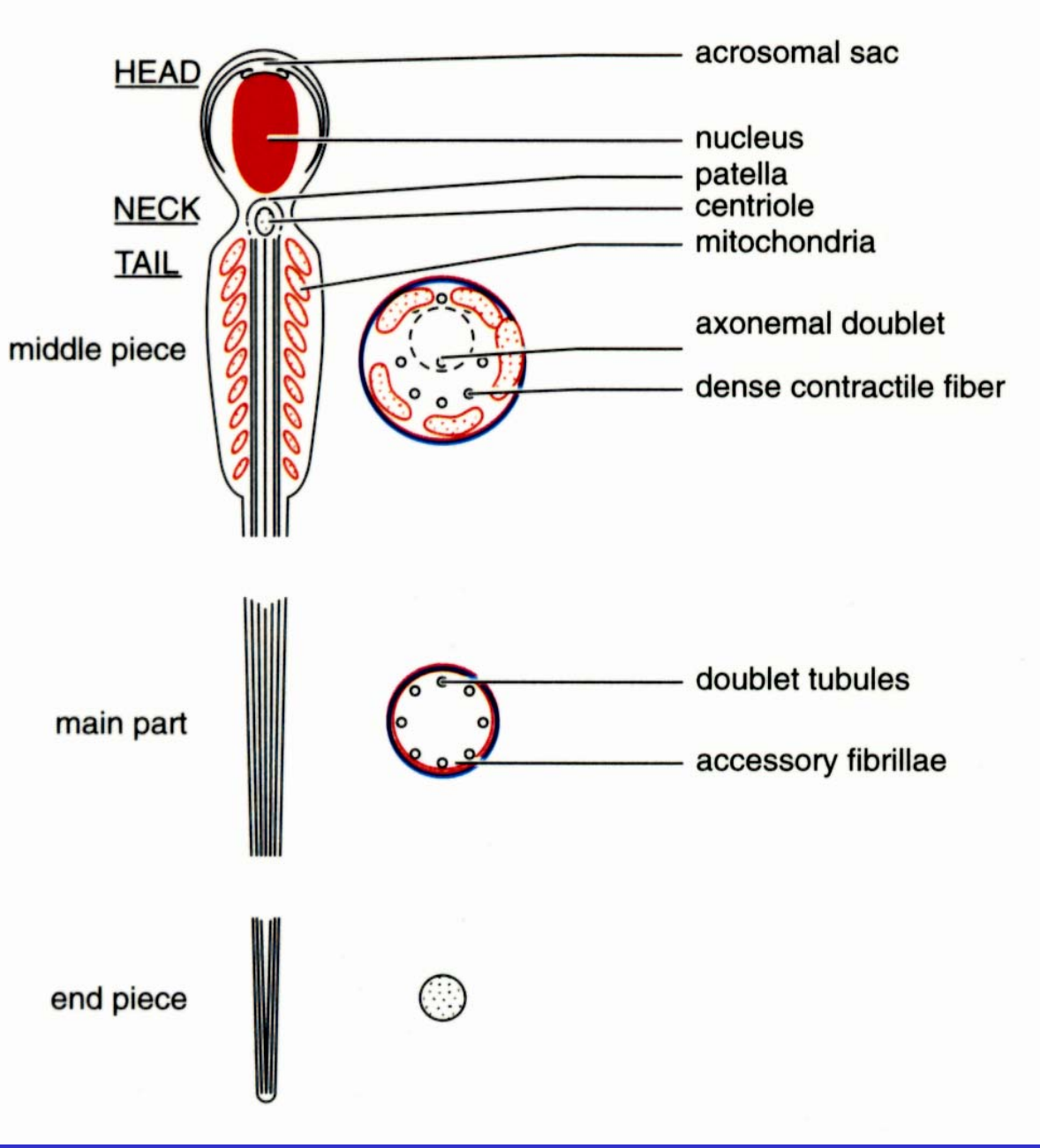
From KL Moore, 1977

Sperm Anatomy

Head (nucleus - meiosis completed)
Acrosome

Neck (junction)

Tail (middle piece; end piece) – mitochondria, microtubule system



From Brookes and Zietman, 1998

Sperm – Egg Fusion

Sperm swimming penetrates the Corona Radiata

Sperm binding to the zona pellucida – ZP3 is critical

Binding induces the Acrosomal Reaction
- Membrane fusion
- Everts Acrosomal sac - releases hydrolytic enzymes (acrosin is a membrane bound serine protease)

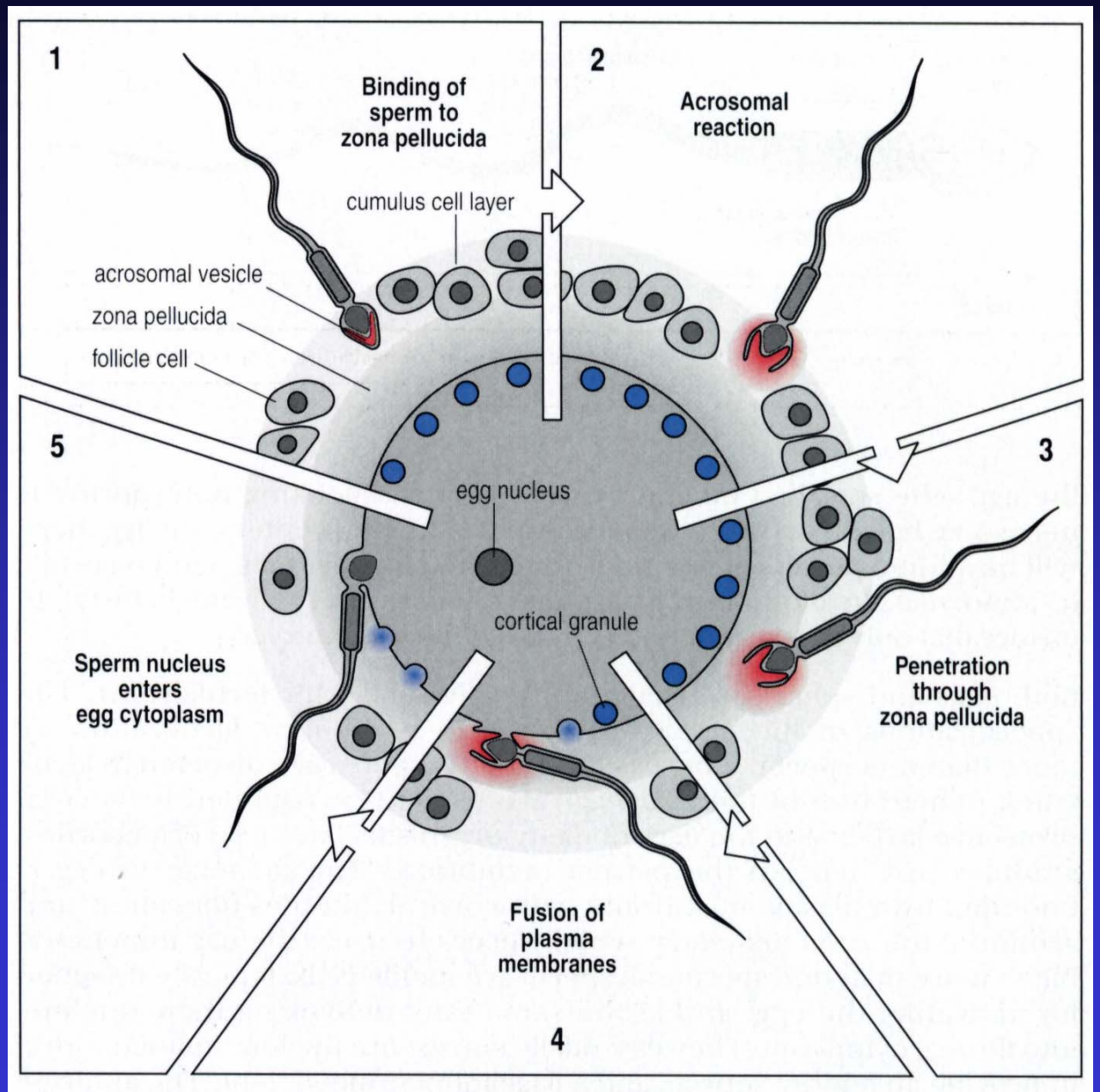
Cell membrane fusion

Prevention of polyspermy
- fast block - membrane depolarization
- slow block - Ca^{++} mediated cortical granule vesicle fusion with membrane; hydrates perivitelline space, zona pellucida elevates

Metabolic activation of egg - Ca^{++} mediated – increase intracellular pH

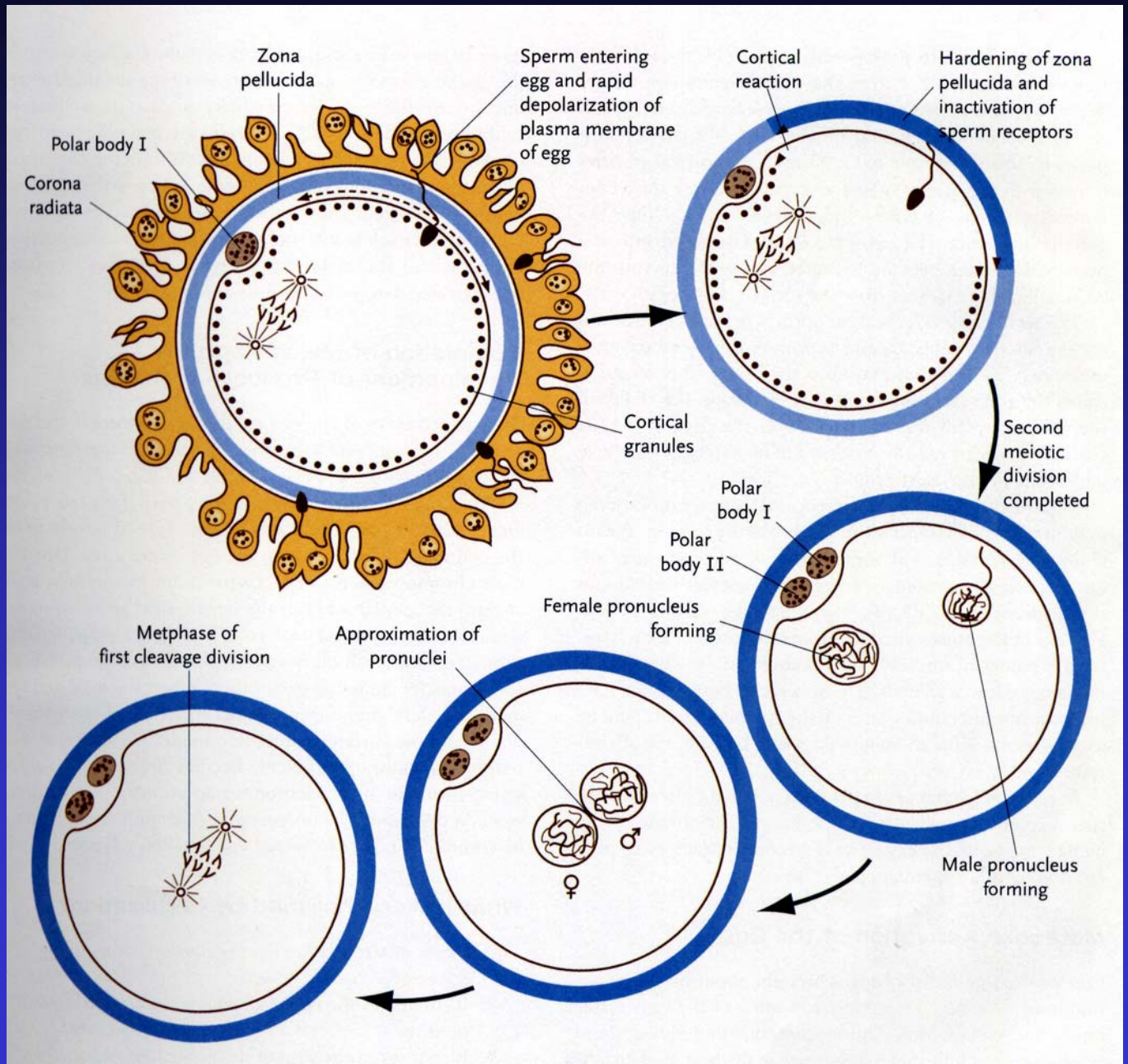
From L Wolpert, 1998

Acrosome reaction

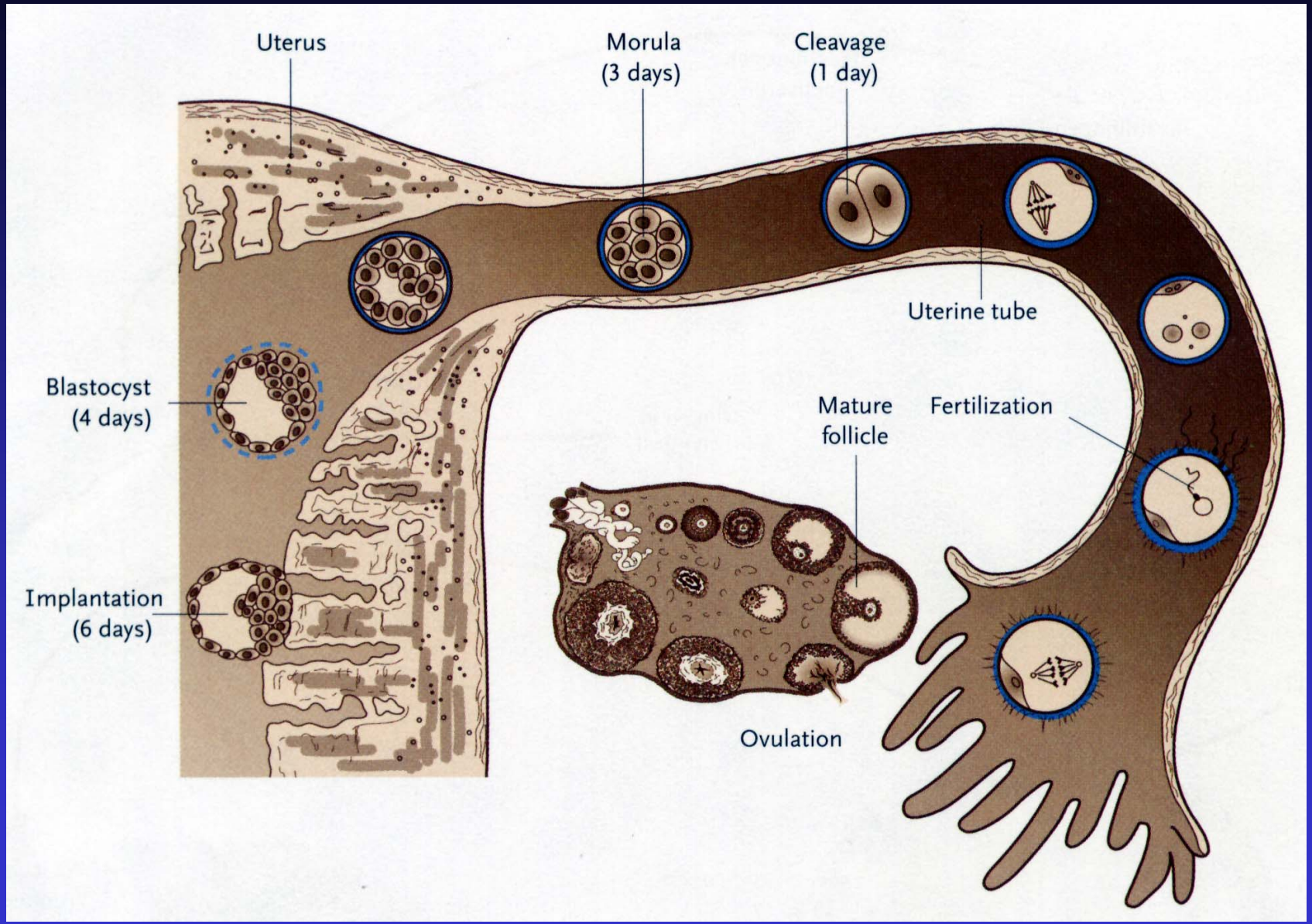


From BM Carlson, 1999

Fertilization



Fertilization occurs in the ampulla of the uterus

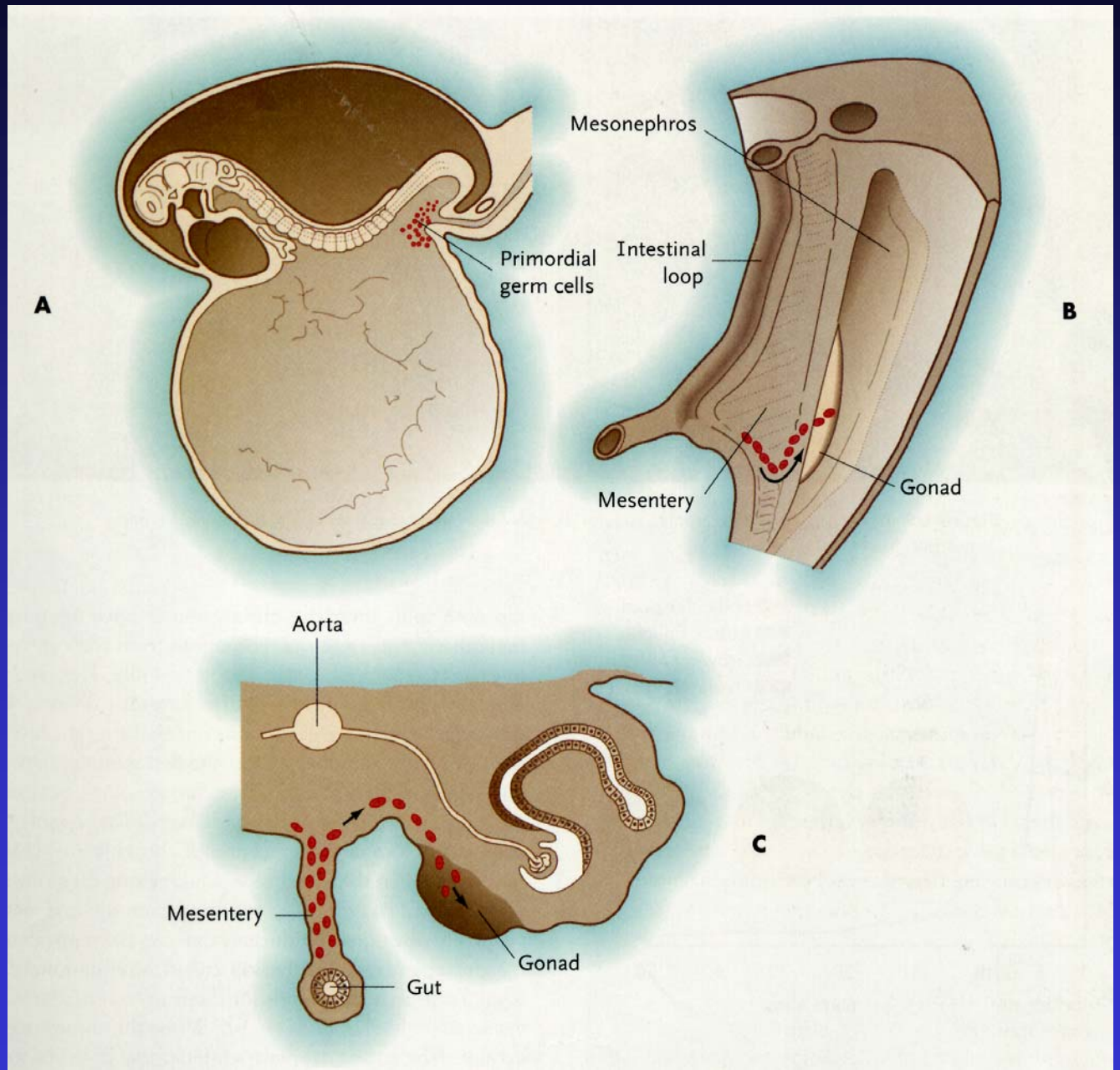


From BM Carlson, 1999

Gametogenesis

- Spermatogenesis, oogenesis
- Germ cells originate from yolk sac of embryo (parent)
- Migration into genital ridge
- Primary sex cords (compact strands of tissue)
- Mitosis
- Female - ovary, sex cords cells → ovarian follicle
- Male - testis, sex cord cells → Sertoli cells of the seminiferous tubules
- Sex cord cells are essential for gametogenesis.

Gametogenesis – Germ Cells



From BM Carlson, 1999

Meiosis

Meiosis occurs during gametogenesis
    1 round of DNA replication → 2 divisions

2n (diploid) → 4n (diploid) → 2n (haploid) → 1n (haploid)

Ploidy = # of each unique chromosome set

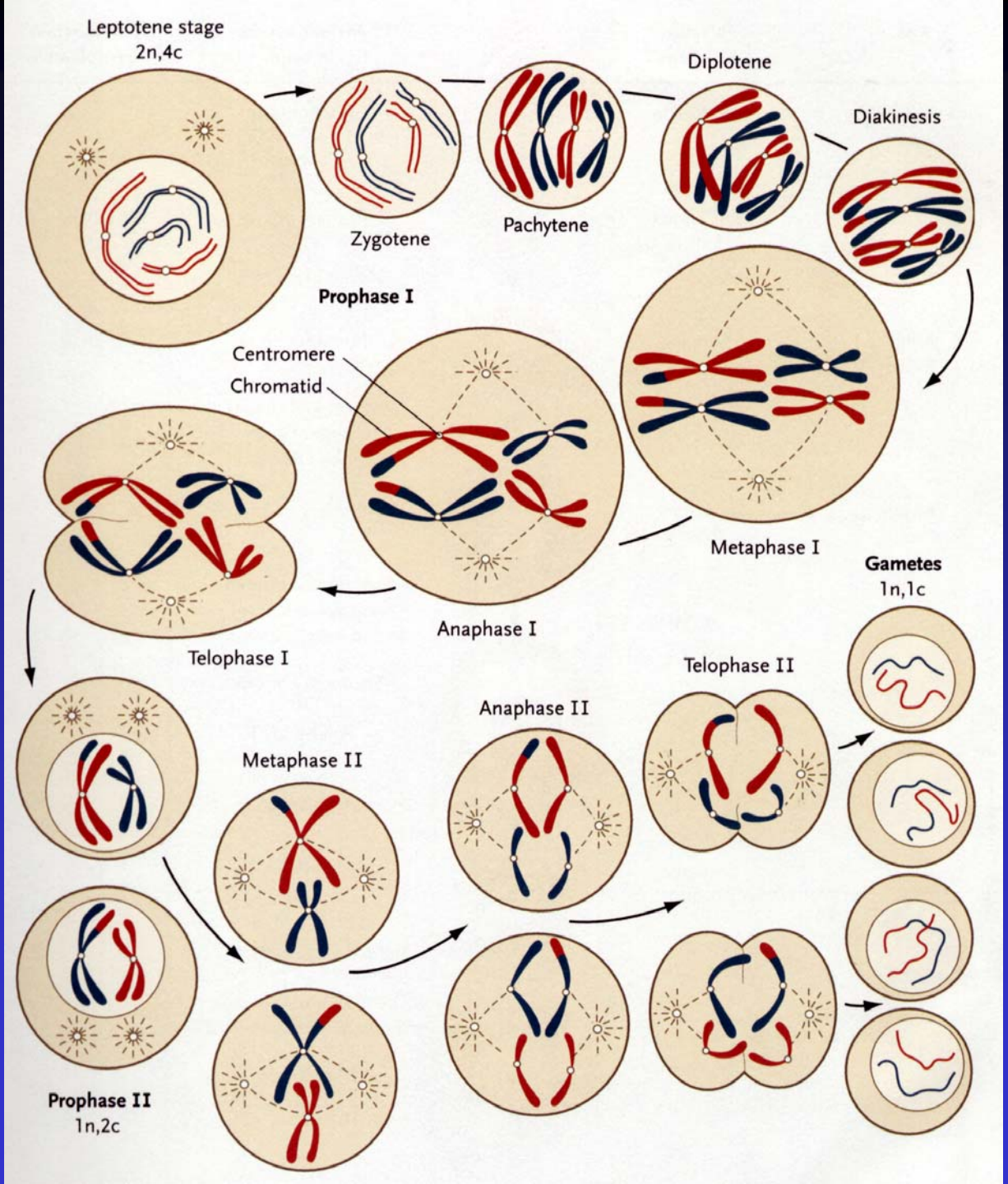
n = number of copies of each unique DNA set

46 Chromosomes - 22 pairs - autosomes, 2 sex chromosomes
    female is XX
    male is XY

Nomenclature: 46,XX or 46,XY

Recombination occurs during meiosis

Meiosis



From BM Carlson, 1999

Anomalies

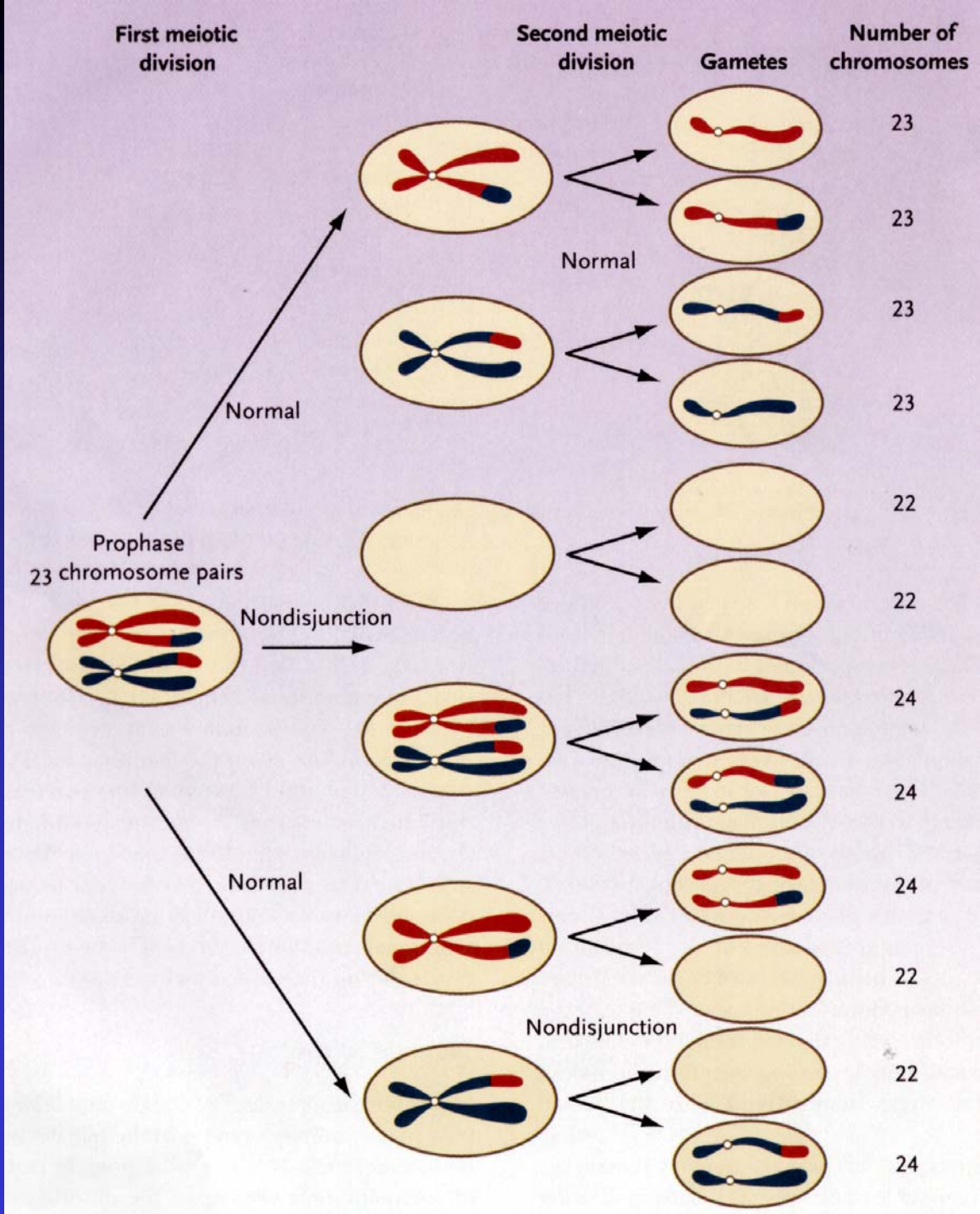
Non-Disjunction - Mis-segregation of chromosomes

Aneuploidy = any deviation from 46,XX or 46,XY

Aneuploidy of entire genome = triploidy, tetraploidy
in humans this is rare and lethal

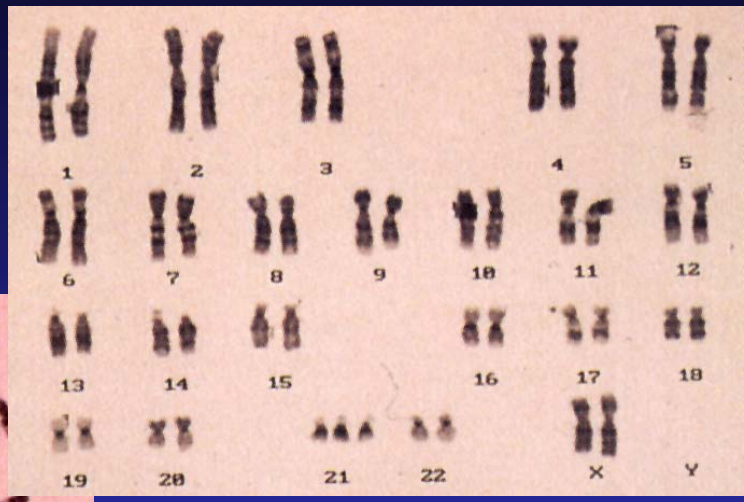
Aneuploidy of single chromosome:
hypodiploid (e.g. monosomy)
hyperdiploid (e.g. trisomy)

Nondisjunction



From BM Carlson, 1999

Karyotype / Trisomy 21

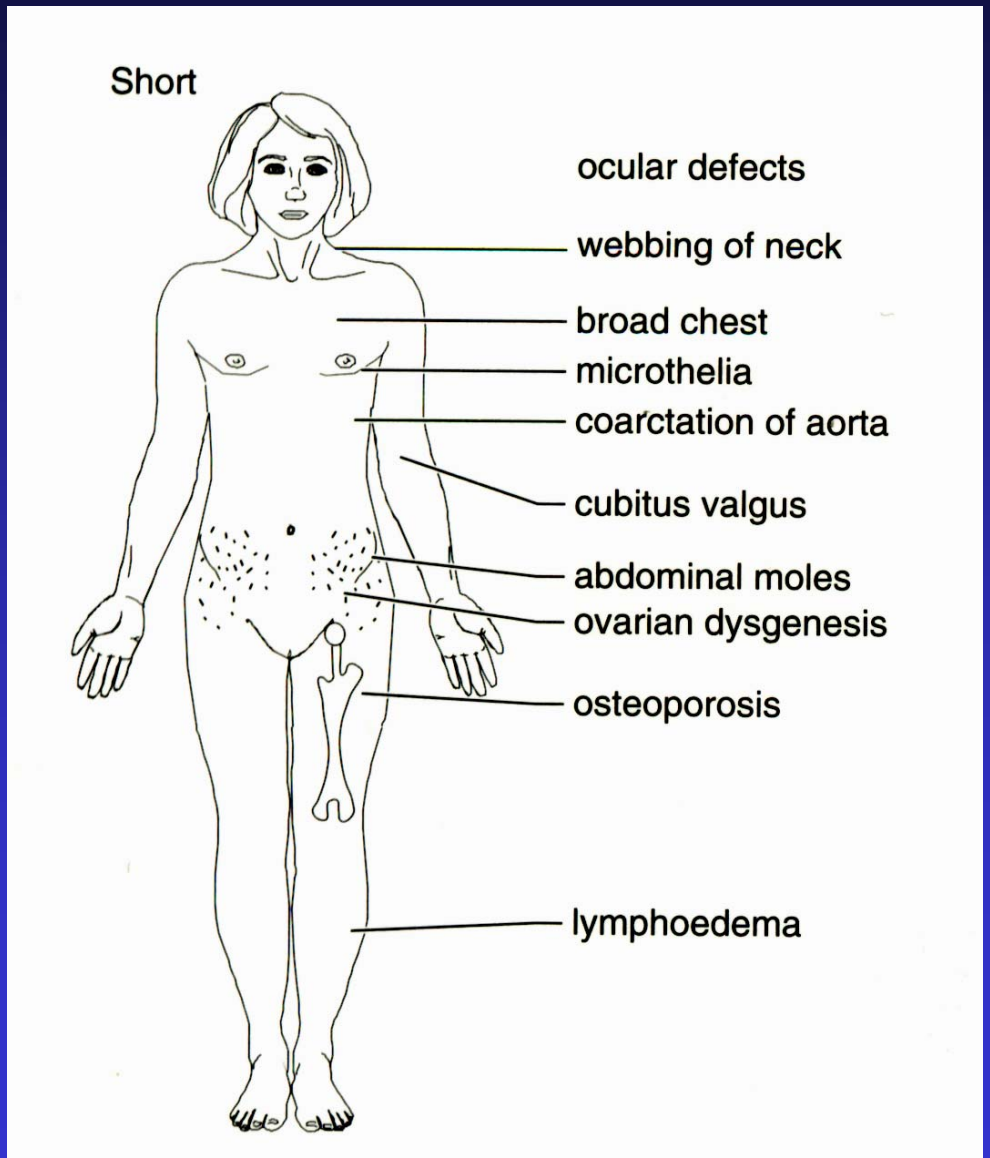


Down Syndrome
80% maternal
Over 300 Characteristics:
Flat facial features
Protruding tongue
Cardiac defects
Mental deficiencies

From Brookes and Zietman, 1998

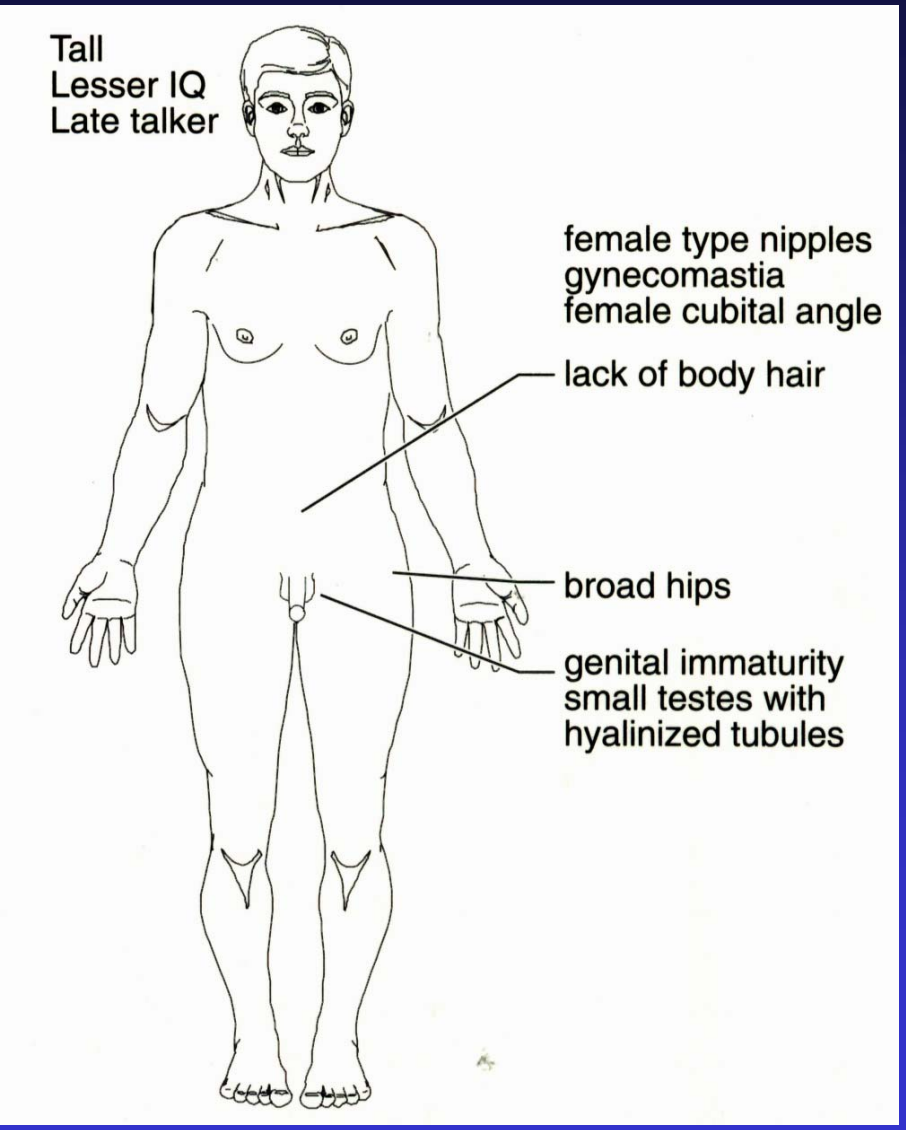
Turner's Syndrome
45,XO

From Brookes and Zietman, 1998



Female
Monosomy
1:5000
75% paternal X is missing
Short stature
Ovarian disgenesis
Broad chest

Klinefelter's Syndrome 47,XXY or 48,XXXY



Male

Sterile

Breasts

Testicular atrophy

From Brookes and Zietman, 1998

Male Reproductive Tract

Testis (seminiferous tubules) – differentiation

Epididymis – biochemical maturation

Ductus deferens (vas deferens)

Ejaculatory duct and inputs:

- seminal vesicle
- prostate gland
- bulbourethral gland

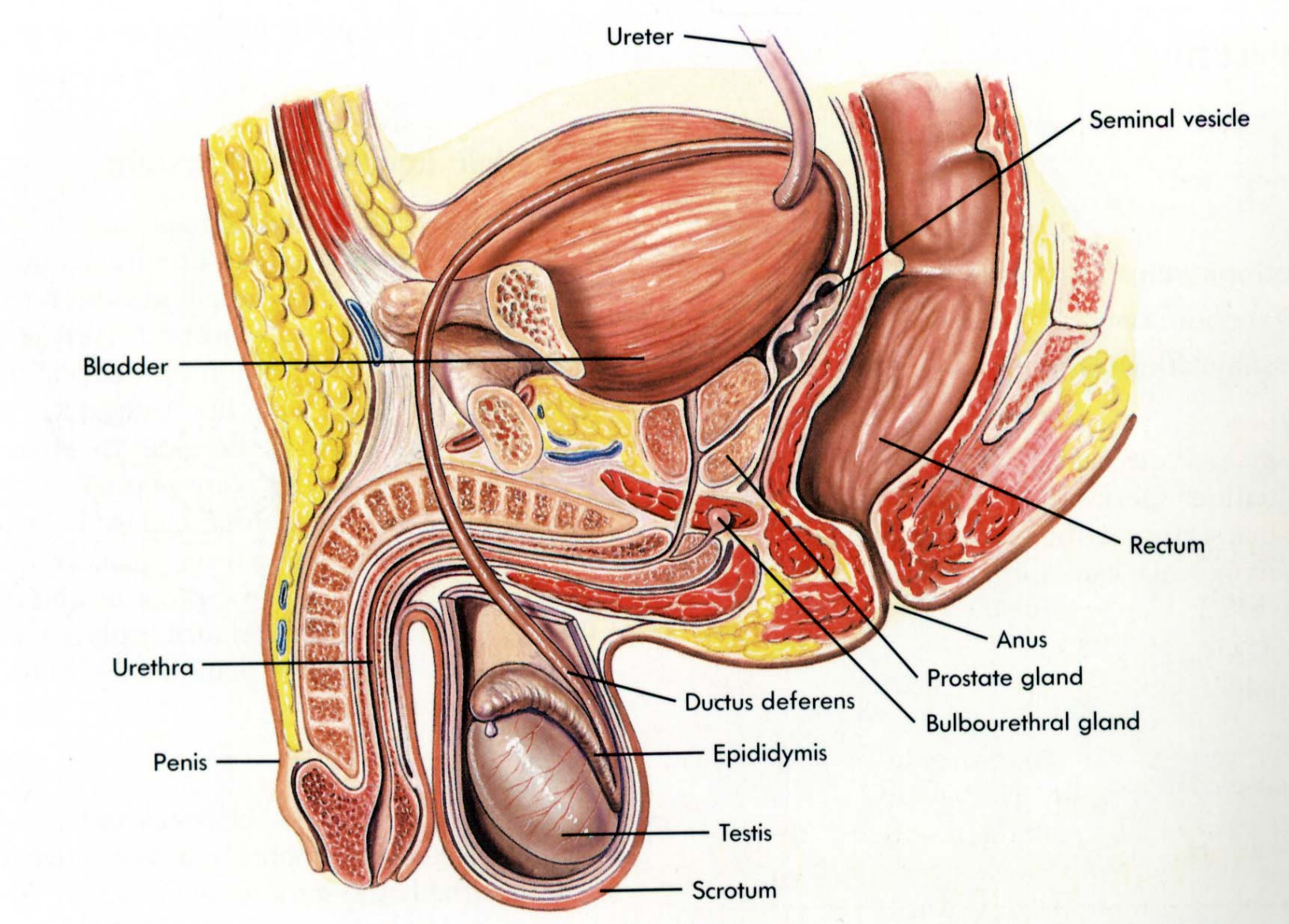
Urethra - out the penis

Ejaculate – 25 to 250 million sperm

Capacitation - final step of maturation

- acrosome changes induced in the female genital tract

Male Reproductive Tract

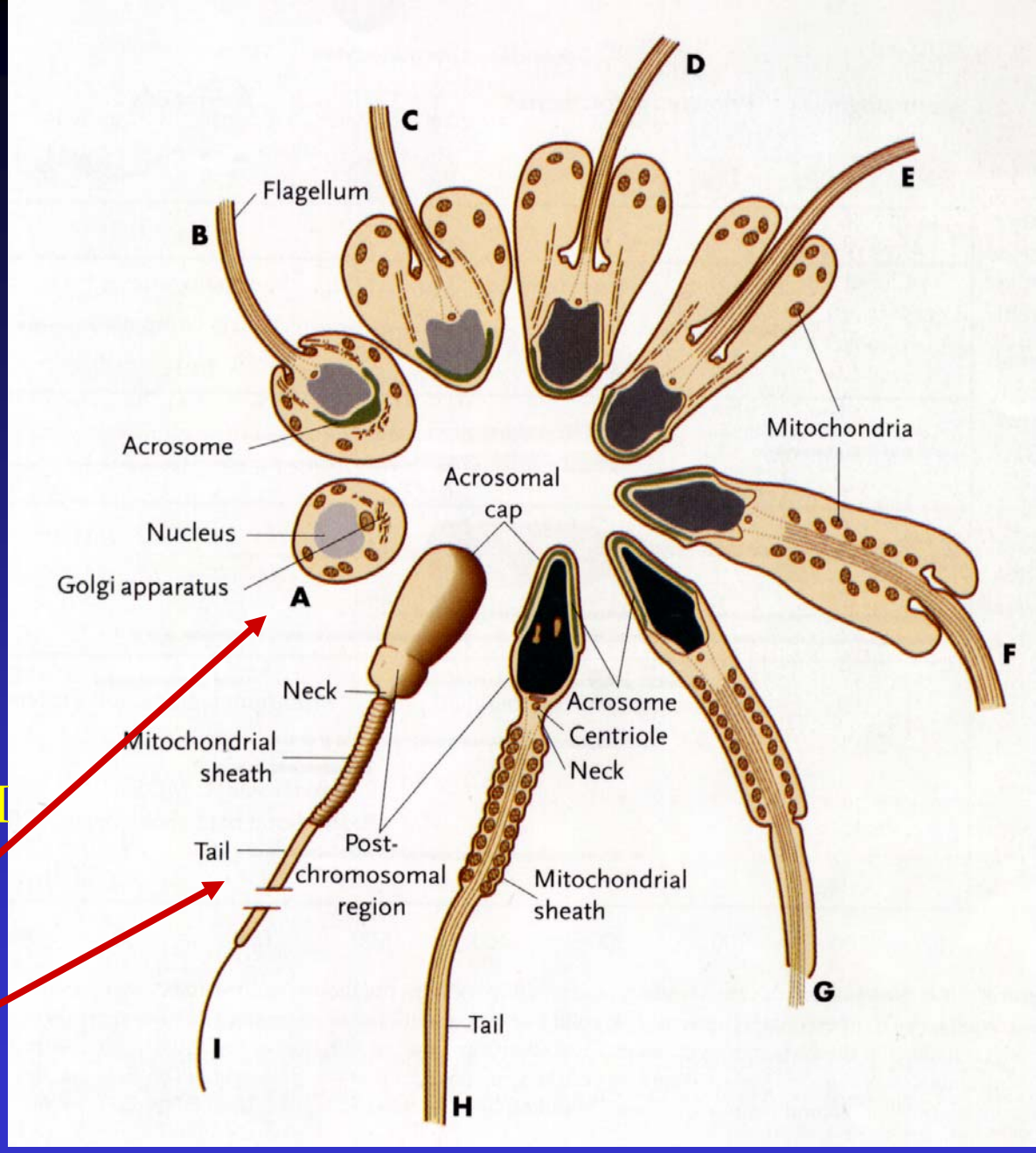


From Seeley, Stephens and Tate, 1989

Spermatogenesis

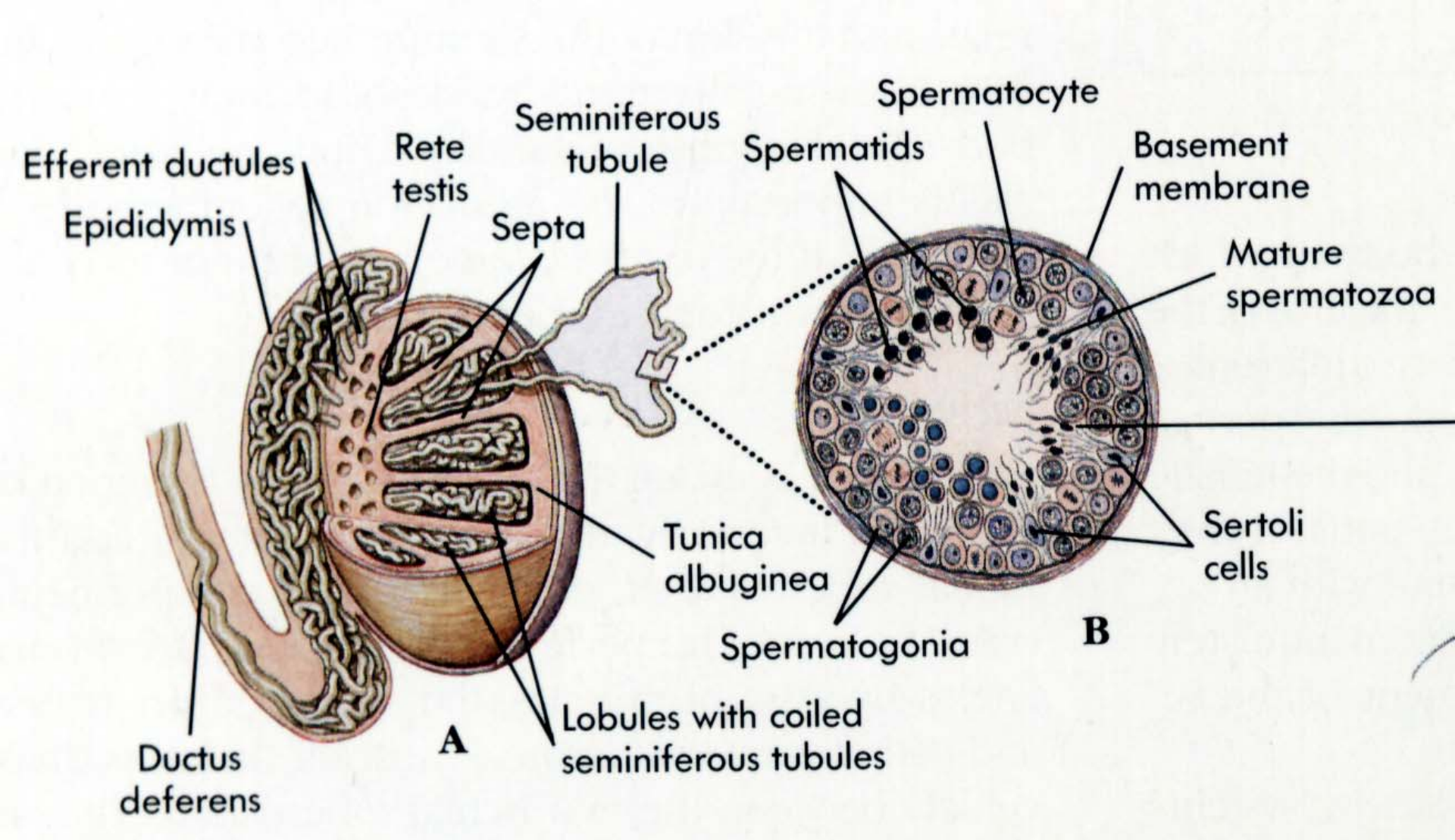
Before puberty:
Spermatogonia multiply
Puberty → Meiosis
Meiosis: equal division
Spermatogonia
    type A – stem cell
    type B – differentiation
I° spermatocyte - meiosis I
II° spermatocyte - meiosis II

Spermiogenesis
    Spermatids
    Spermatozoa



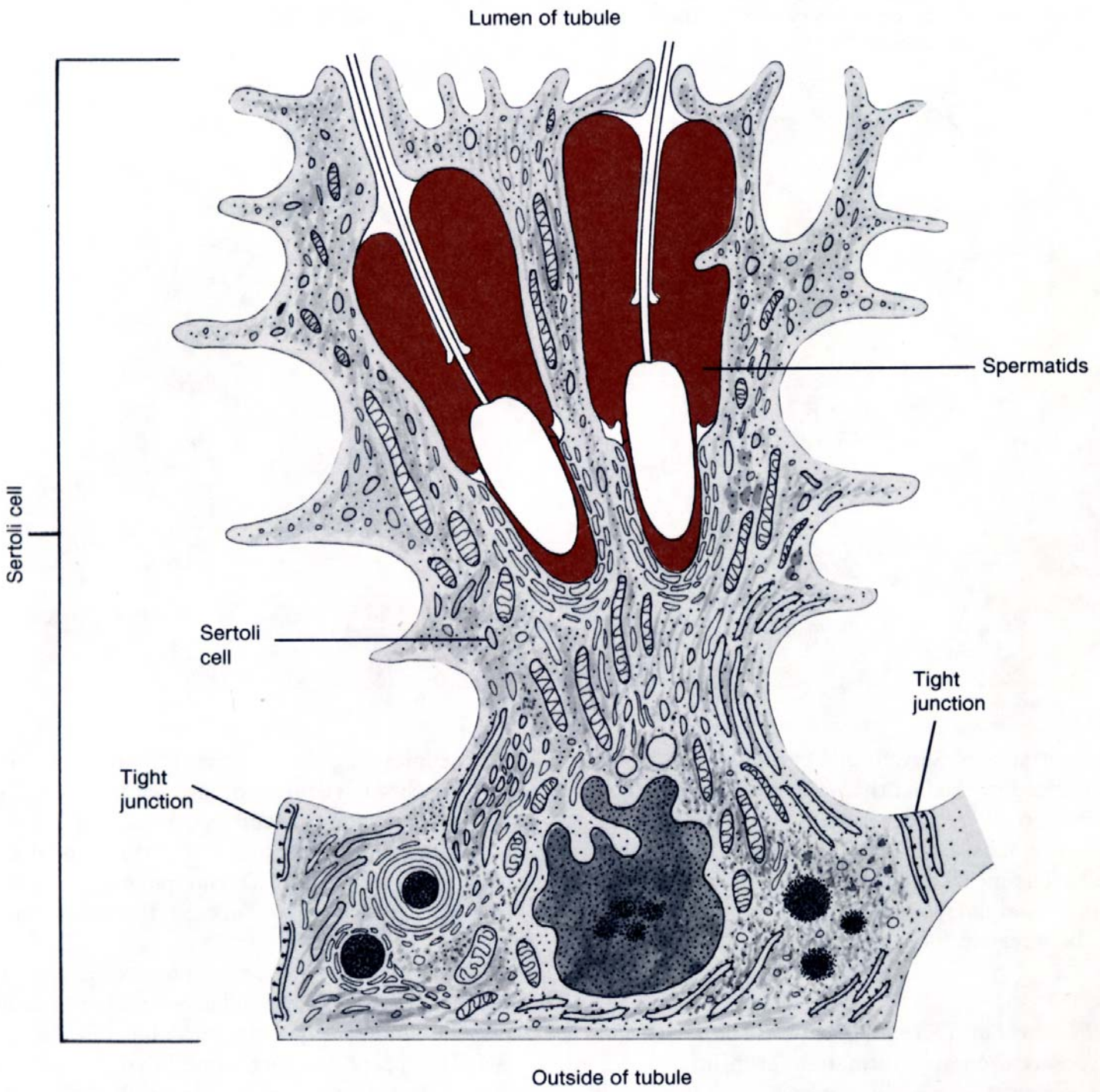
From BM Carlson, 1999

Seminiferous Tubules



From Seeley, Stephens and Tate, 1989

Sertoli Cells



From SI Fox, 1984

Female Reproductive Tract

Ovary - Oogenesis

Uterine (Fallopian) Tube

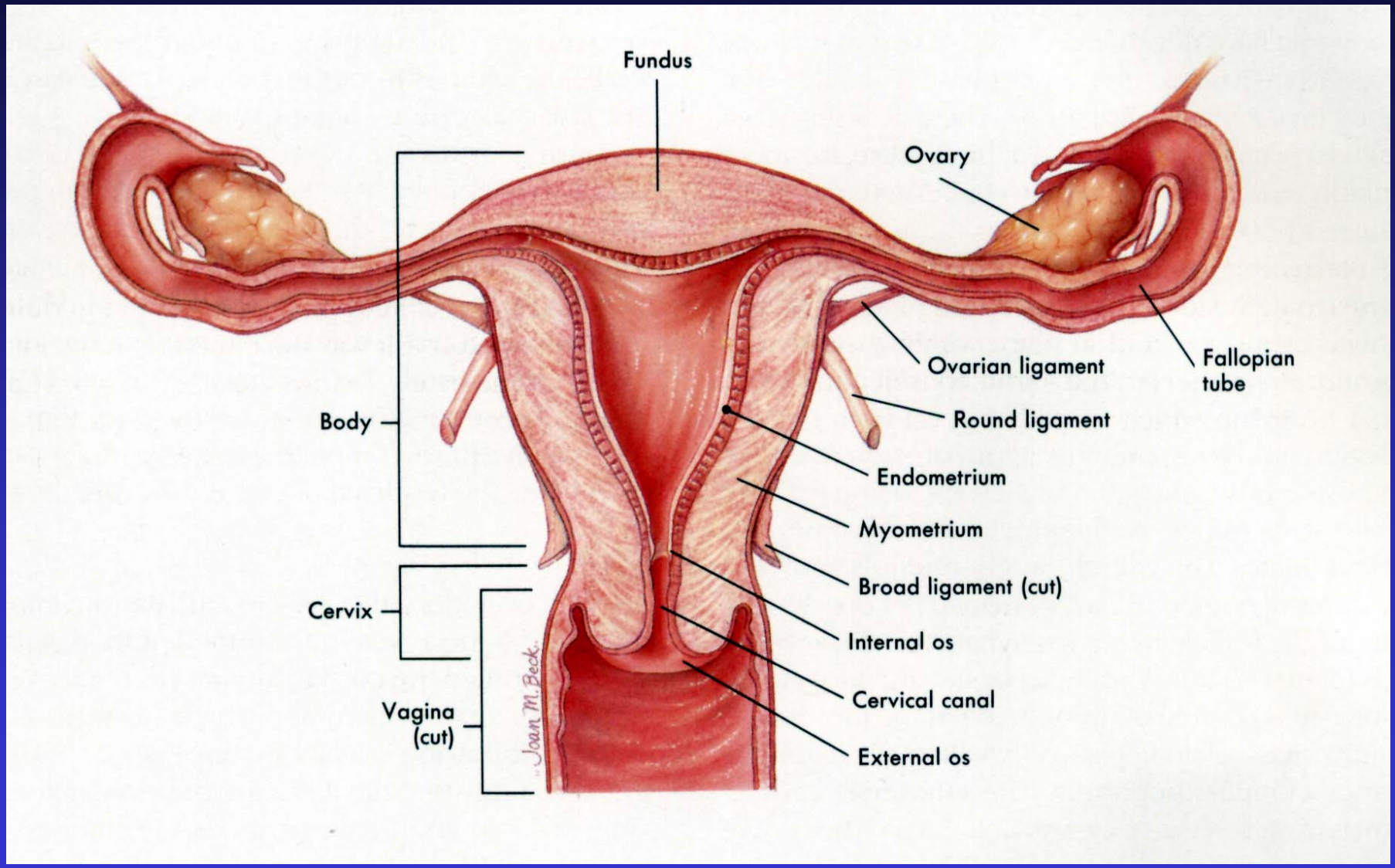
- Fimbriare (finger like projections of Infundibulum)
- Infundibulum
- Ampulla – Fertilization
- Isthmus

Uterus - endometrium, myometrium, perimetrium

Cervix

Vagina

Female Reproductive Tract



From Seeley, Stephens and Tate, 1989

Oogenesis

Oogonia – mitosis to 5th month, 7 million at birth

Atresia of oogonia degeneration: Puberty - 40,000; Ovulated - 400

Meiosis - initiated in newborn

1st Block of Meiosis → 1st prophase – called **Primary oocyte**

Primary oocyte – Large nucleus → **germinal vesicle**

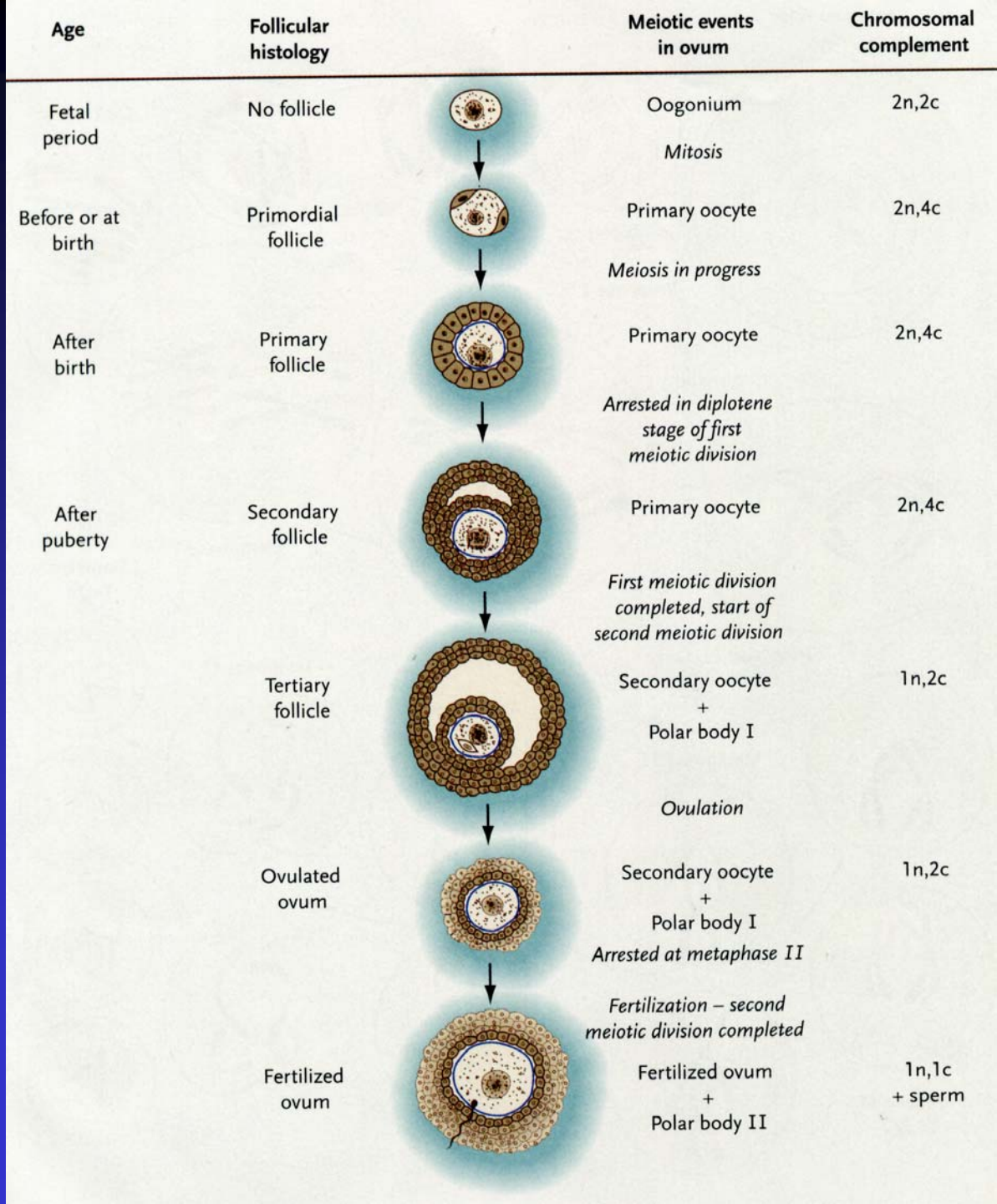
After Puberty - 1st meiosis completed just prior to ovulation

Unequal meiosis → **secondary ooctye** and **1st polar body**

2nd block of meiosis is at metaphase of 2nd division

Fertilization releases 2nd block

Oogenesis



Age	Follicular histology	Meiotic events in ovum	Chromosomal complement
Fetal period	No follicle	Oogonium	2n,2c
		Mitosis	
Before or at birth	Primordial follicle	Primary oocyte	2n,4c
		Meiosis in progress	
After birth	Primary follicle	Primary oocyte	2n,4c
		Arrested in diplotene stage of first meiotic division	
After puberty	Secondary follicle	Primary oocyte	2n,4c
		First meiotic division completed, start of second meiotic division	
	Tertiary follicle	Secondary oocyte + Polar body I	1n,2c
		Ovulation	
	Ovulated ovum	Secondary oocyte + Polar body I	1n,2c
		Arrested at metaphase II	
		Fertilization – second meiotic division completed	
	Fertilized ovum	Fertilized ovum + Polar body II	1n,1c + sperm

From BM Carlson, 1999

Follicle

Follicle cells (from sex cords) surround the Primary oocyte

The Follicle is the oocyte plus follicle cells

Primordial follicle **- follicle cells** partially surround oocyte

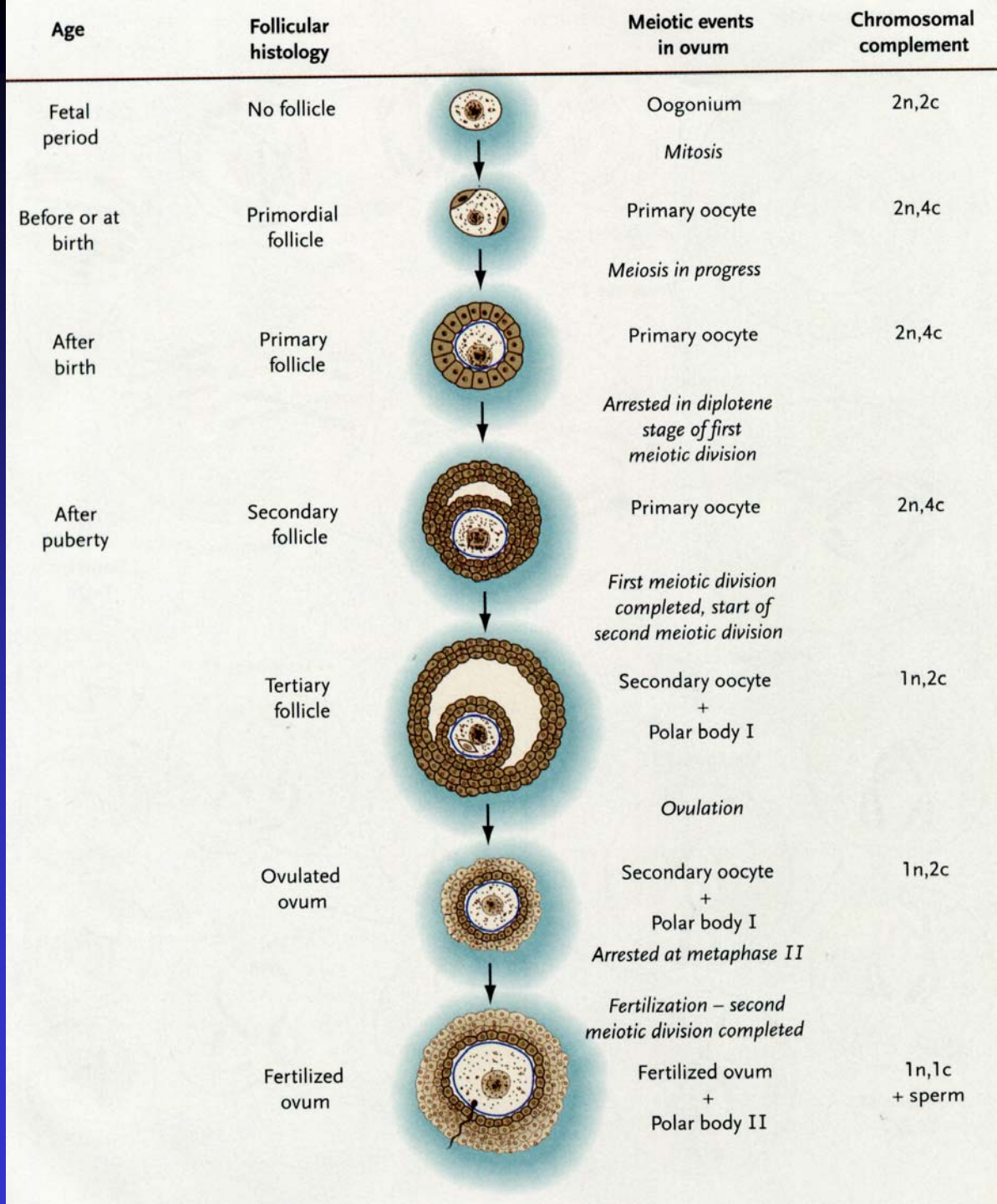
Primary follicle – follicle cells form a complete layer
Follicle cells form gap junctions with the oocyte and produce **Meiotic inhibitory factor**
Follicle cells are called granulosa cells

Granulosa cell layer enclosed by the membrana granulosa, a basement membrane that acts as a barrier to capillaries

Zona pellucida secreted by oocyte and follicle cells – with microvillar connections between the two.

Ovary cells form 2 more layers – theca interna, theca externa

Oogenesis



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		Fertilization – second meiotic division completed	
	Fertilized ovum	Fertilized ovum + Polar body II	1n,1c + sperm

From BM Carlson, 1999

Follicle Development

Secondary follicle – formation of the antrum (cavity)
fluid filled, liquor folliculi
Hormone production, androgens and estrogen

Tertiary or Graffian follicle – 12 hours prior to ovulation. cumulus oophorus = mound of cells that house the secondary oocyte

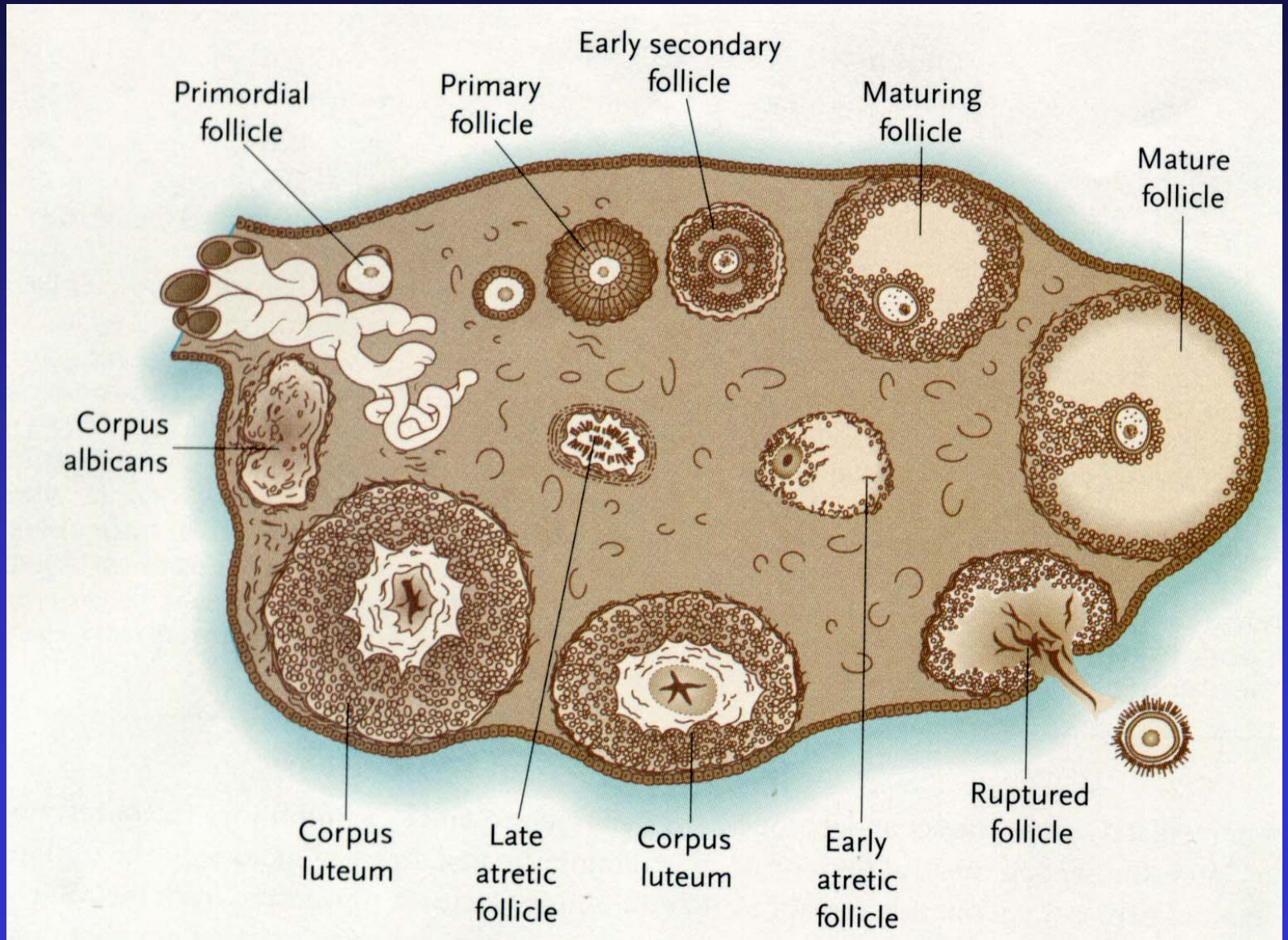
Oogenesis controlled by cycles (Menstrual) of hormone release:
Hypothalamus → **gonadotropin releasing hormone** (GnRH)
Anterior pituitary → **Gonadotropins**, includes **luteinizing hormone** (LH) and **Follicle stimulating hormone** (FSH)

Ovulation - tertiary follicle protrudes like a blister on the surface of the ovary – then bursts in response to LH and FSH

Corpus Luteum – Follicle after ovulation – hormone producing Progessterone

From BM Carlson, 1999

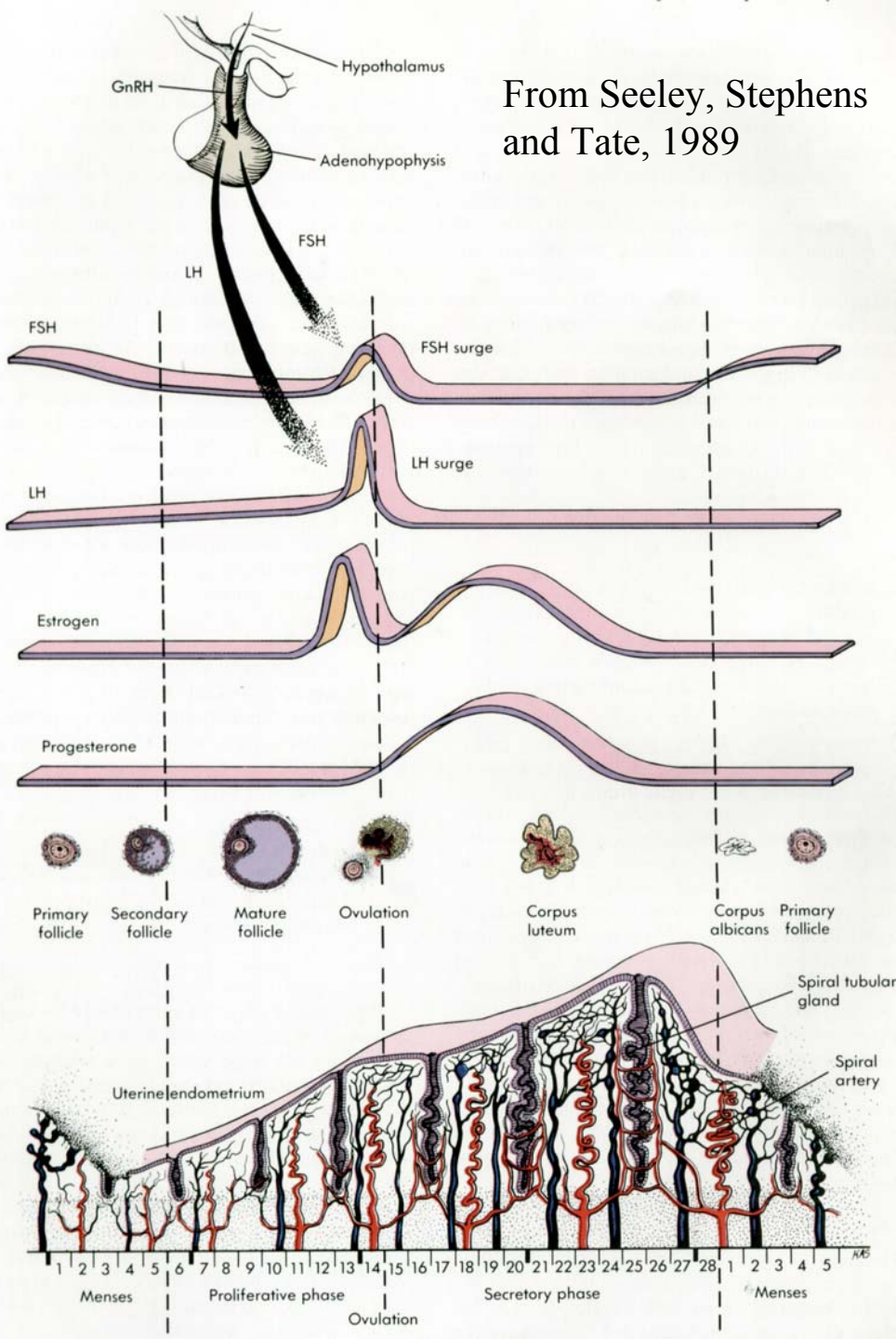
Follicle Development



Hormonal Control of Menstrual Cycle

From SS Mader, 1992

From Seeley, Stephens and Tate, 1989



Menstrual Cycle
Menstrual Phase

Day 1-5 - Menstrual Phase

Progesterone-dependent (corpus luteum)

Uterus: Low progesterone – constriction of arteries veins

Sloughing of the endometrium

Ovaries: Folliculogenesis - 5-12 primordial follicles initiated

Primary follicles - squamous to cuboidal cell layer

Secretion of zona pellucida

Day 5-14 - Proliferative Phase

Day 13-14 - Ovulation

Day 14-28 - Secretory Phase

Menstrual Cycle
Proliferative Phase

Day 5-14 - Proliferative Phase

- Estrogen-dependent (produced by granulosa cells)
- Uterus: Endometrial stroma thickens (2-3-fold)
  - Uterine glands elongate
  - Spiral arteries grow
  - Epithelial cells become ciliated
- Ovaries: Growing follicles - cell proliferation, multilayered
  - One follicle dominates – antrum formation, fluid uptake
  - Surrounding cells form theca interna and theca externa
  - Mature graafian follicle
  - Membrana granulosa - follicle cells lining antrum

Day 13-14 - Ovulation

Day 14-28 - Secretory Phase

Menstrual Cycle
Ovulation

Day 13-14 – Ovulation - Estrogen surge induces LH and FSH surge

- Uterus: Proliferative phase continues
- Ovaries: Oocyte resumes meiosis
  - Germinal vesicle breakdown
  - Metaphase in 20 hours
  - Unequal division – II^o oocyte and 1st polar body
  - 2^{nd} meiotic block
  - Cumulus oophorus - detaches and released into antrum
- Ovulation: Day 14, follicle becomes vascularized
  - Bulges from the surface of ovary - stigma - small protrusion
  - Follicle wall thinning → cumulus-oocyte complex released
  - Ovulated ovum collected by the oviduct

Day 14-28 - Secretory Phase

Menstrual Cycle
Secretory Phase

Day 1-5 - Menstrual Phase

Day 5-14 - Proliferative Phase

Day 13-14 - Ovulation

Day 14-28 - Secretory Phase

- Progesterone-dependent (corpus luteum)
- Uterus: secretory phase - increase vasulature
  - Spiral arteries and spiral veins
  - Formation of glandular structures
  - Uterine epithelium becomes secretory
- Ovaries: Corpus luteum forms from ruptured follicle
  - Produces Progesteron
  - Corpus luteum degenerates without implantation

Fertilization/Implantation

Day 15 – Fertilization

Unfertilized oocytes die **12-24 hours** after ovulation

Fertilization usually occurs in ampulla

Day 20 - Implantation

Implantation of the fertilized embryo occurs in the uterus

Uterine cells (trophoblast) produce Human Chorionic Gonadotrophin (hCG)

hCG – maintains the corpus luteum (i.e. progesterone production)

Hormonal Control of Menstrual Cycle

From SS Mader, 1992

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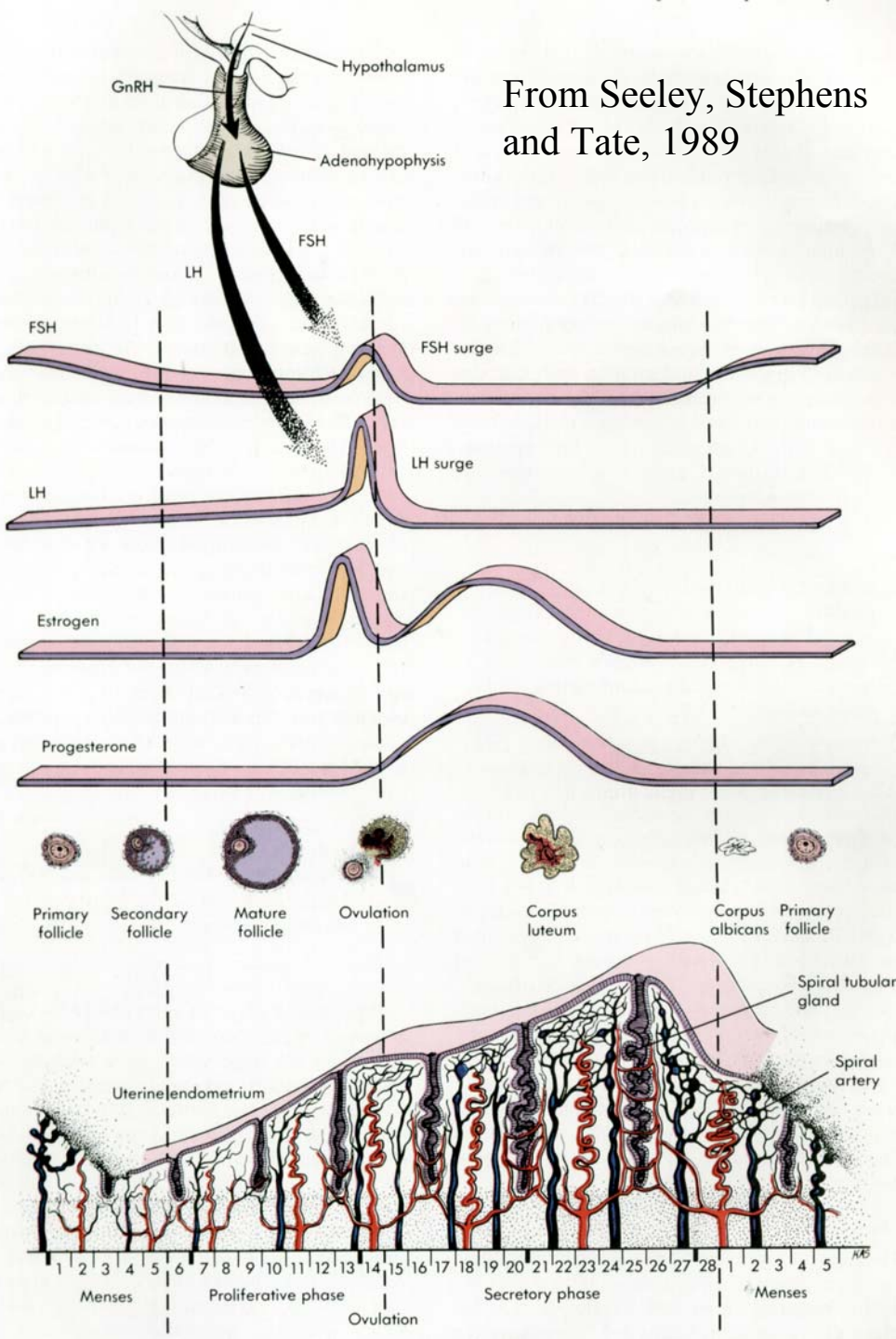


Estrogen

17β–estradiol, Steroid, from testosterone

Testosterone produced by thecal cells of the follicle – LH induced

Testosterone passes to granulosa cell of the follicle

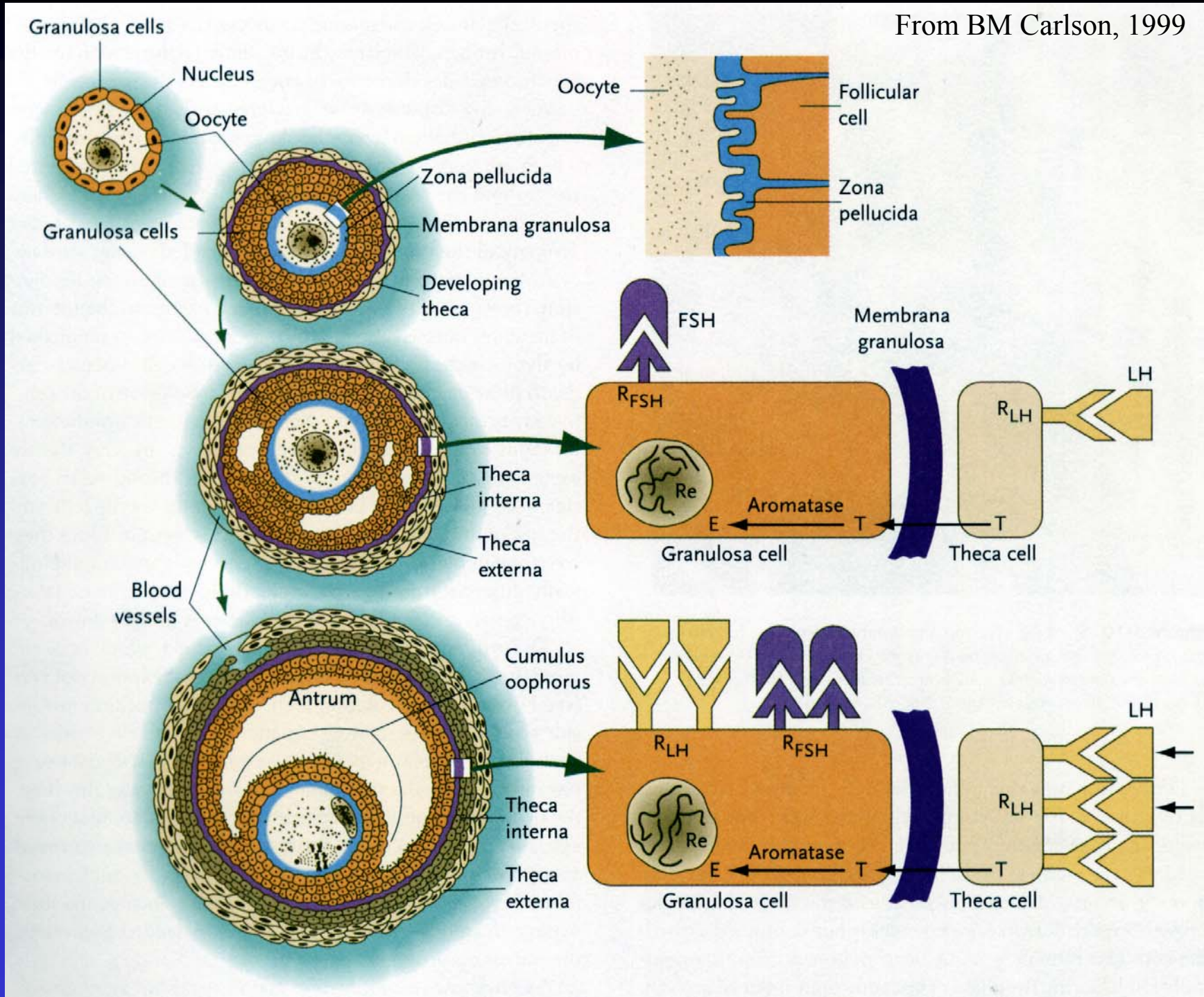
Granulosa cells express aromatase (enzyme) – FSH induced

Aromatase catalyzed reaction testosterone to 17β–estradiol

17β–estradiol released into the circulation, activates nuclear estrogen receptor – ligand-dependent transcription factor

Multiple Influences: Hypothalamus – GnRH (gonadotrophin releasing hormone – LH surge; Uterus - Proliferative phase; Breasts; Body fat; Bone growth

From BM Carlson, 1999



Progesterone

Steroid produced by granulosa lutein cells after ovulation – corpus luteum

Progesterone secretion by corpus luteum for 10 days – without implantation – it undergoes luteolysis – progesterone levels decrease – induces menstrual flow

Maintenance of Progesterone secretion by human chorionic gonadotropin (HCG) produced by the developing placenta

During pregnancy thecal lutein cells also produce progesterone

Progesterone released into the circulation, activates nuclear progesterone receptor – ligand-dependent transcription factor

FSH- Follicle Stimulating Hormone

Glycoprotein, 35 Kd, Released by Anterior Pituitary

(+) Hypothalamus, GnRH, gonadotropin releasing hormone

(-) Ovaries (granulosa cells), Inhibin (32 Kd), cirulation

Females: → production of estrogen by follicle cells

Menstrual Cycle:

days 5-14 – proliferative phase, estrogen: follicle development
day 14 – ovulation – FSH surge

Males: → production of Androgen binding protein by Sertoli cells

LH – Luteinizing Hormone

Glycoprotein, 28 Kd, Released by Anterior Pituitary

(+) Hypothalamus, GnRH, gonadotropin releasing hormone

(-) Ovaries (granulosa cells), Inhibin (32 Kd), cirulation

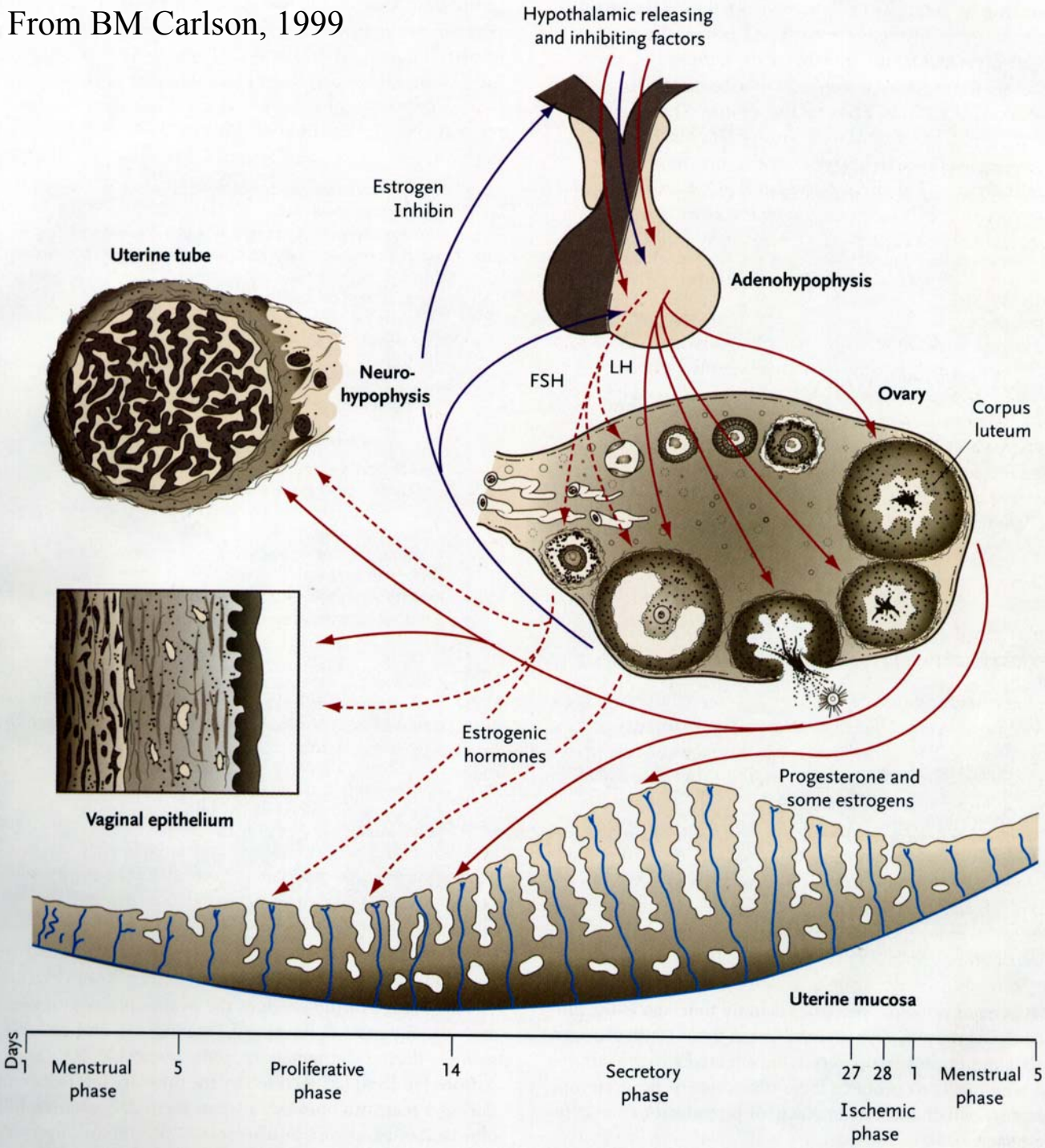
Females: → production of progesterone by follicle cells

Menstrual Cycle:

- day 14 – LH surge induces ovulation and transforms the graafian follicle into the corpus luteum
- days 14-28 – Secretory phase, LH required for progesterone production

Males: → Induces enzymes required for testosterone synthesis in Leydig cells

From BM Carlson, 1999



Hormones Influence Spermatogenesis

Hypothalamus

▼

GnRH

▼

Anterior Pituitary

▼

LH

▼

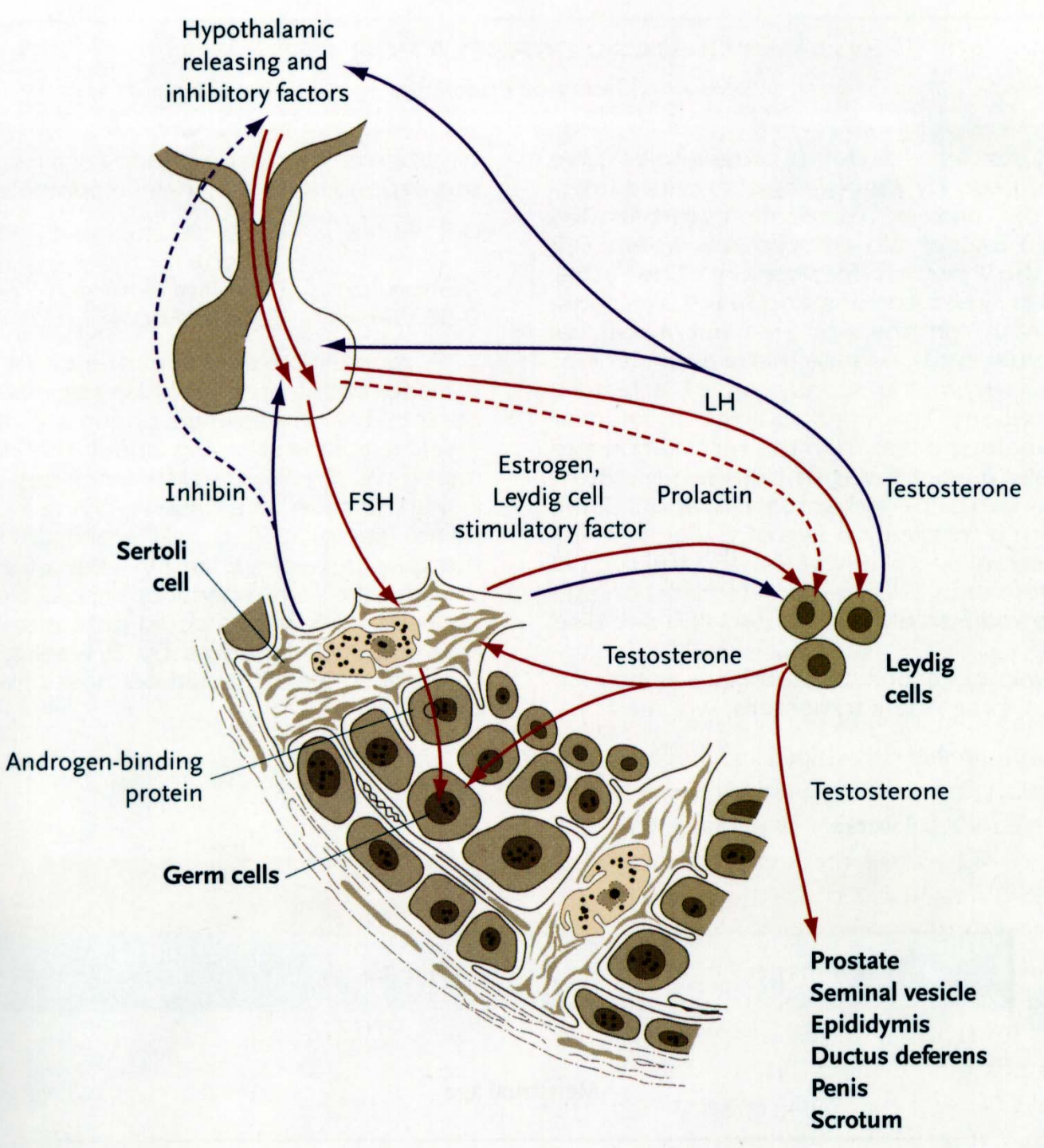
Leydig Cells

▼

Testosterone

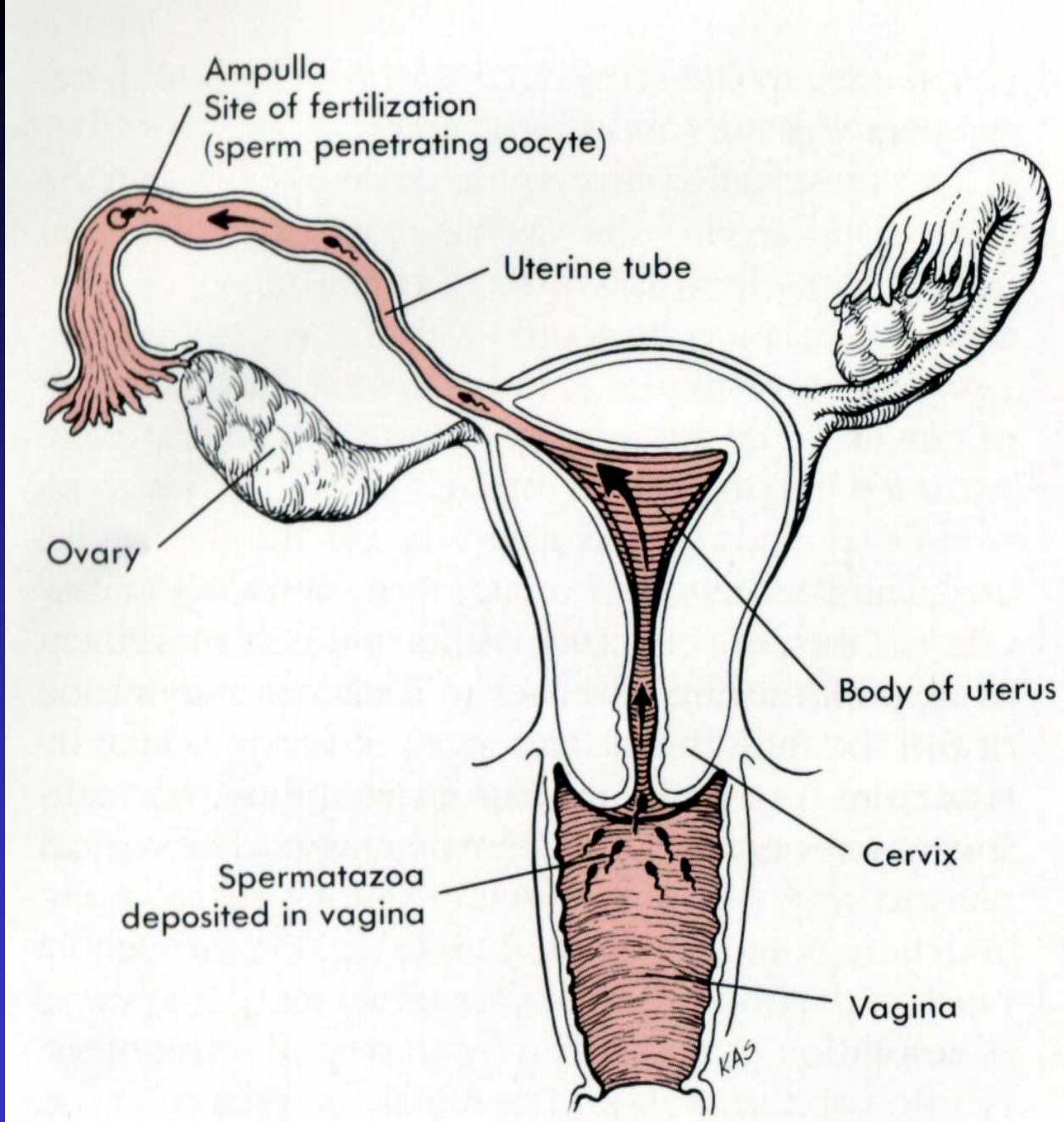
▼

Serotoli Cells



From BM Carlson, 1999

Sperm Transport



From Seeley, Stephens and Tate, 1989

Birth Control Methods

Rhythm

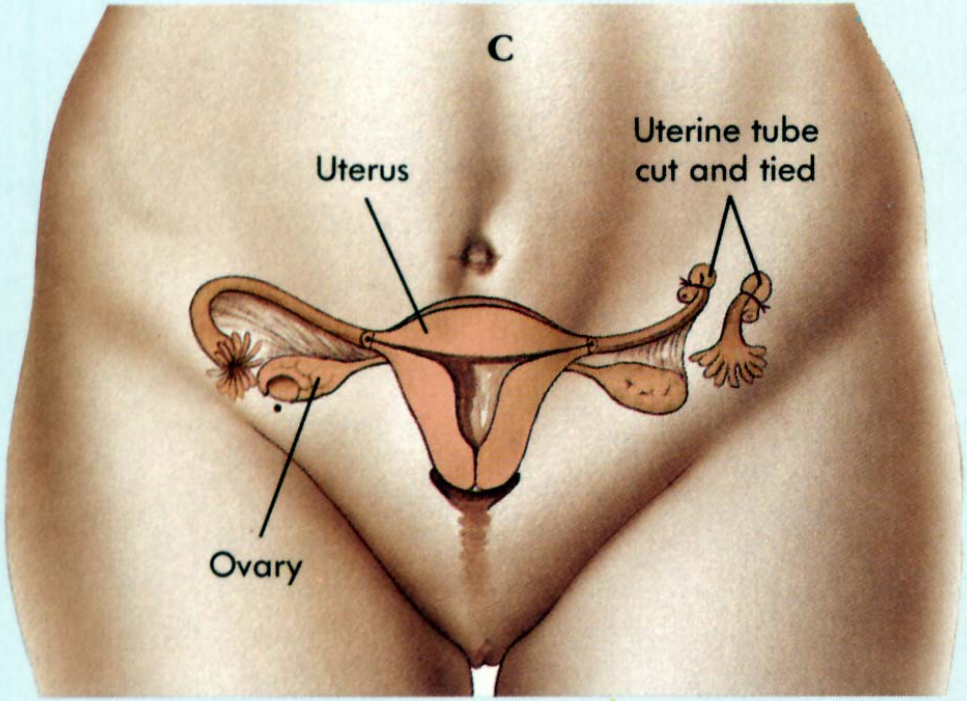
Barriers – condoms, diaphragm, cervical cap

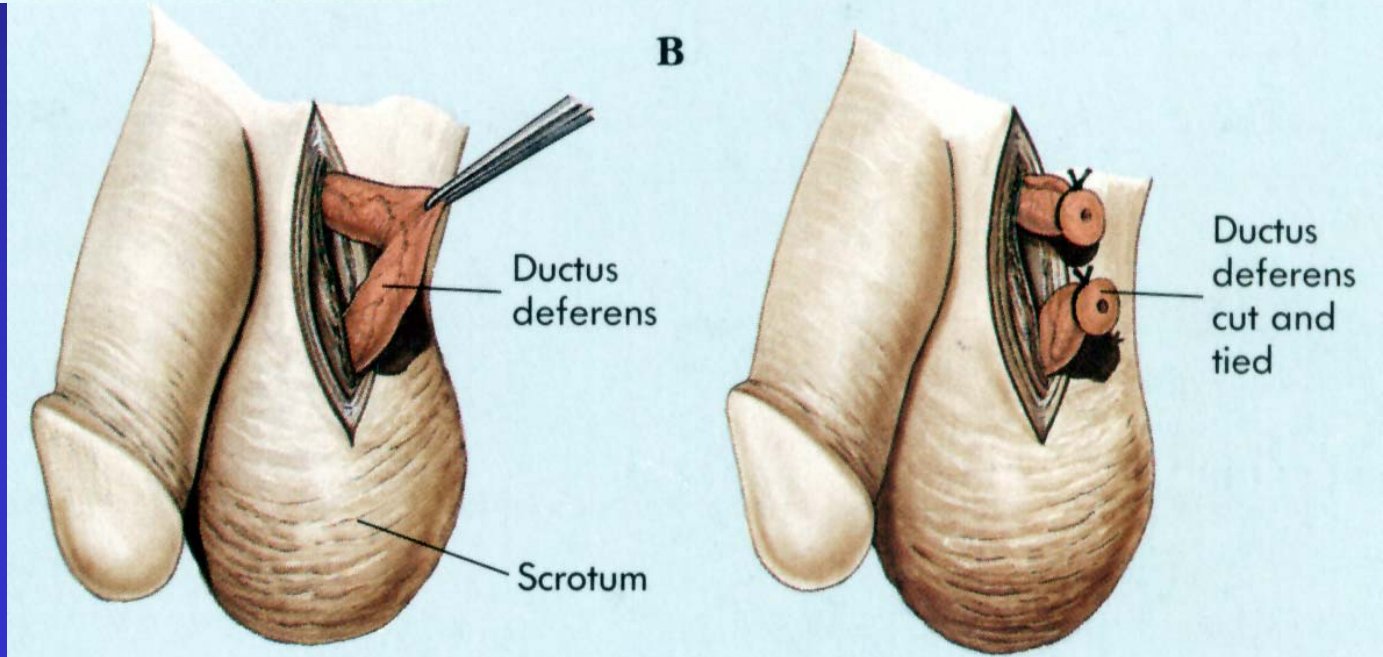
Pill (estrogen/progestin) – inhibits ovulation

IUD (intrauterine device) – mechanical interference

RU-486 – progesterone antagonist – induces menses

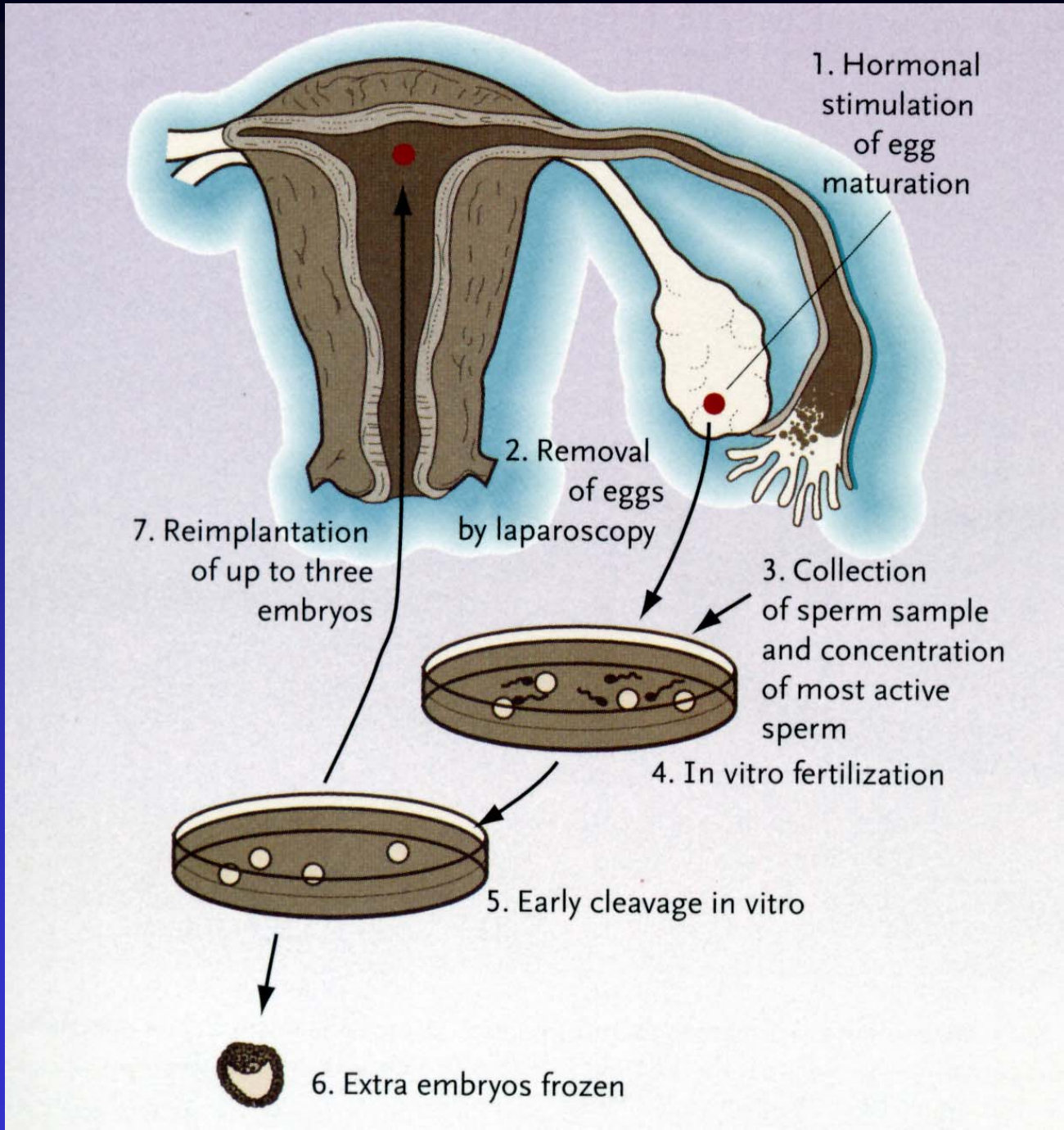
Sterilization – vasectomy / fallopian tube ligation





From Seeley, Stephens and Tate, 1989

In Vitro Fertilization



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