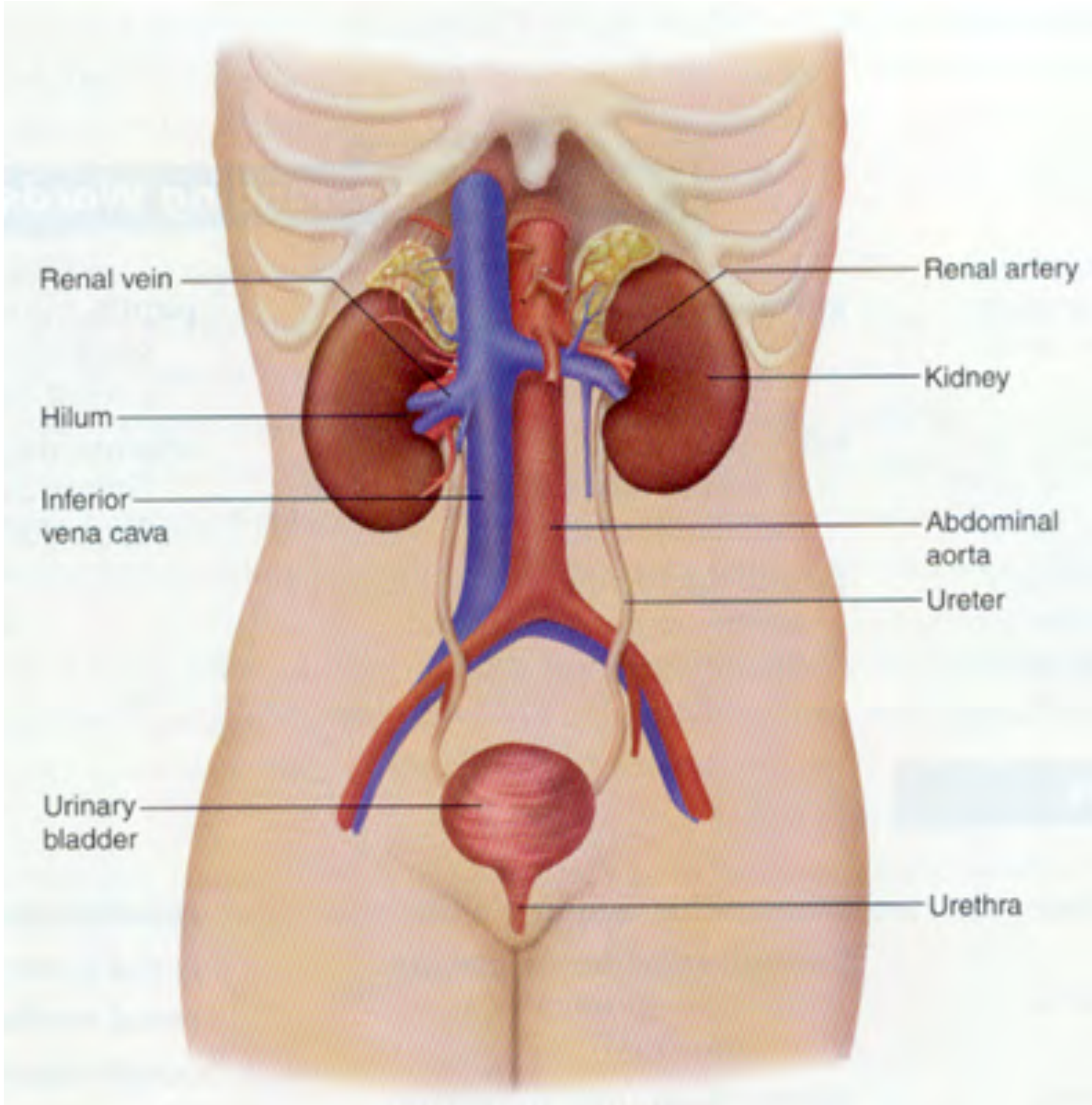
Spring Elective

2018 Spring

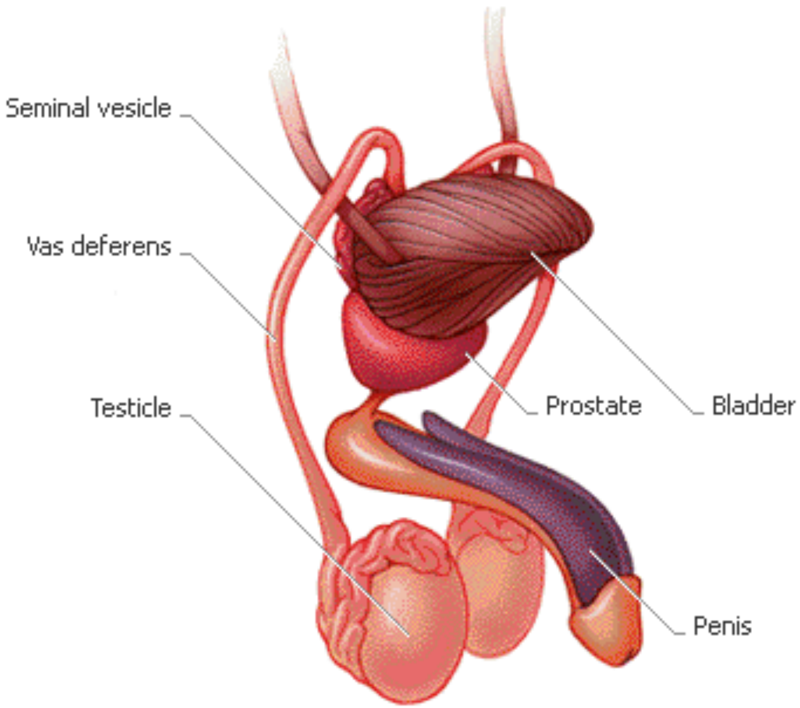
Genito-Urinary system


Renal vein
Renal artery
Kidney
Hilum
Inferior vena cava
Abdominal aorta
Ureter
Urinary bladder
Urethra

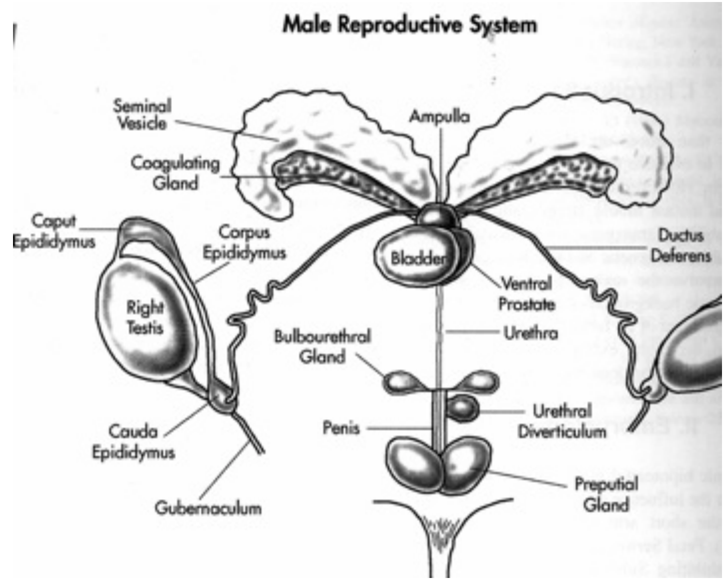
Human Uterus,
fallopian tubes,
Ovaries

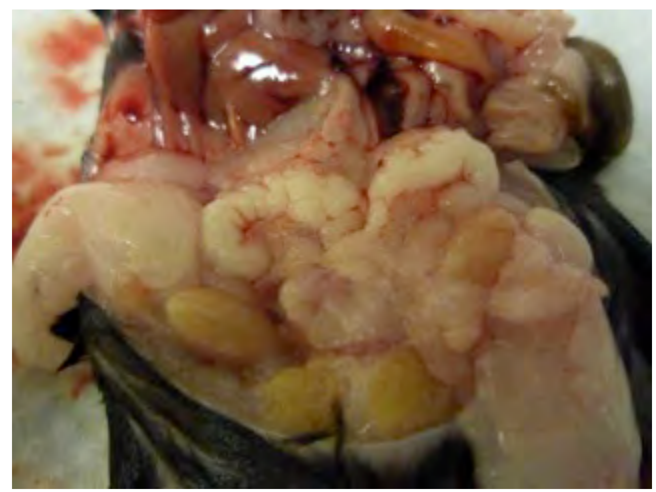
Mouse bi-cornuate uterus,
tubes and ovaires

Human Male Reproductive system



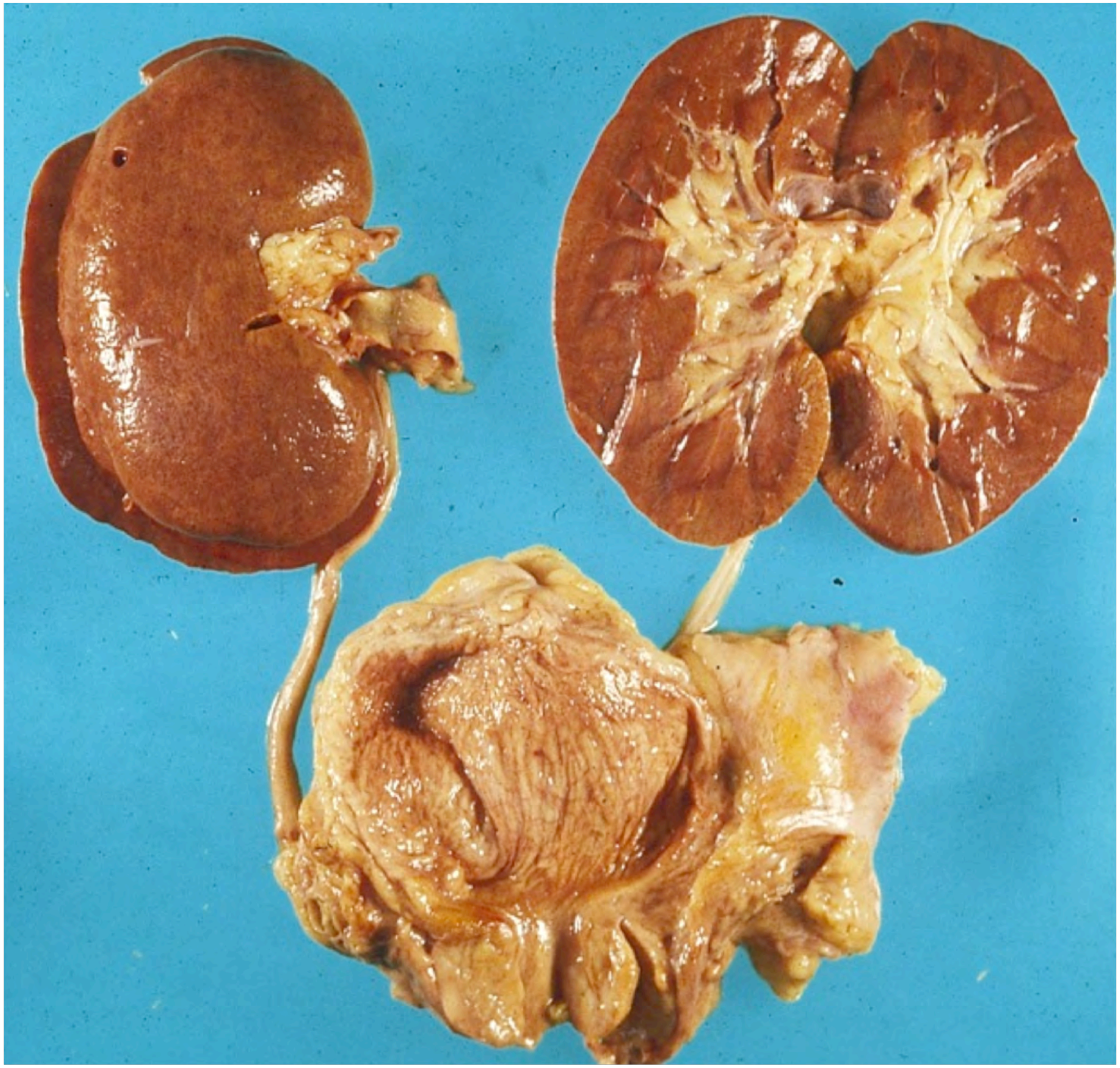
Mouse



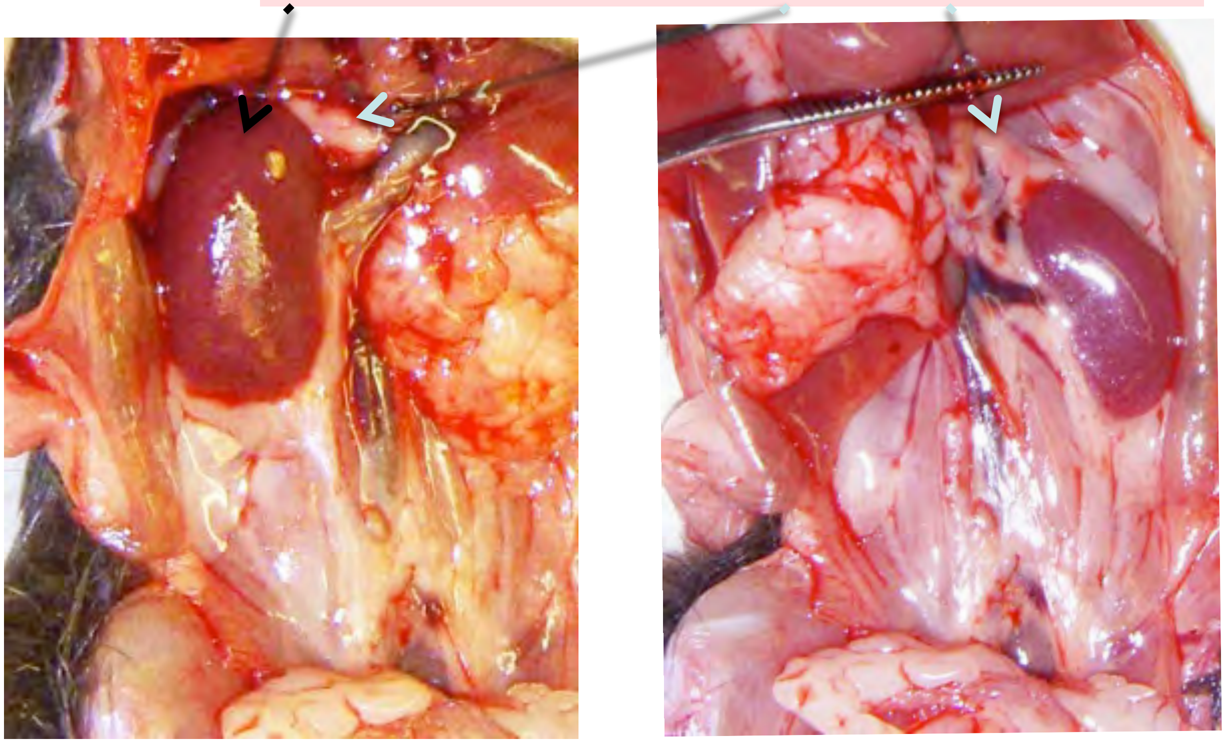


The mouse seminal vesicles are very prominent

Human kidneys, ureters, bladder, prostate



Mouse kidneys, adrenals



Alan J. Davidson et al., 2008.
Mouse kidney development

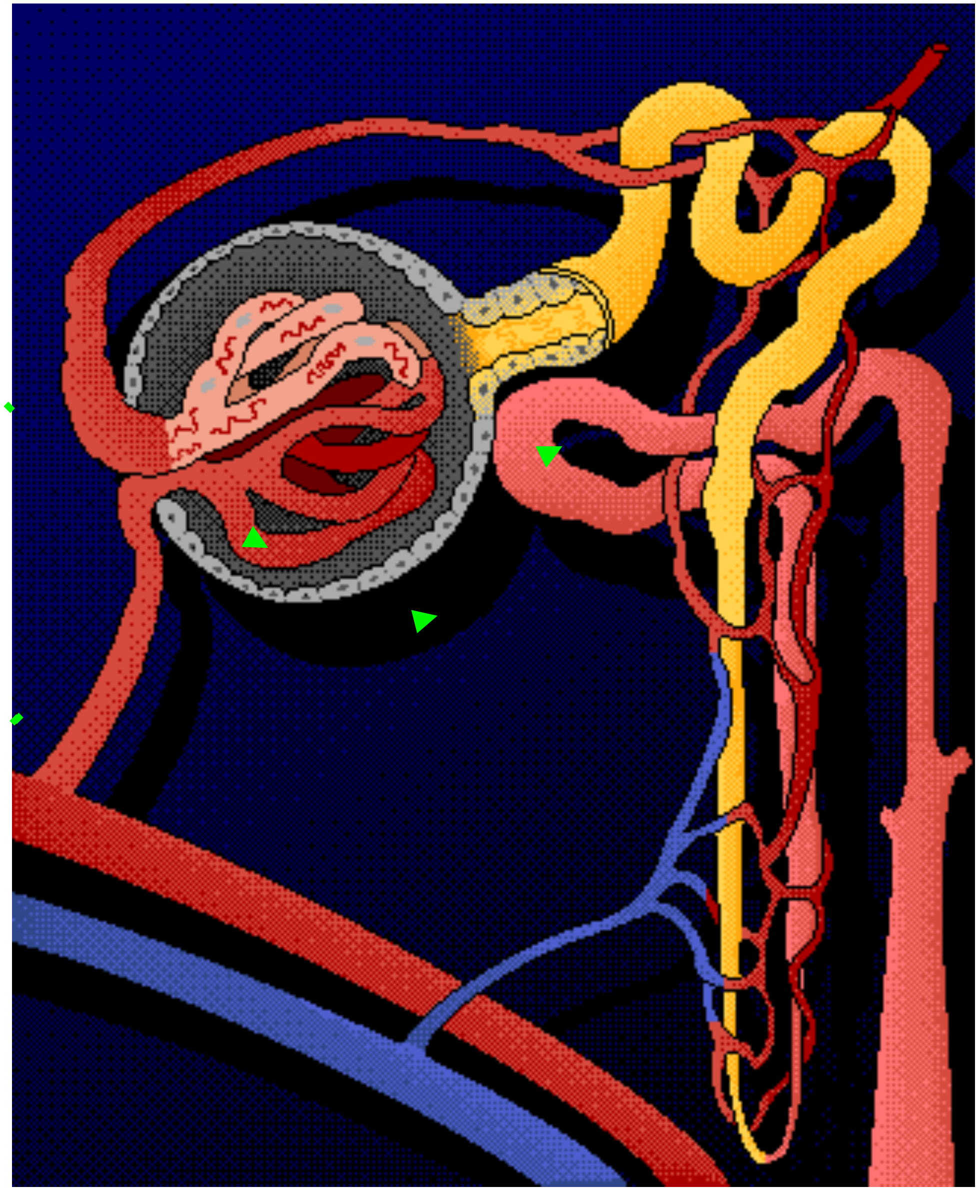
TYPES OF CAPILLARIES

Continuous	No gaps between endothelial cells	Basal Lamina present	Most common
Fenestrated	Endothelial cells separated by gaps of 60-80 nm	Basal Lamina present	Kidney Intestine Endocrine organs
Fenestrated2	Gaps	THICK BASAL lamina	Glomeruli of kidney
Sinusoidal	Gaps	Discontinuous Basal Lamina	Liver Spleen Bone Marrow

The Nephron

- <u>Filtration</u>: Glomerulus

- <u>Secretion & Reabsorption</u>: Proximal tubule, loop of Henle, and Distal tubule



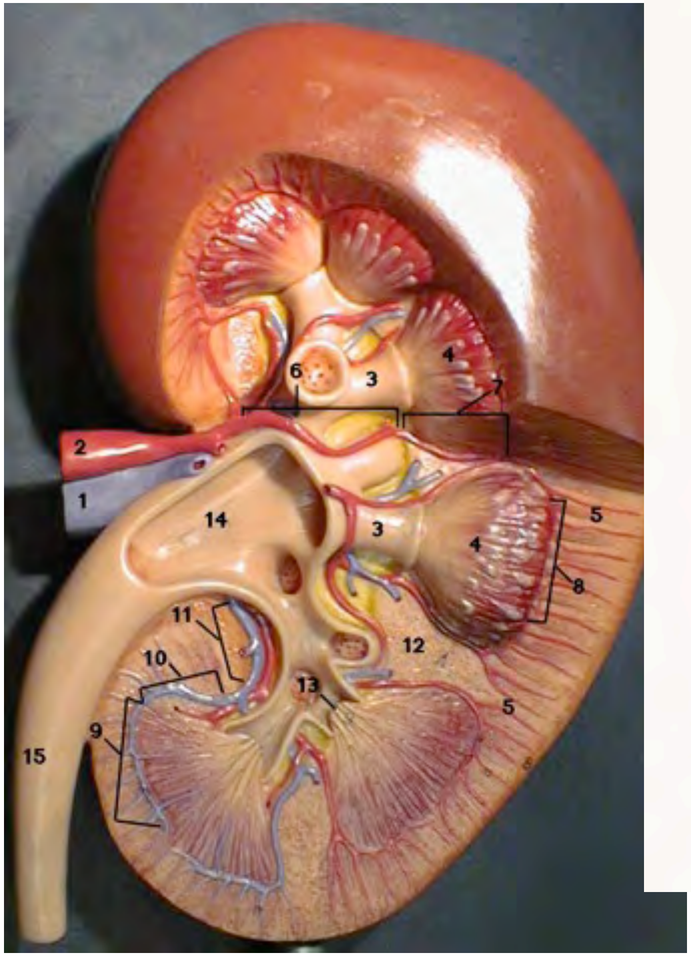
Nephron segments

- Bowman's capsule
- Proximal tubule
- Loop of Henle
- Distal tubule
- Collecting duct
- Peritubular capillaries and vasa recta

Glomerulus: Filtration of molecules

- ~40 nM threshold/ 60 kD
  - Inulin 5 kD —----fully filtered

    (also not secreted/reabsorbed or metabolized in the tubule, hence it is used as a tracer to measure Glomerular Filtration Rate)
  - Alb 70 kD---- largely excluded
- Favors cations because it is negatively charged due to heparan sulfation of basement membrane;
  - thus negatively charged proteins such as albumin are preferentially excluded
  - albuminuria can be largely a result of charge alteration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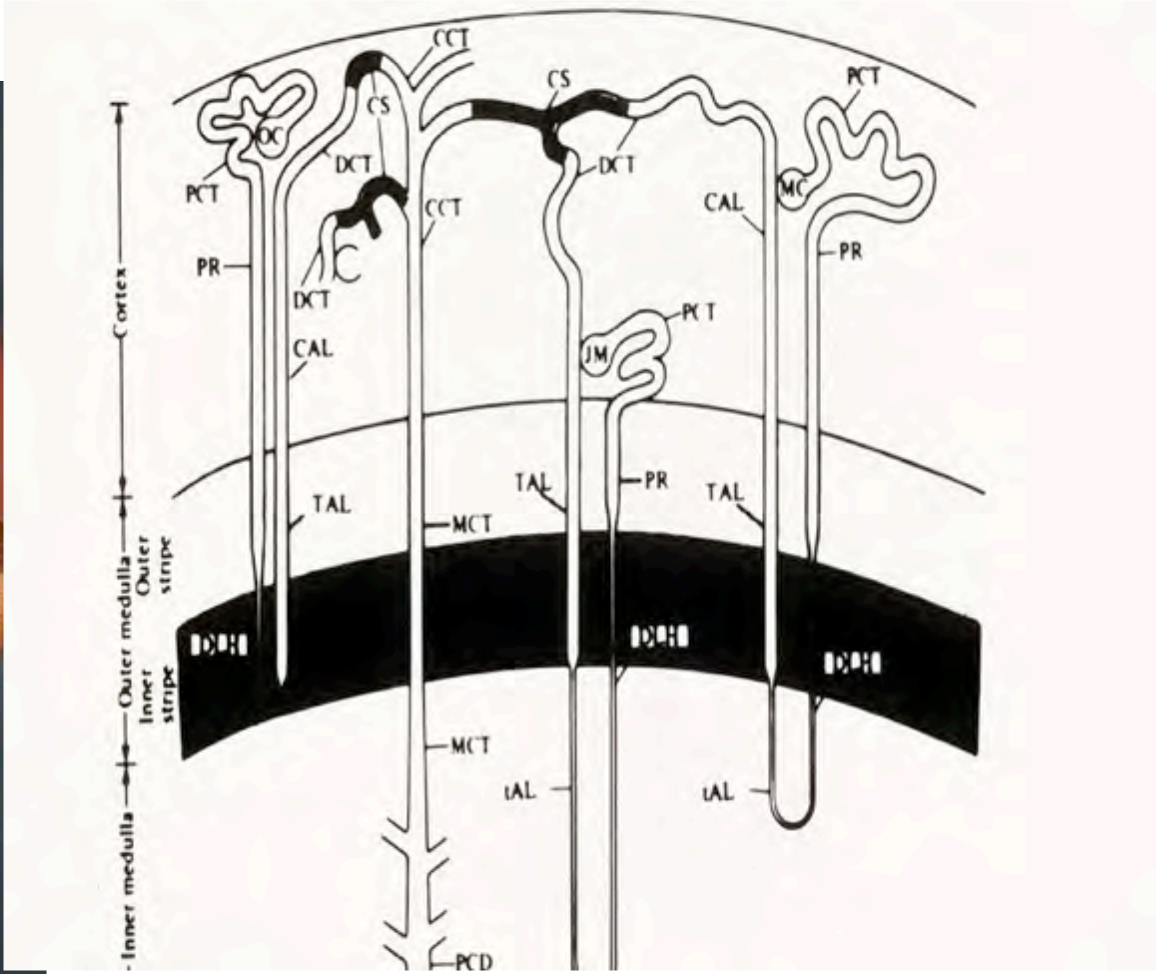
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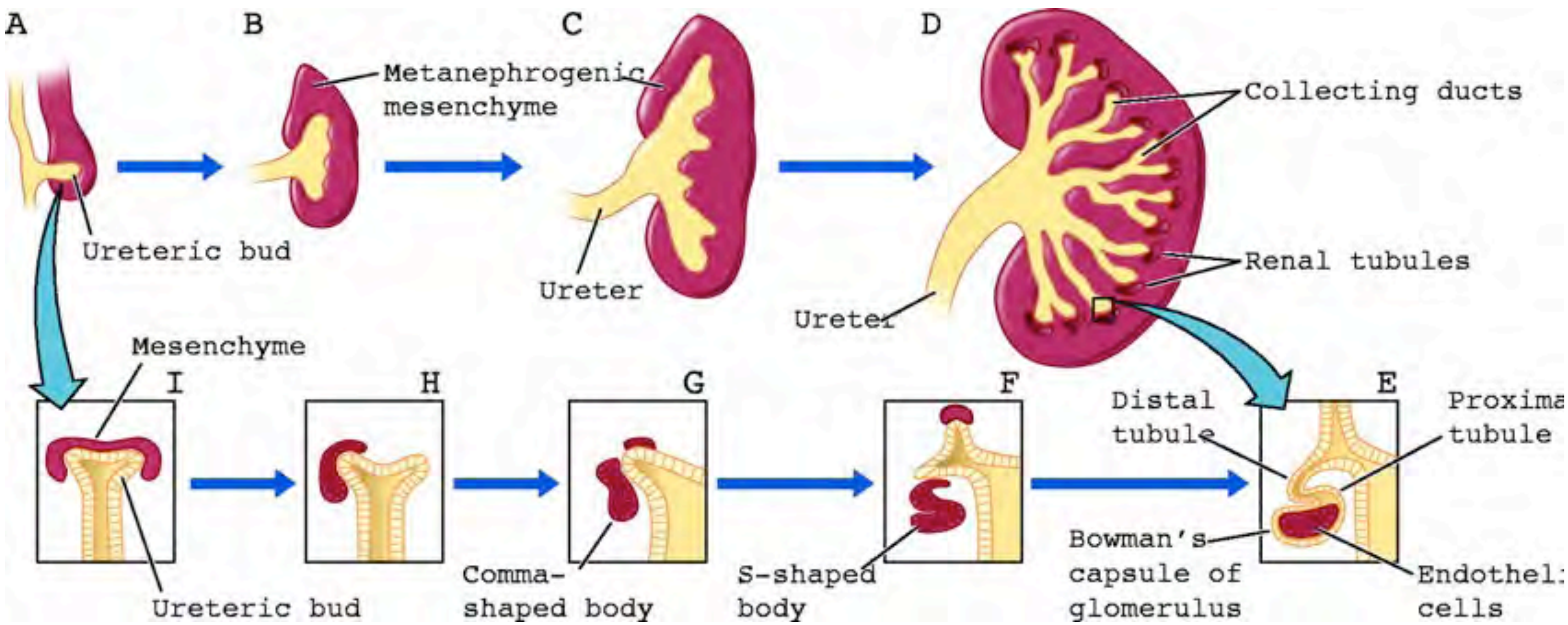
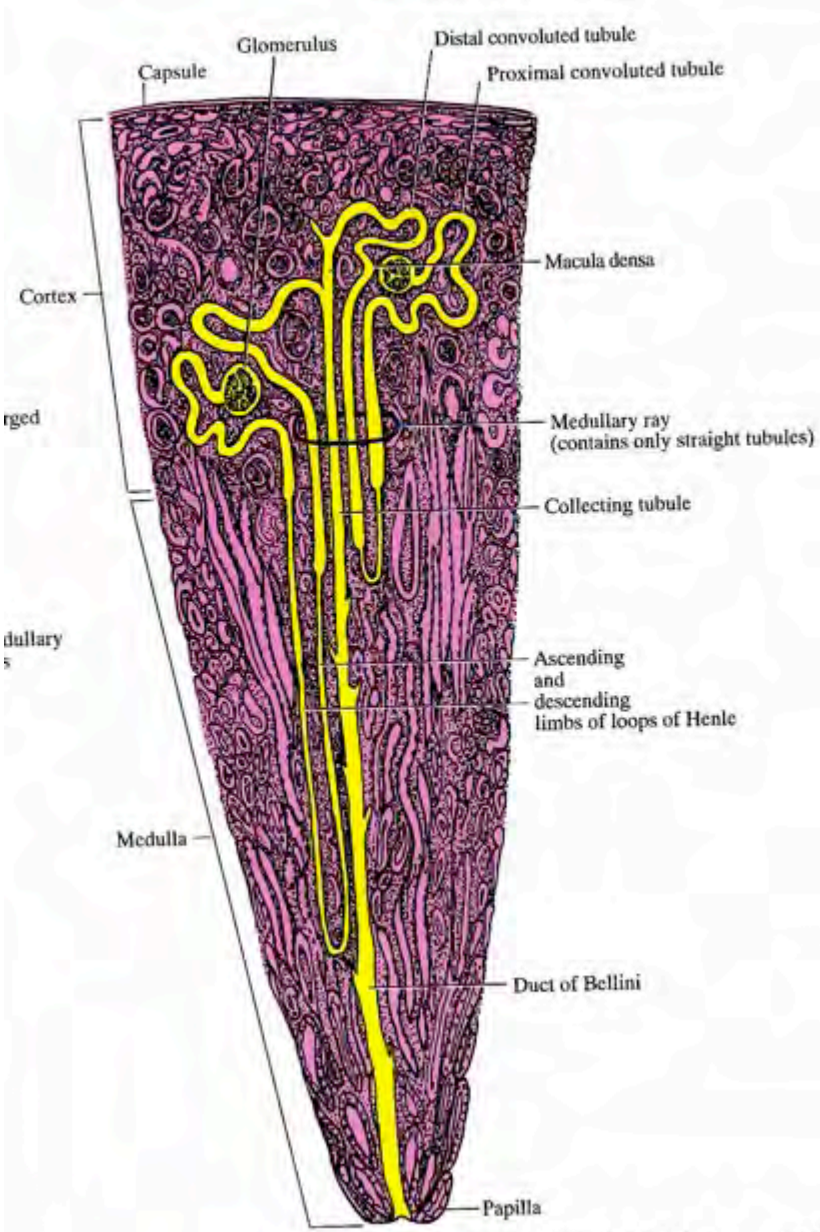
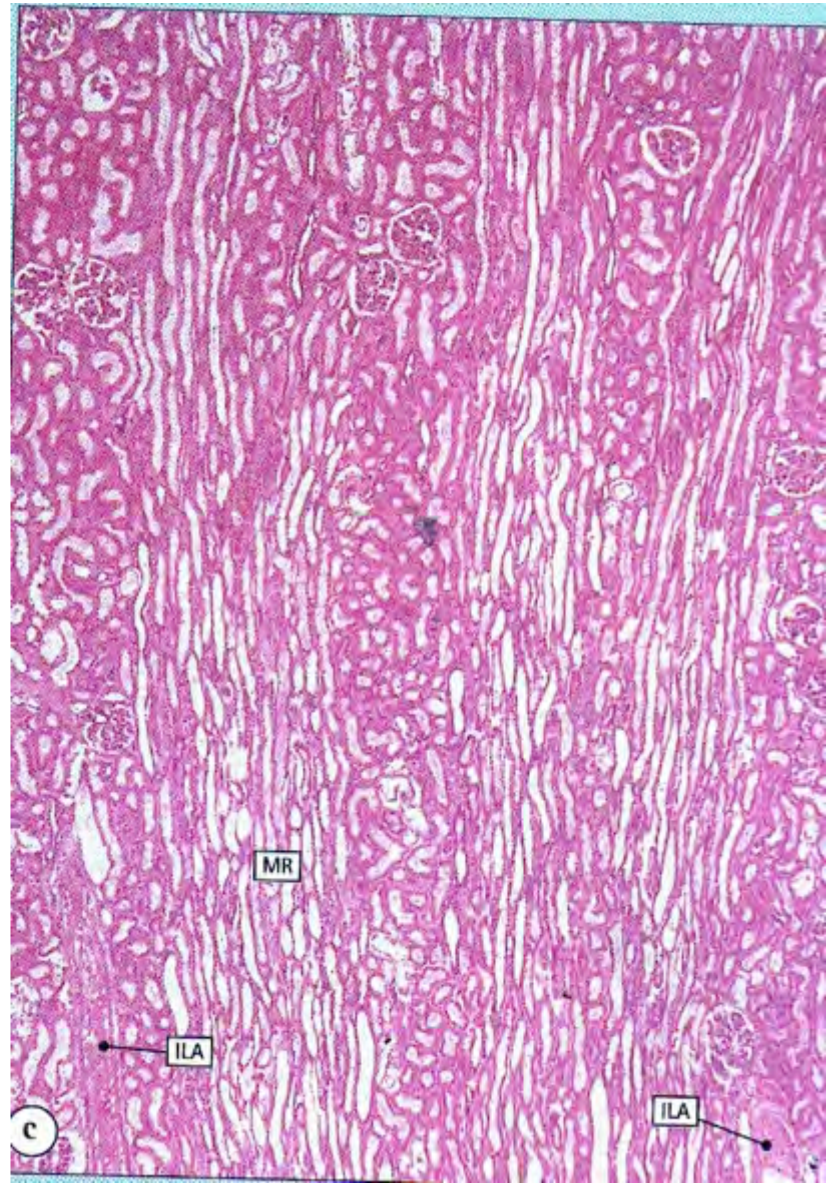
DLH
MCT
tAL
tAL
PCD
Cortex
Outer medulla
Outer stripe
Inner stripe
Inner medulla

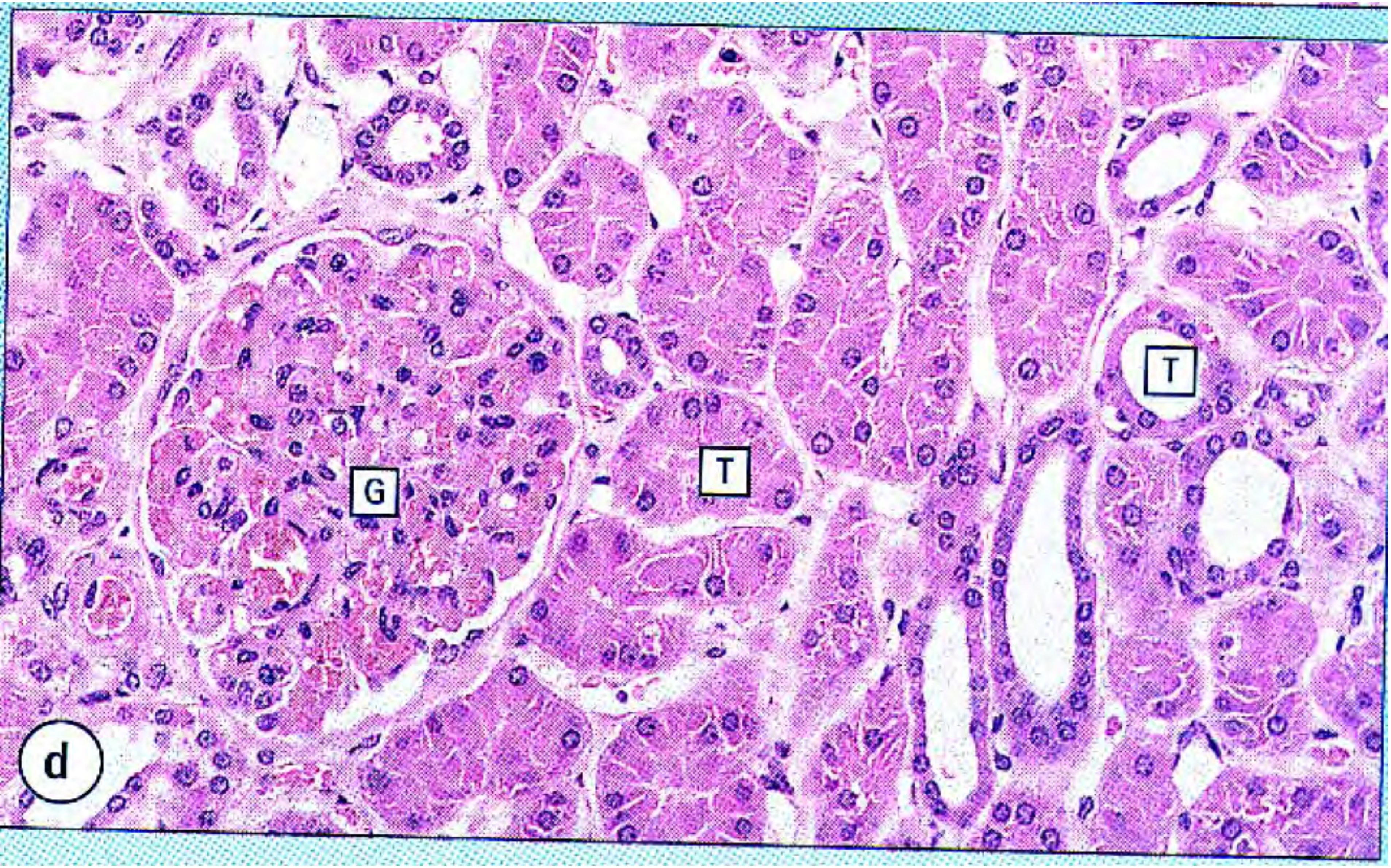


Continued growth and transformation of mesenchymal cell clusters results in epithelialization and tubulogenesis, ultimately forming the portion of the nephron comprising the glomerulus, proximal tubule, loop of Henle, and distal tubule.

Kidney Structure



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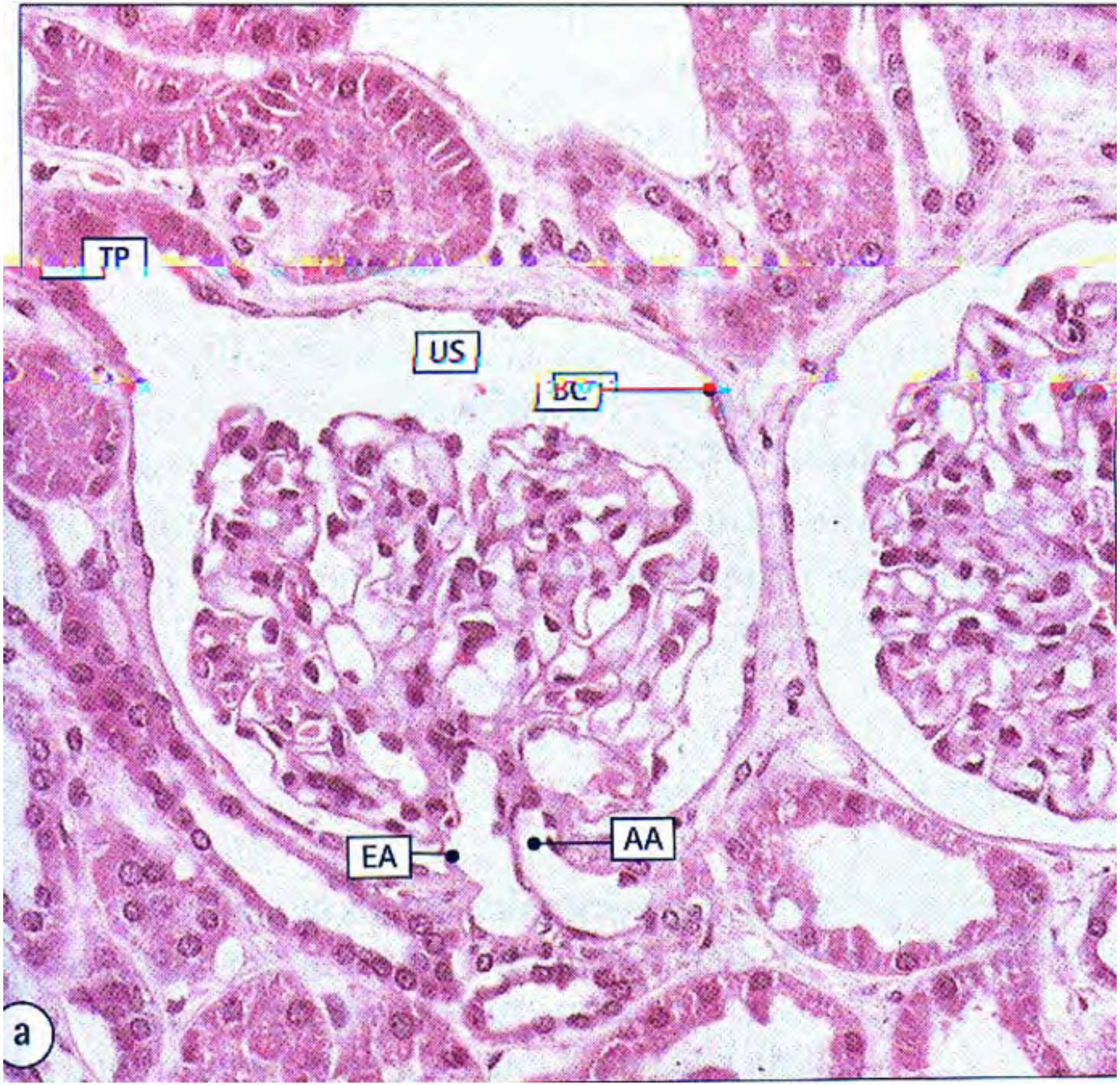
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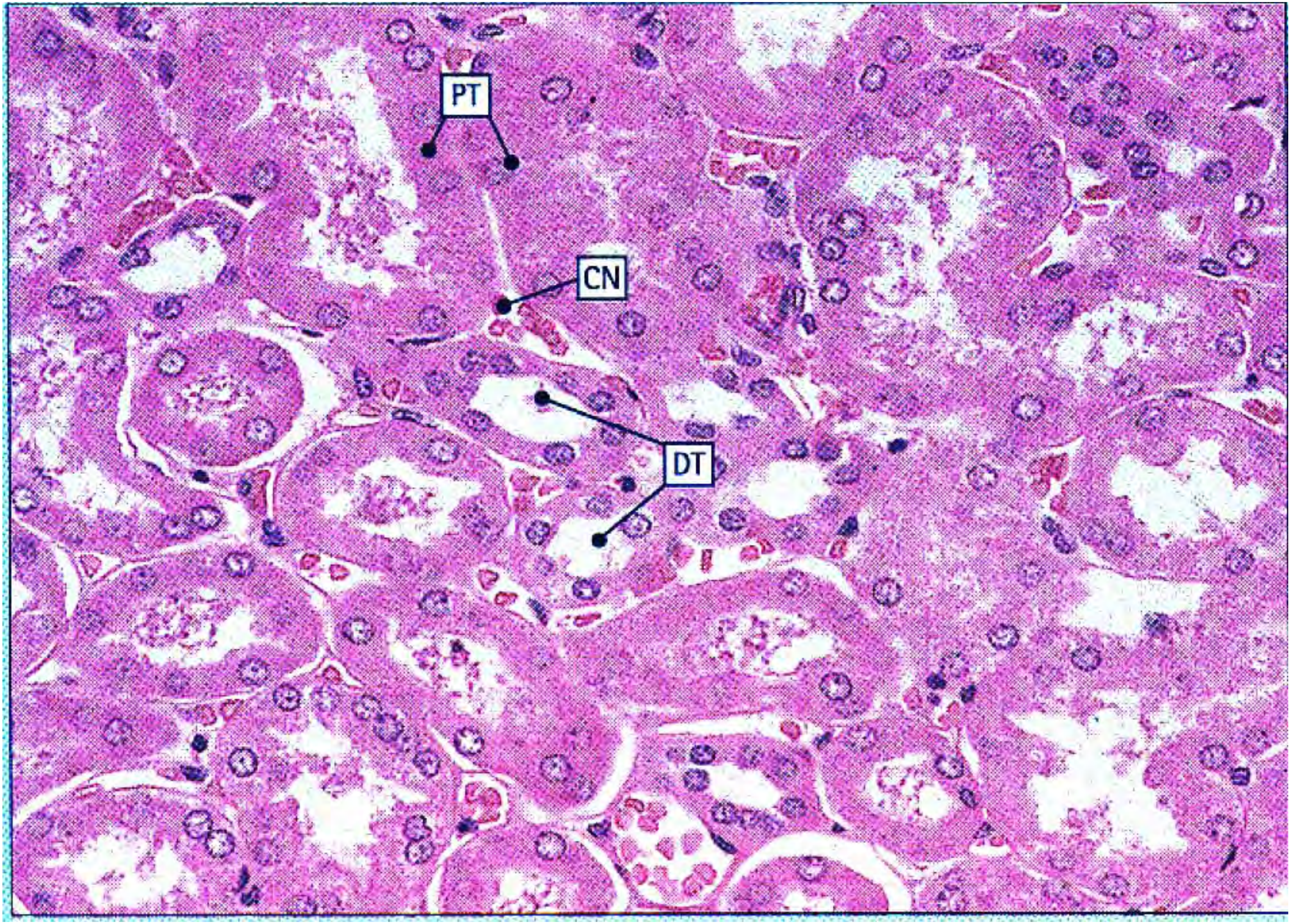
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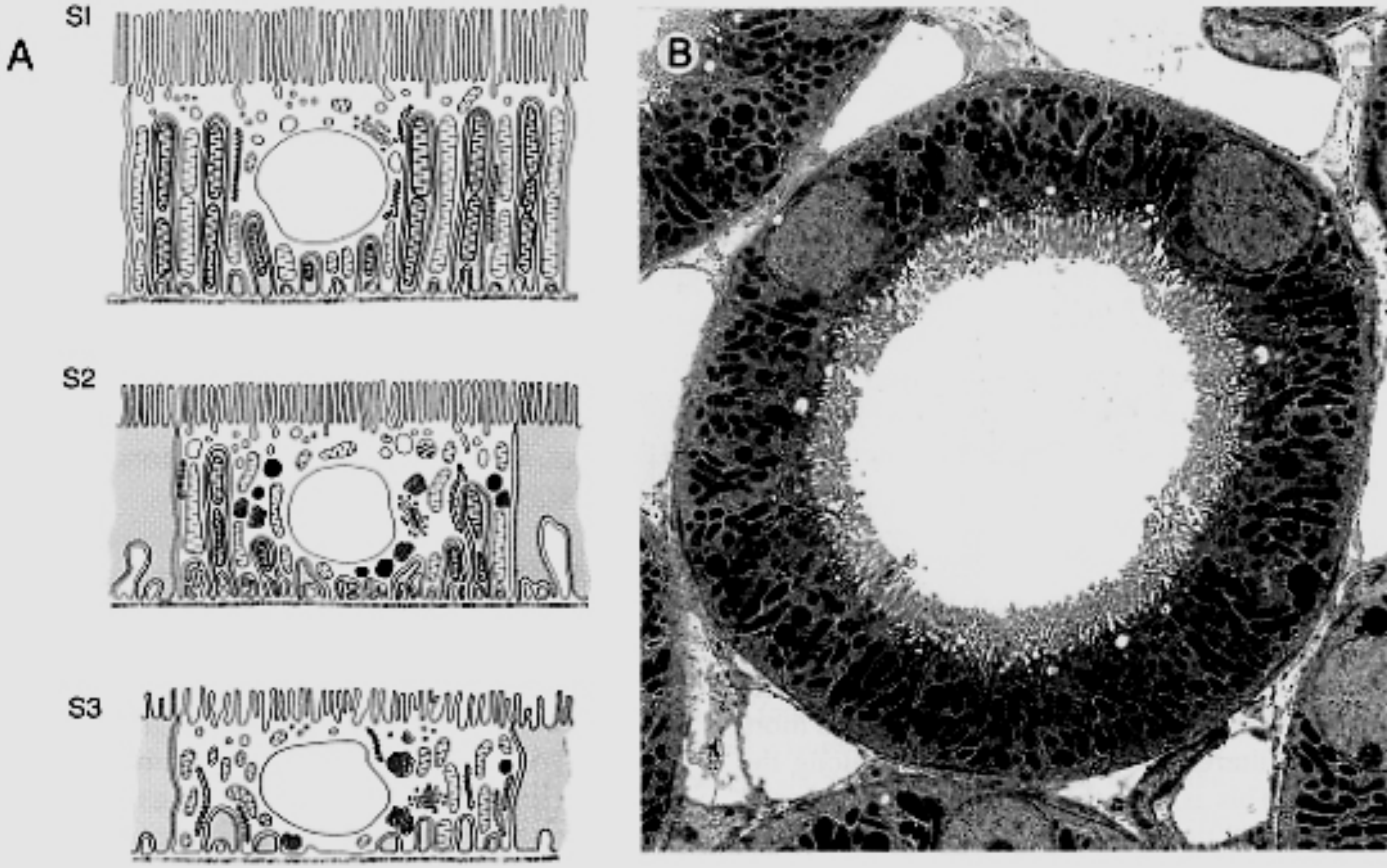


FIGURE 7 Proximal tubule. The proximal tubule consists of three segments: S1, S2, and S3. The left panel shows schematic diagrams of the typical cells from these three segments, the right panel shows a cross section of the S1 segment. The S1 begins at the glomerulus, and extends several millimeters, before the transition to the S2 segment. The S3 segment, which is also called the proximal straight tubule, descends into the renal medulla to the inner medulla. The proximal tubule is characterized by a prominent brush border, which increases the membrane surface area by a factor of about 40-fold. The basolateral infoldings, which are lined with mitochondria, are interdigitated with the basolateral infoldings of adjacent cells (in these diagrams, processes that come from adjacent cells are shaded). These adaptations are most prominent in the first parts of the proximal tubule, and are less well developed later along the proximal tubule.

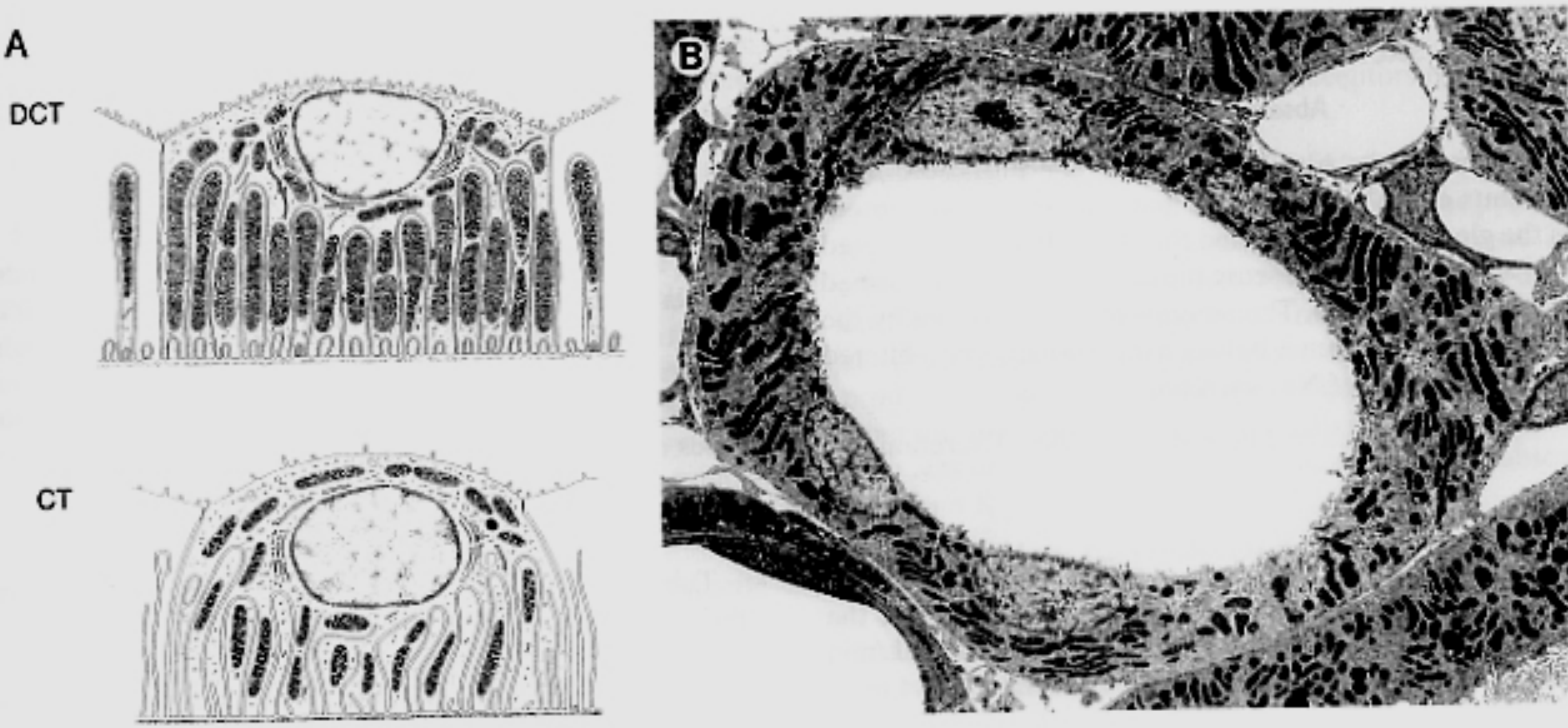
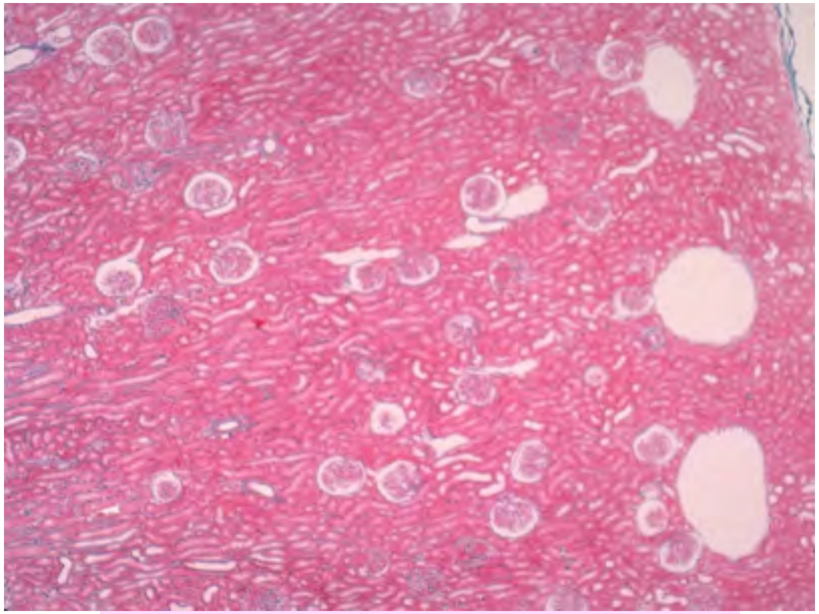
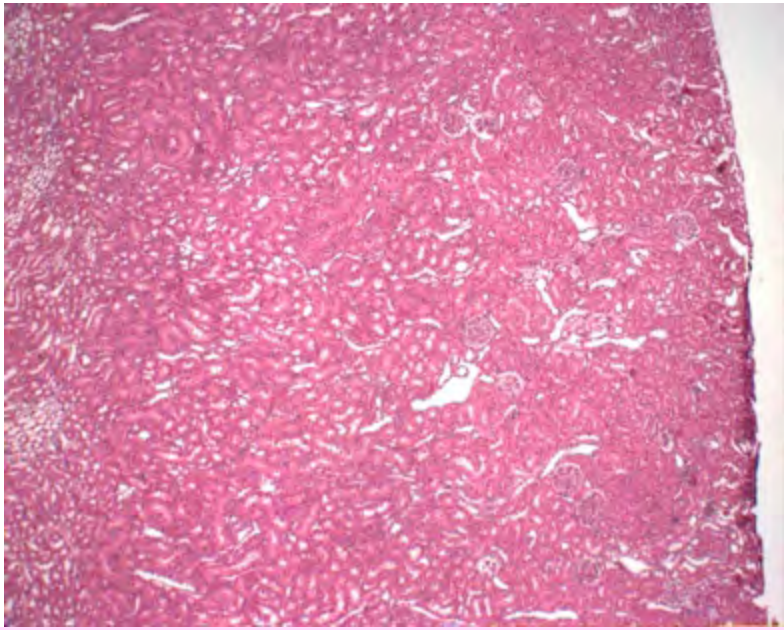


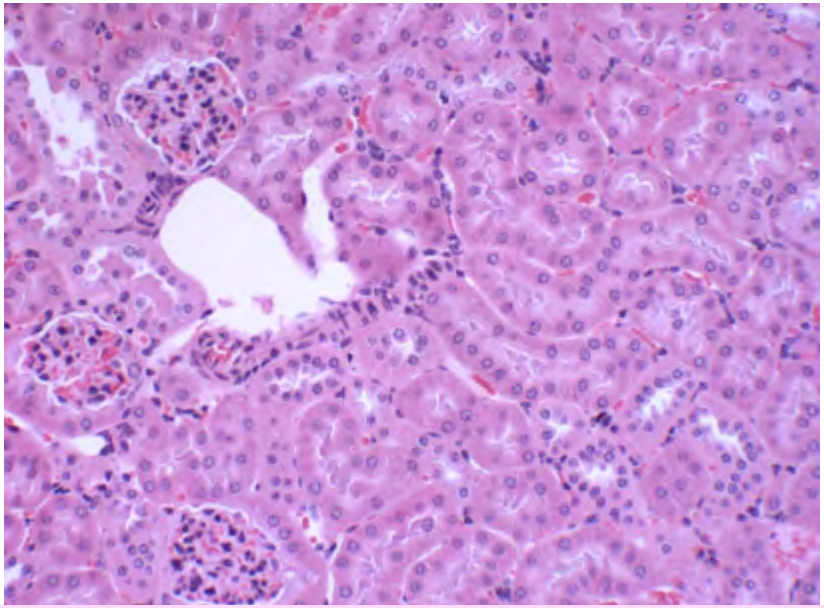
FIGURE 9 Distal convoluted tubule. The distal convoluted tubule is customarily divided into two parts: the true distal convoluted tubule (DCT, shown schematically on the left, and in cross-section on the right) and the connecting tubule (CT), where cell morphology is somewhat more similar to collecting duct.



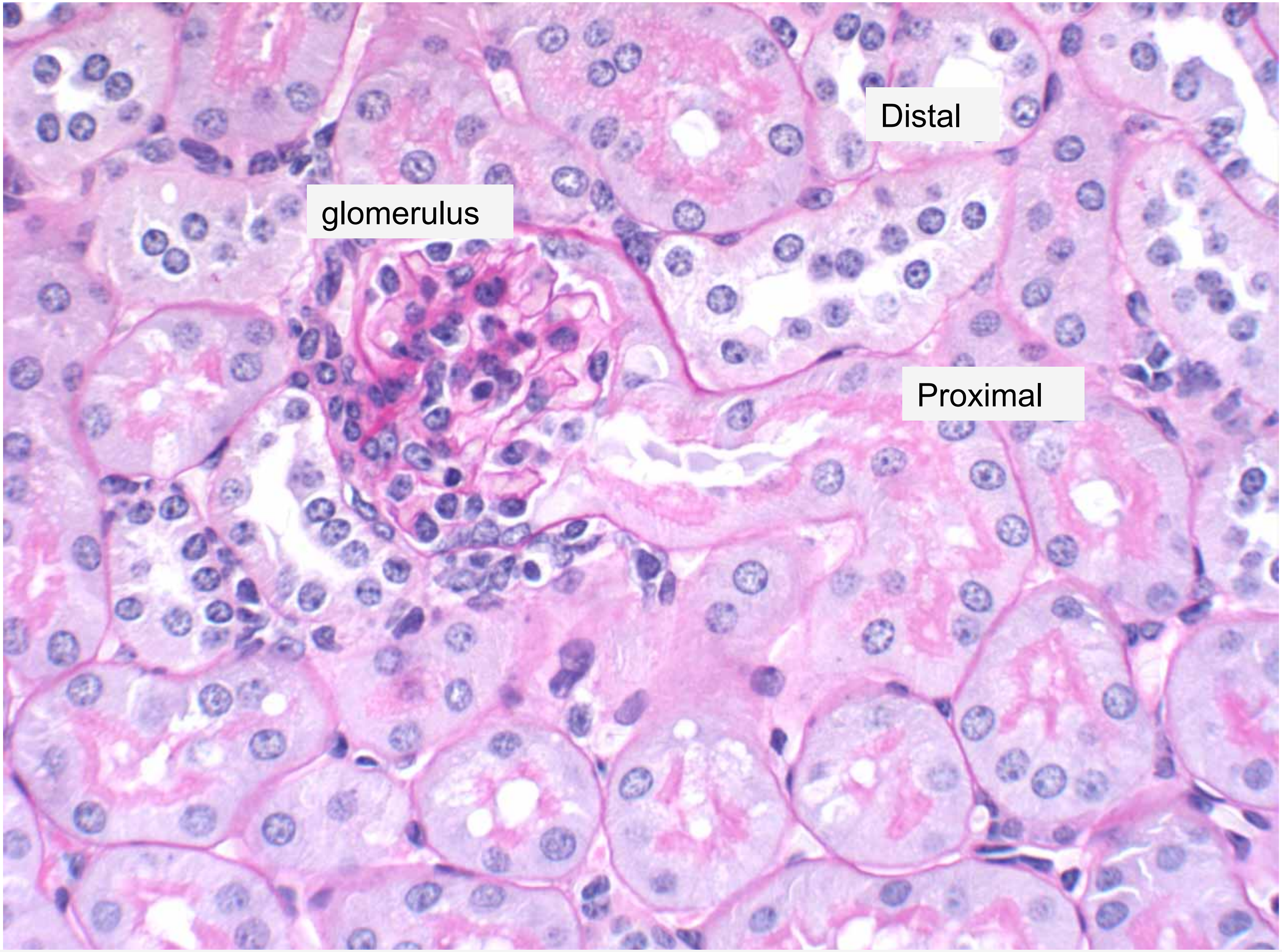
H&E of human Kidney x40 magnification



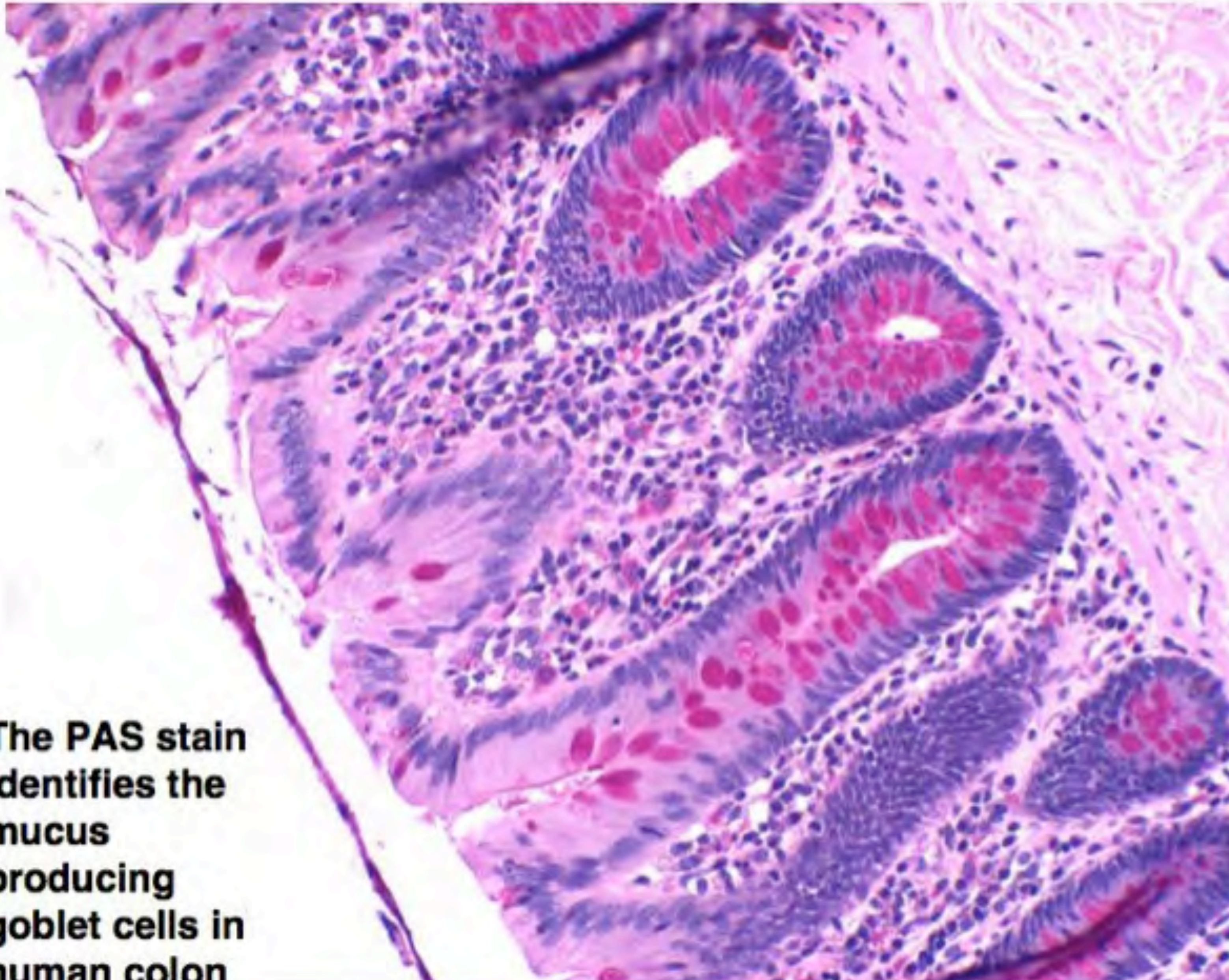
H&E of mouse Kidney x40 magnification



H&E of mouse Kidney x200 magnification

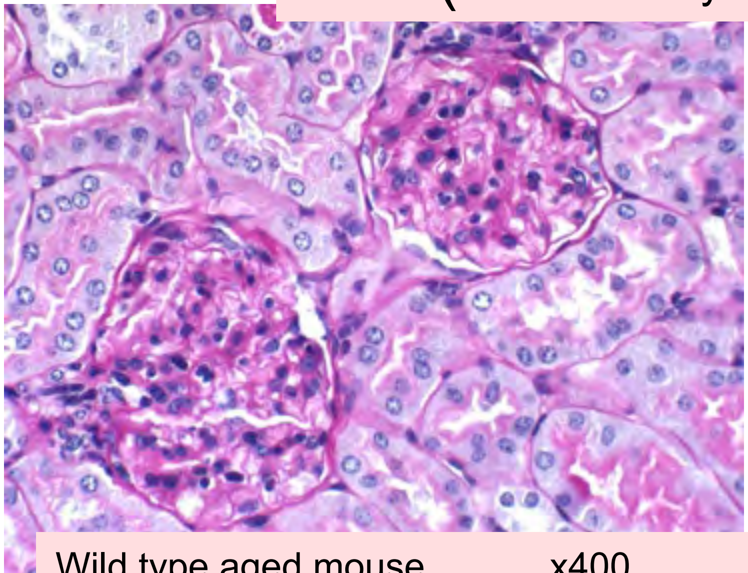


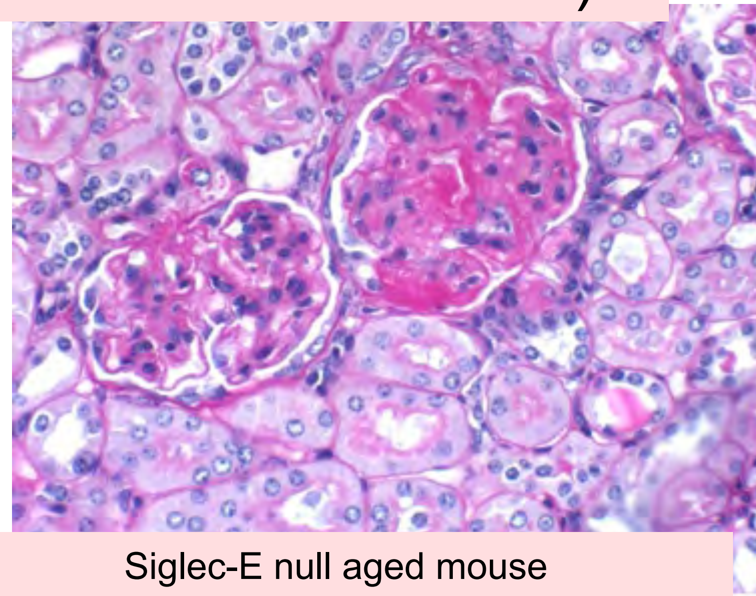
PAS stain (Periodic Acid Schiff) highlights basement membranes (carbohydrate structures)



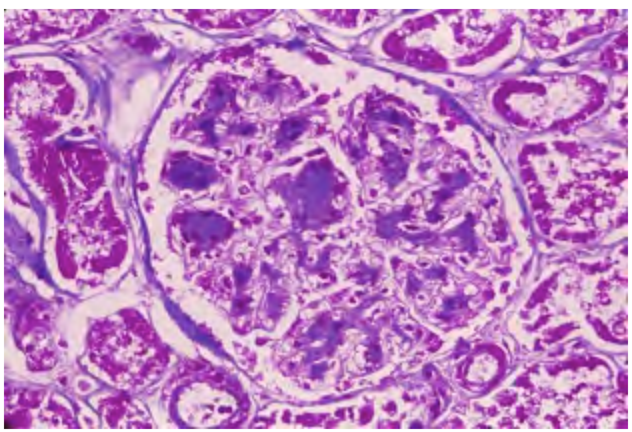
The PAS stain identifies the mucus producing goblet cells in human colon

PAS (mouse kidneys sectioned at 3 micron thickness)

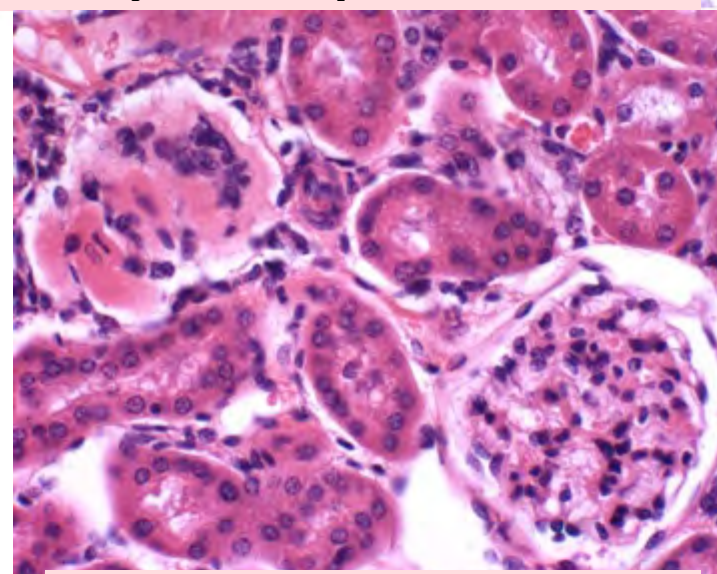




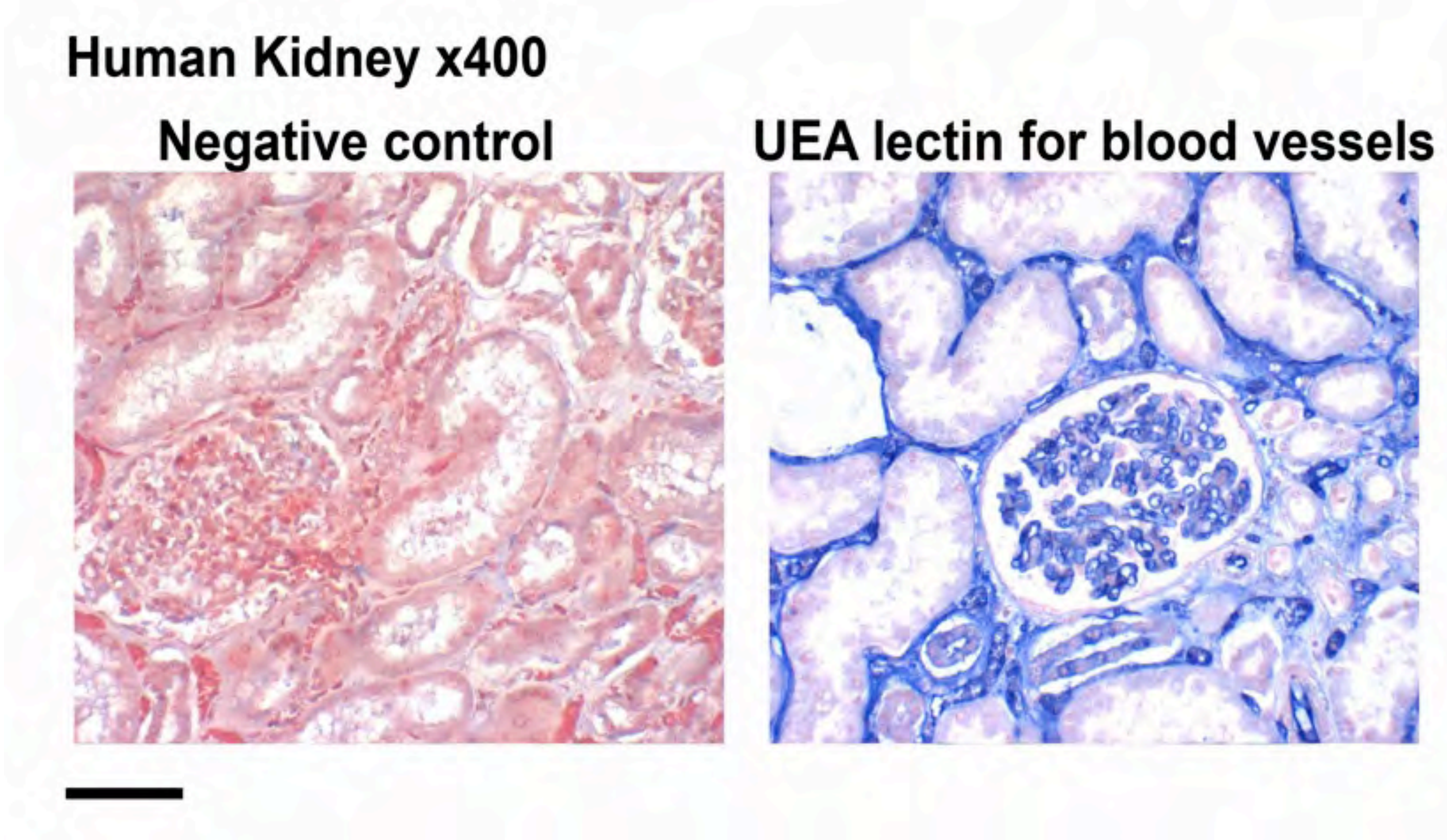
Wild type aged mouse x400 Siglec-E null aged mouse



Human Kidney with Expanded nodular formations in glomerular capillaries -- positive staining with PAS-- in diabetic glomerulosclerosis



H&E of same mouse kidney x400



Capillaries of the glomerulus highlighted with the UEA lectin

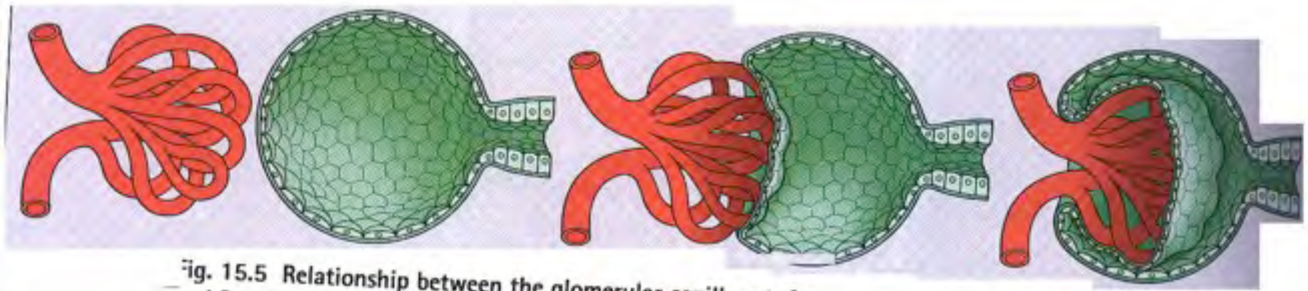
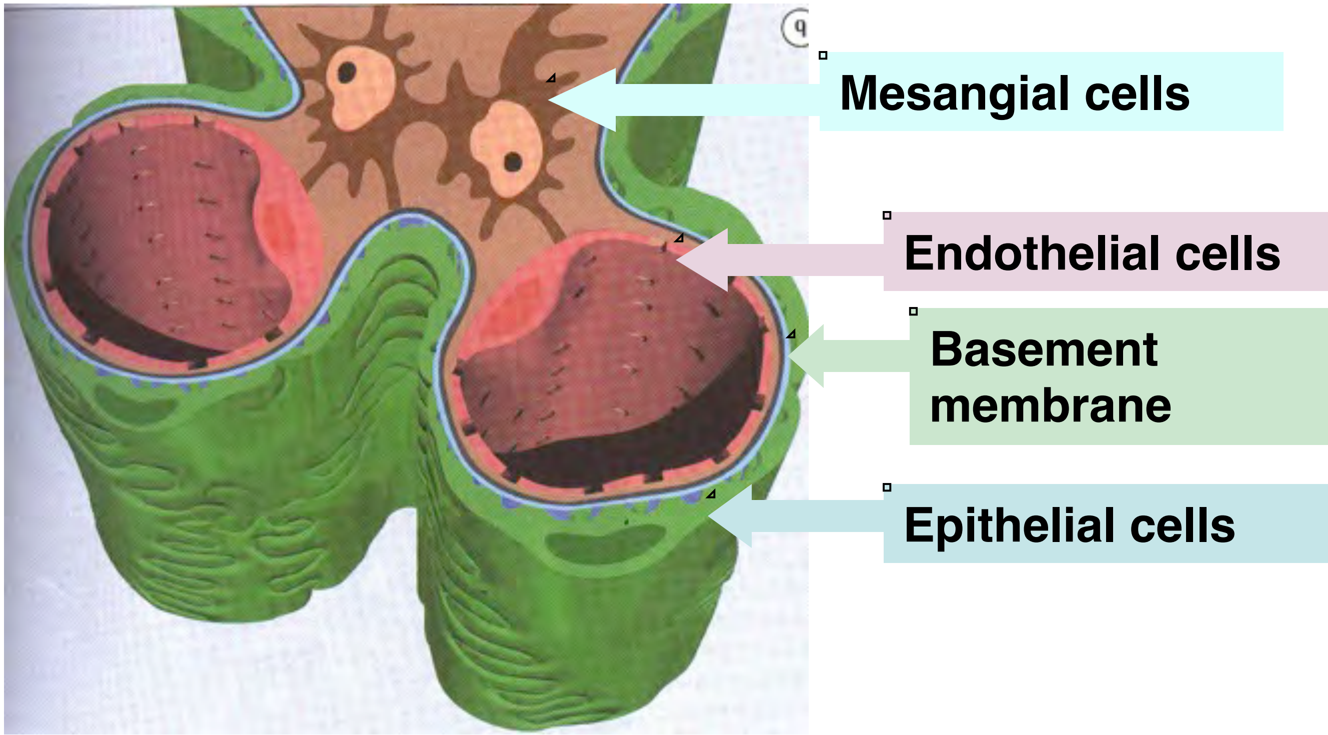
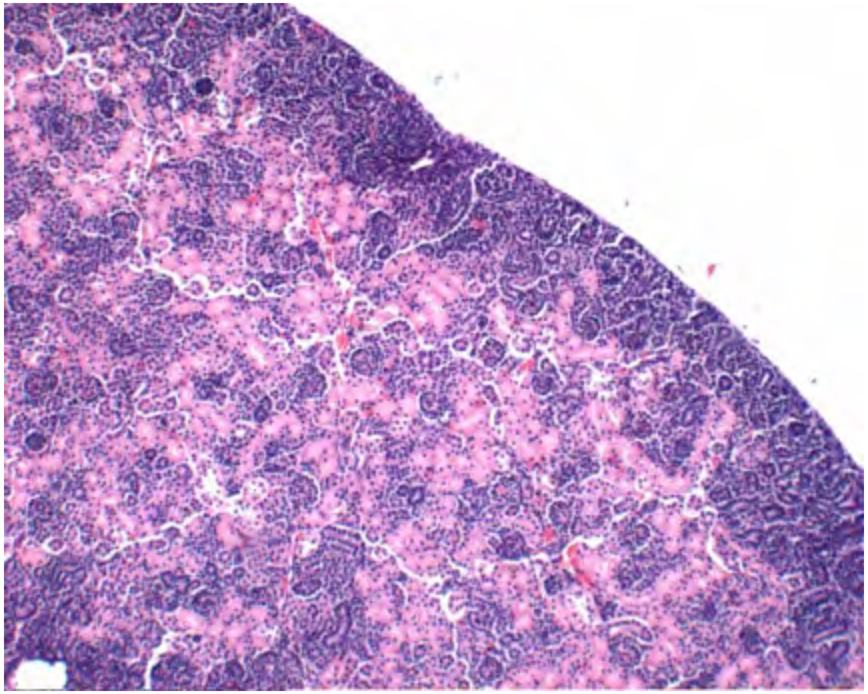
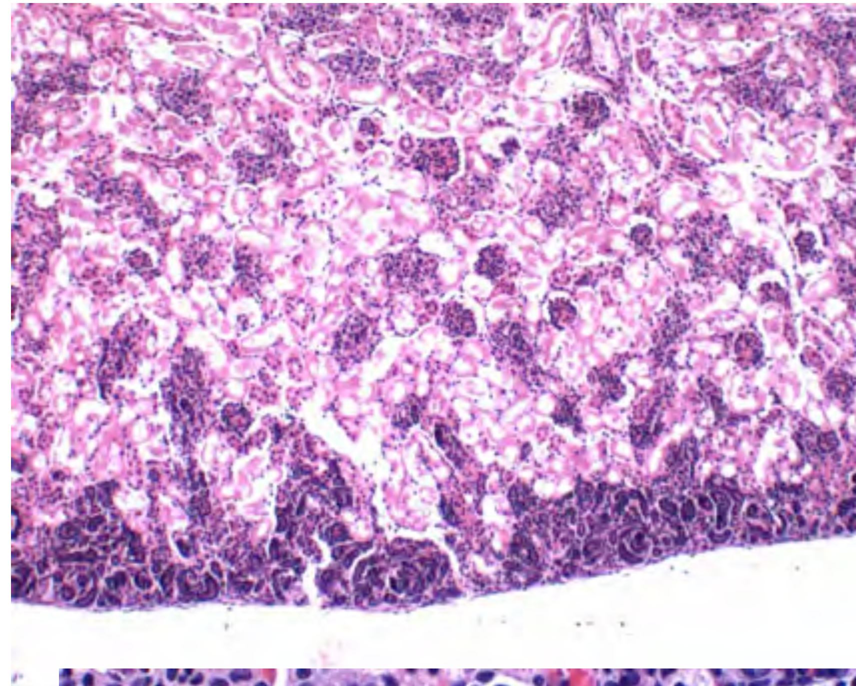
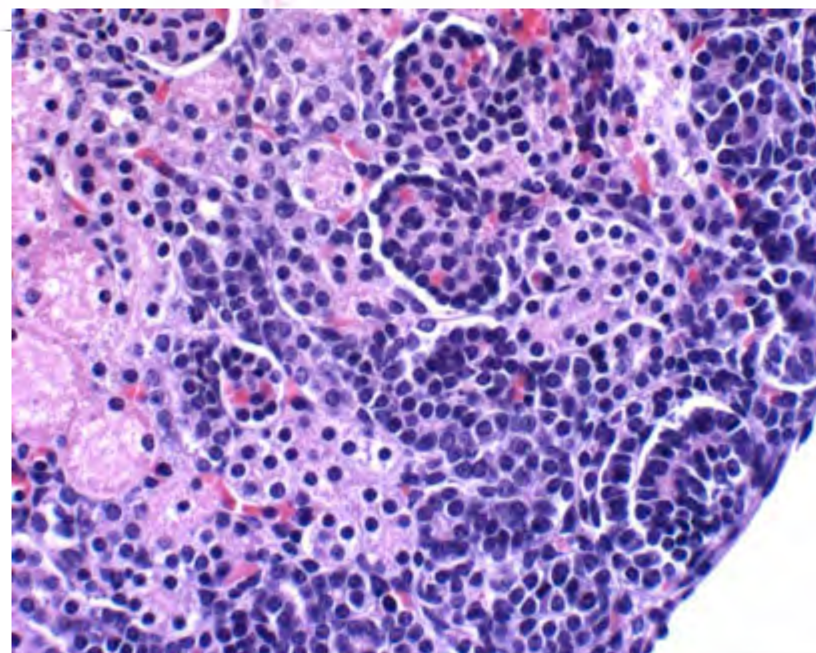


Fig. 15.5 Relationship between the glomerular capillary tuft and Bowman's capsule.





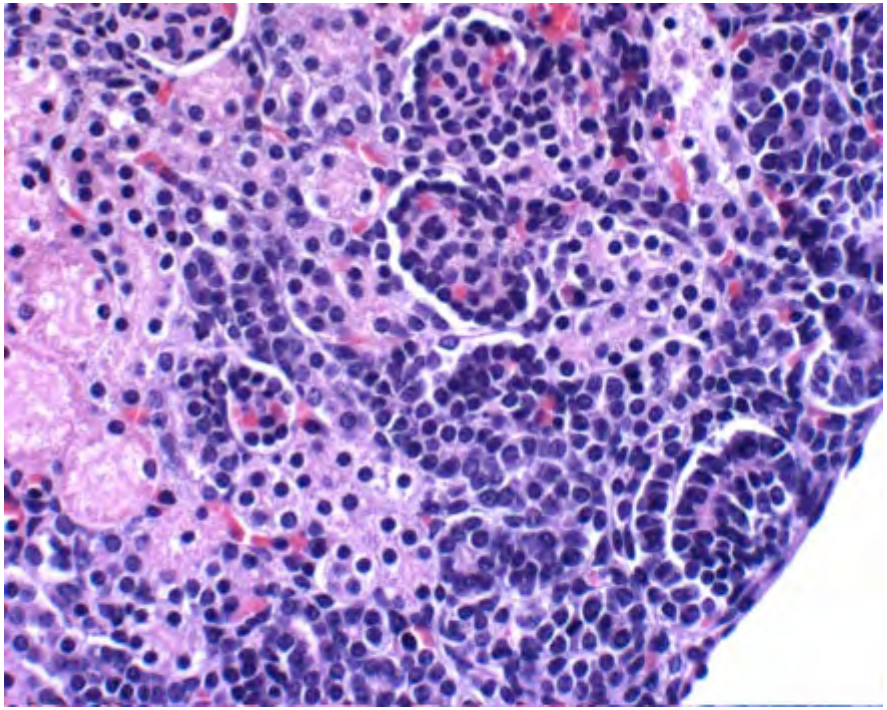
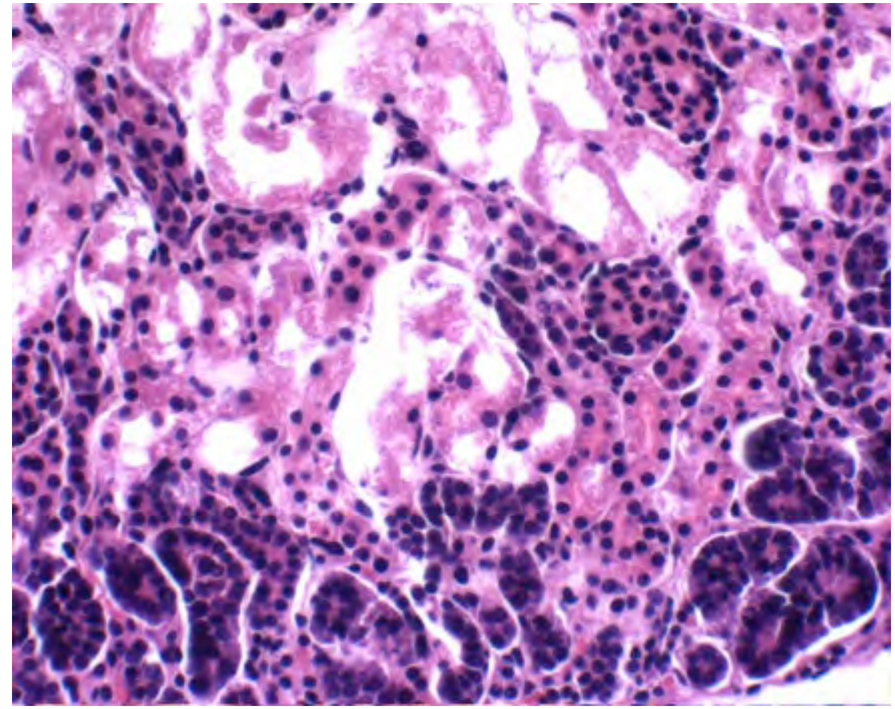




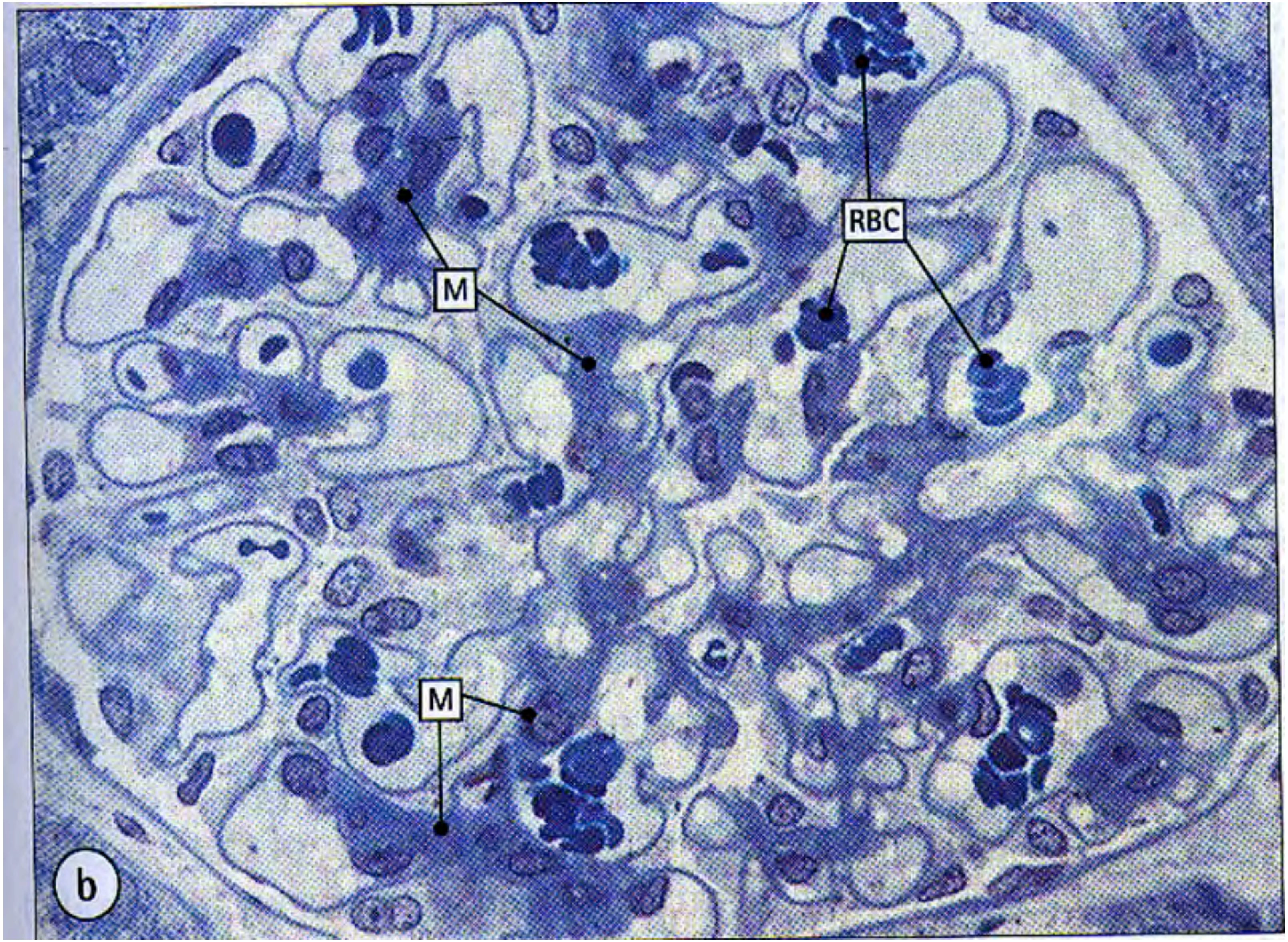
H&E of Embryo d16.5

Mouse Kidney cortex with

developing glomeruli

H&E of Embryo d 16.5 Mouse Kidney cortex x400 magnification



Thin section of glomerulus

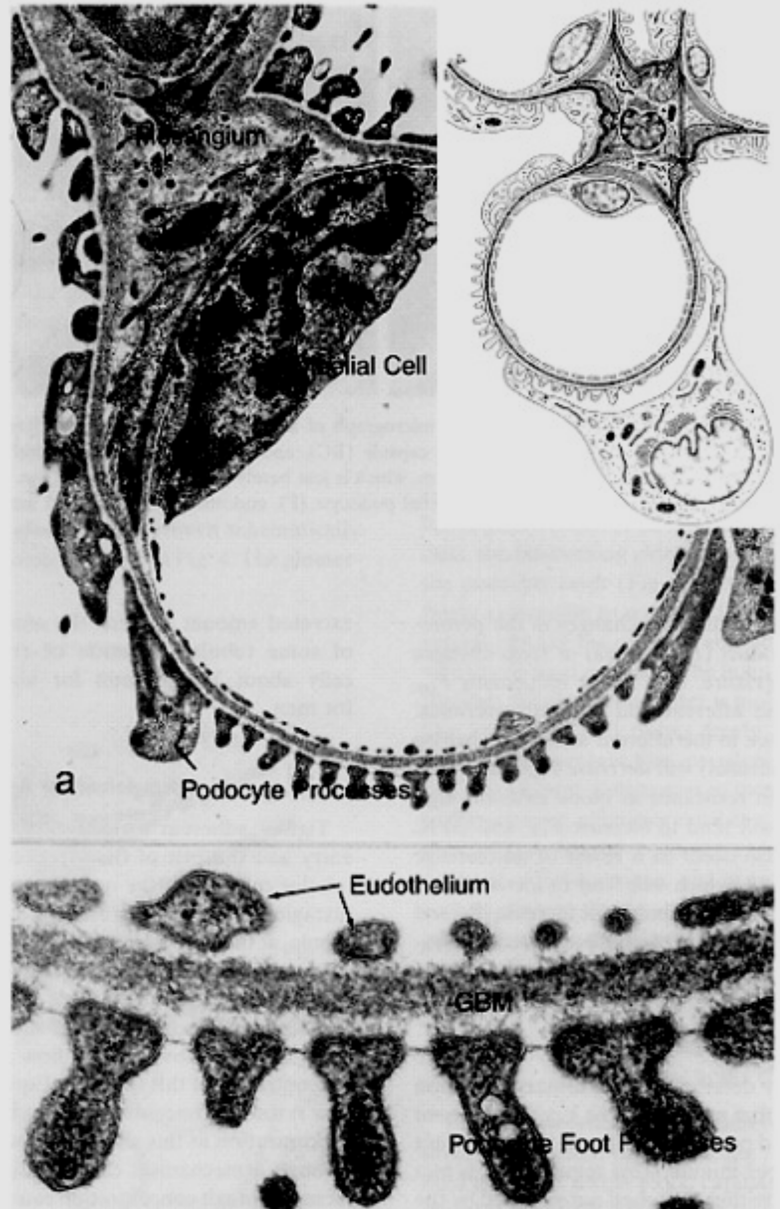


FIGURE 5 Structure of the glomerular capillary loop and the filtration barrier. (a) A single capillary loop showing the endothelial and foot process layers and the attachments of the basement membrane to the mesangium. Pressure in the glomerular capillary bed is substantially higher than in other capillaries. As shown in the diagrammatic insert, the mesangium provides the structural supports which permit these cells to withstand these high pressures. (b) The glomerular filtration barrier.

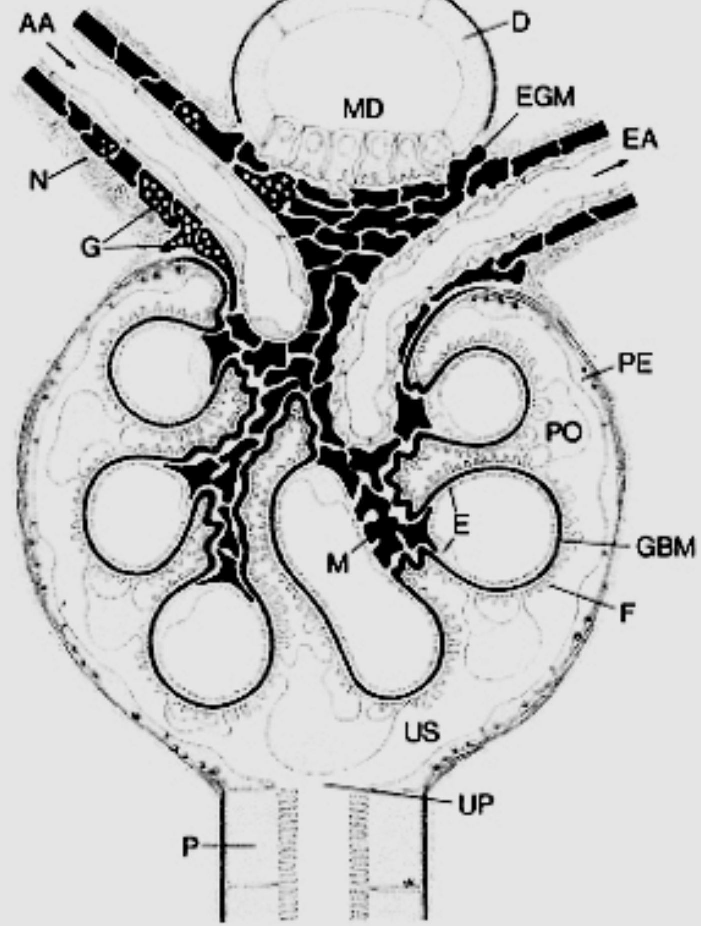
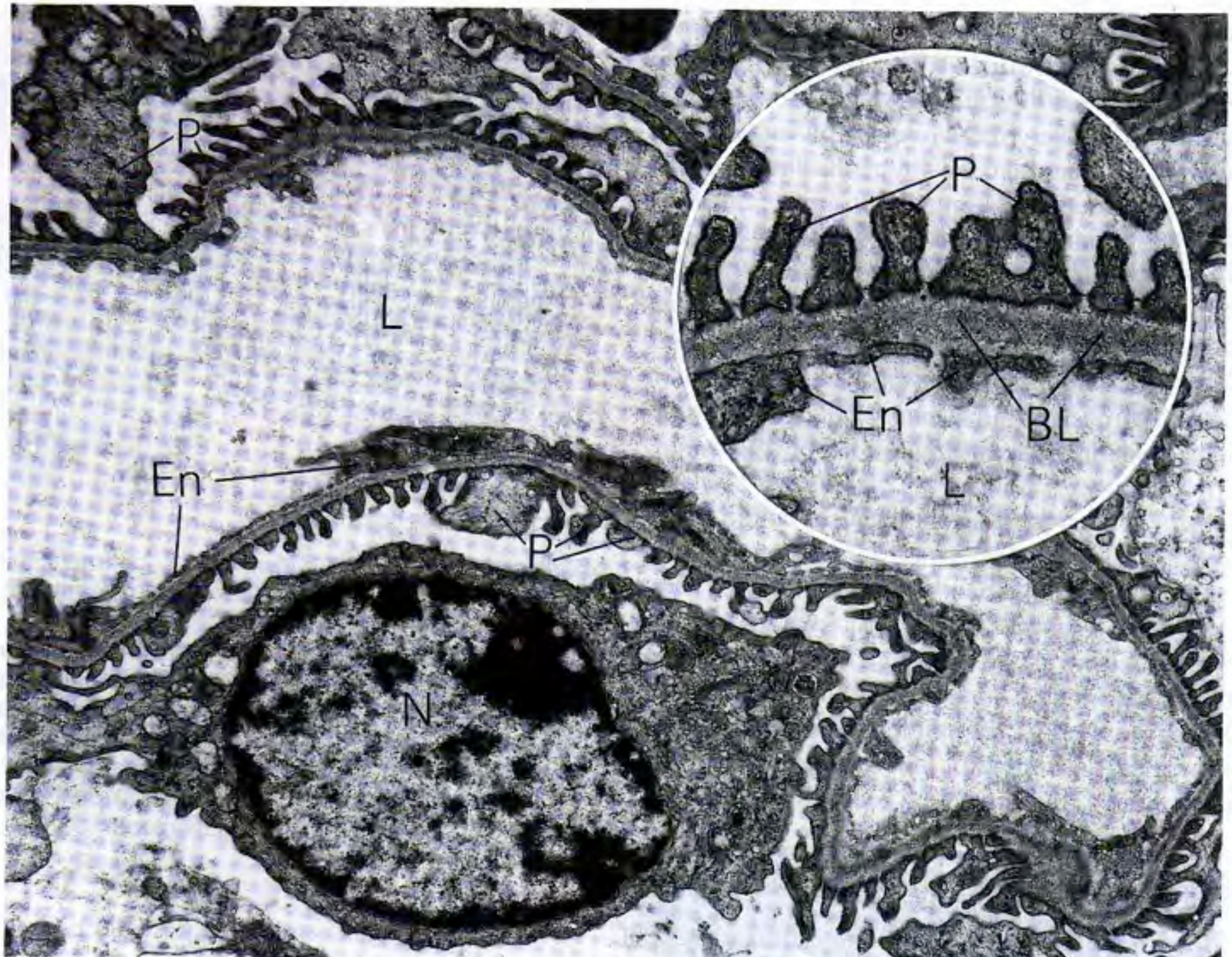


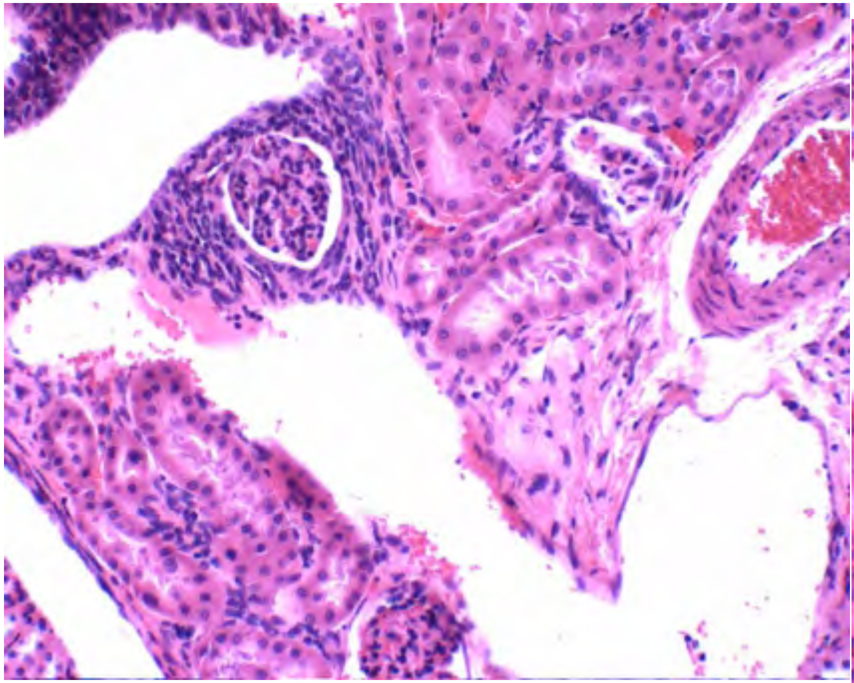
FIGURE 3 Anatomy of the glomerulus and juxtaglomerular apparatus. Schematic diagram of a section of a glomerulus and its juxtaglomerular apparatus. Structures shown are as follows: afferent arteriole (AA), efferent arteriole (EA), macula densa (MD), distal tubule (D), juxtaglomerular granular cell (G), sympathetic nerve endings (N), mesangial cell (M), extraglomerular mesangial cell (EGM), endothelial cell (E), epithelial podocyte (PO), with foot process (F), parietal epithelial cell (PE), glomerular basement membrane (GBM), urinary space (US), urinary pole (UP), and proximal tubule (P).

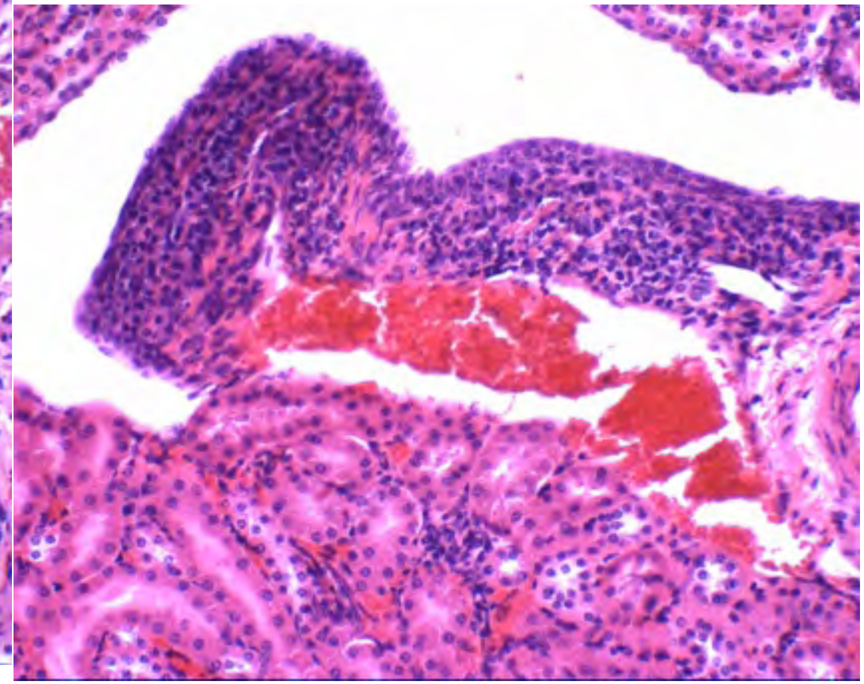
Primer on Kidney Diseases; NKF



Electron micrograph of a kidney glomerulus ...

	A	B	C
1	C57BL/6 blood chemistry normal ranges		n ~= 400
2	age ~ 2-5 months		
3		mean	sd
4			
5	Glucose (mg/dL)	196.7	91.2
6	Urea nitrogen (mg/dL)	21.4	4.4
7	Creatinine (mg/dL)	0.2	0.2
8	Bicarbonate (mEq/L)	15.9	3.2
9	Chloride (mEq/L)	107.5	4.2
10	Sodium (mEq/L)	150.5	3.9
11	Potassium (mEq/L)	5.0	1.1
12	Calcium (mg/dL)	9.0	0.4
13	Direct bilirubin (mg/dL)	0.1	0.1
14	Total bilirubin (mg/dL)	0.4	0.2
15	Albumin (g/dL)	1.4	0.2
16	Total protein (g/dL)	4.2	0.3
17	Phosphorus (mg/dL)	8.0	1.6
18	AST (SGOT) (IU/L)	72.7	36.3
19	ALT (SGPT) (IU/L)	38.7	25.9
20	Alkaline phos, total (IU/L)	101.5	32.2
21			
22	LIPID PANEL (n~=50)		
23	Lipase (U/L)	53.0	12.9
24	Cholesterol (mg/dL)	98.6	17.9
25	HDL-chol. (mg/dL)	78.6	21.9
26	LDL-chol. (mg/dL)	12.2	8.6
27	Triglycerides (mg/dL)	67.8	26.1
28			





Pathology of kidney:

Inflammation:

---glomerular = glomerulonephritis,-autoimmune

---tubular=pyelonephritis

hyperplasia, accumulations:

fibrosis/scarring, cysts

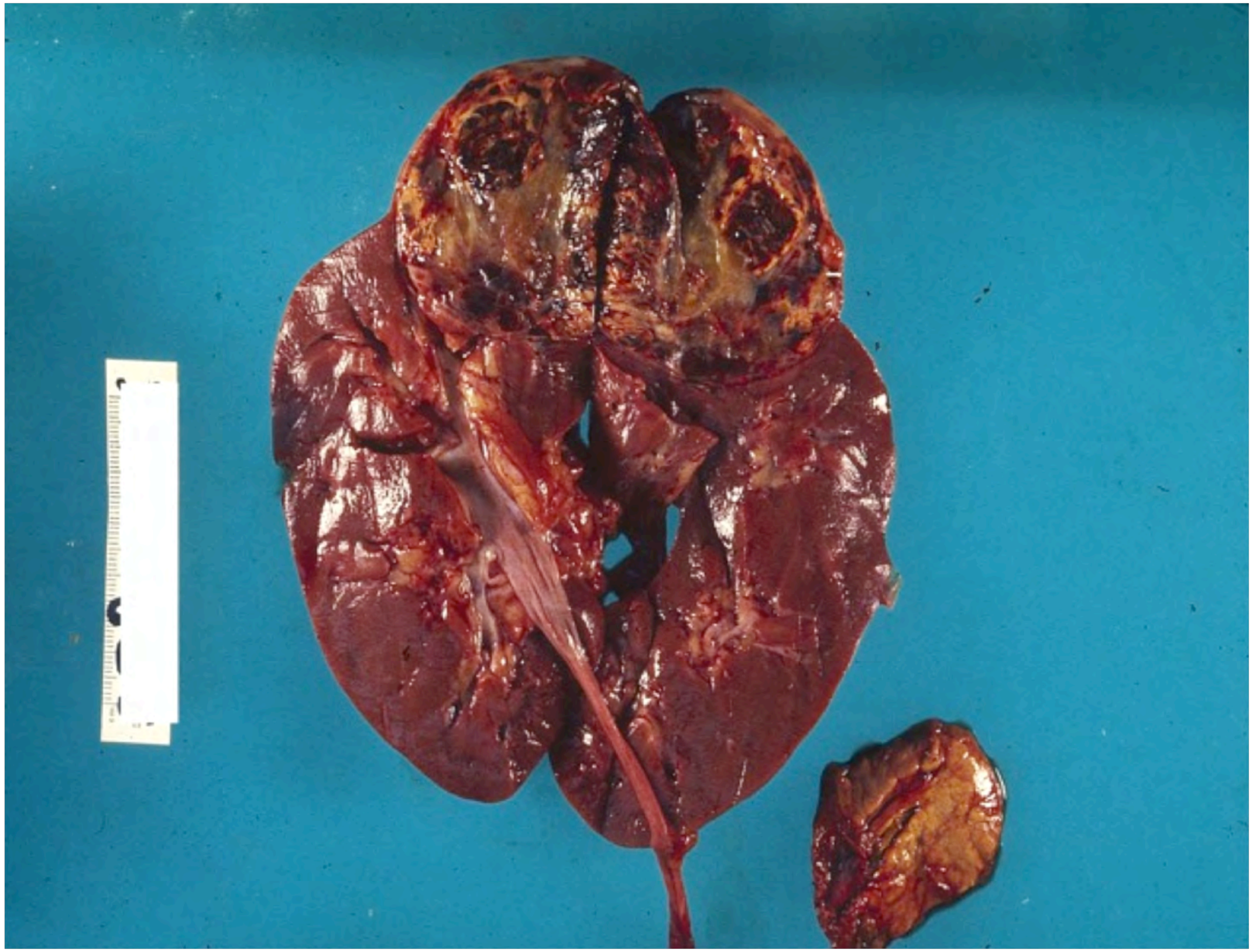
Infarct

Cancer: **primary adenocarcinomas or metastatic**

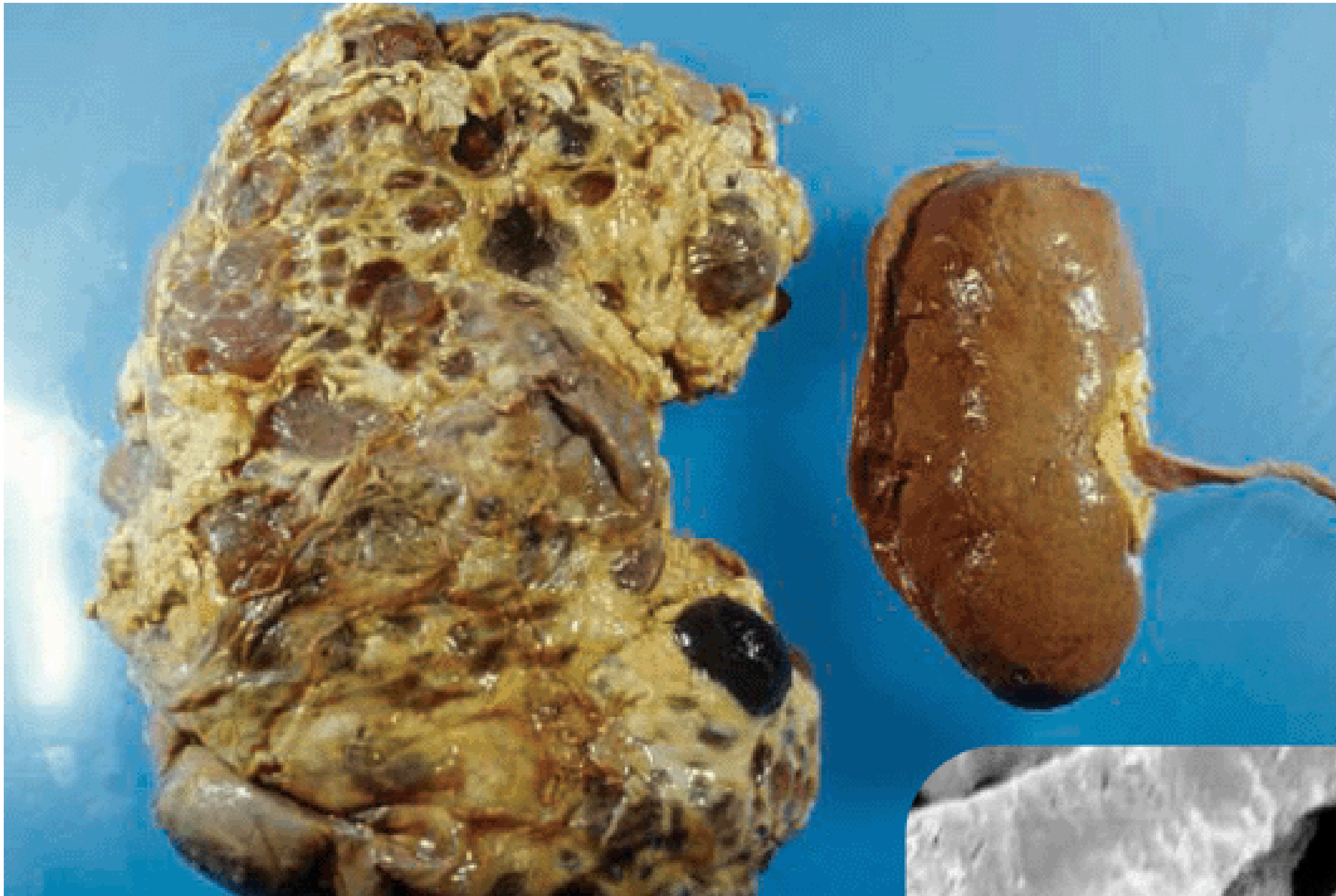
Simple cysts in human kidney

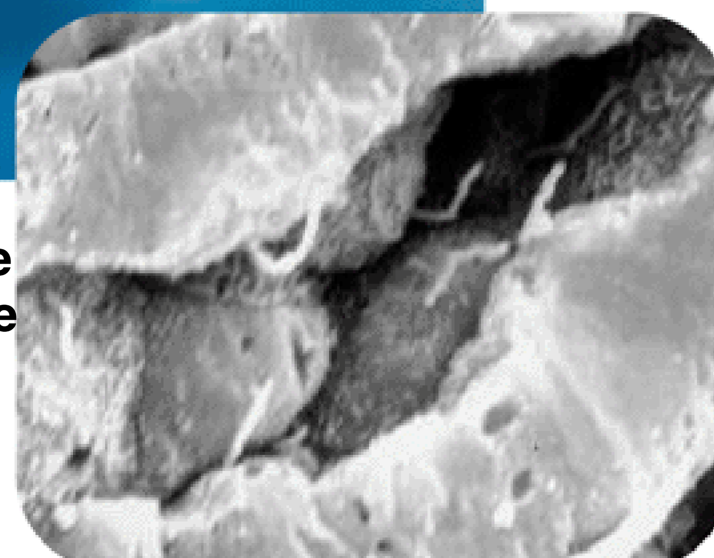
http://www-medlib.med.utah.edu

As mice age, the kidneys develop similar cysts due to chronic pyelonephritis (Tubules inflammation, scarring and repair) with consequent stasis



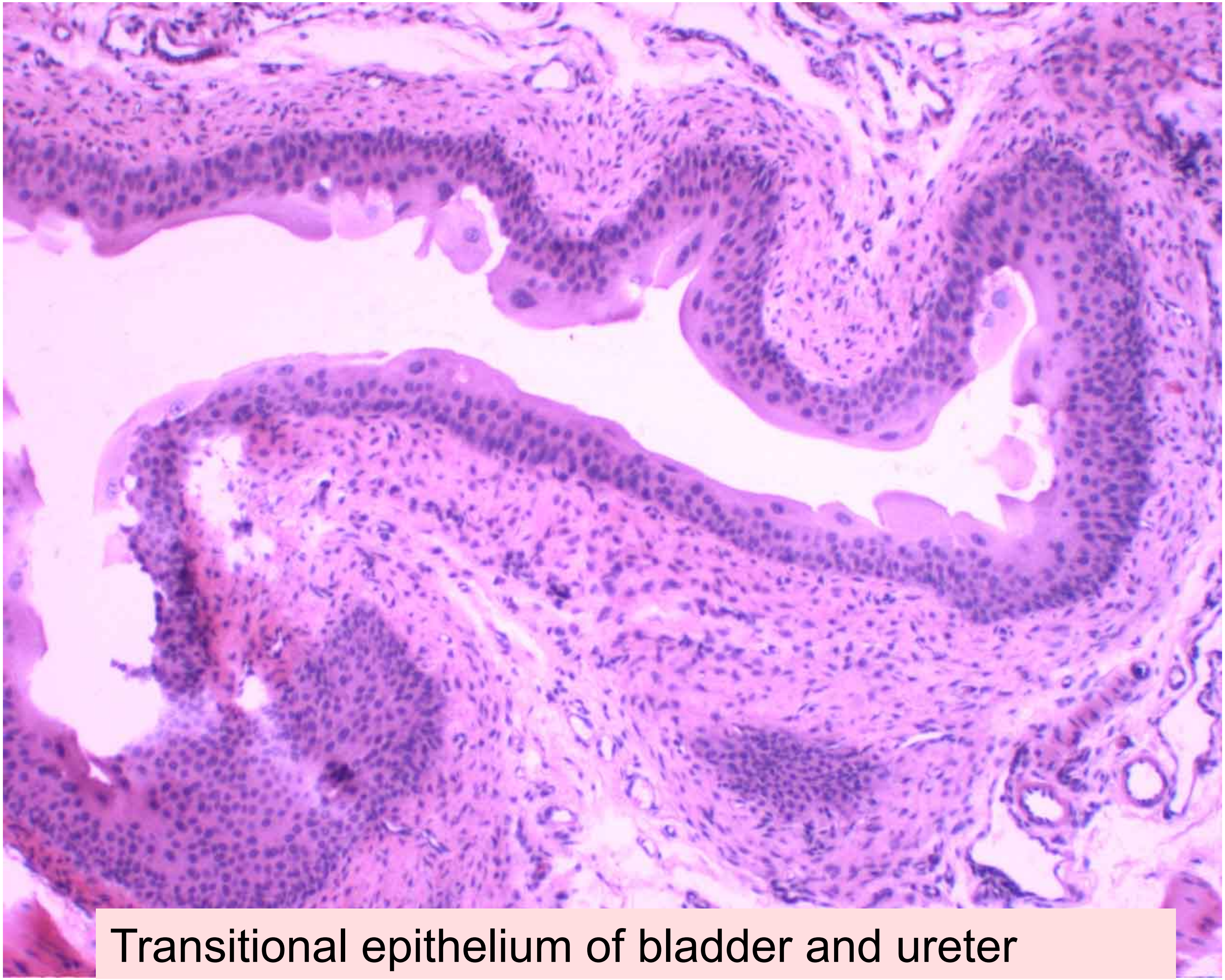
Resected renal cell carcinoma, at upper pole of the kidney



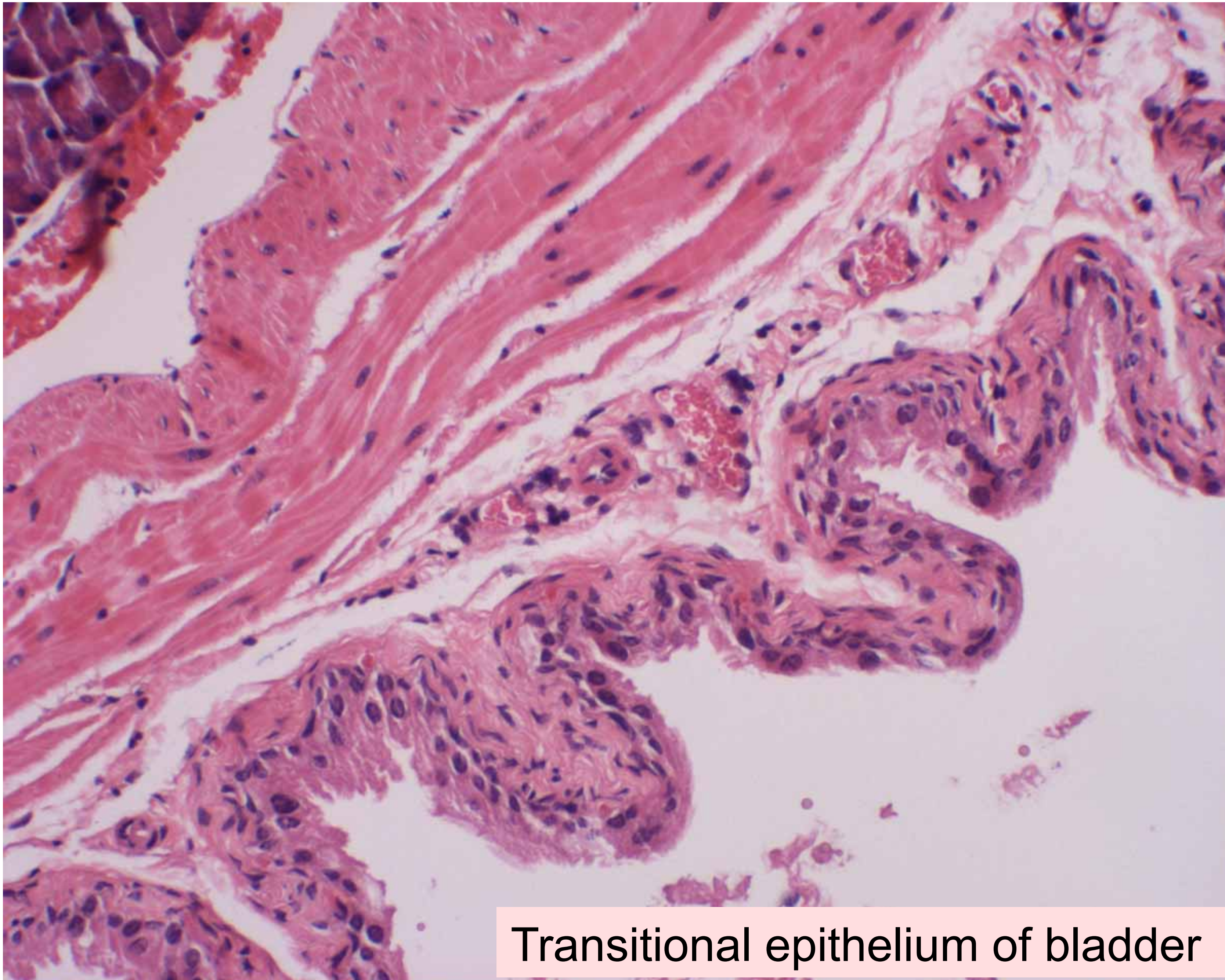


Compared to a normal kidney (*right*), those from people with polycystic kidney disease (*left*) are enlarged and ravaged with cysts. Defects in the primary cilia on kidney tubule epithelial cells (*inset*) lead to the devastation. Science Oct 14, 2005

H&E of mouse Kidney Pelvis x40 magnification



Transitional epithelium of bladder and ureter



Transitional epithelium of bladder

Histologic highlights within the Female and Male Reproductive systems

Uterus, Fallopian Tubes, ovaries

Human

Mouse

Stages of ovarian follicular development

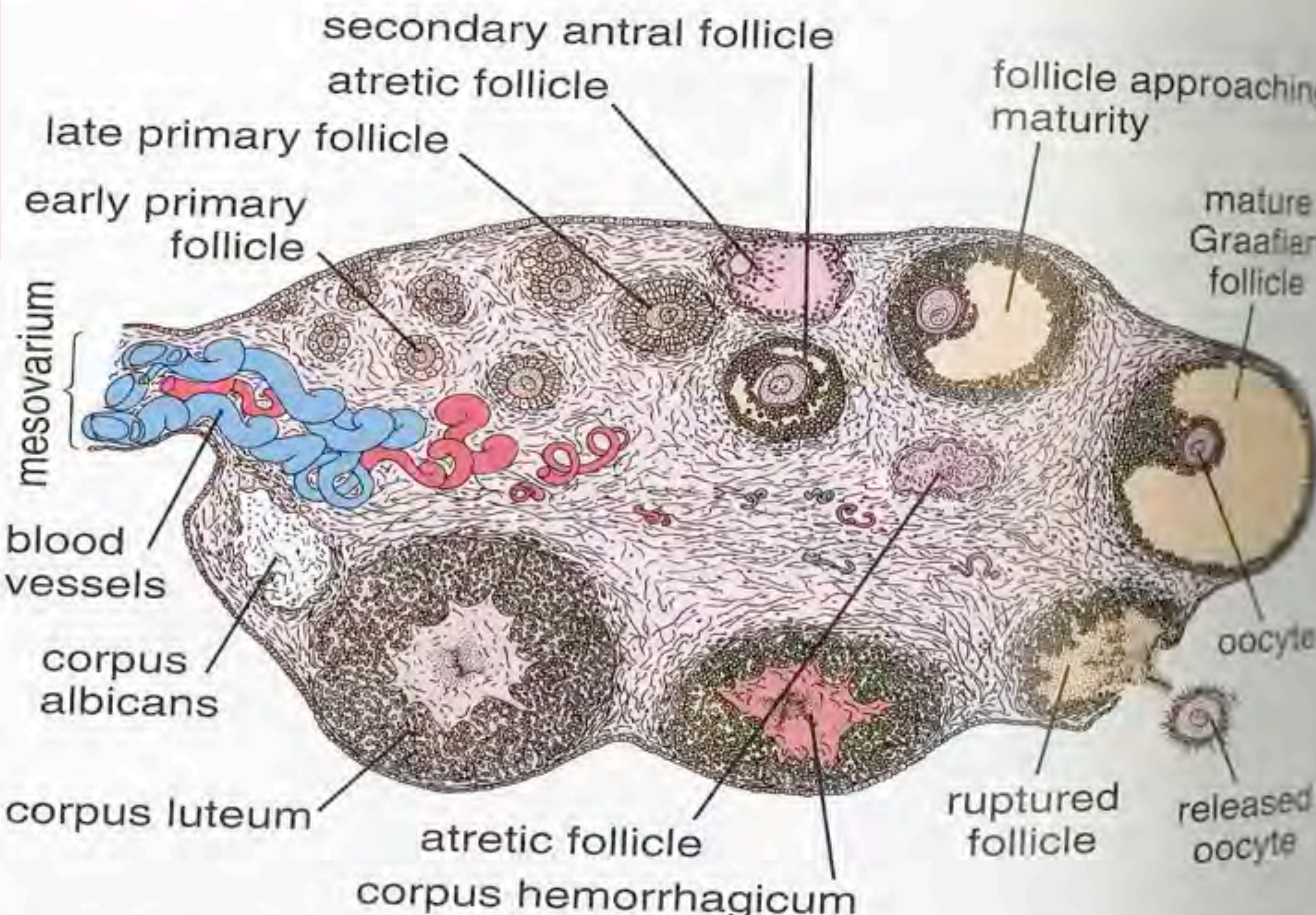


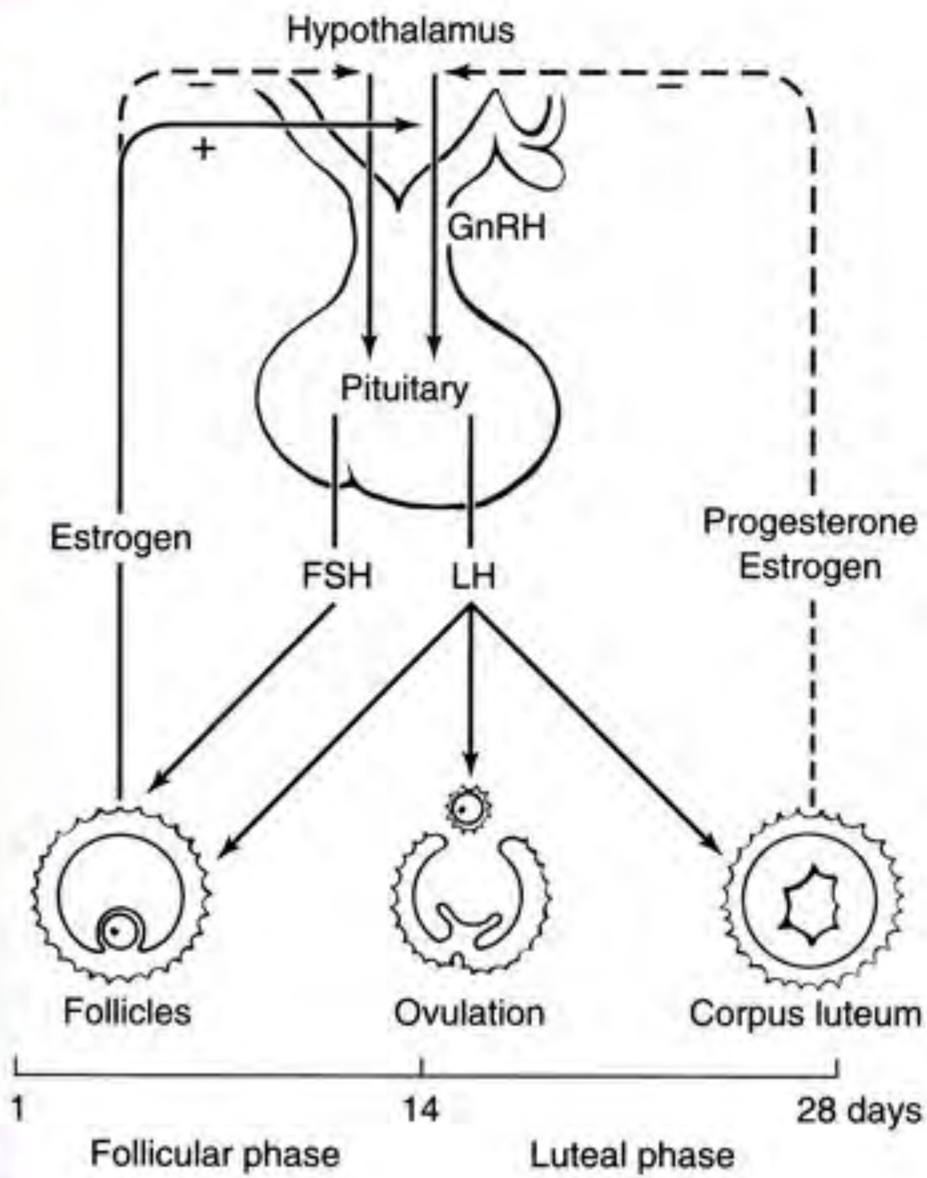
FIGURE 23.2 Schematic drawing of a section through the ovary. This section shows, in clockwise order, stages of follicular development from the early primary follicle to the mature (Graafian) follicle. Changes in the follicle after ovulation lead to development of the corpus luteum and eventually the corpus albicans. Note the highly coiled blood vessels in the hilum and medulla of the ovary.

Hormonal control of the Ovary

At the time of menstruation, **Follicular Stimulating Hormone (FSH)** from the pituitary, initiates follicular growth.

At the time of the maturation of the follicle, the **estrogen** rise leads (via the hypothalamic interface) to the "positive feed-back" effect, and a release of **Luteinizing Hormone (LH)** occurs over a 24-48 hour period.

This 'LH surge' triggers ovulation.

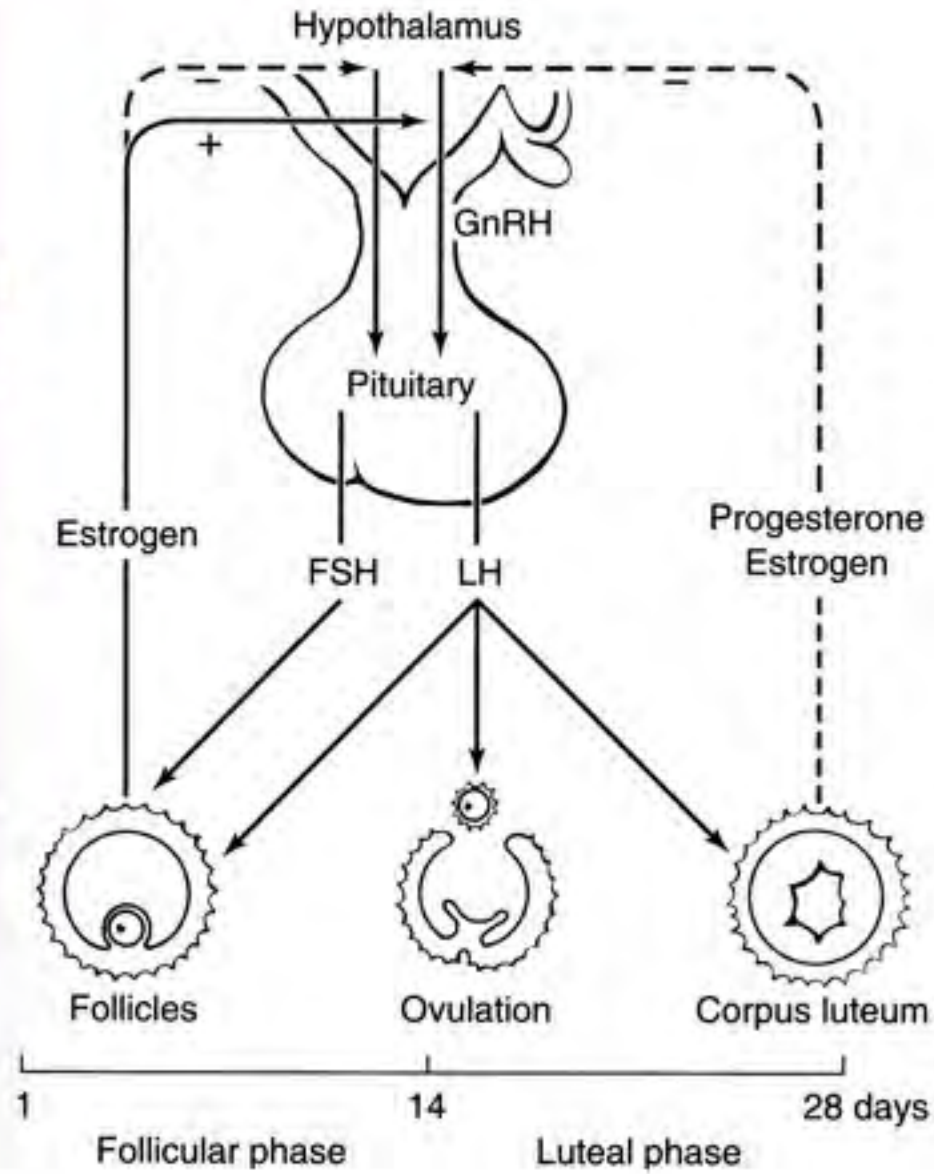


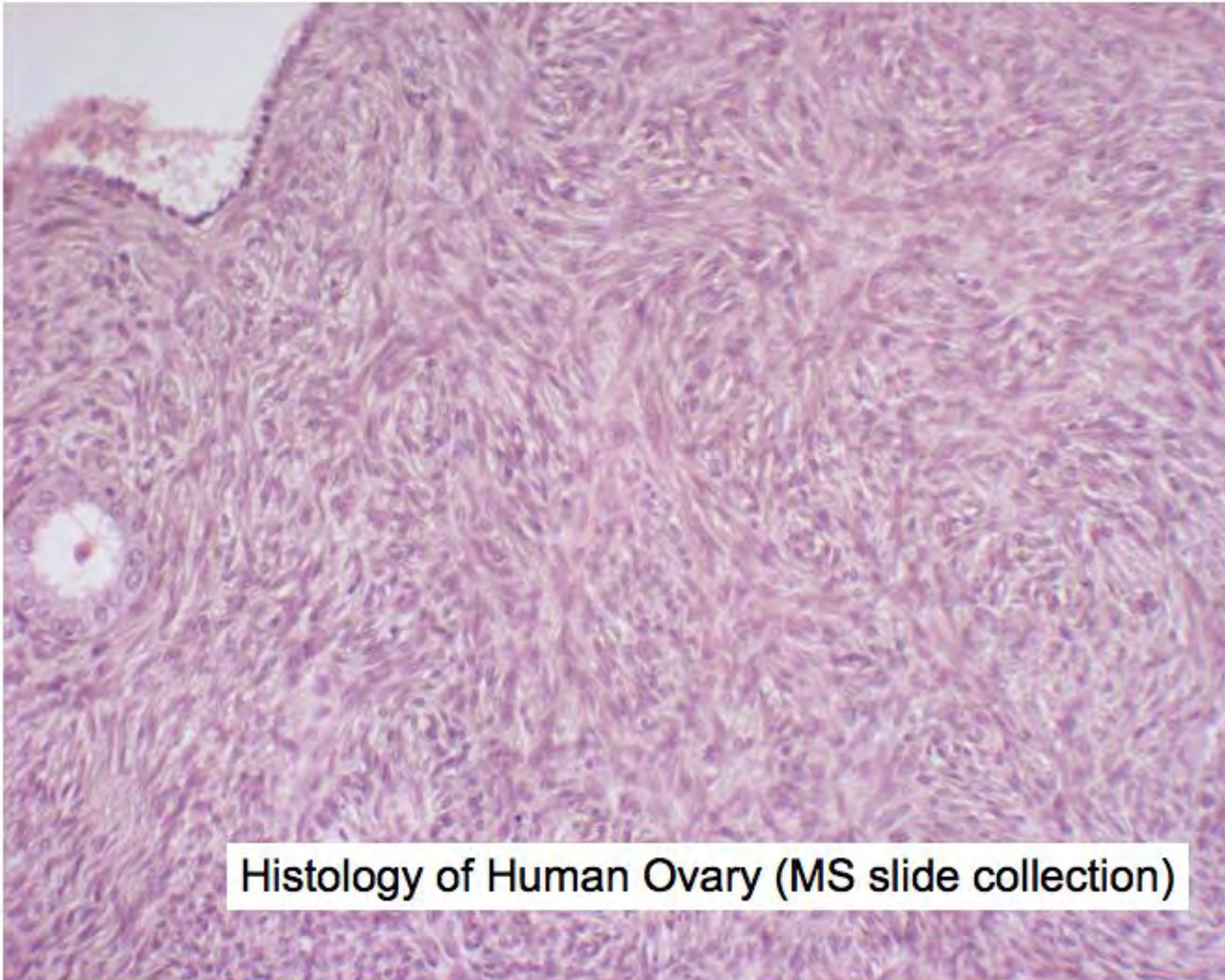
Hormonal control of the Ovary

The LH surge not only releases the egg, but also initiates the conversion of the residual follicle into a corpus luteum.

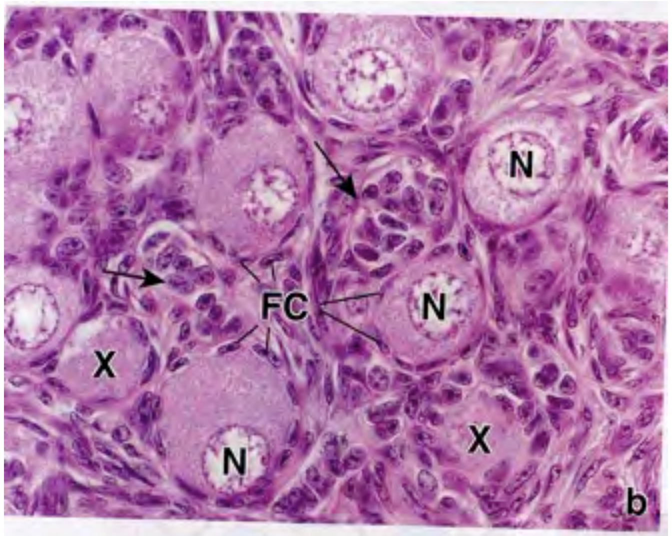
The corpus luteum in turn, produces progesterone to prepare the endometrium for a possible implantation .

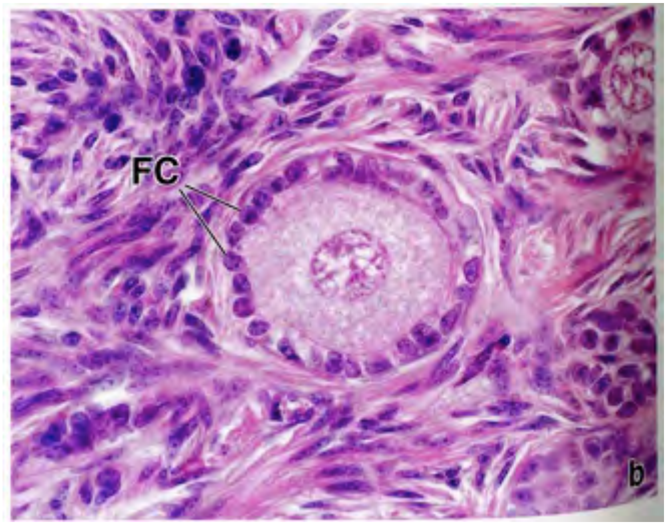
If there is no pregnancy, corpus luteum is cleared



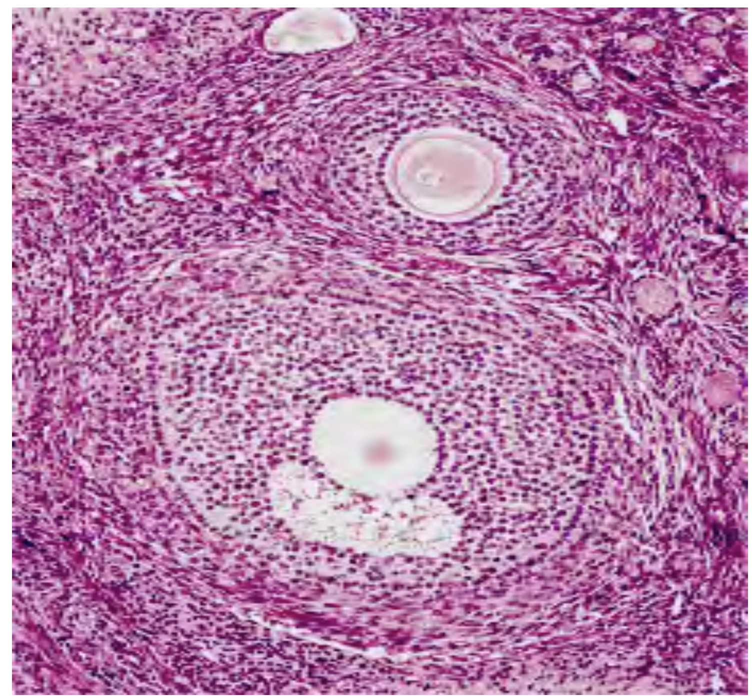


Histology of Human Ovary (MS slide collection)





Stages of development of the ovarian follicle



Fluid in antrum of secondary follicle

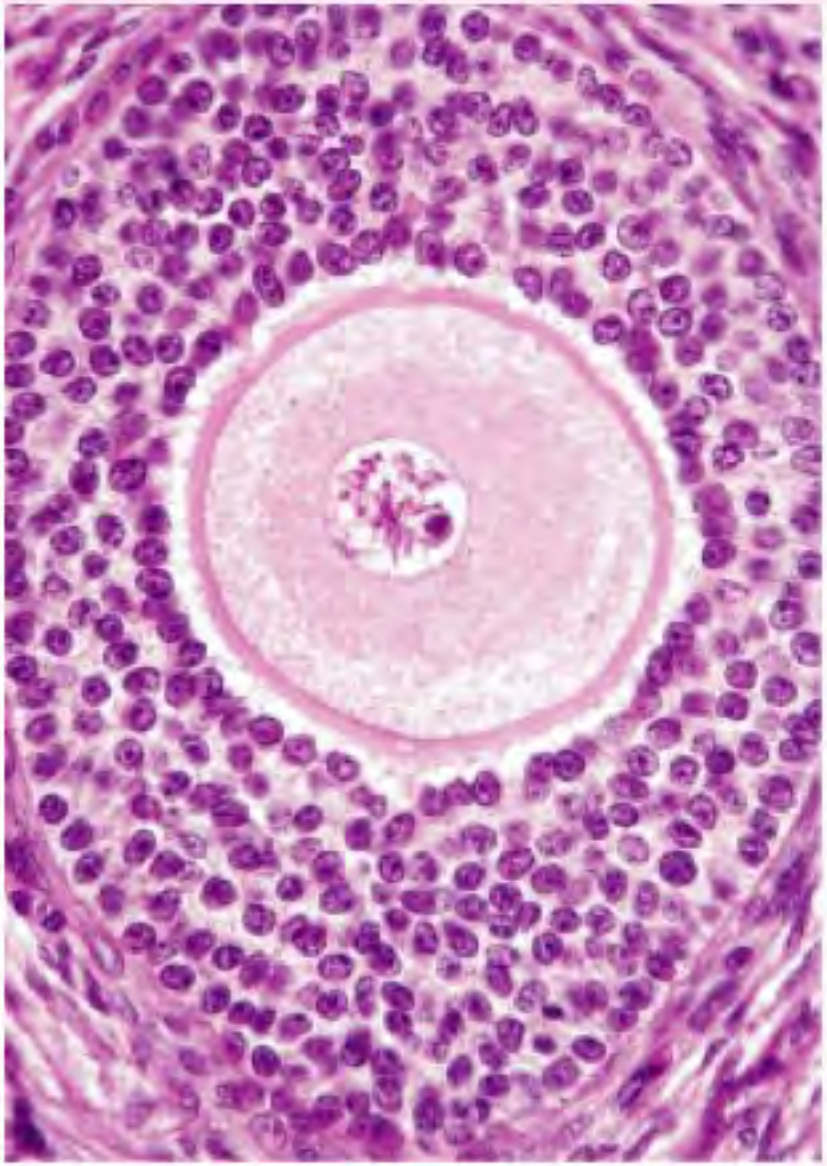
Stages of Ovarian follicle maturation

Primary Follicle

- oocyte
- zona pellucida
- granulosa cells
- theca folliculi

The **Zona Pellucida**: an acellular acidophilic glycoprotein ring that surrounds the oocyte

The primary follicle increases in size with the proliferation of the granulosa cells under the influence of FSH, Growth factors and calcium ions



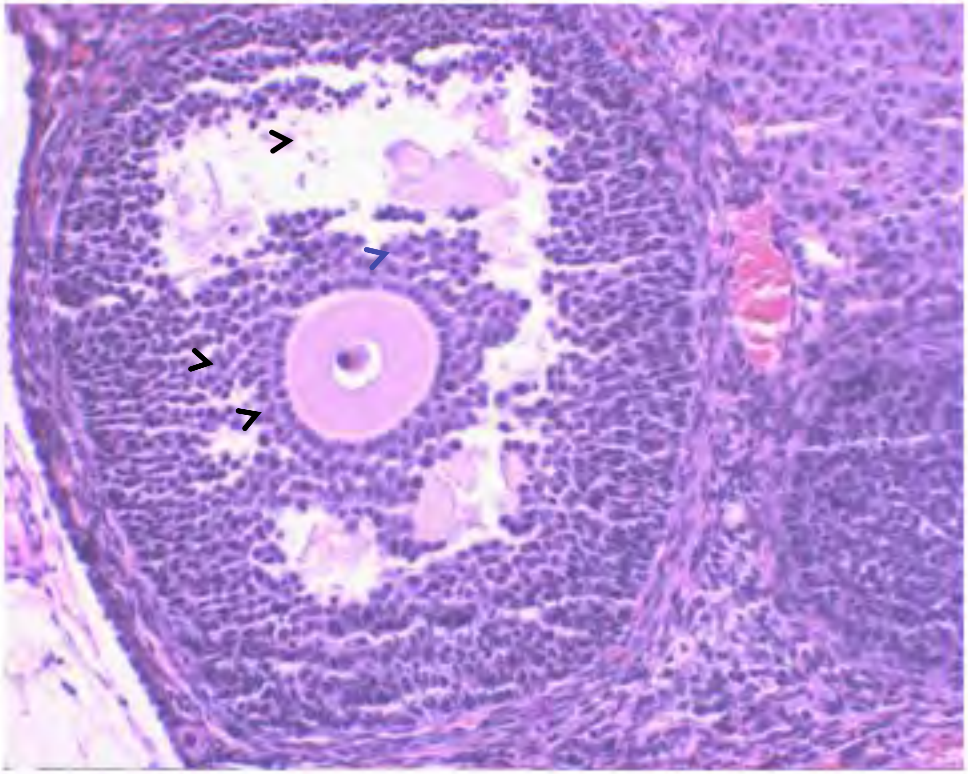
Stages of Ovarian follicle maturation

liquor folliculi

cumulus oophorus

corona radiata

Zona pellucida



Mature or Graafian follicle
(~10 mm diameter)

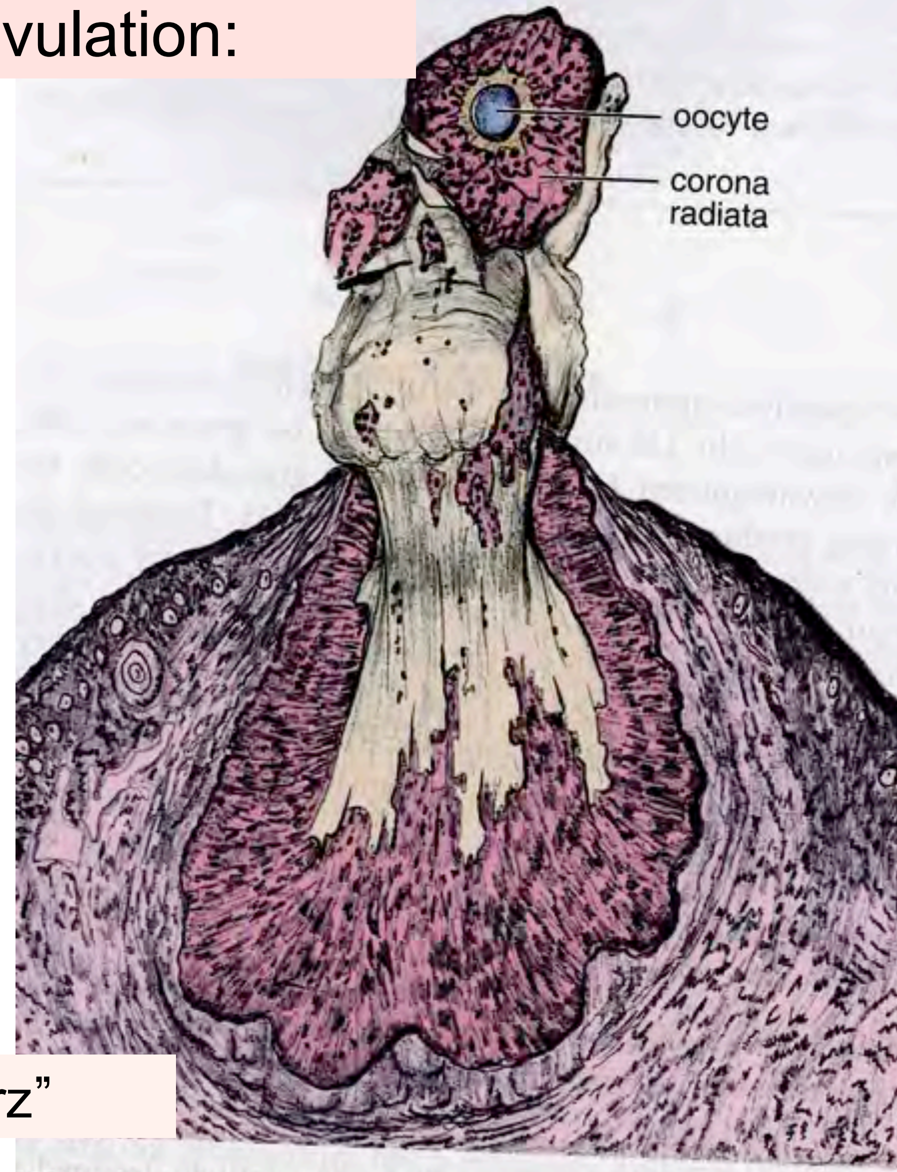
Mature or Graafian follicle and ovulation:

Bulges from the ovarian surface

The Primary oocyte resumes the First Meiotic division, forming the Secondary oocyte and the first polar body

Just as the Secondary oocyte enters the Second meiotic division, Ovulation occurs

“mittelschmerz”



IGURE 23.8 Ovulation. This drawing shows a rabbit oocyte, surounded by the cumulus oophorus, being expelled from the ruptured varian follicle. (Based on Weiss L, Greep RO. Histology, 4th ed. New ork: McGraw-Hill, 1977.)

OVARIES

Corpus luteum (yellow body --after ovulation)

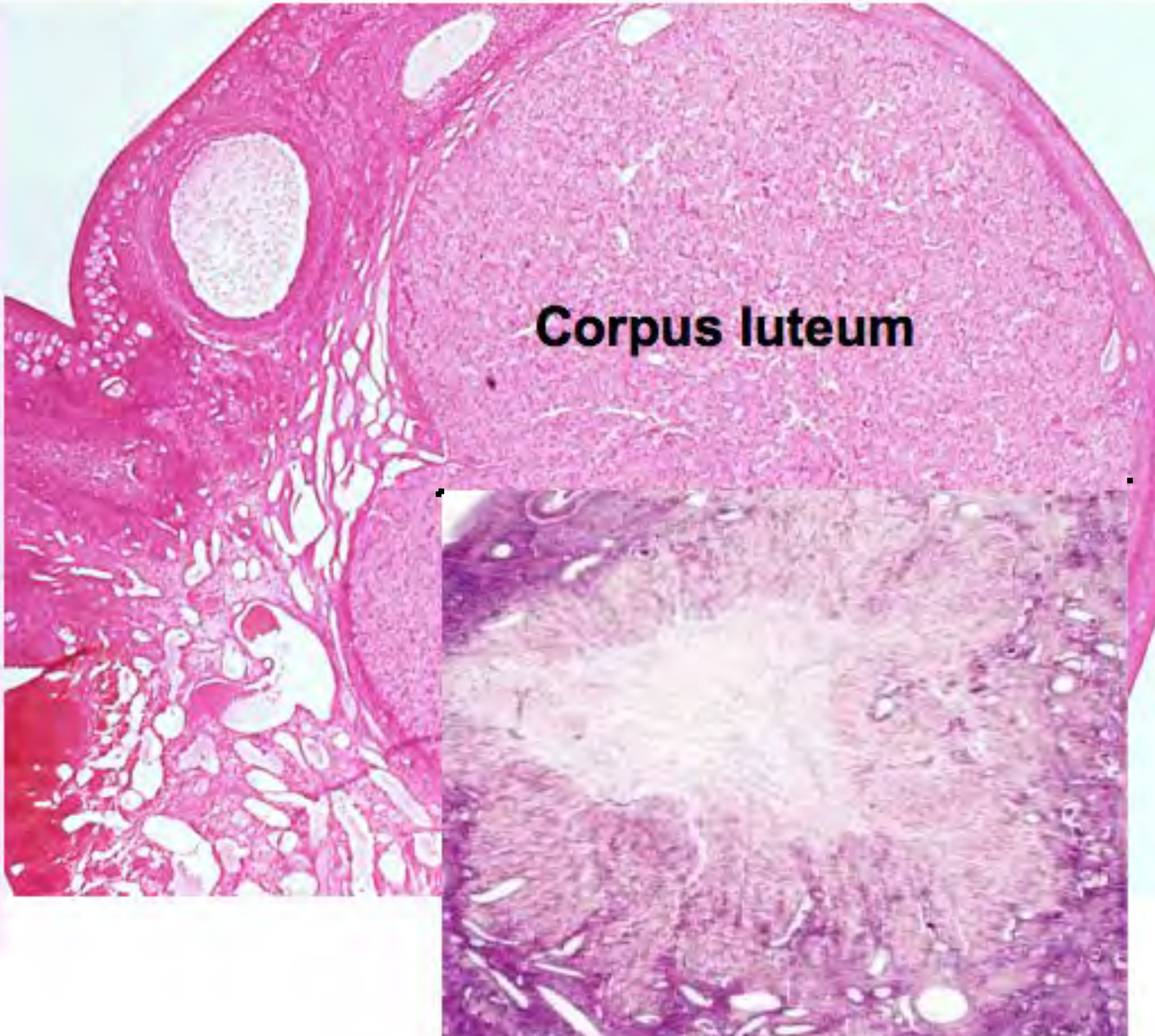
http://library.med.utah.edu/WebPath/FEMHTML/FEM045.html

Stages of Ovarian follicle maturation

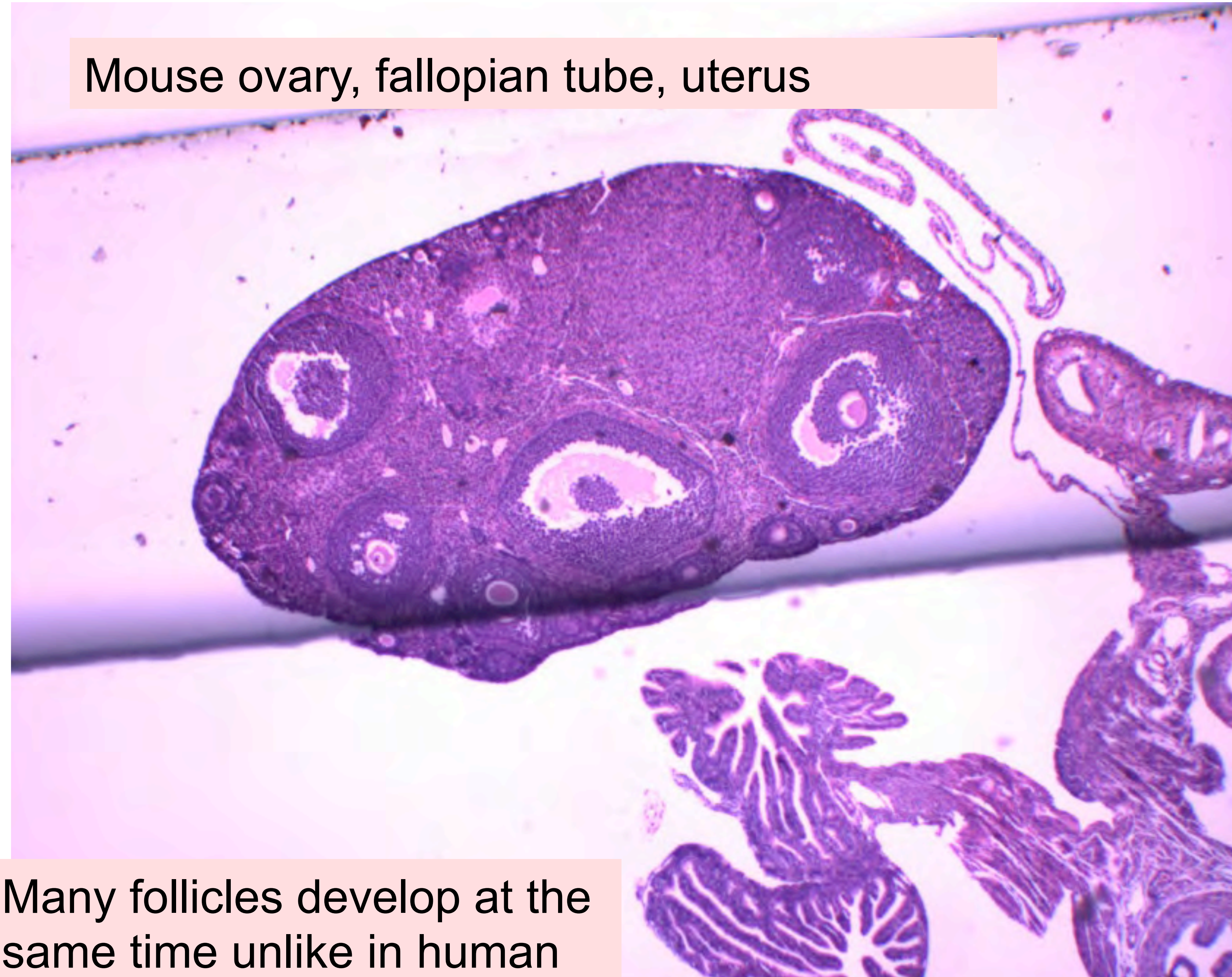
Following ovulation, the follicle the **corpus luteum** starts producing **progestogens.**

If fertilization does not occur, it undergoes atresia after 10-14 days

If fertilization does occur, it persists for about 6 months, stimulated by **placental human chorionic gonadotropin.**

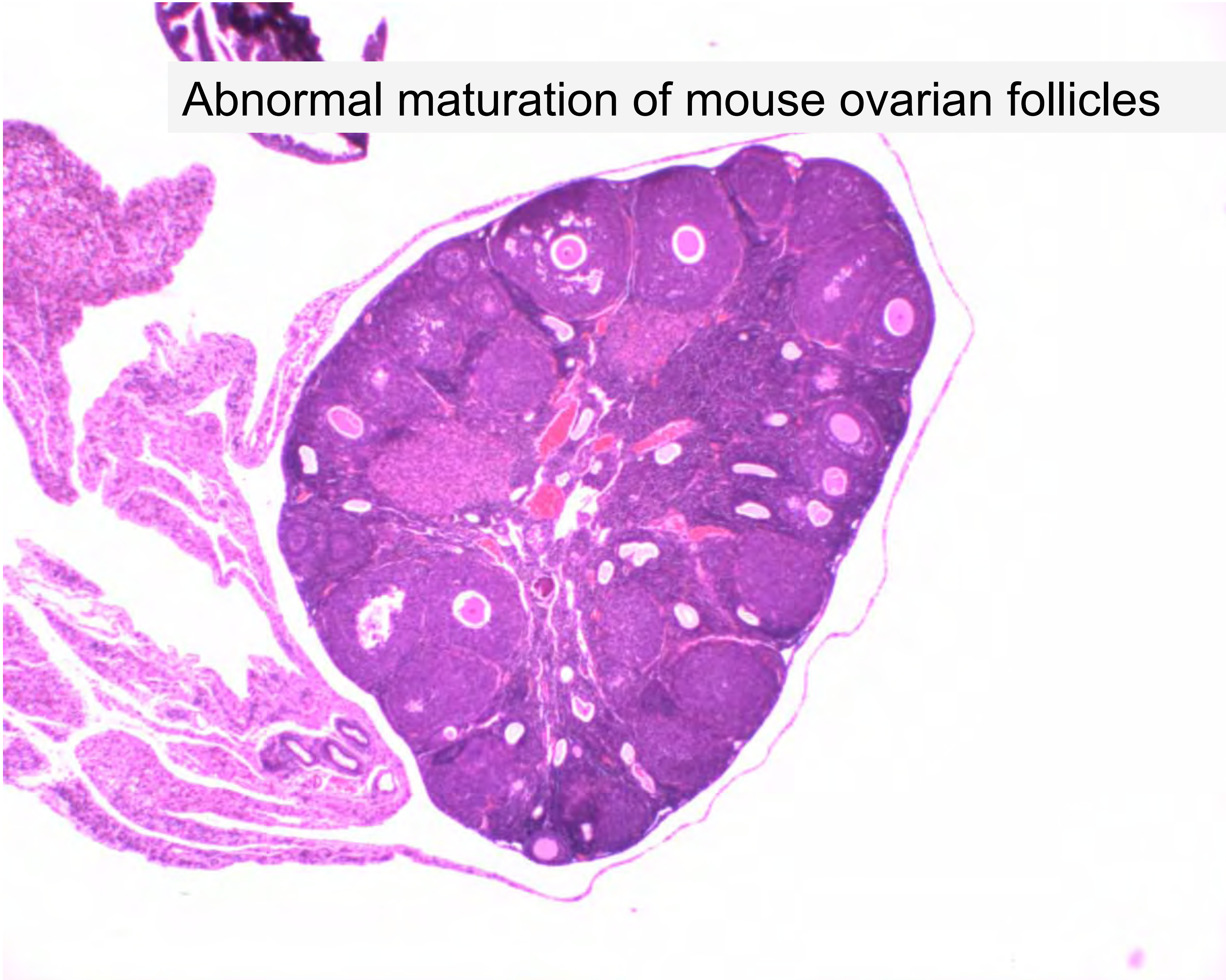


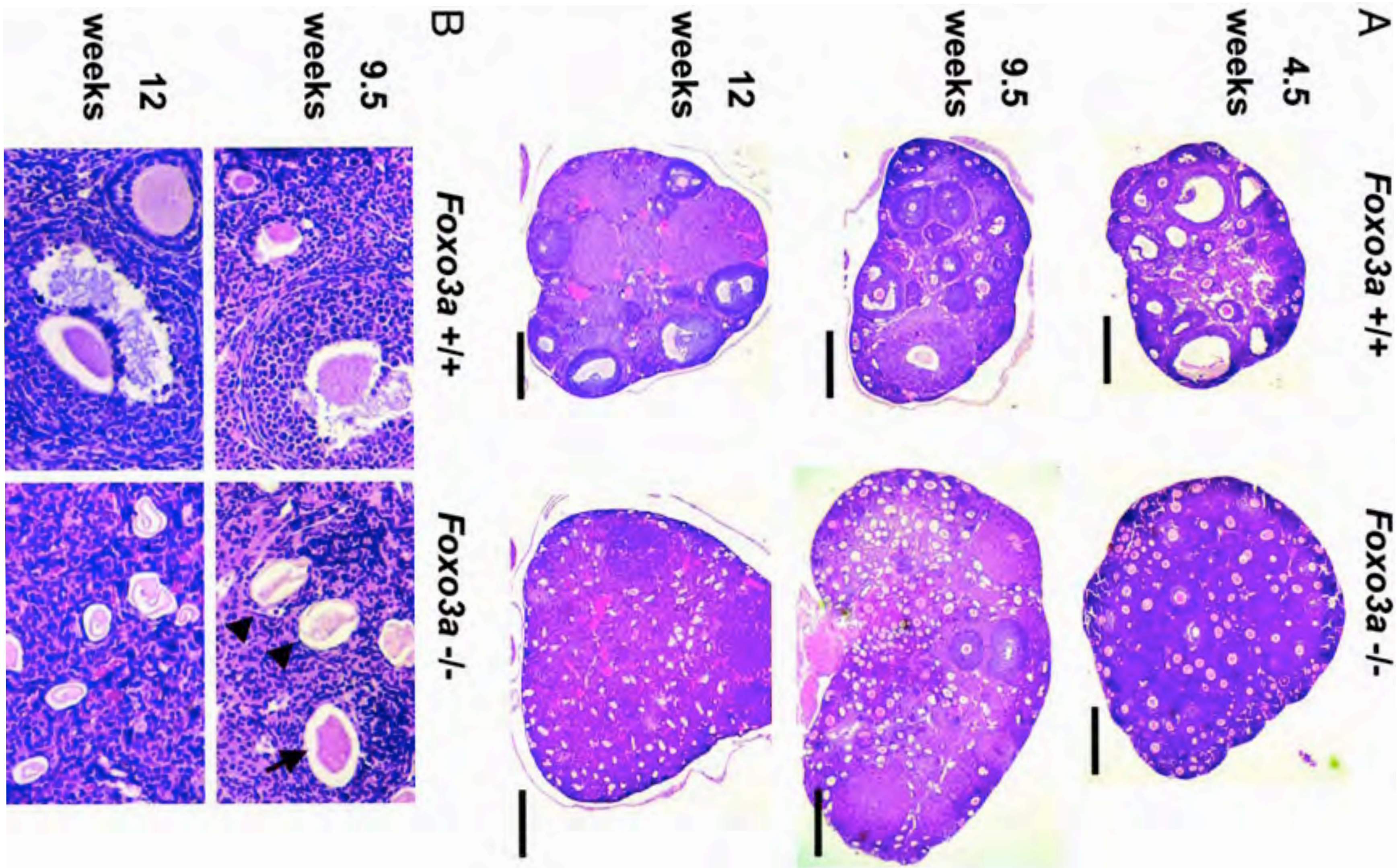
Mouse ovary, fallopian tube, uterus



Many follicles develop at the same time unlike in human

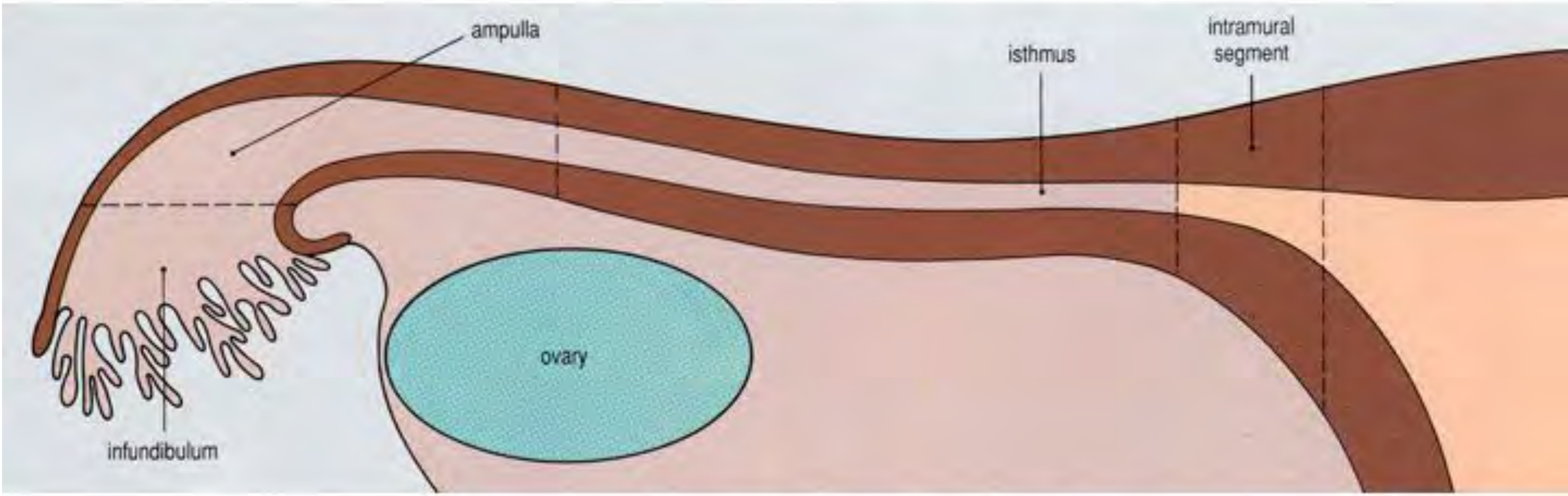
Abnormal maturation of mouse ovarian follicles





Hosaka T, Biggs WH 3rd, Tieu D, Boyer AD, Varki NM, Cavenee WK, Arden KC. Proc Natl Acad Sci U S A. 2004 Mar 2;101(9):2975-80

Fallopian Tube

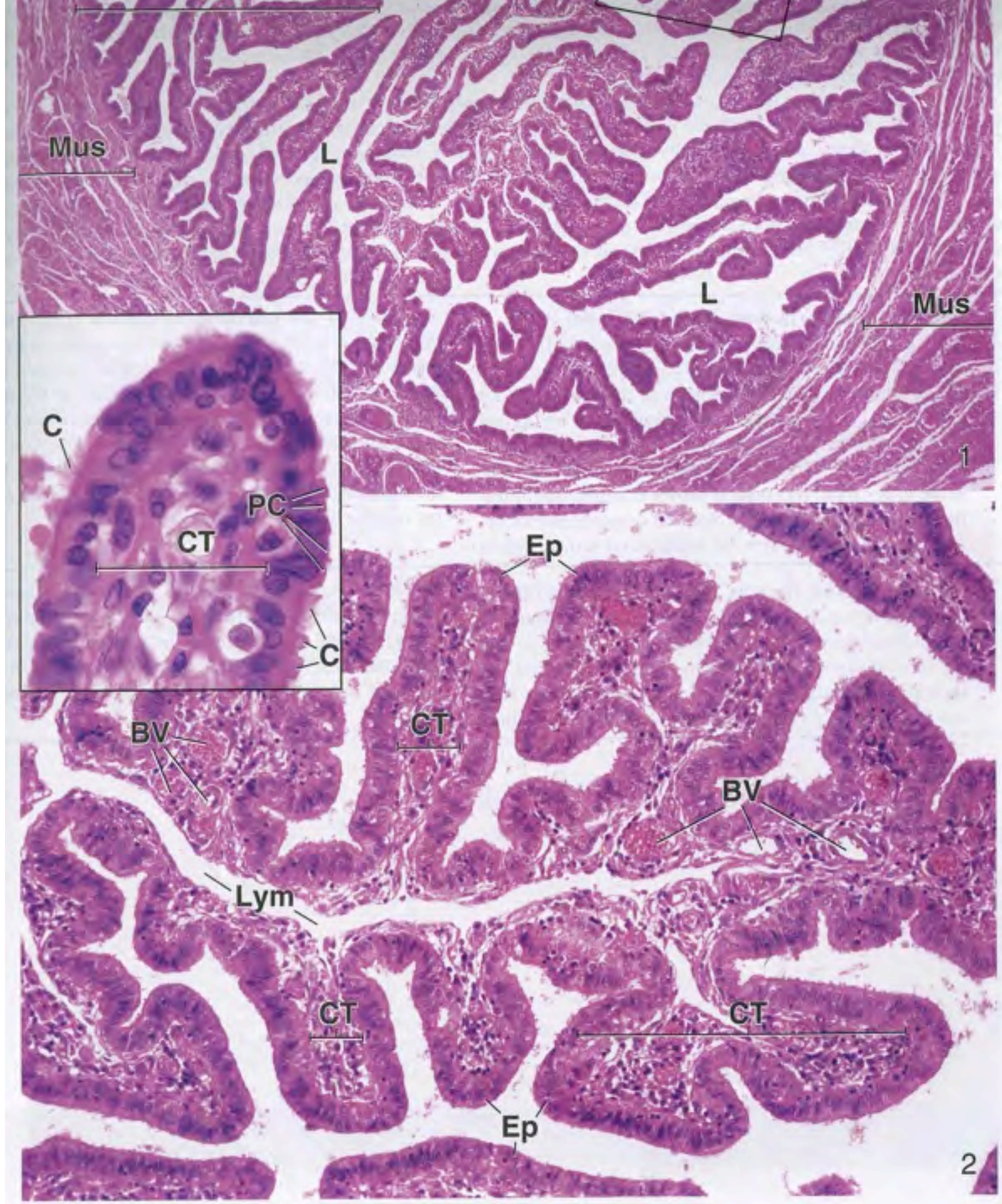


The Fallopian tubes are paired structures (upto about 12 cm in length and 7 mm in diameter)

They are the site of fertilization and development of the early embryo to the blastocyst stage

4 regions:

- infundibulum
- ampulla
- isthmus
- intramural region



Fallopian tube at different magnifications

Fallopian Tube, epithelium

Mucosa consists of simple columnar epithelium

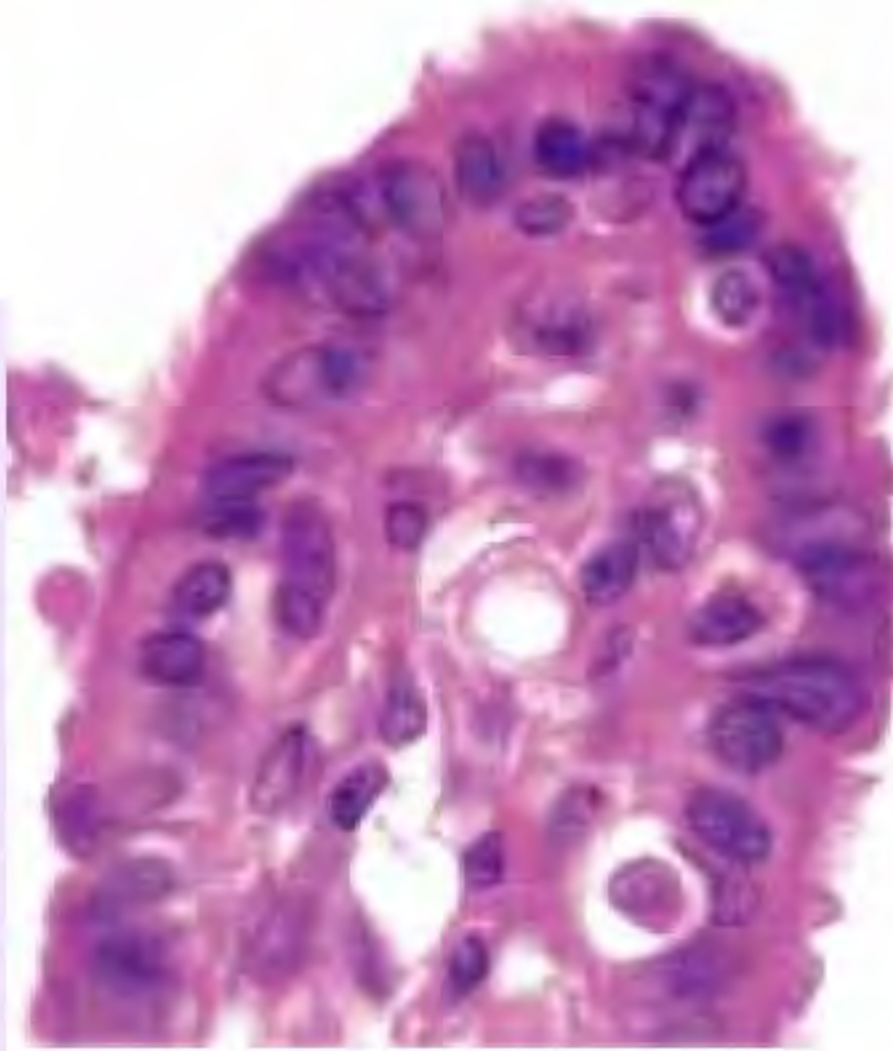
2 types of epithelial cells:

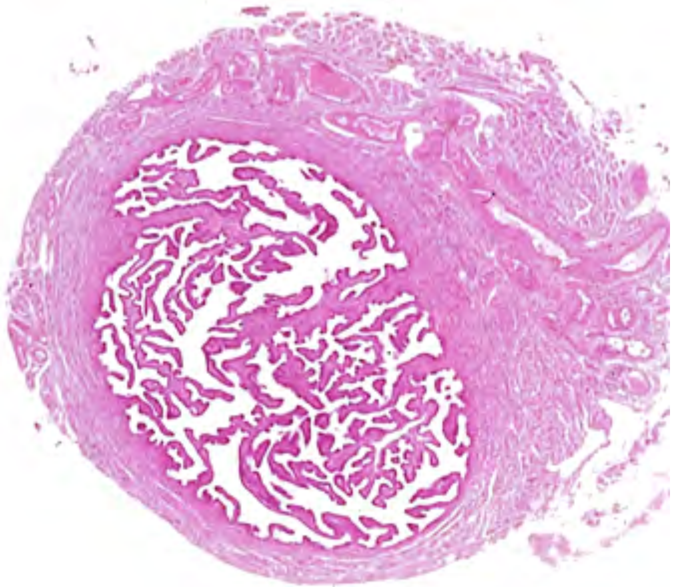
•**ciliated cells,** especially in the fimbrial portion to assist with *ovum transport (and sperm transport)*

• **secretory cells** (peg cells):

--*ovum nutrition*

--*sperm capacitation*

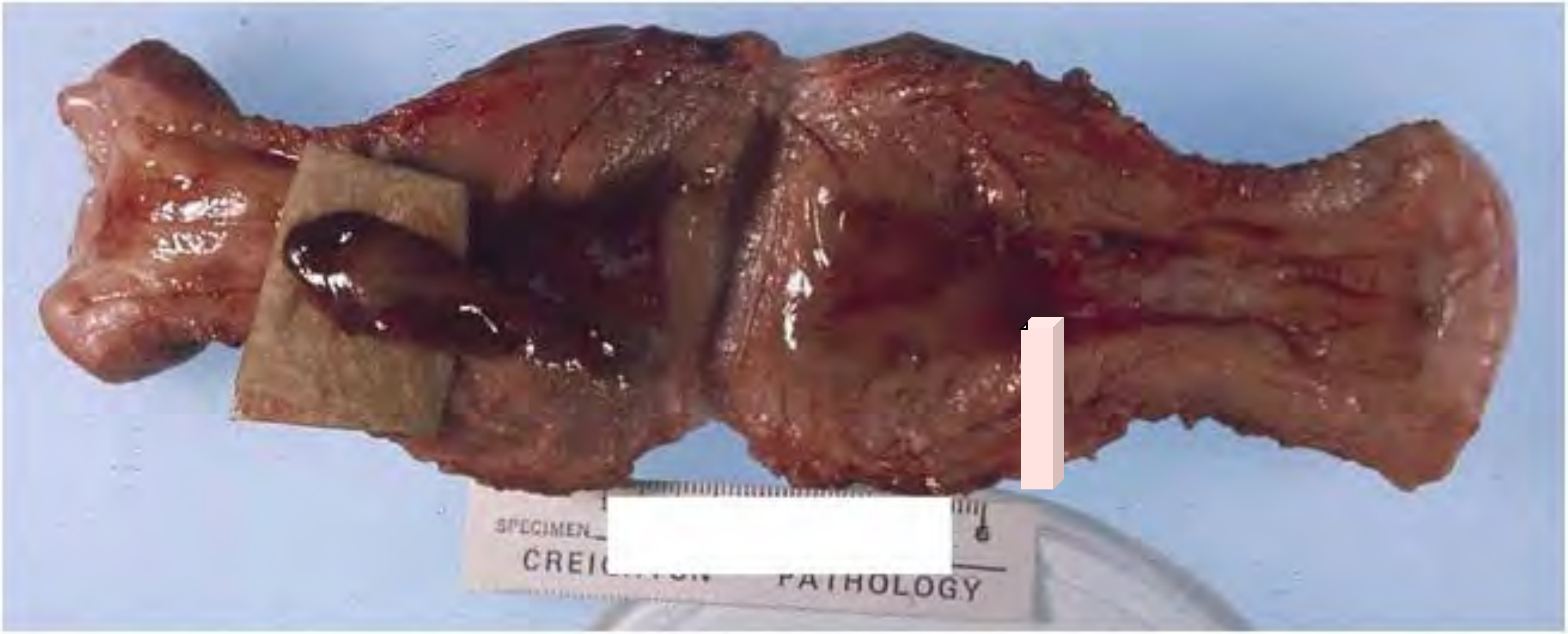




Normal human fallopian tube with highly folded mucosa at the ampulla which is the usual site of fertilization

Abnormal human fallopian tube which are both blocked and dilated after infectious events

UTERUS

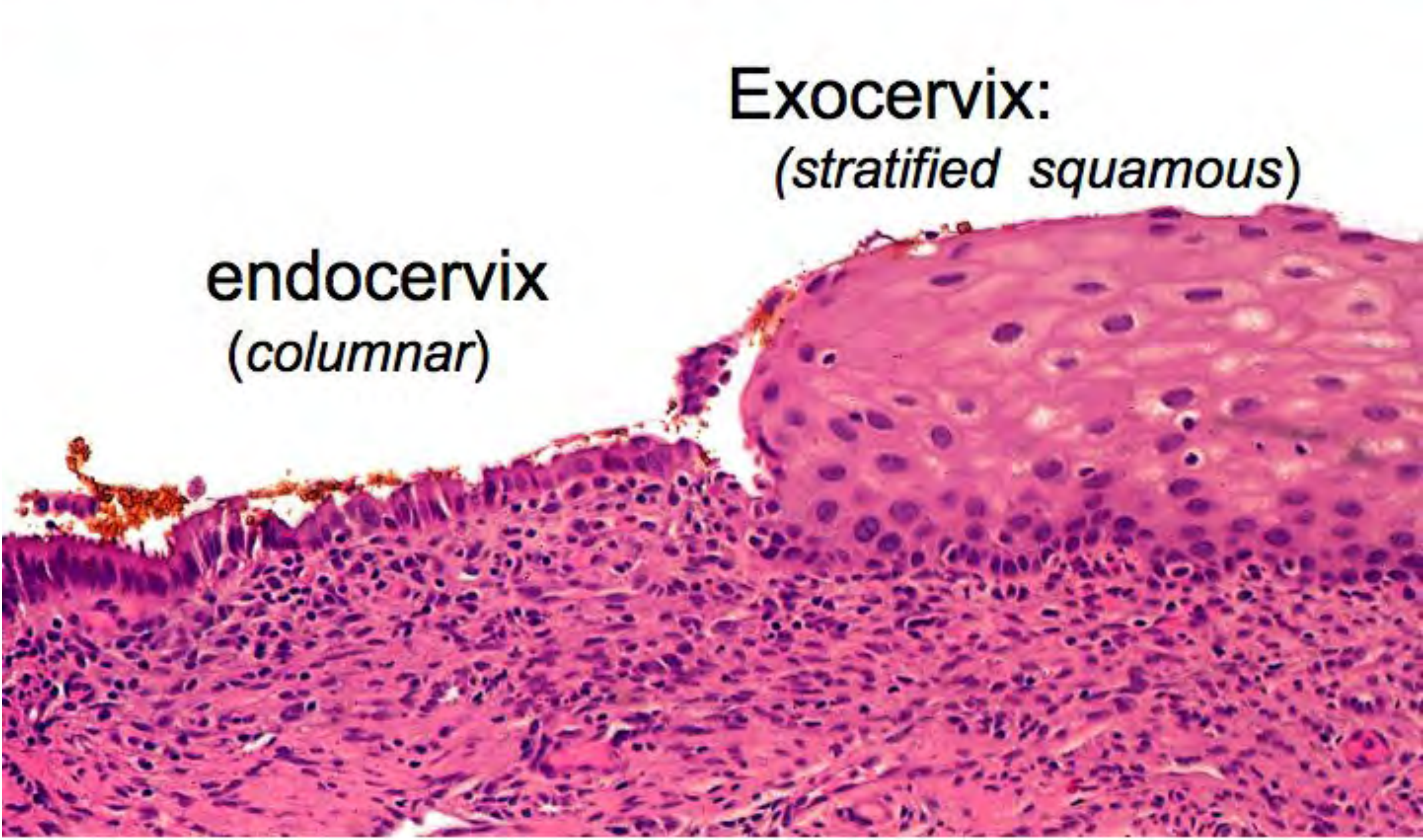


The Uterus is a hollow, muscular pear-shaped organ (~6.5 cm long, 3.5 cm wide and 2.5 cm thick

It has a body with a an upper fundus and a distal cervix

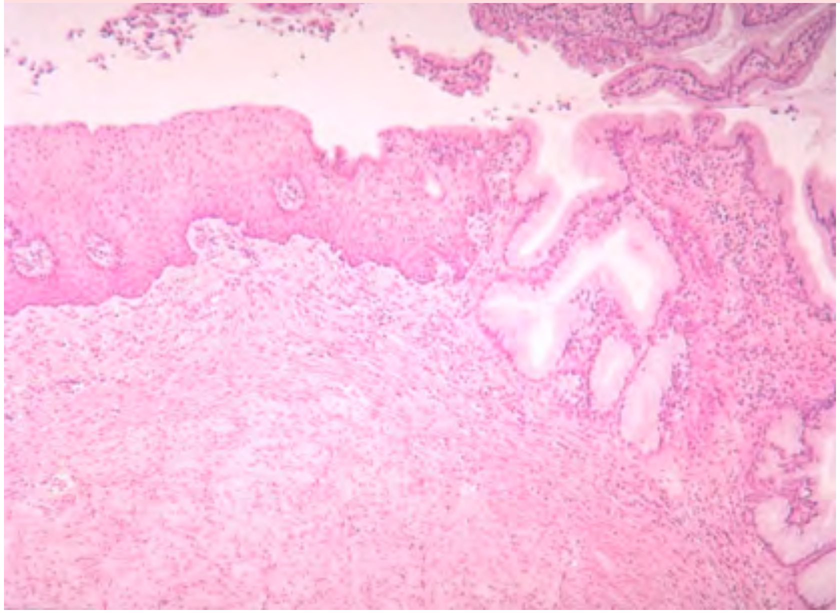
There are 3 layers: the endometrium, myometrium and serosa

Abrupt squamo-columnar junction

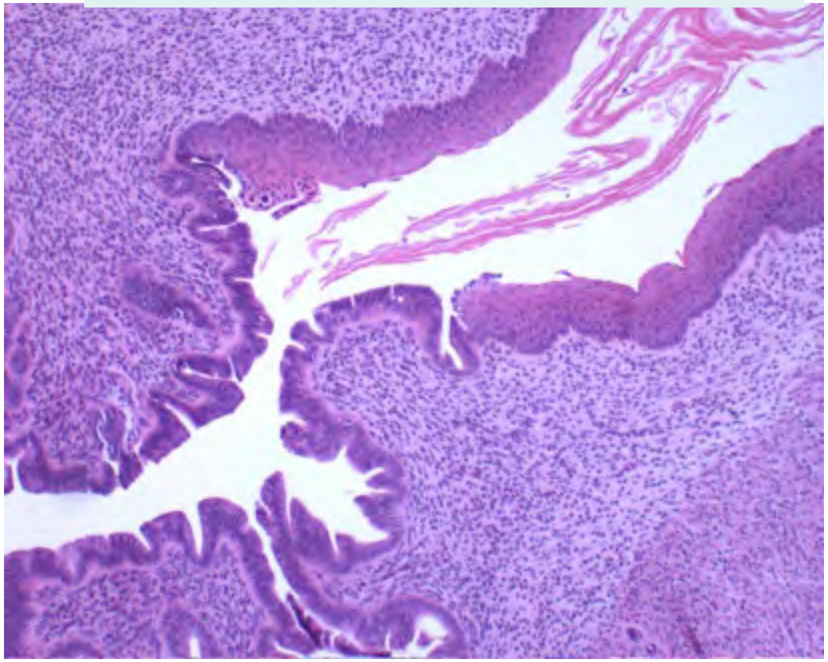


Squamo-columnar junction of cervix

Human ecto and endo cervix



Mouse endo and ecto cervix



Differences from Human Menstrual Cycle
One of the main differences between the rodent and the human cycle, other that the overall time it takes for a full cycle, is that the peaks of estrogens and progesterone are typically separated in humans, whereas these overlap in rodent.

In the mouse, the estrous cycle is divided into 4 stages (proestrus, estrus, metestrus, and diestrus) and repeats every 4 to 5 days unless interrupted by pregnancy, pseudopregnancy, or anestrus.

http://www.biobserve.com/downloads/maria-gulinello/Rodent-Estrous-Cycle.pdf

Behavioral Core

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Behavioral Core Facility
Albert Einstein College of Medicine

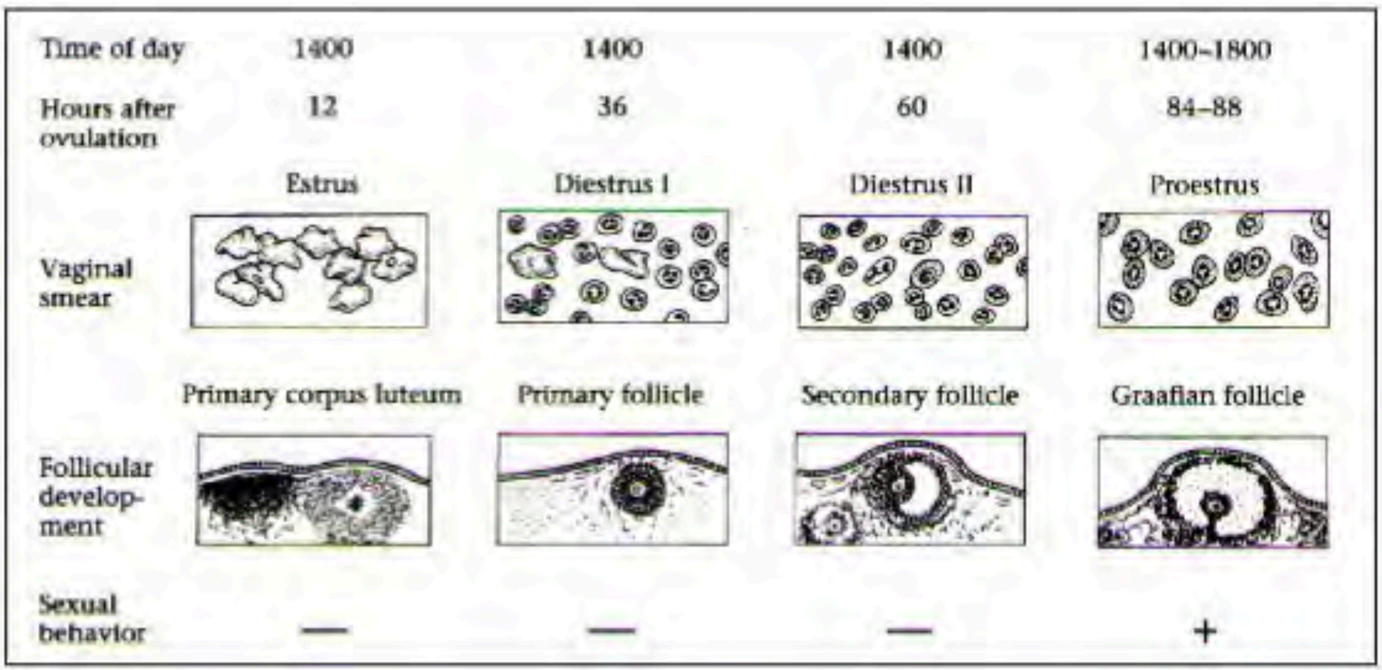
<u>Behavioral Core Protocols and Training</u>

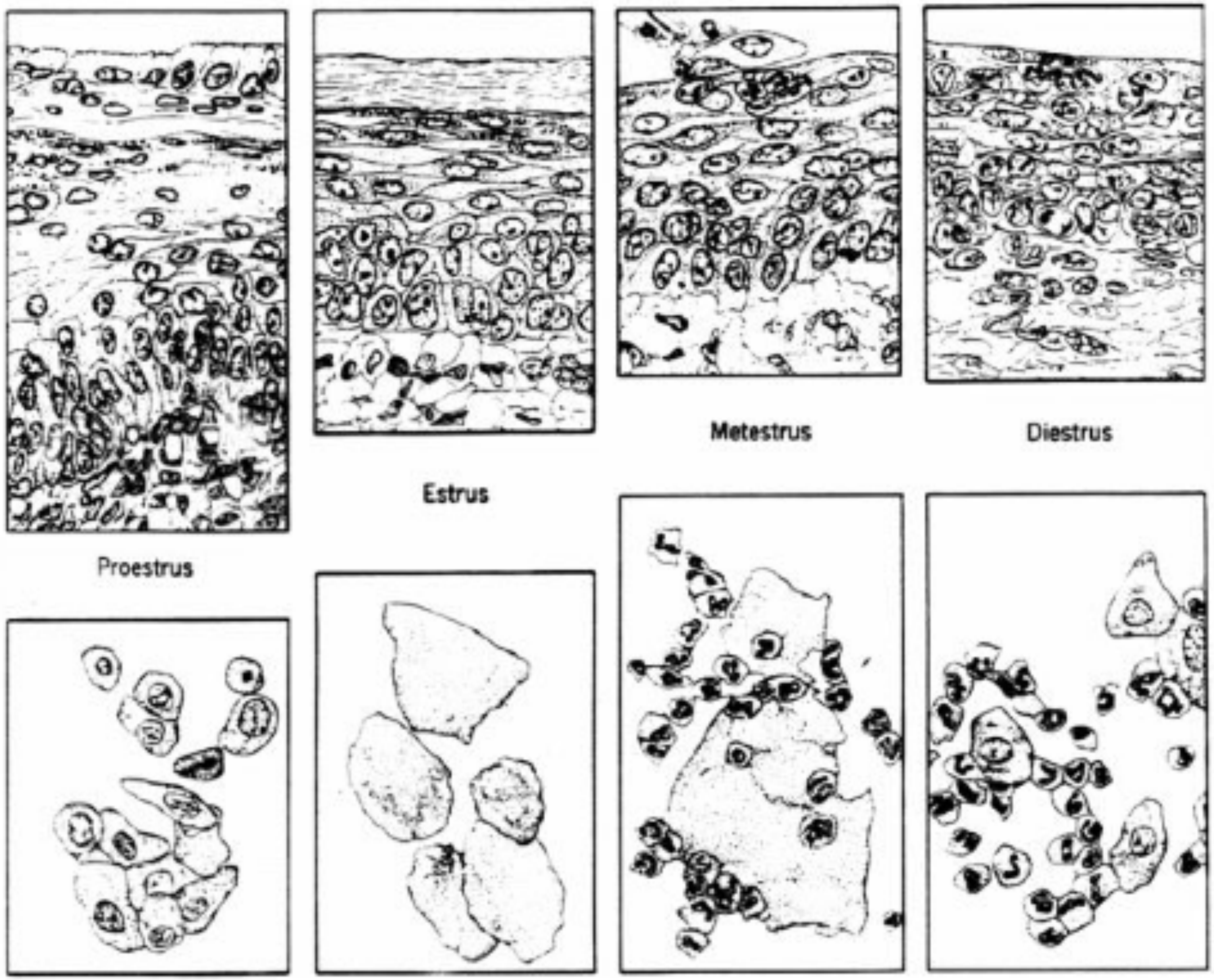
<u>Estrous Cycle Staging</u>

The Rodent Estrous Cycle

Rats and mice are spontaneous ovulators – i.e. they do not need the presence of males to induce ovulation. There is some evidence the stimulation from male rodents can induce and or/hasten ovulation, but it is not obligatory. Rats are mice typically have a 4-6 day cycle which consists of 4 stages – estrus, proestrus, diestrus I (a.k.a metestrus) and diestrus II.

Protestrus is defined by the presence of nucleated epithelial cells that are round. However, sometimes these cornify rapidly, especially in mice. If you are having trouble distinguishing between P and E, you should probably consider any slide in which nucleated cell predominate to be P, even if these cells are not the smooth round shape you are expecting. **Estrus** is characterized by non-nucleated, cornified epithelial cells. **Metestrus** (or Diestrus I) typically has a low cell number, often with a lot of cell debris. **Diestrus II** contains mostly lymphocytes.




Proestrus
Estrus
Metestrus
Diestrus

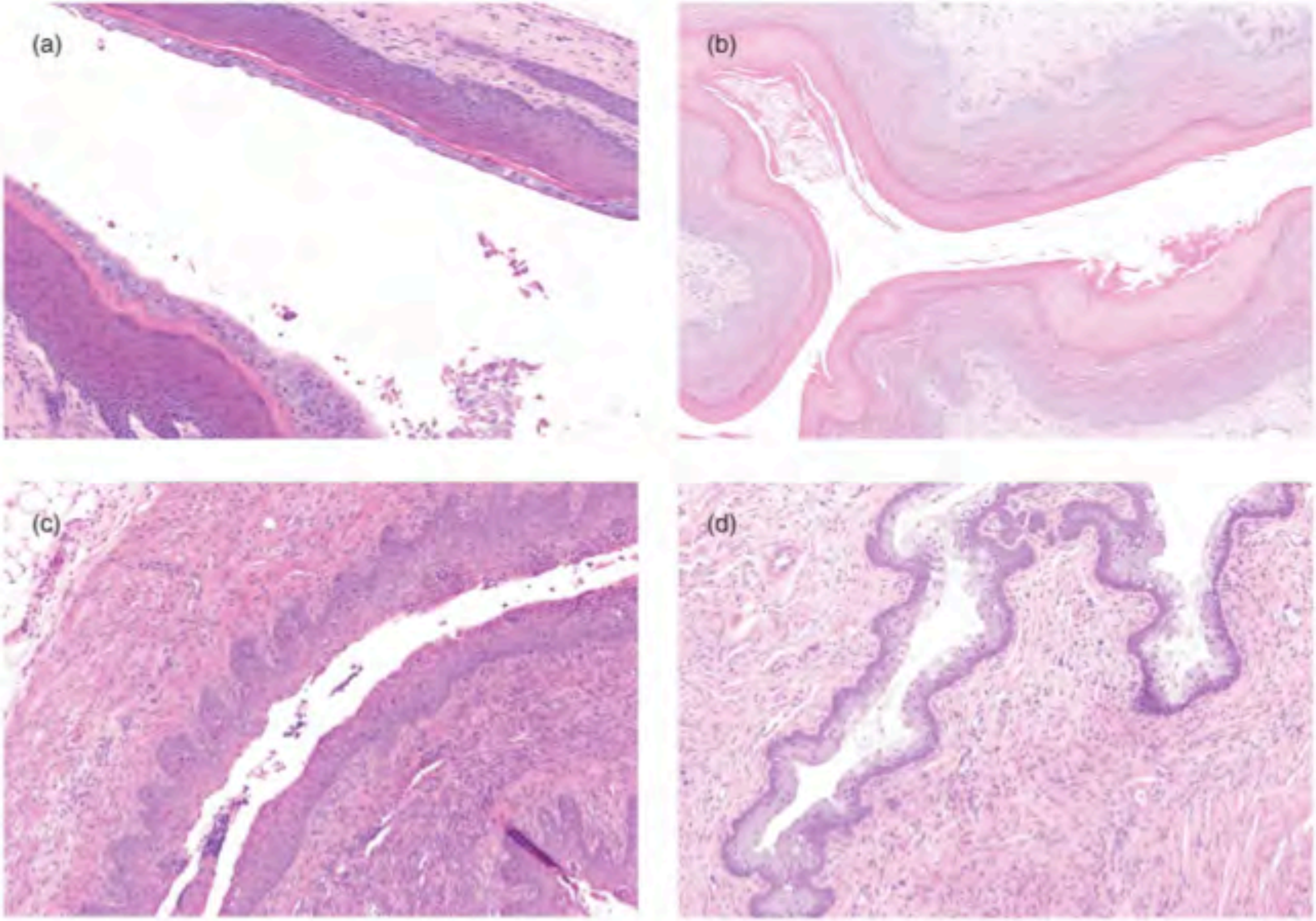


Figure 6.12 Vaginal epithelium changes morphology with stage of oestrous cycle. (a) Proestrus, (b) oestrus, (c) metoestrus, (d) dioestrus.

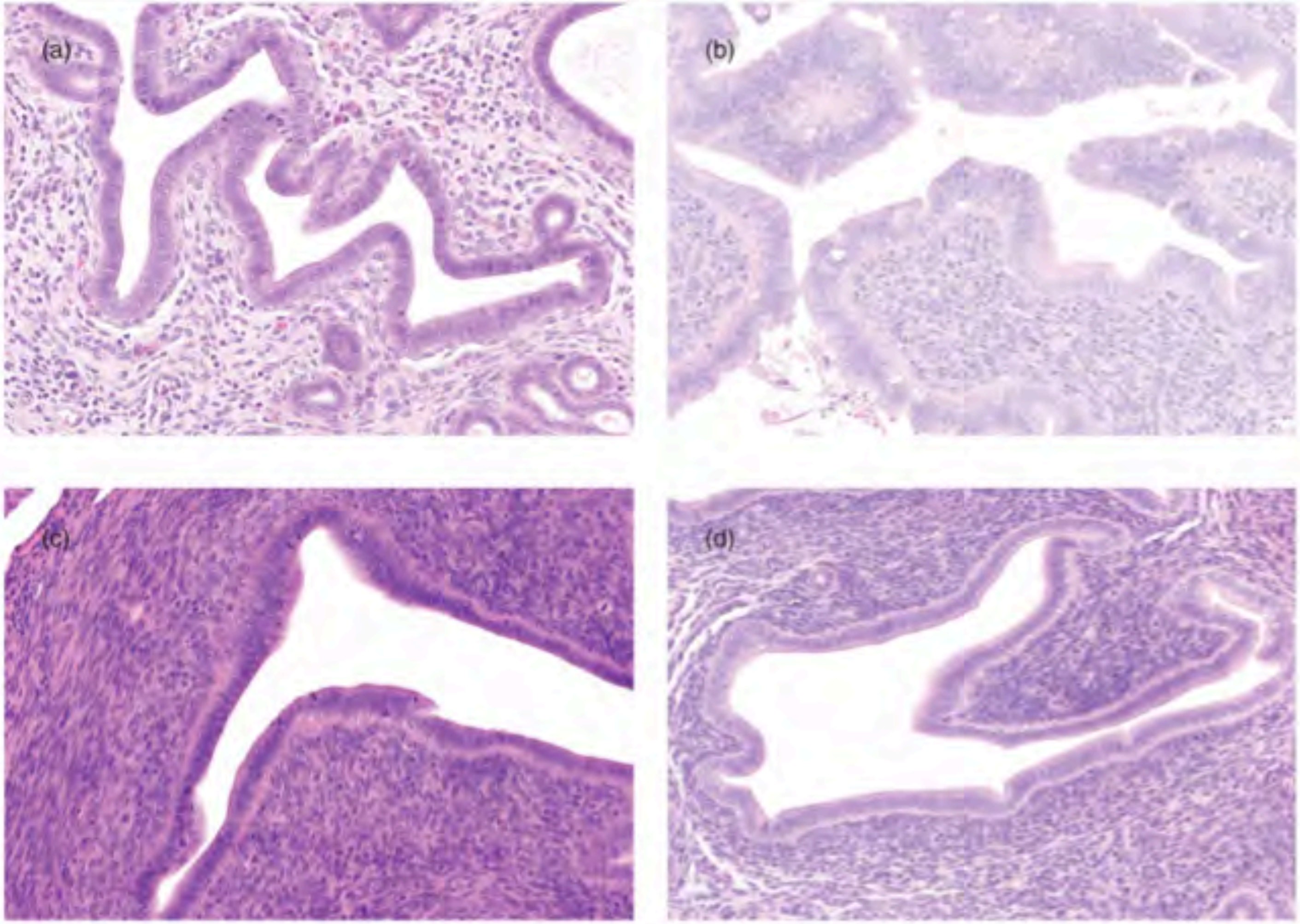


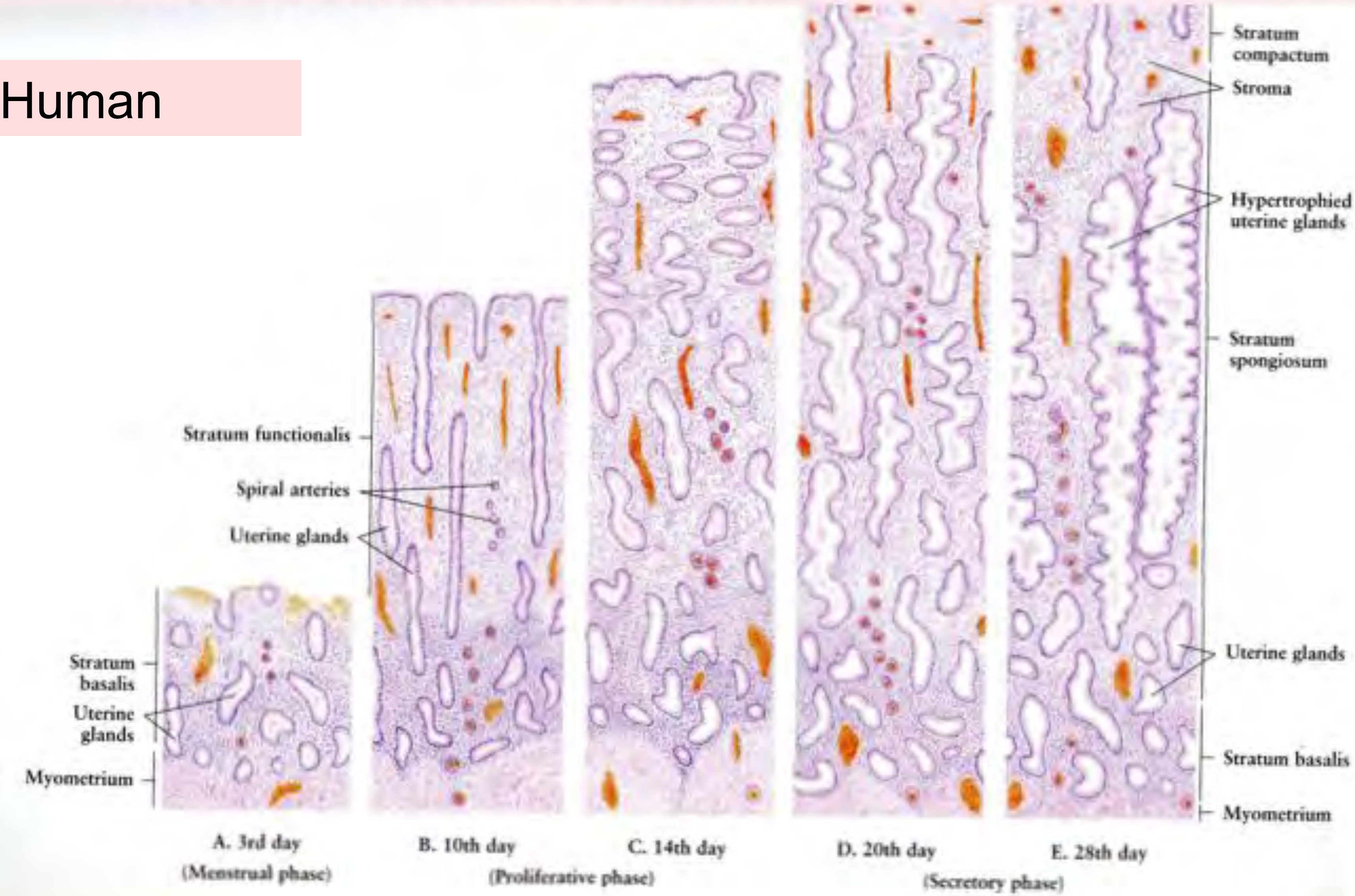
Figure 6.10 Uterine endometrium changes morphology with stage of oestrous cycle. (a) During proestrus the epithelium may contain mitoses and the stroma may be oedematous, (b) epithelium starts to vacuolated and degenerate in oestrus, (c) mitoses are seen towards the end of metoestrus, (d) the epithelium is at its lowest in dioestrus.

A Practical Guide to the Histology of the Mouse, First Edition. Cheryl L. Scudamore.

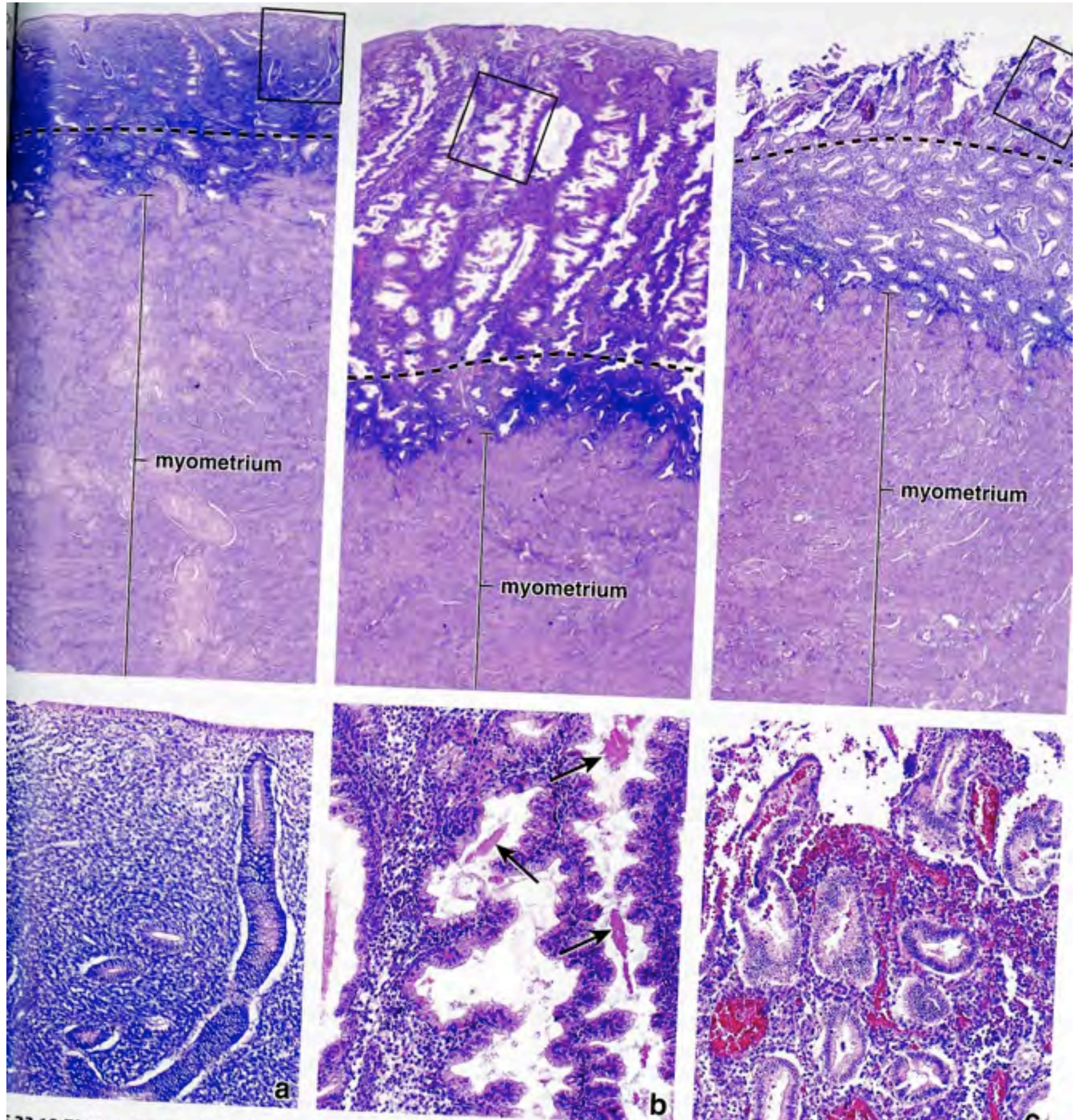
Published 2014 by John Wiley & Sons, Ltd. Companion Website: www.wiley.com/go/scudamore/mousehistology

Uterine endometrium changes during the menstrual hormonal cycle

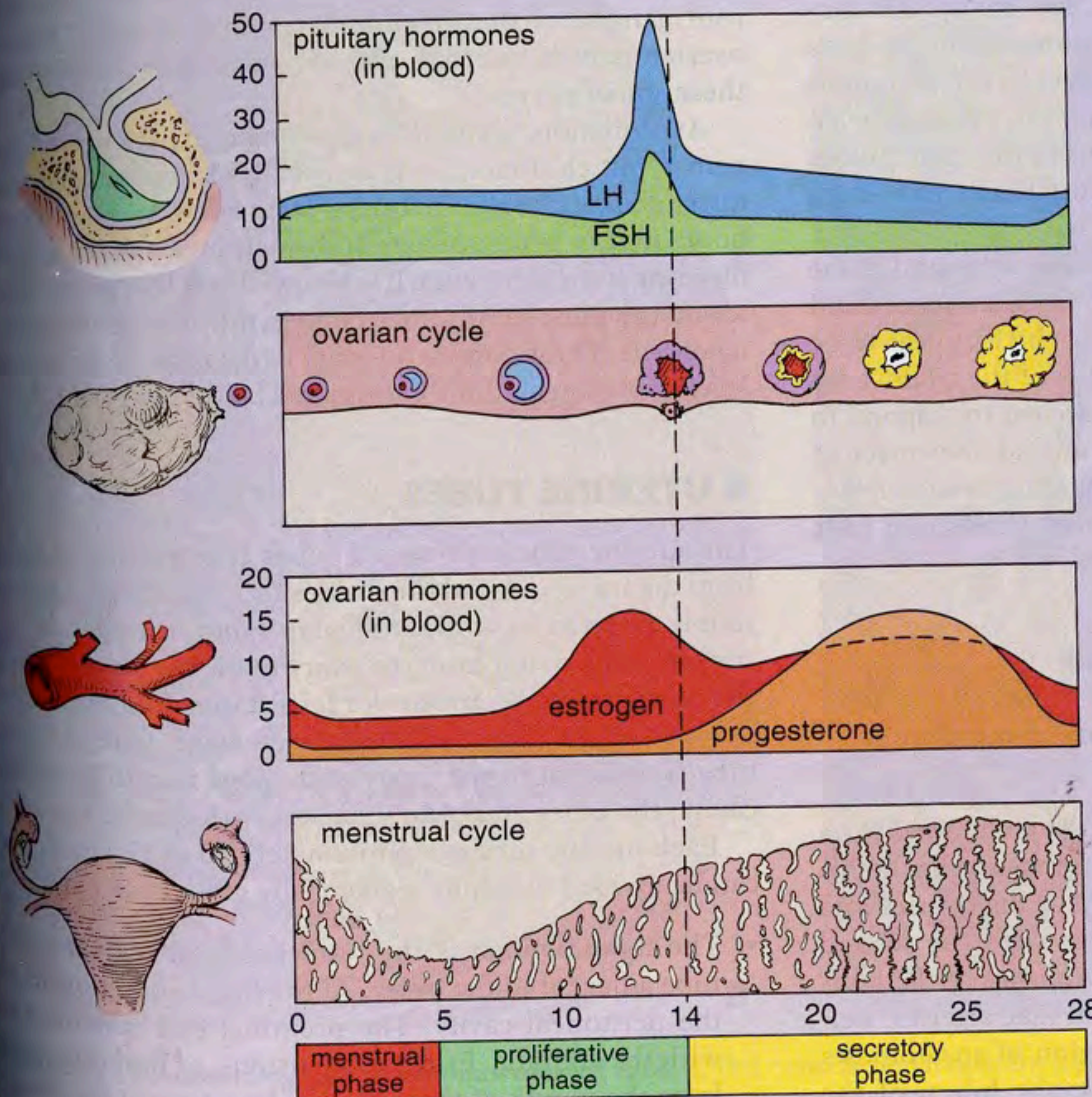
Human



Uterine endometrium changes during the human menstrual cycle

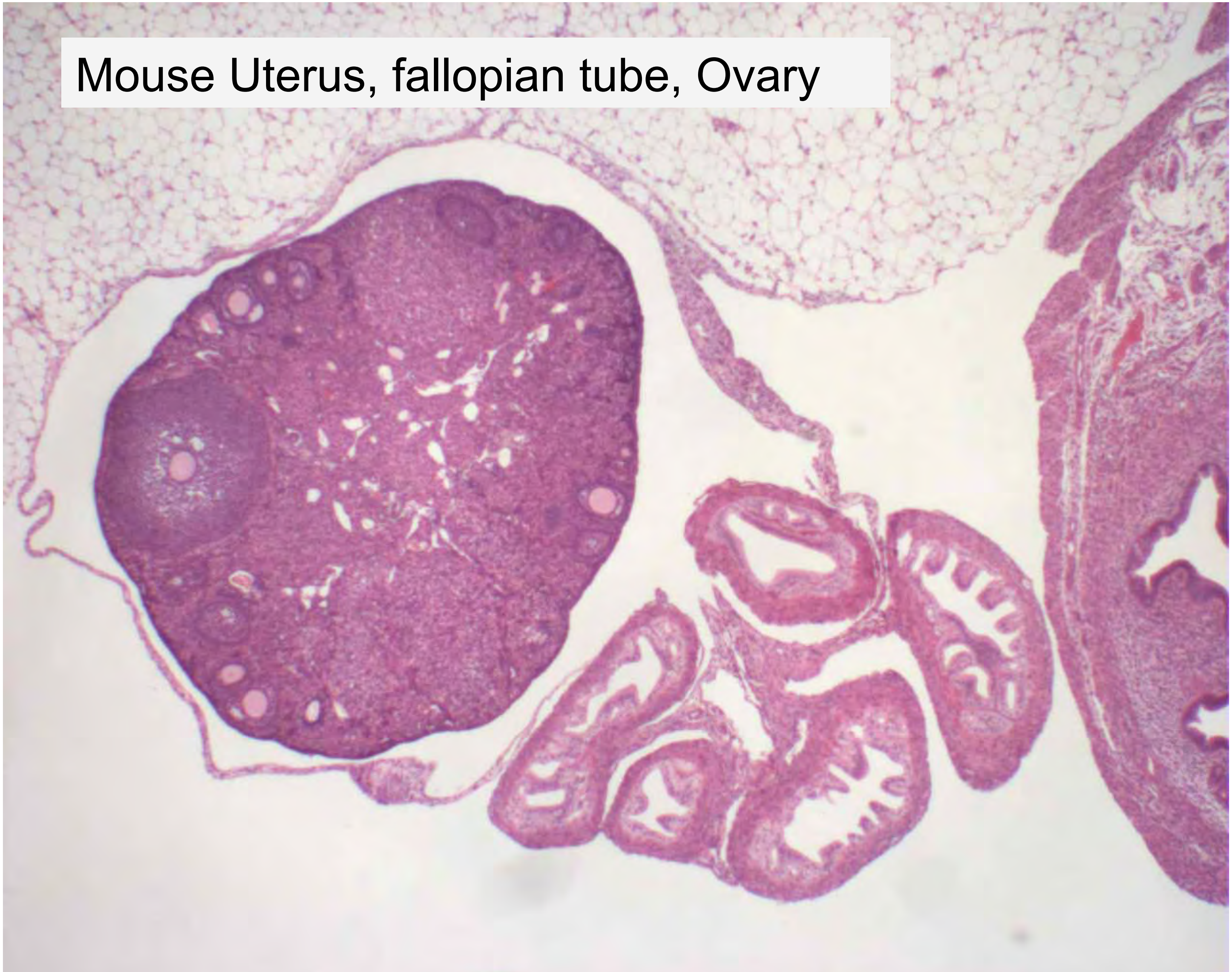


23.19 Photomicrographs of the uterine lining in proliferative, secretory

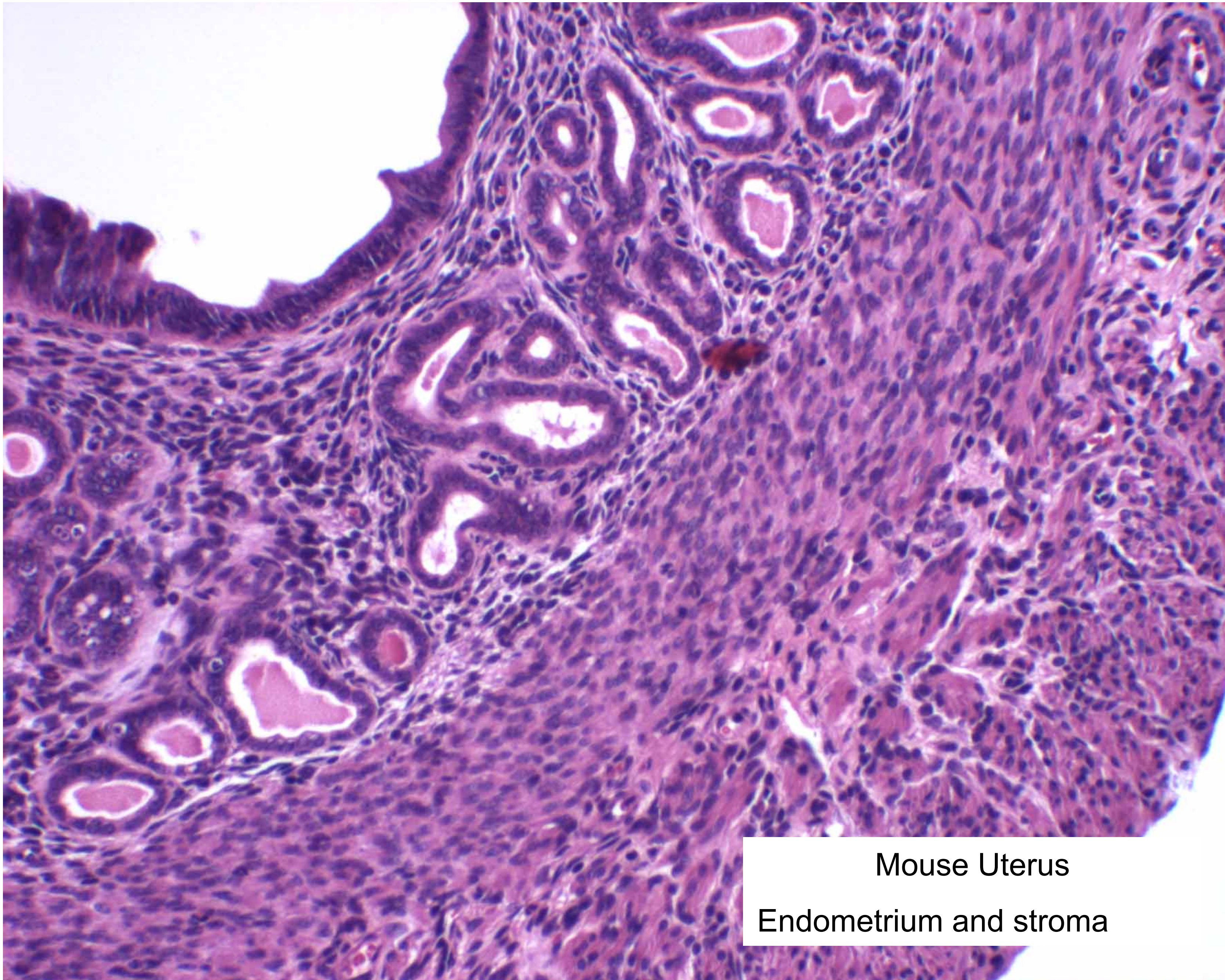


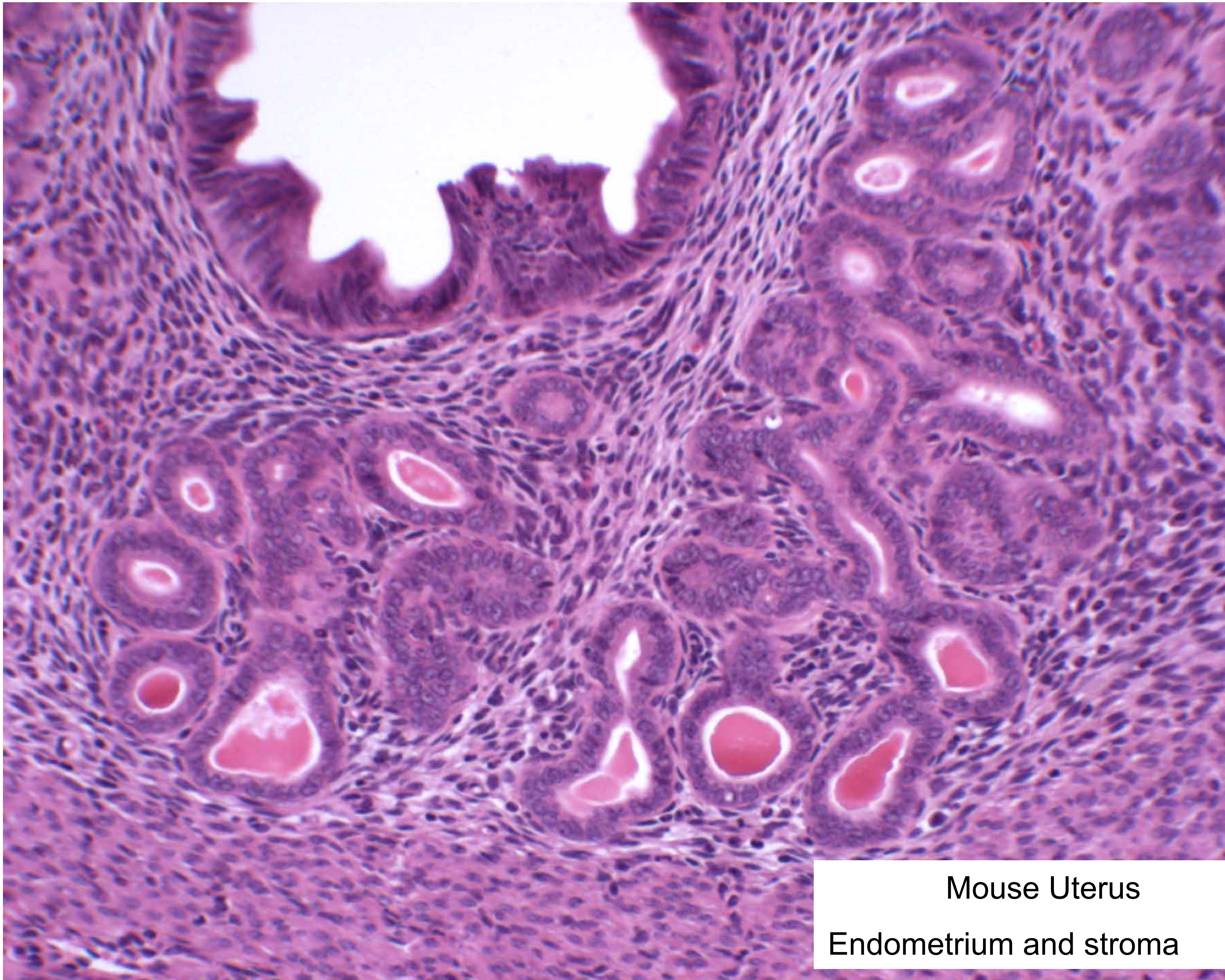
50
40
30
20
10
0
pituitary hormones
(in blood)
LH
FSH
ovarian cycle
20
15
10
5
0
ovarian hormones
(in blood)
estrogen
progesterone
menstrual cycle
0
5
10
14
20
25
28
menstrual phase
proliferative phase
secretory phase

A section through a portion of the human uterus


Mouse Uterus, fallopian tube, Ovary

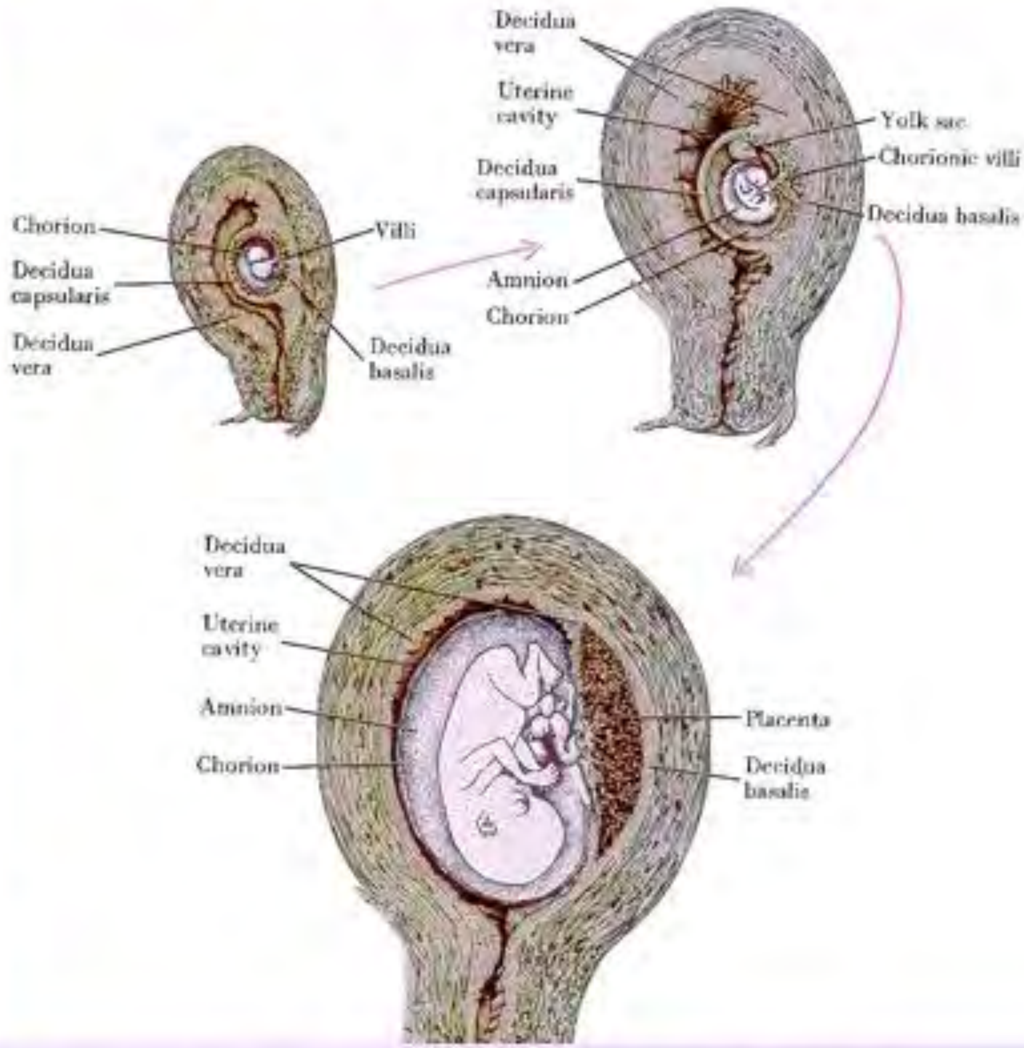

Mouse Uterus


Mouse Uterus
Endometrium and stroma


Mouse Uterus
Endometrium and stroma

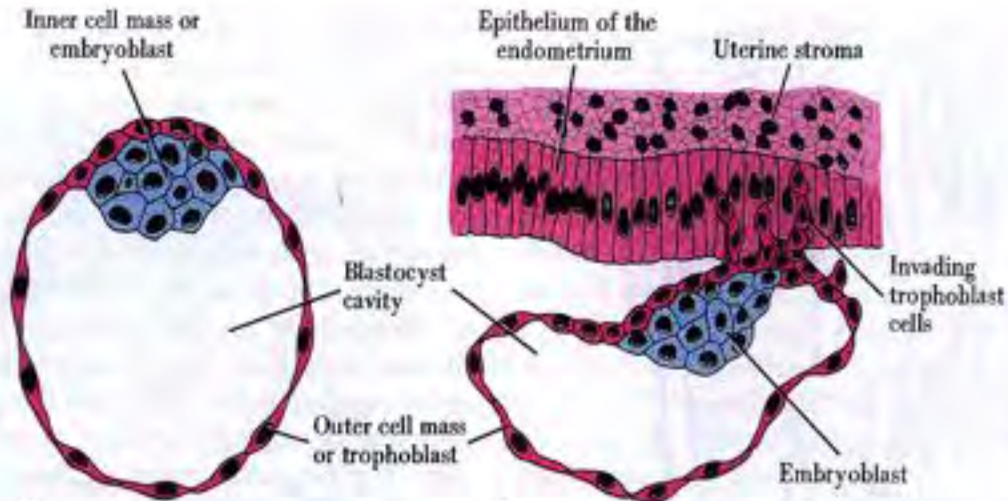
Human Placenta

If fertilization and implantation occur, a gravid phase replaces the menstrual phase of the cycle and decline of the endometrium is delayed until after parturition. The endometrium is converted into decidual cells, which form the basal part of the placenta.



The placenta is a major endocrine organ producing steroid and protein hormones

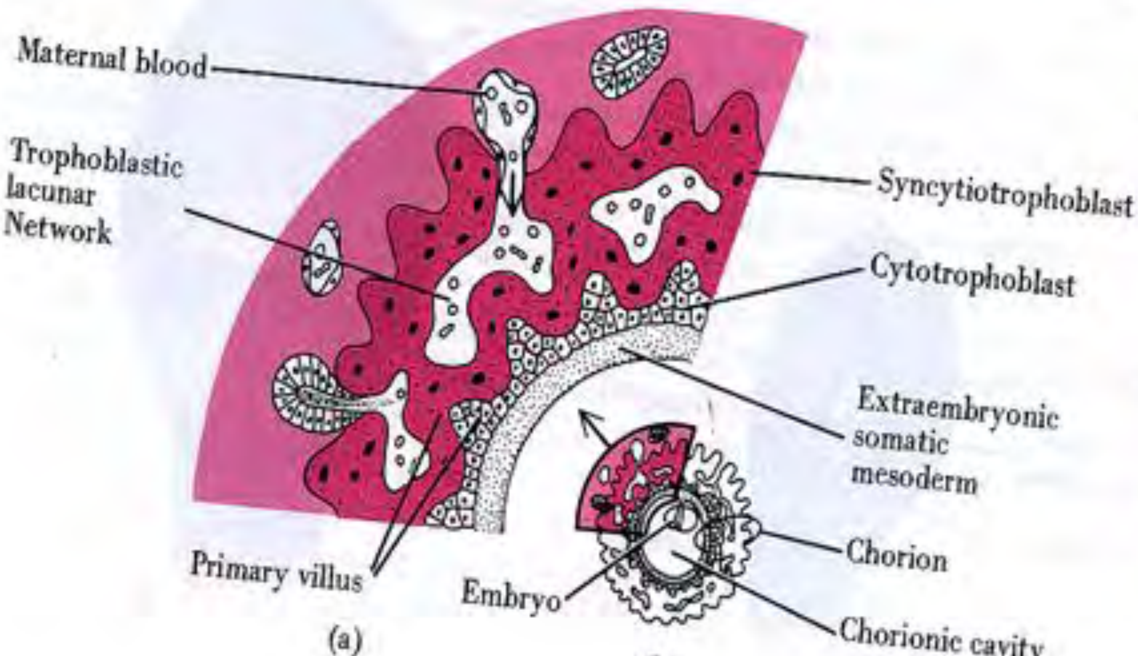
Human Placenta



A. B.

Early stages of implantation

Human day 4, day 5

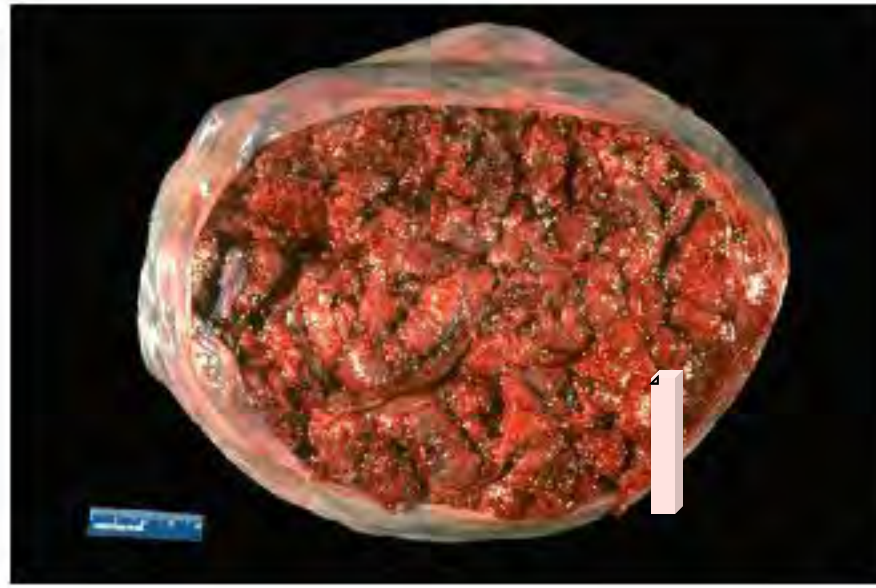


(a) (b)

Early stages of placental development

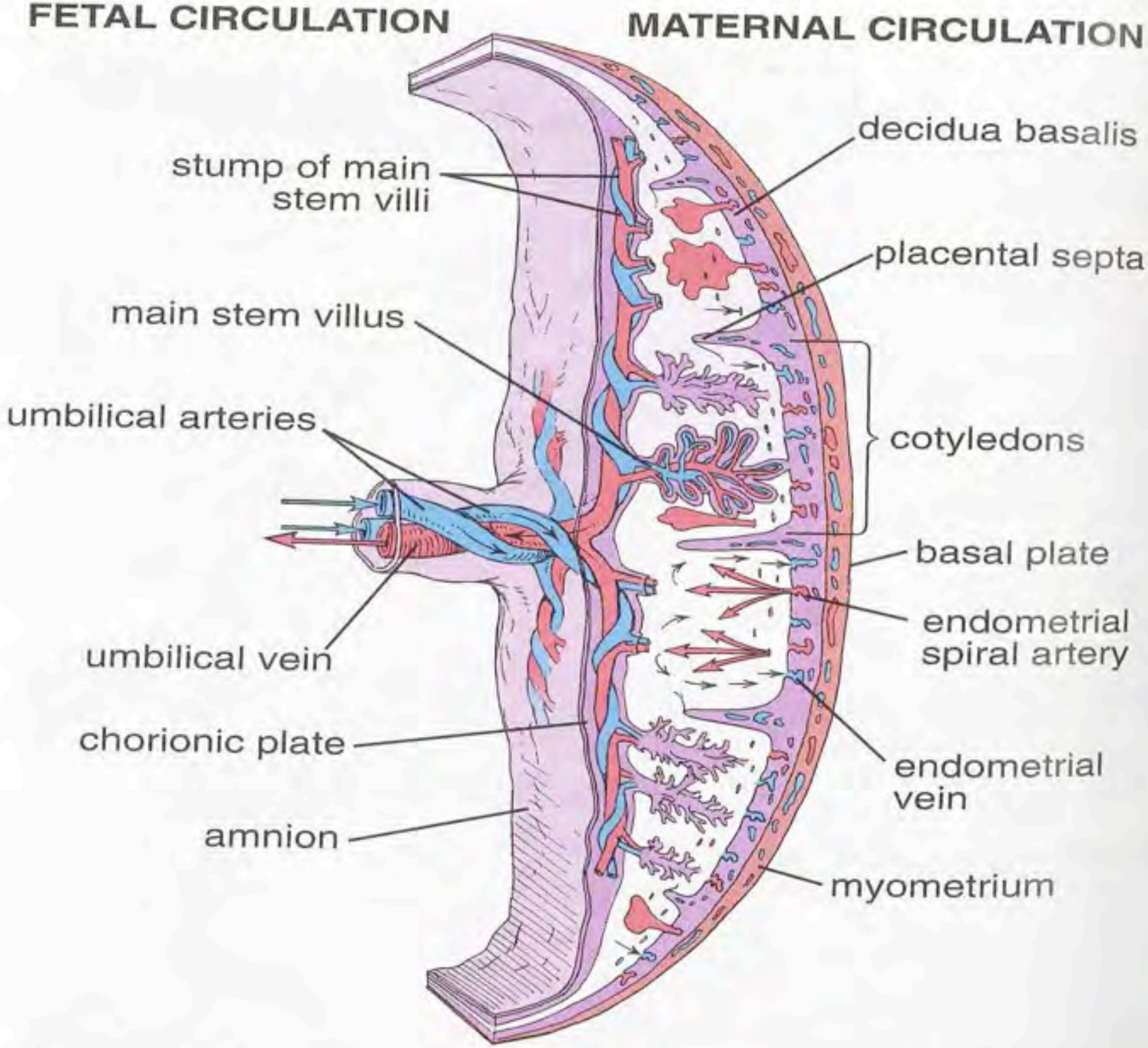
Human day 14

Human Placenta



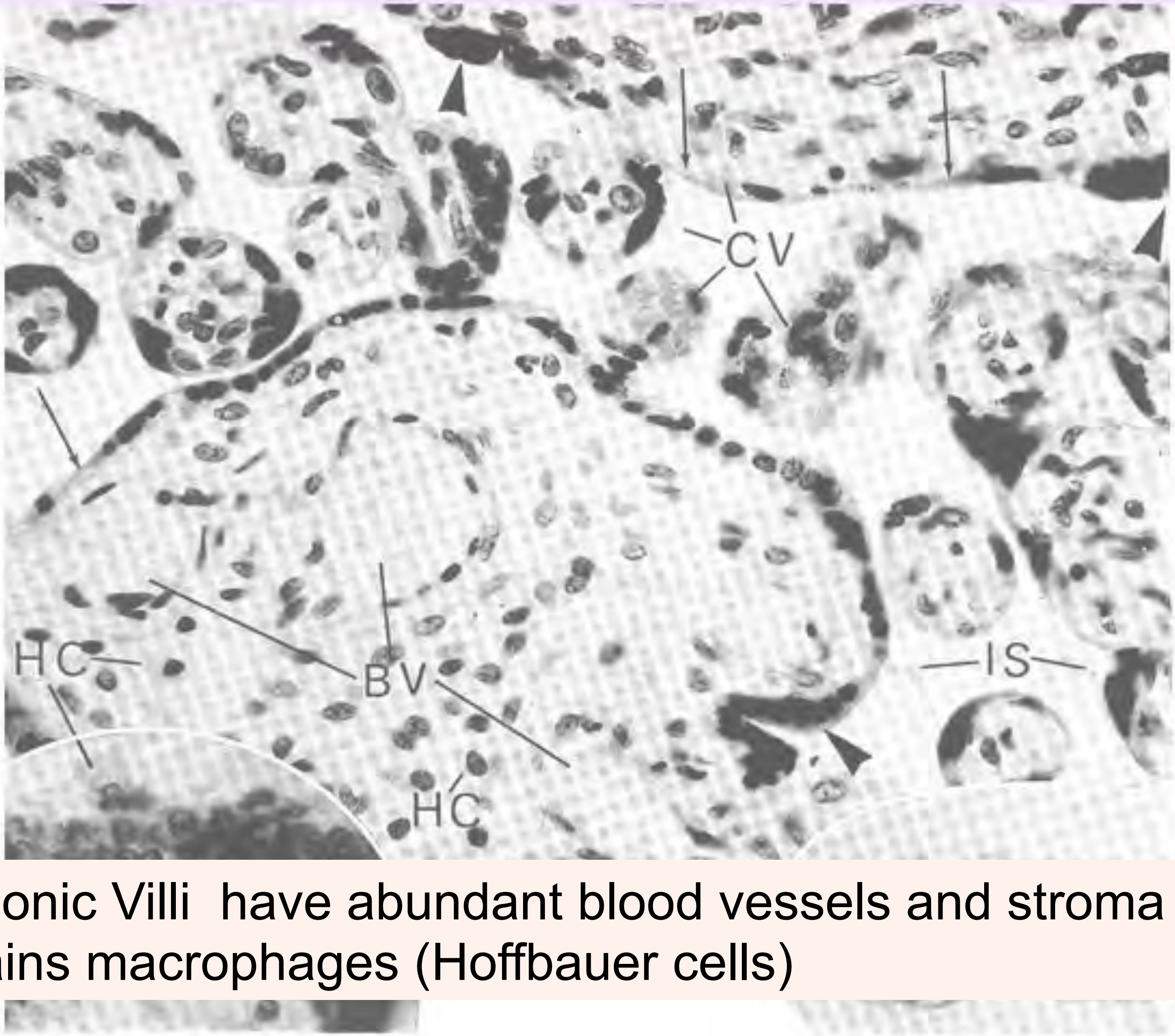
Fetal surface: Shiny, covered with amnion
Maternal surface: Uterine/decidual surface

Human Placenta : diagram



gittal section of the uterus (*left*) with the developing embryo shows the

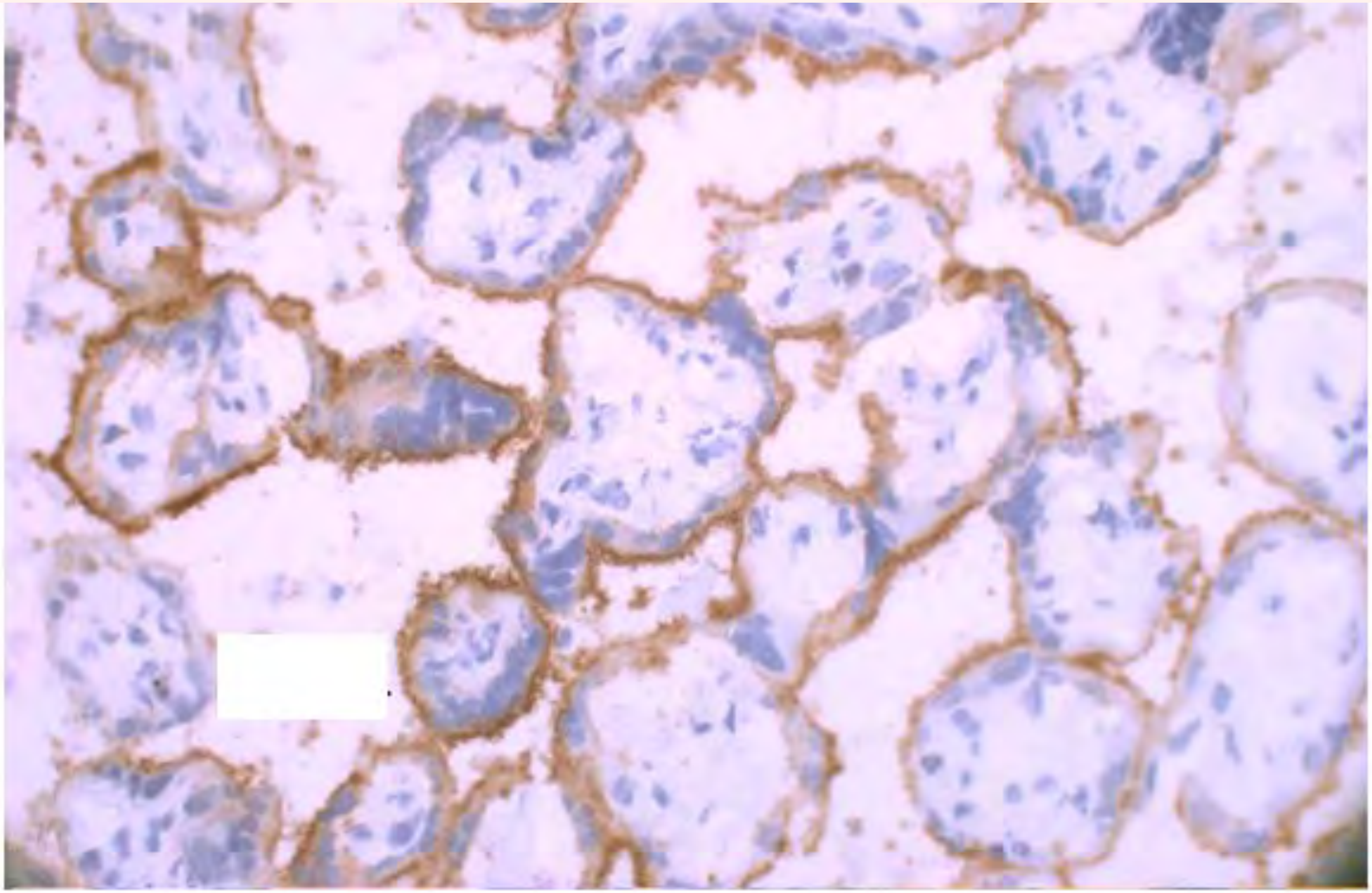
Histology of Human Placenta



Chorionic Villi have abundant blood vessels and stroma contains macrophages (Hoffbauer cells)

Histology of Human Placenta,IHC

Chorionic Villi sections show trophoblast which is composed of an inner Cytotrophoblast and an outer multi-nucleated Syncytiotrophoblast.



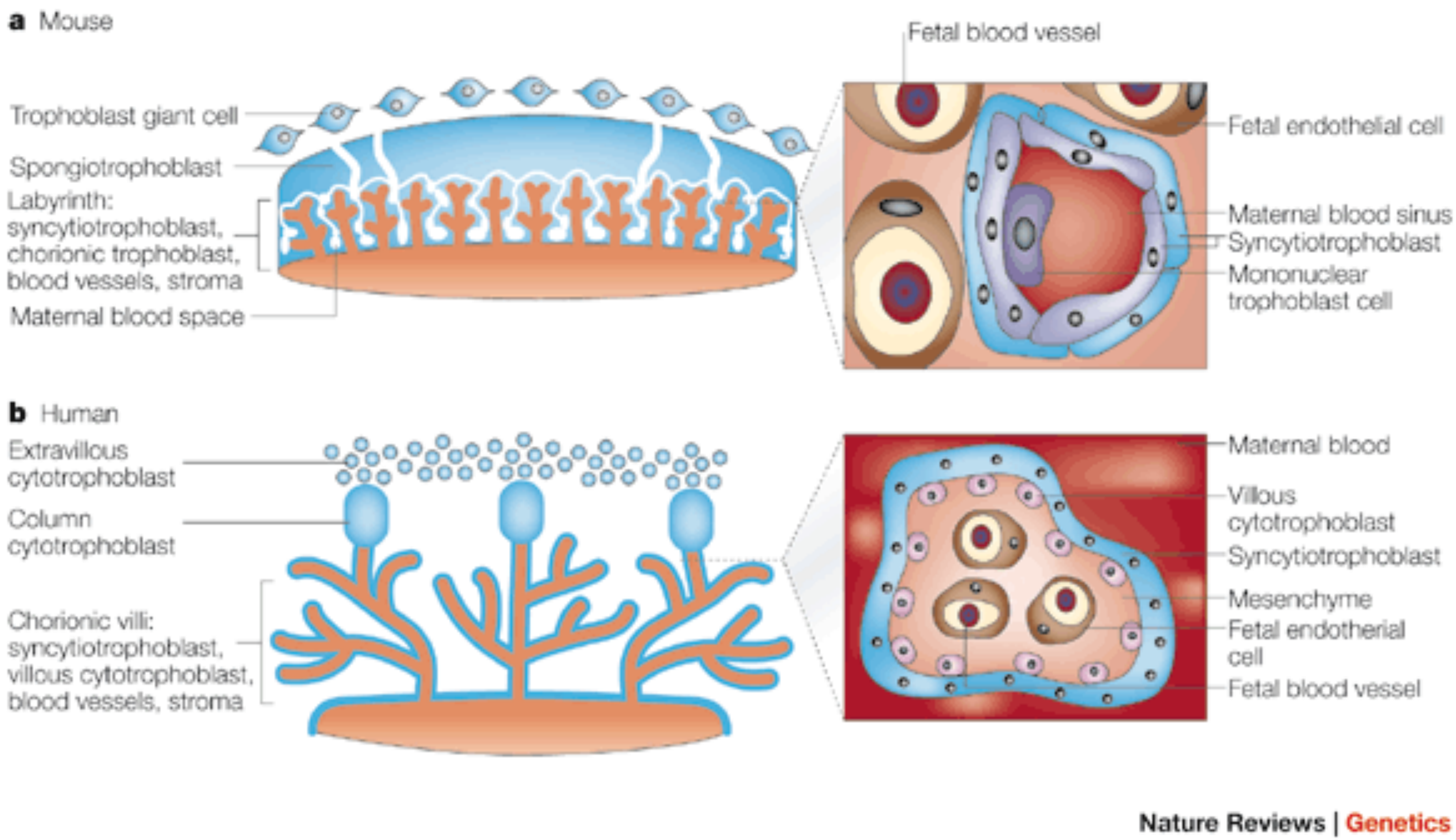


FIGURE 2 | Comparative anatomy of the mouse and human placenta.
Placental development: Lessons from mouse mutants Janet Rossant & James C. Cross Nature Reviews Genetics 2, 538-548 July 2001

Placenta (2002), **23**, 3–19
doi:10.1053/plac.2001.0738, available online at http://www.idealibrary.com on IDEAL

CURRENT TOPIC

Comparative Developmental Anatomy of the Murine and Human Definitive Placentae

P. Georgiades[a], A. C. Ferguson-Smith and G. J. Burton

Department of Anatomy, University of Cambridge, Downing Street, Cambridge, CB2 3DY, UK
Paper accepted 28 August 2001

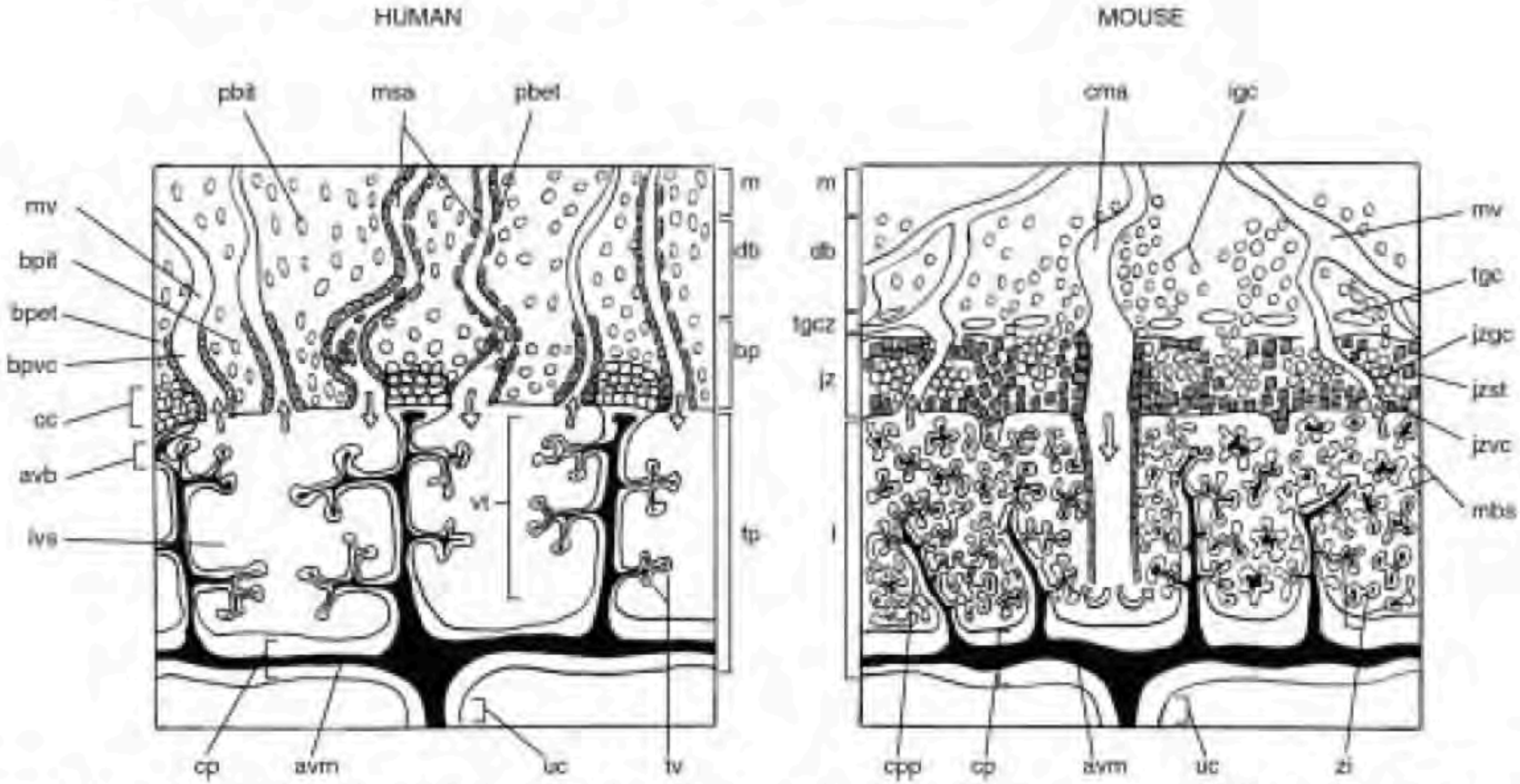
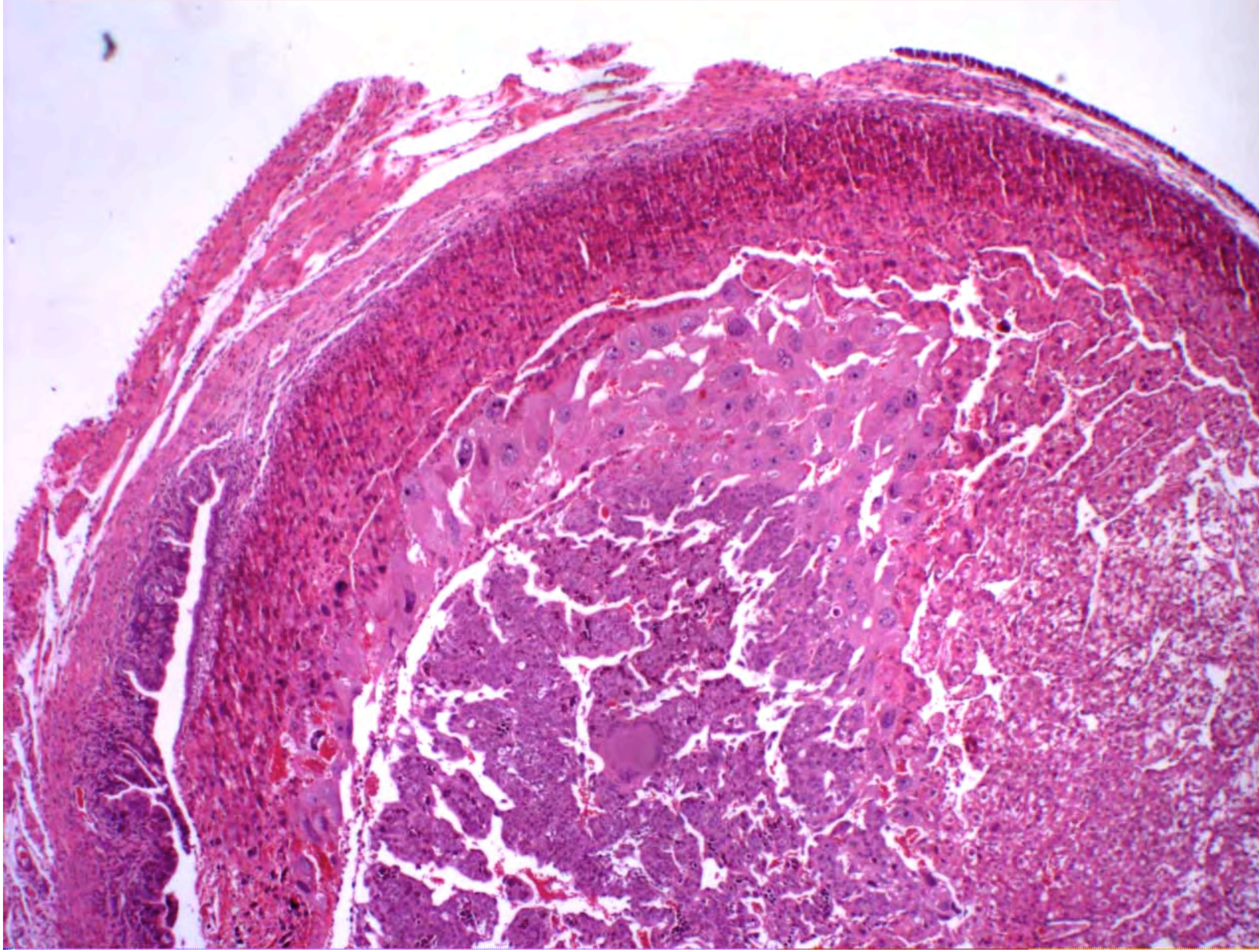
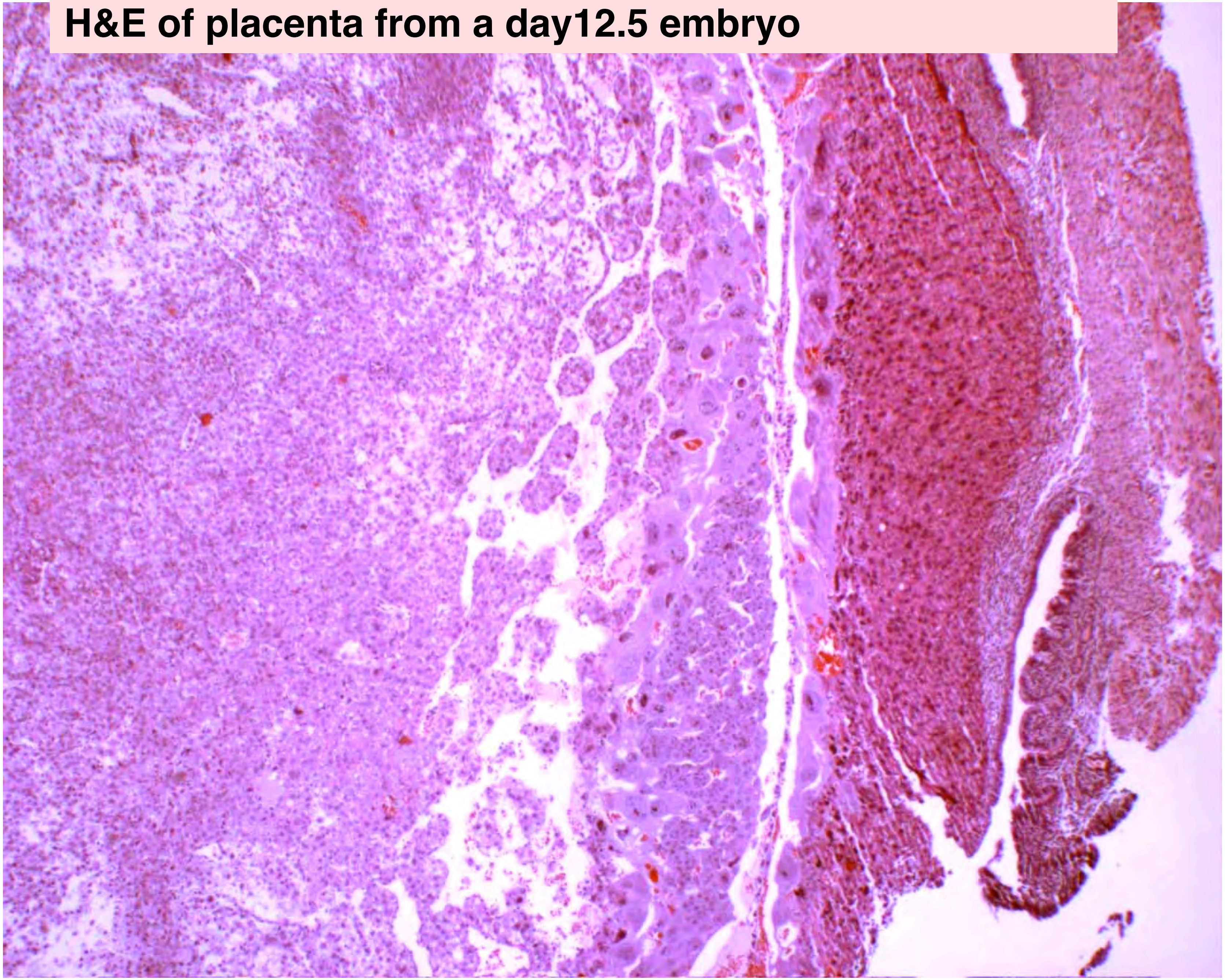


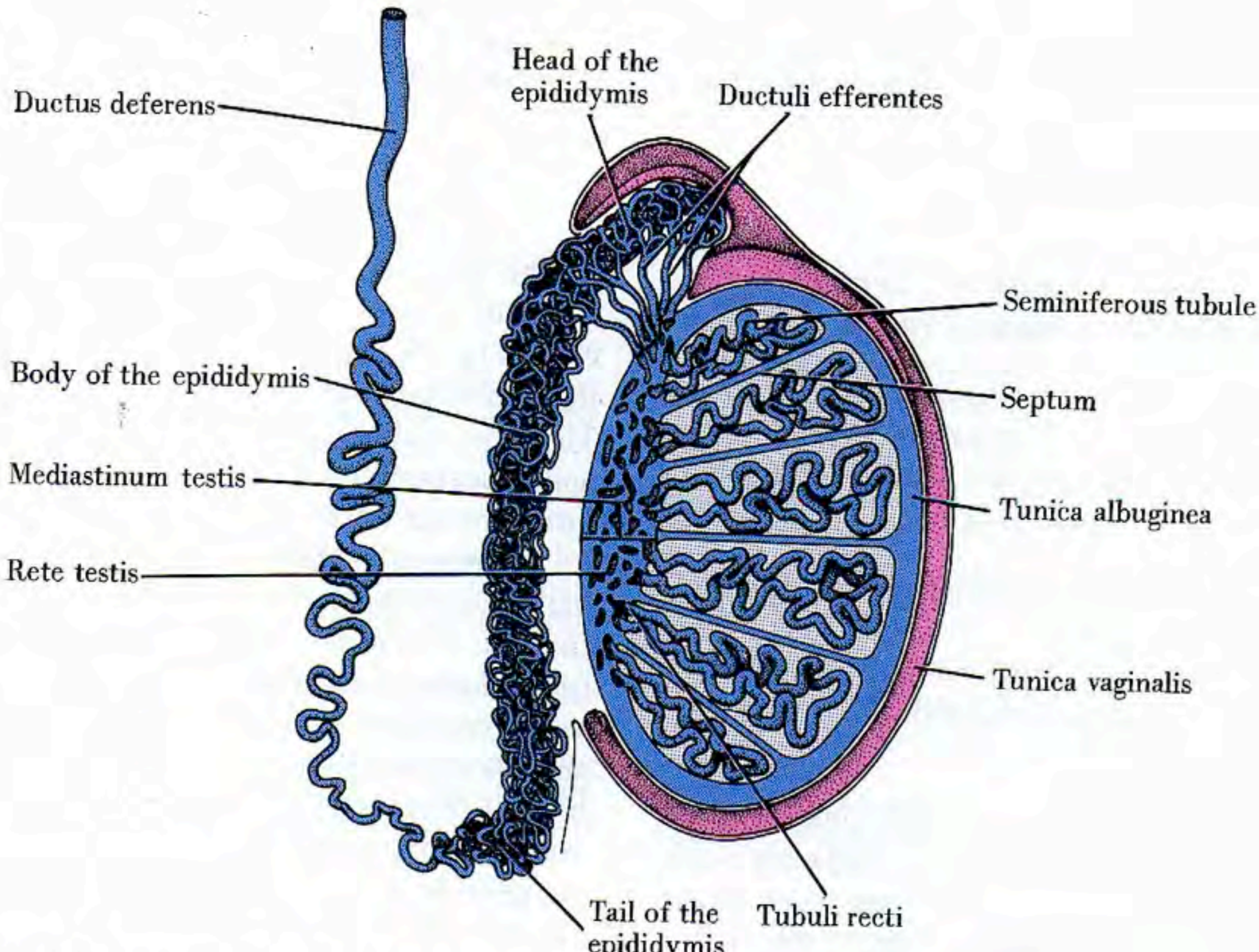
Figure 1. A simplified diagrammatic representation of the major regions and some cell types of human and murine placentae during the third trimester and the last fifth of gestation respectively. This is a cross-sectional view with the plane of sectioning being perpendicular to the flat (fetal) surface of the placenta. The side of the placenta facing the mother (maternal side) is at the top of the picture and that facing the fetus (fetal side) at the bottom. Note that one way of distinguishing the extent of the basal plate (*bp*) of the human placenta is the extent of endovascular trophoblast lining the lumen of maternal veins (*mv*). Although it is impossible to show in two dimensions, the zona intima (*zi*) regions of the murine labyrinth (*l*) are actually maze-like ramifications of the main chorionic plate projections (*cpp*). In both species, the venous and arterial channels of the junctional zone (*jz*) and basal plate (*bp*) are lined by endovascular trophoblast. The same applies to the labyrinthine part of the murine central maternal artery (*cma*). Arrows depict the direction of maternal blood flow within the utero-placental circulation. *avb*,

H&E of placenta from a day12.5 embryo

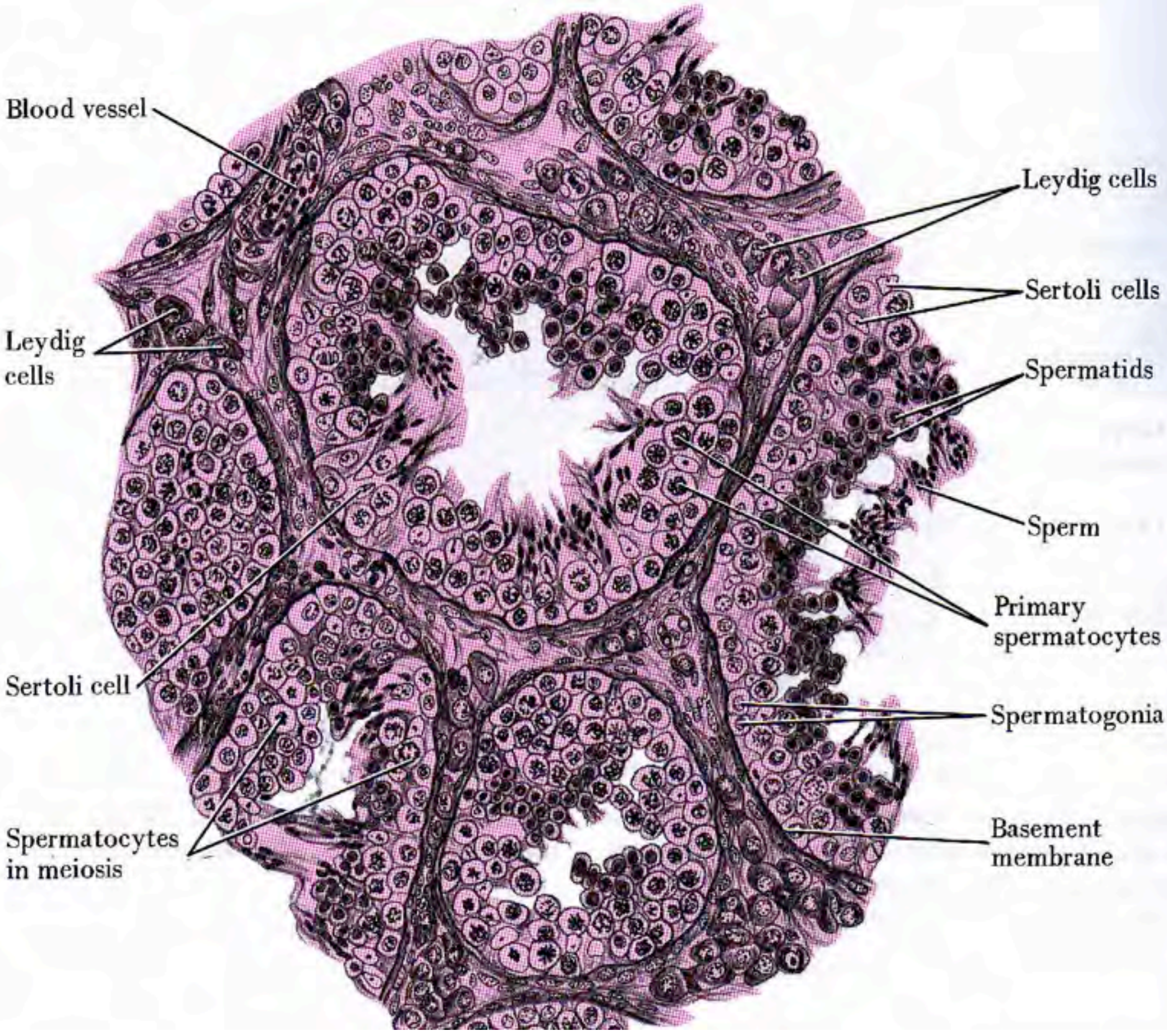


H&E of placenta from a day12.5 embryo





chematic diagram of a longitudinal section ... Dym M: In: Weiss L (ed): Cell and Ti



Blood vessel
Leydig cells
Sertoli cells
Spermatids
Sperm
Primary spermatocytes
Spermatogonia
Basement membrane
Leydig cells
Sertoli cell
Spermatocytes in meiosis

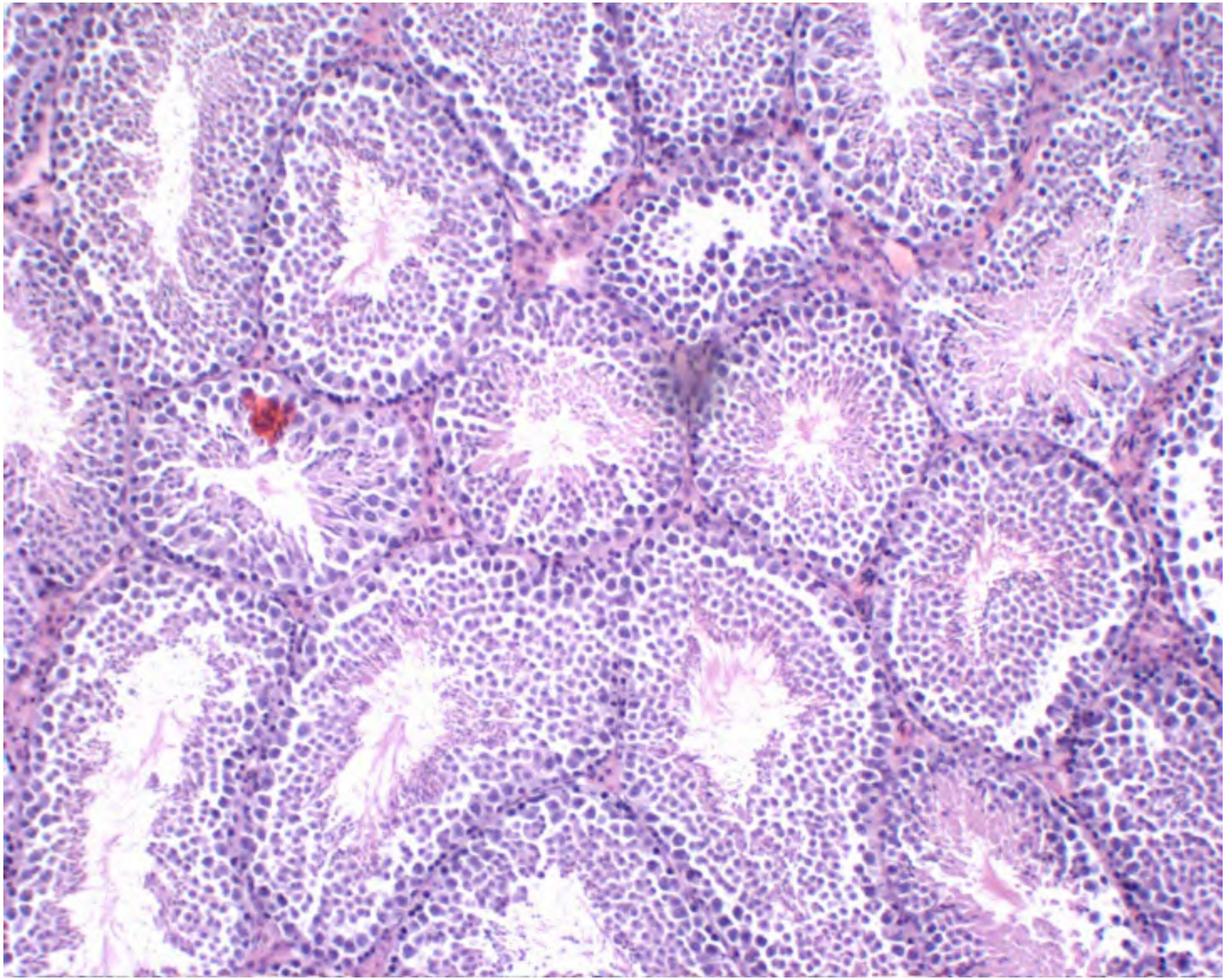
TESTIS: site of the development of spermatozoa and the production of testosterone. Spermatogenesis and testosterone production are controlled by FSH and LH (ICSH -- Interstitial Cell Stimulating Hormone).

Seminiferous tubule - site of spermatogenesis

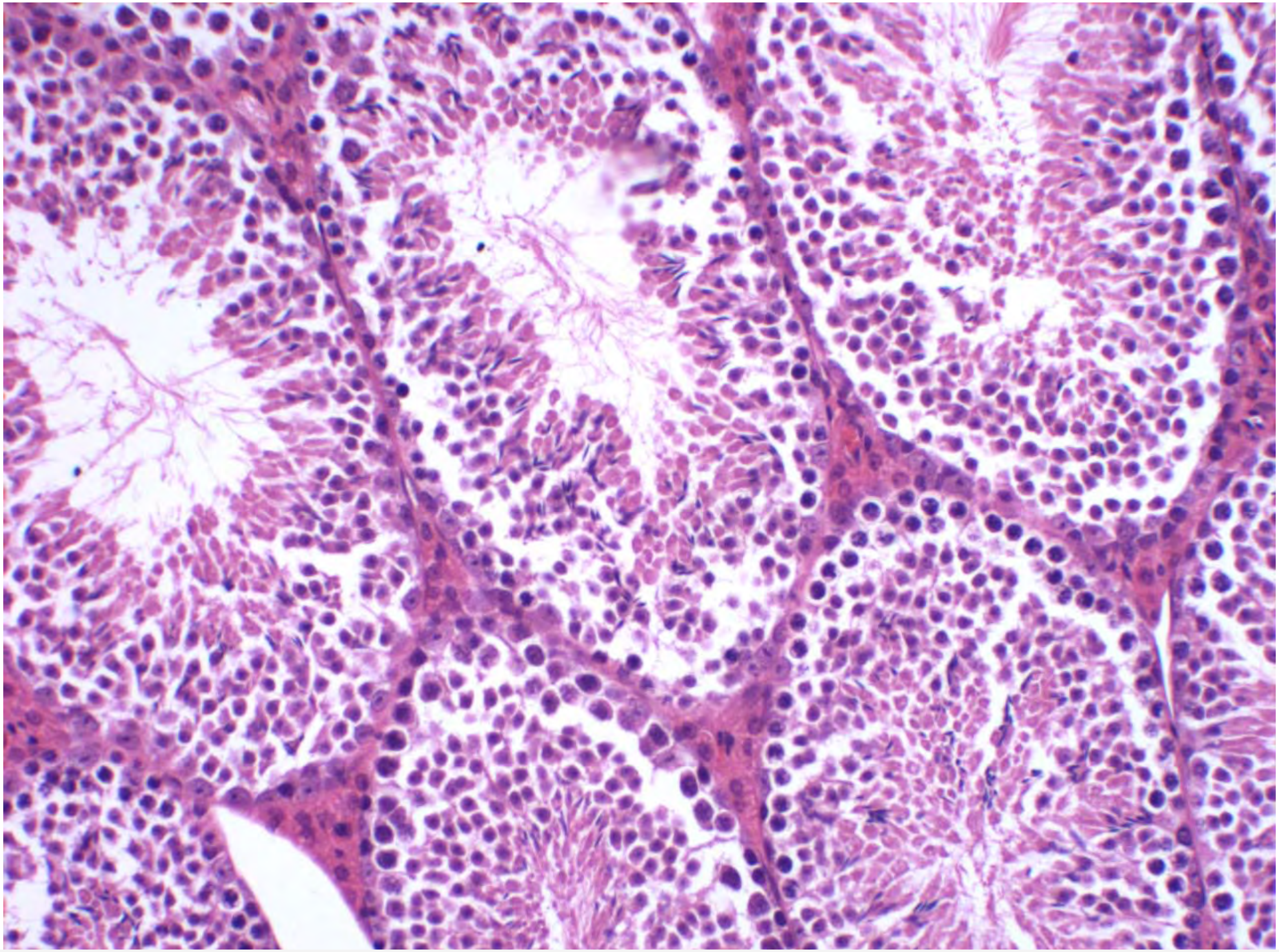
Interstitial cells (Leydig cells) are in the stroma, between the seminiferous tubules, and are the site of testosterone production

Need-to-know

- The germ cell types, from basal location (immature) to luminal location (mature), are, respectively, spermatogonia, spermatocytes, spermatids, and spermatozoa in both the mouse and the human.
- In the mouse, it takes approximately 35 days for spermatogonia to develop into spermatozoa.
- In the human, it takes approximately 70 days for spermatogonia to develop into spermatozoa.



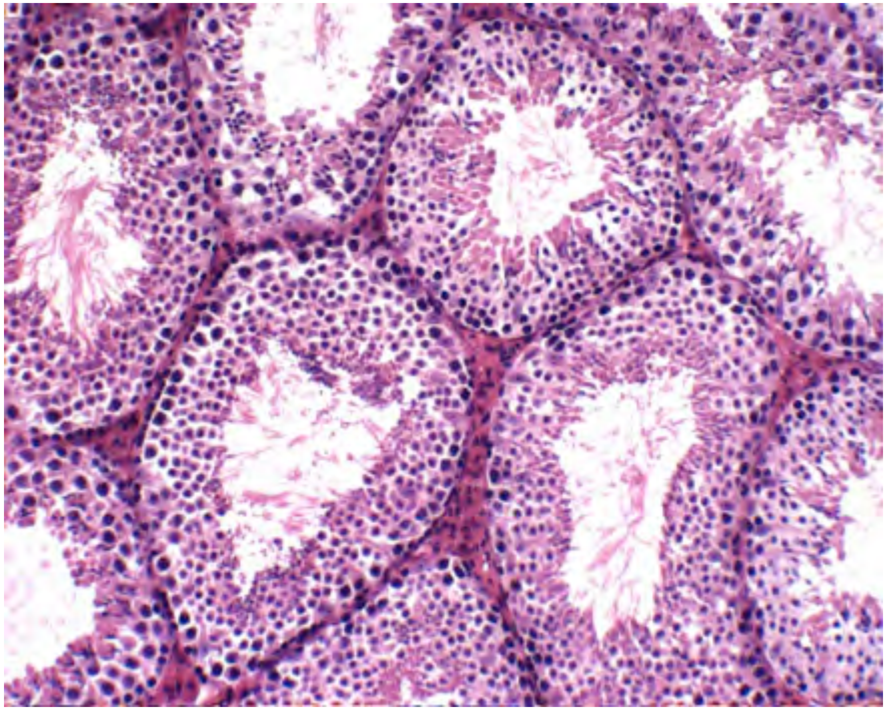
H&E of a section of mouse testis

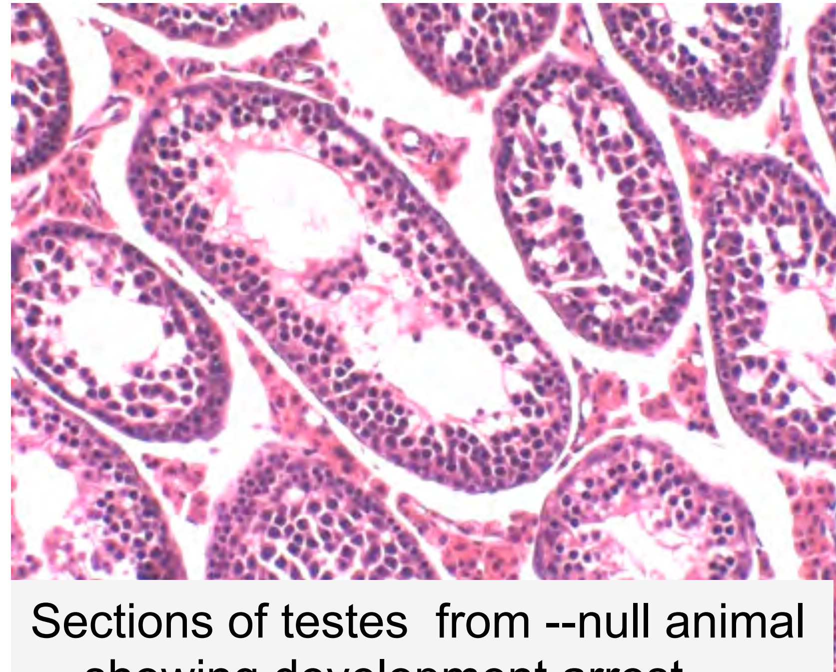


H&E of a section of mouse testis (not fixed well)

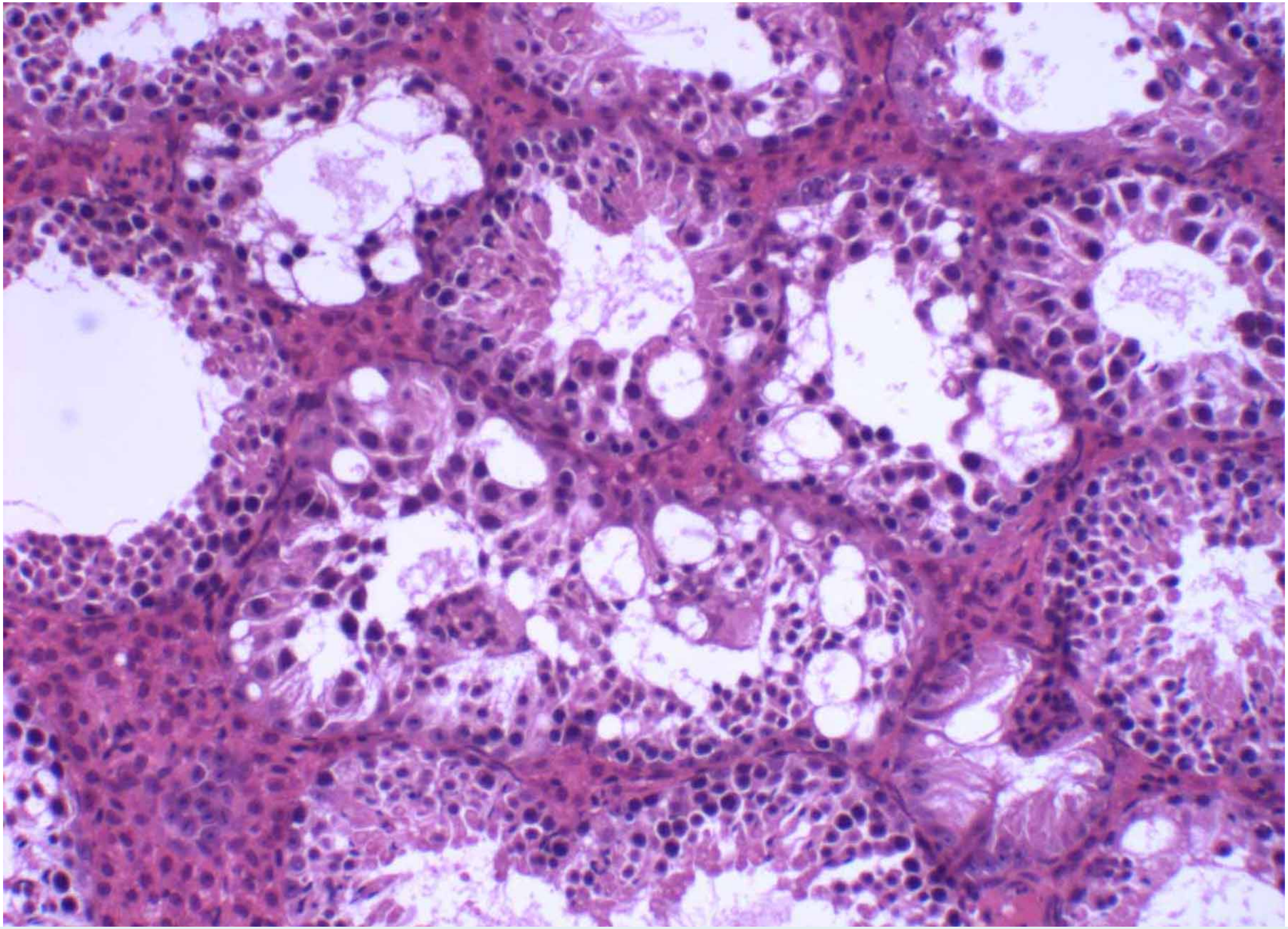
If no IHC needed, fix in Bouin's for 6 hours and wash in 70% alcohol until clear and process into paraffin

Seminiferous tubules with maturing sperm



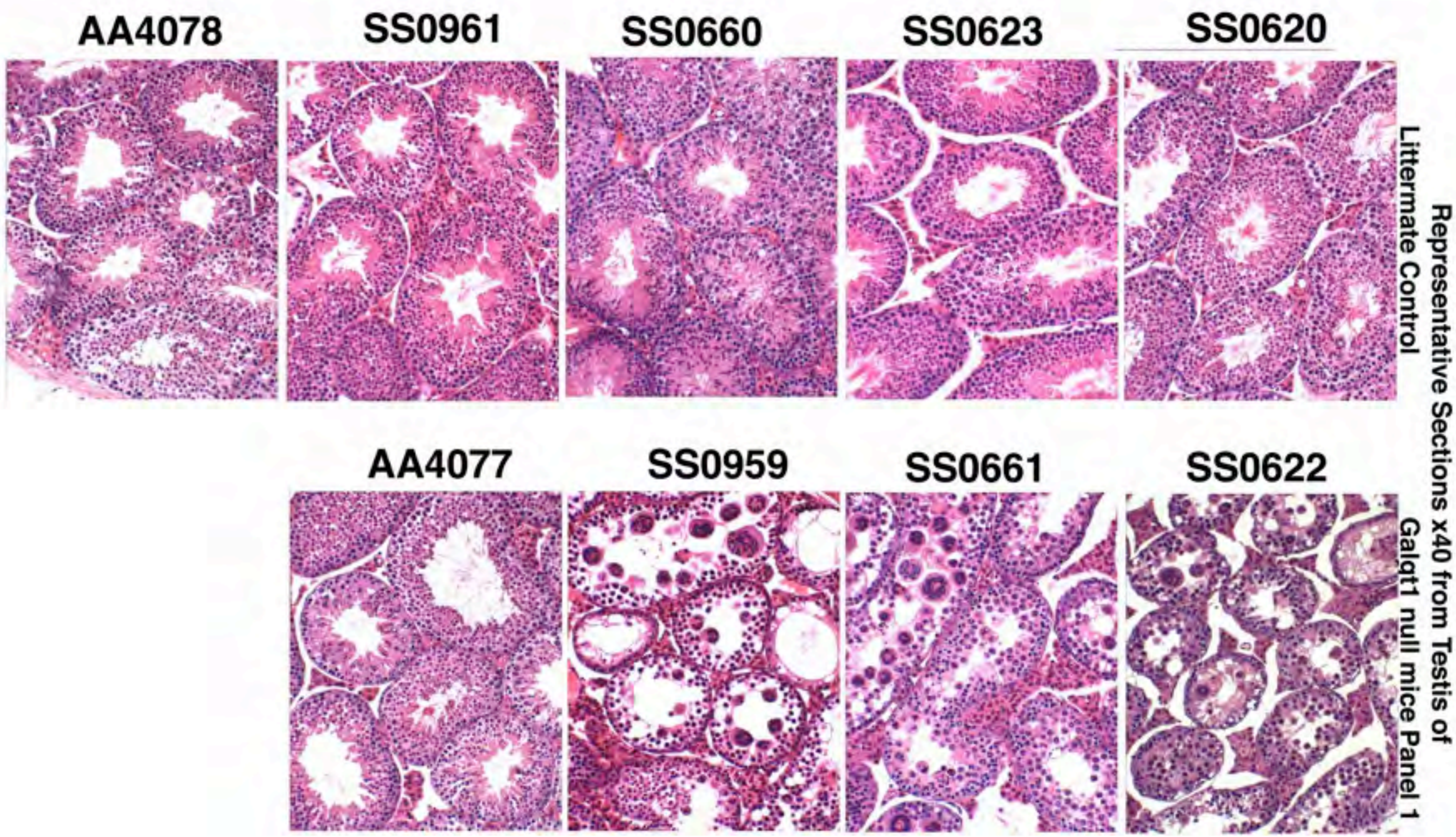


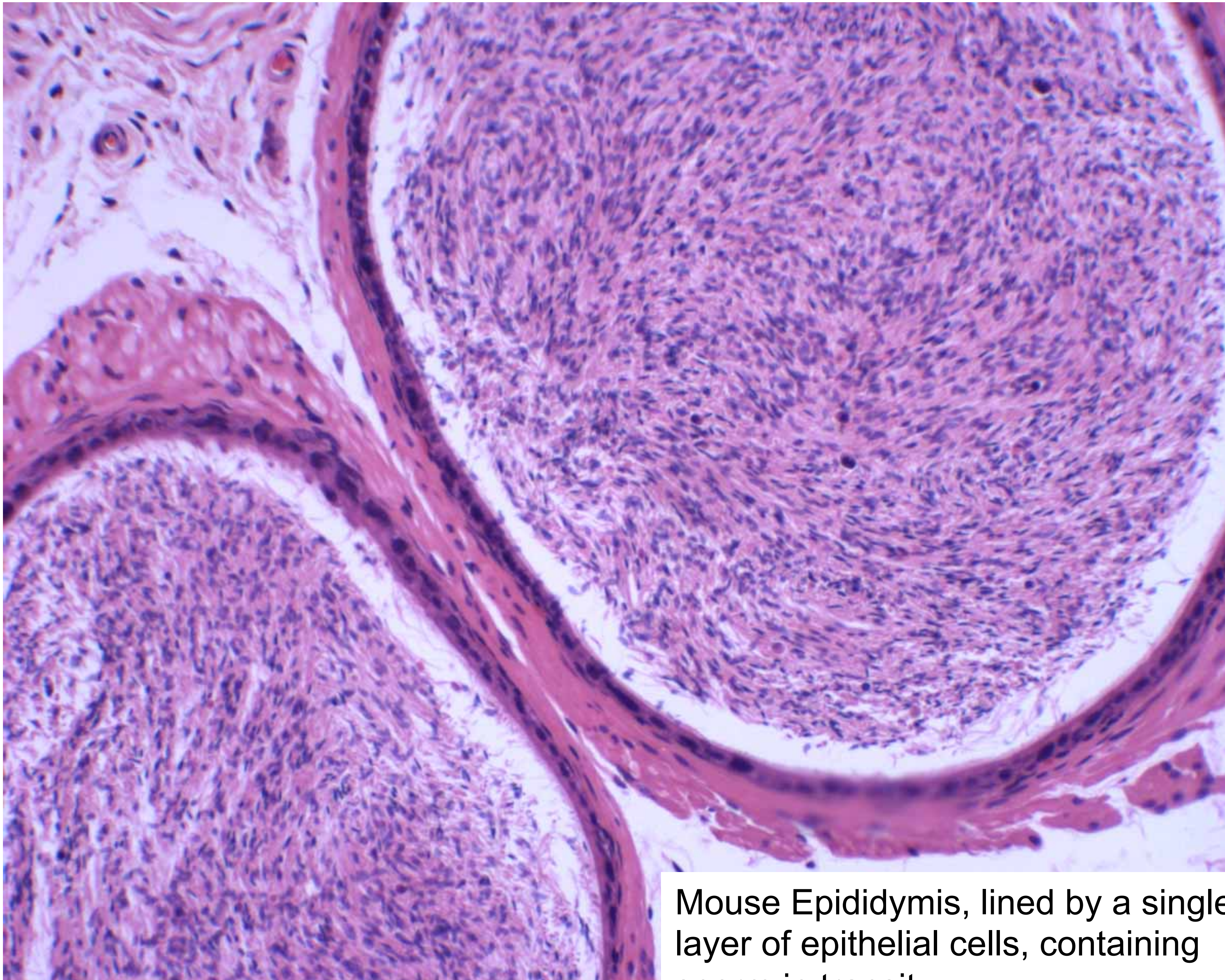
Sections of testes from --null animal showing development arrest



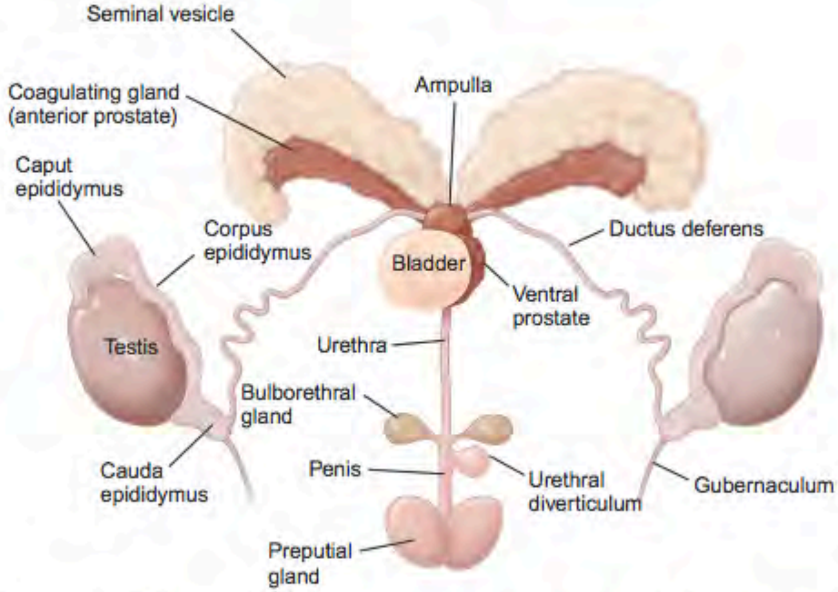
Abnormal degeneration of cells lining seminiferous tubules of mouse testis

H&E of testes from littermate controls and from ---null mice, showing degenerated follicles



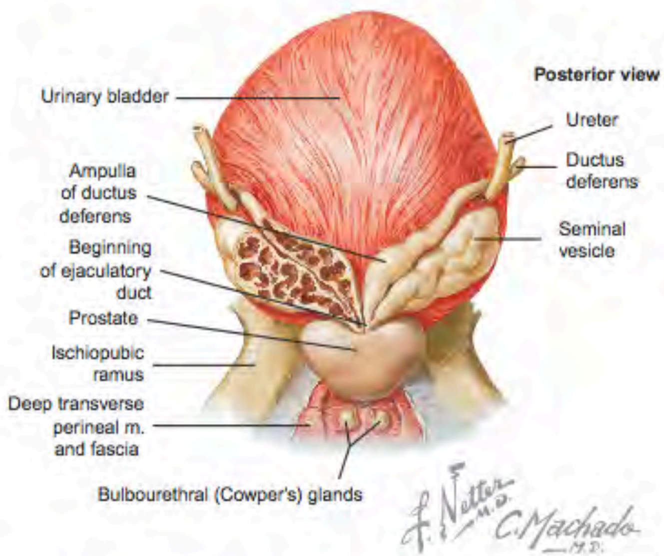


Mouse Epididymis, lined by a single layer of epithelial cells, containing sperm in transit



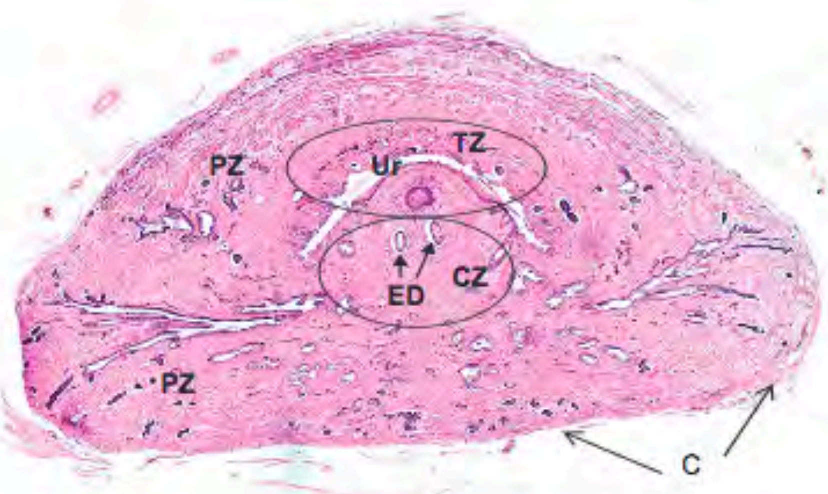
- **Need-to-know**
  - Mice have ampullary and preputial glands.

FIGURE 1 The male mouse reproductive system. The reproductive tract consists of paired testes, epididymis, vas deferens, and the accessory sex glands which consist of paired seminal vesicles, prostate lobes, ampullary glands, bulbourethral glands, preputial glands, and the penis. Source: Adapted with permission from Anatomy of a Laboratory Mouse, Cook, M.J., 1965, with permission from Elsevier.



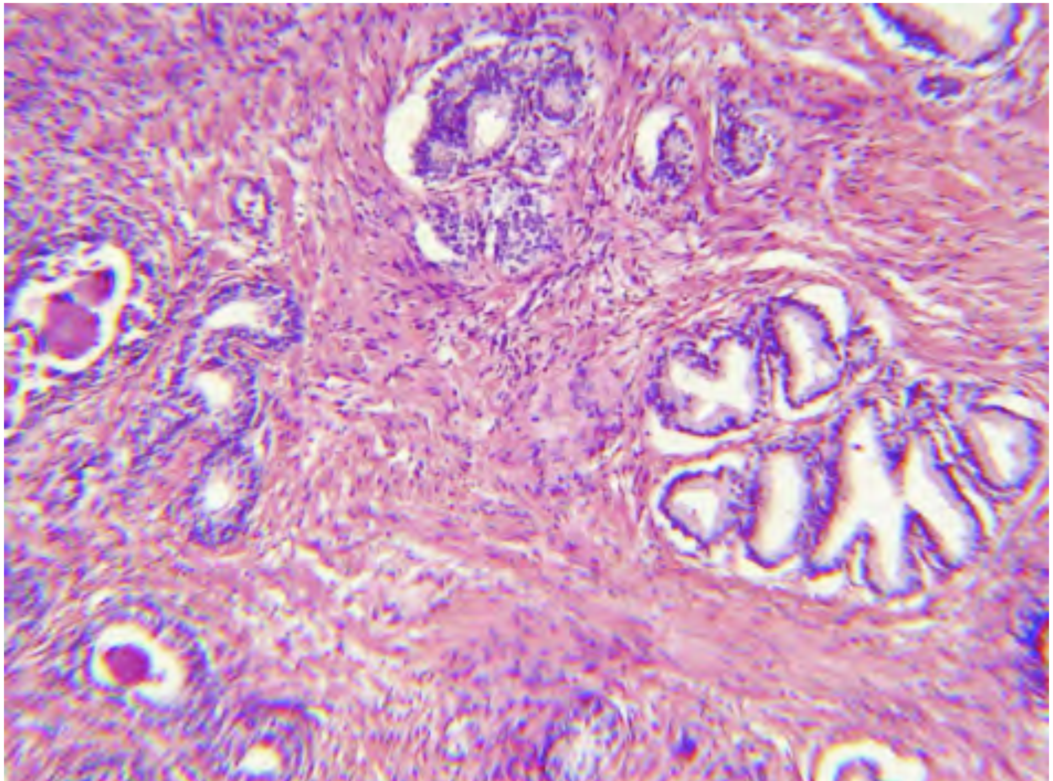
- **Need-to-know**
  - Humans lack ampullary and preputial glands.

FIGURE 2 The male human reproductive system. The reproductive tract consists of paired testes, epididymis, vas deferens, seminal vesicles, bulbourethral glands, prostate gland, and the penis. Source: © Elsevier, Inc., www.netterimages.com.

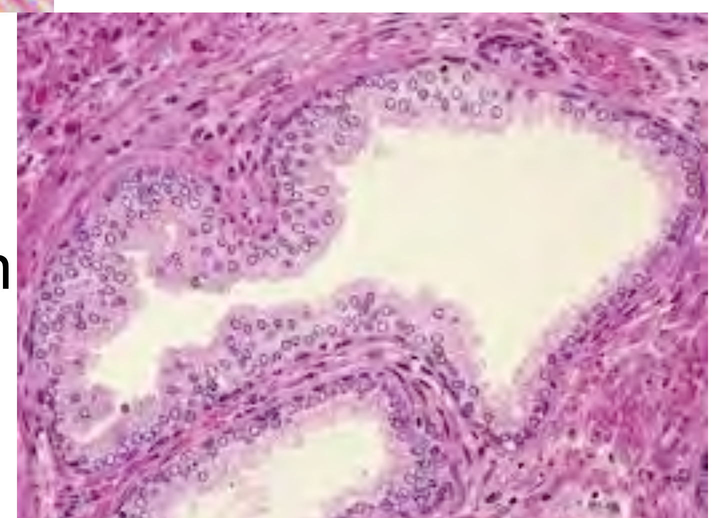


- Need-to-know
  - The mouse prostate is divided into four histologically distinct lobes.
  - The human prostate is divided into zones that are not clearly demarcated from one another but may be characterized by specific predisposition to disease.
  - The human prostate is surrounded by a capsule, whereas the mouse prostate. Lobes are invested and separated by a thin mesothelial-lined capsule/ membrane.

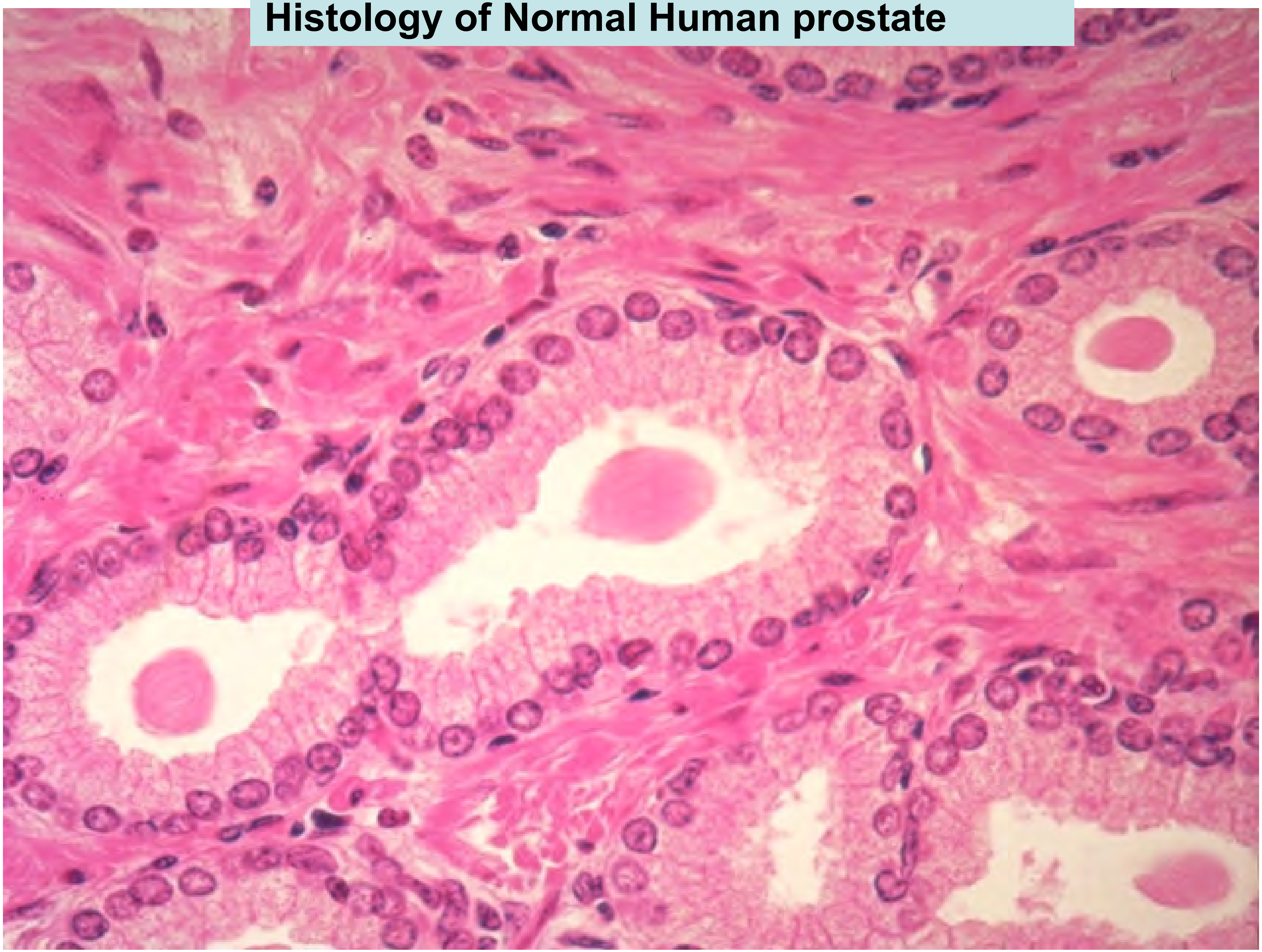
FIGURE 27 Human prostate. The prostrate is alobular, but it is divided into three concentric zones. The central zone (CZ) encircles the ejaculatory ducts (ED), the transition zone (TZ) surrounds the prostatic part of the urethra (Ur), and the peripheral zone (PZ) makes up the bulk of the gland. The human prostate is surrounded by a capsule (C).

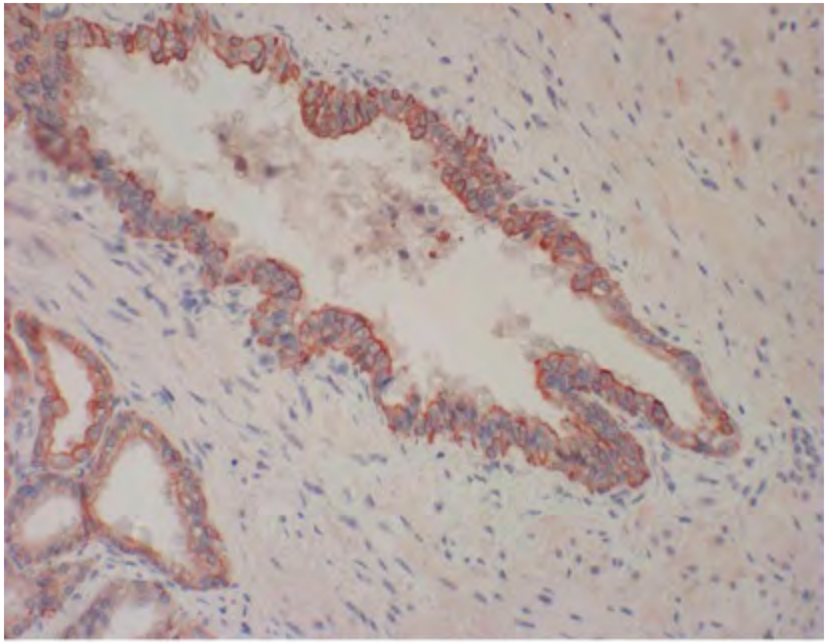


Human prostate:
Tubulo-alveolar glands embedded in fibro-muscular stroma

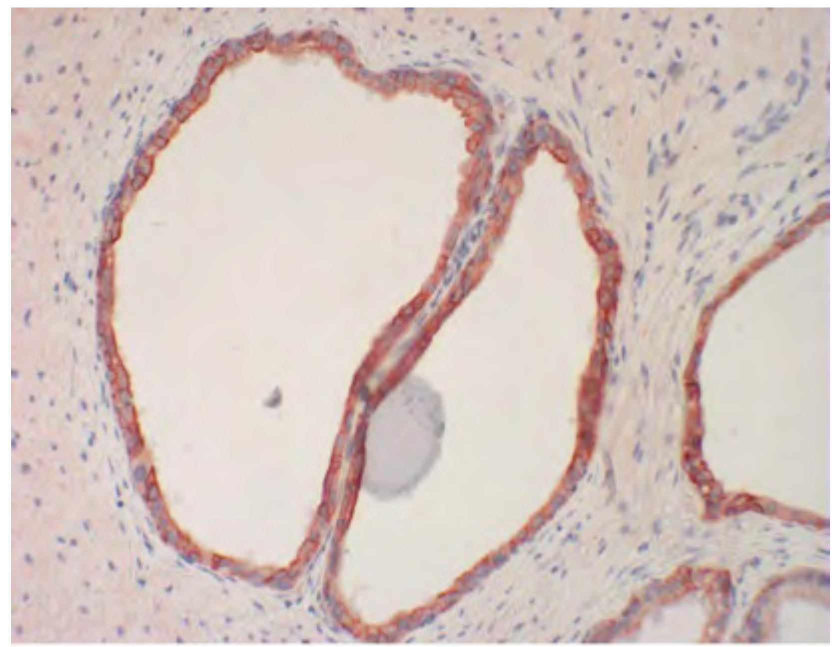


Histology of Normal Human prostate



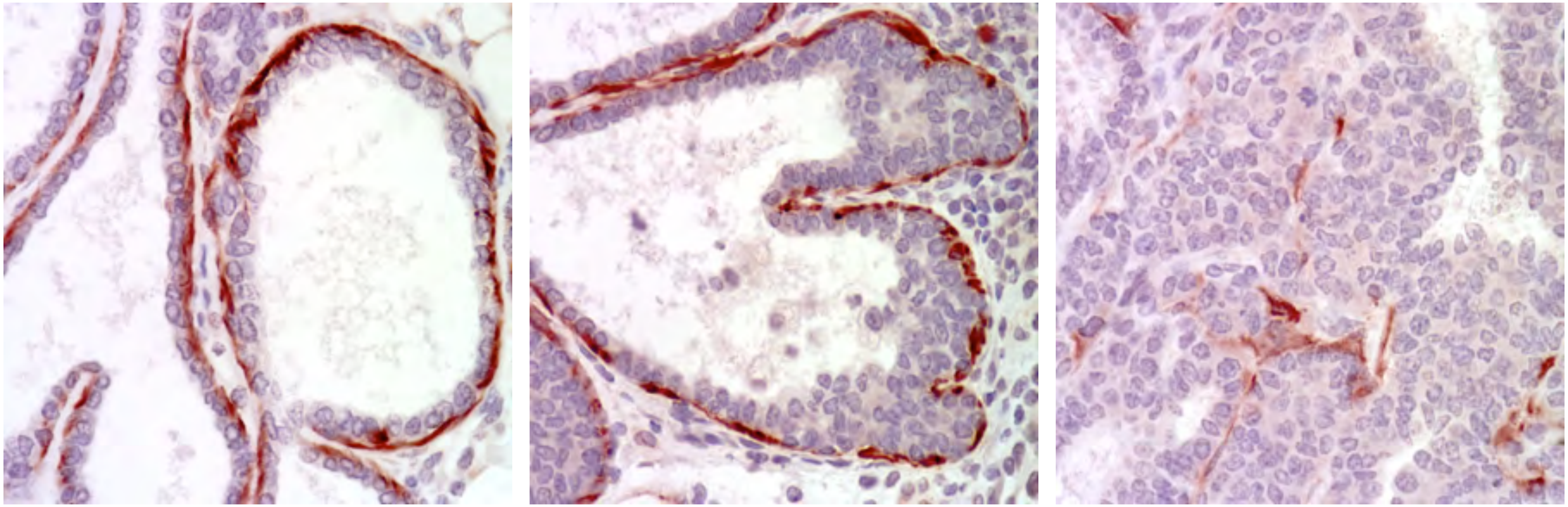


Normal Human Prostate
Single layer of epithelial cells
marked with anti-keratin



Markers of Differentiation

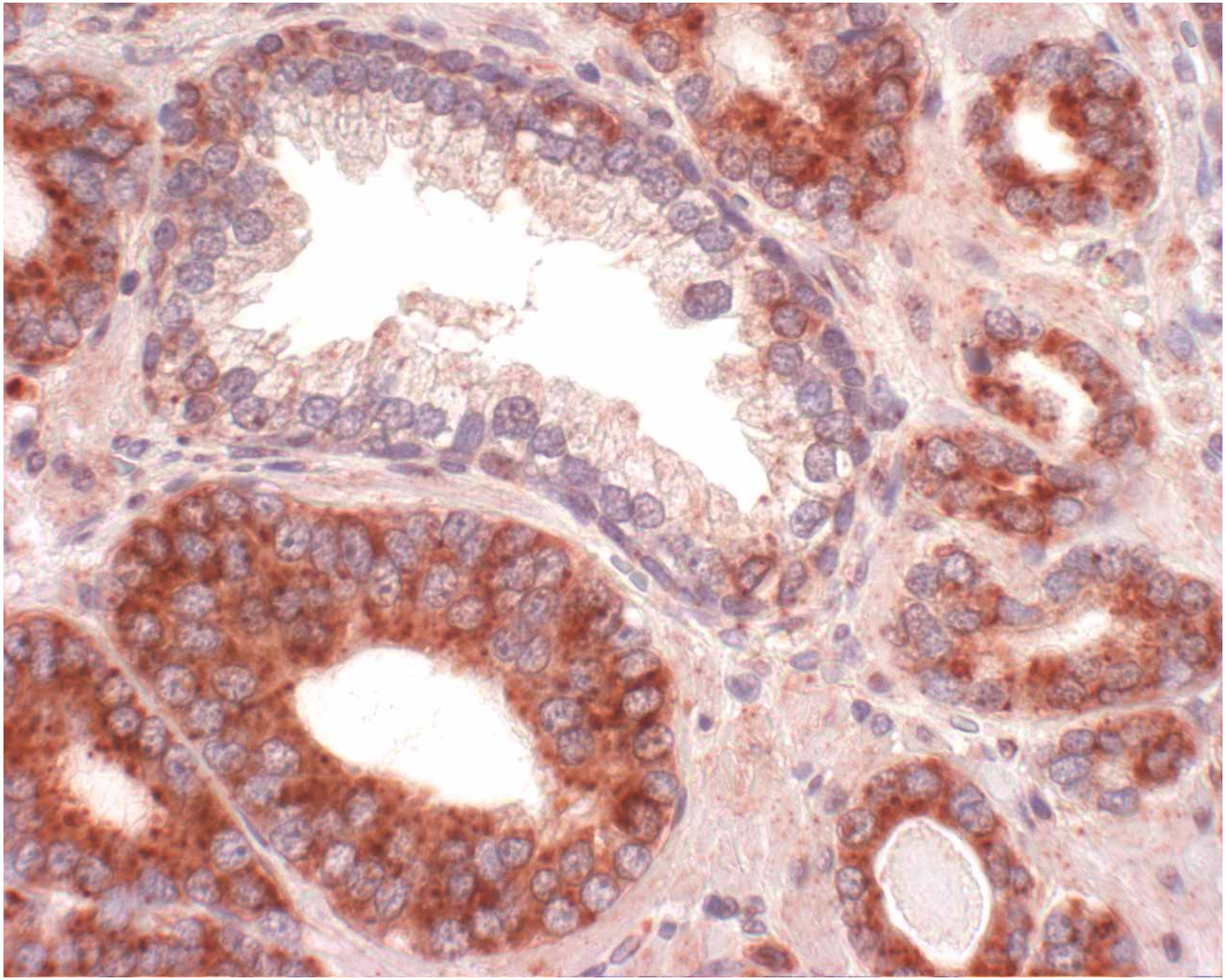
Smooth Muscle Actin (SMA)



Normal

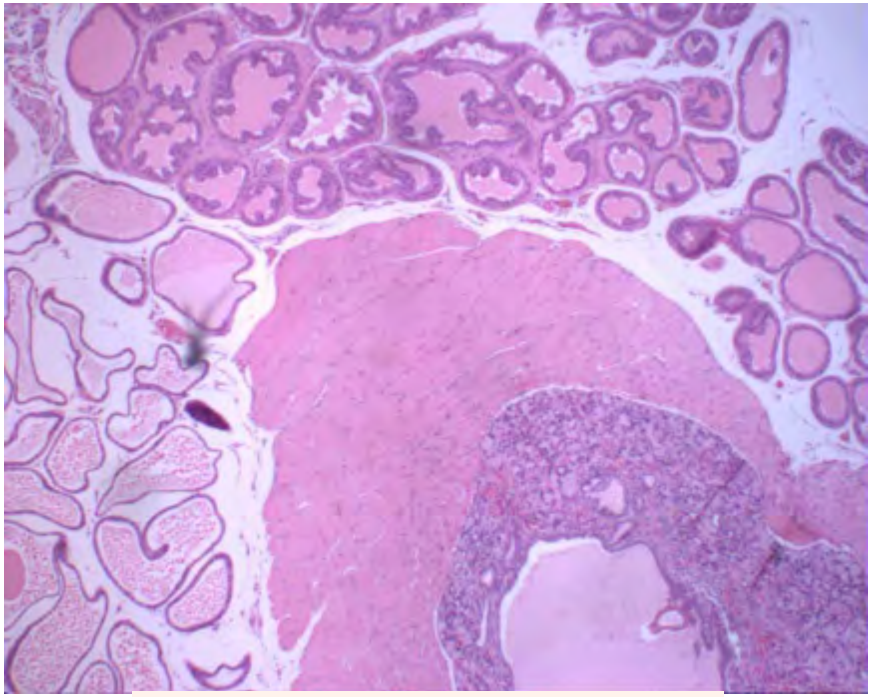
Hyperplasia

Tumor

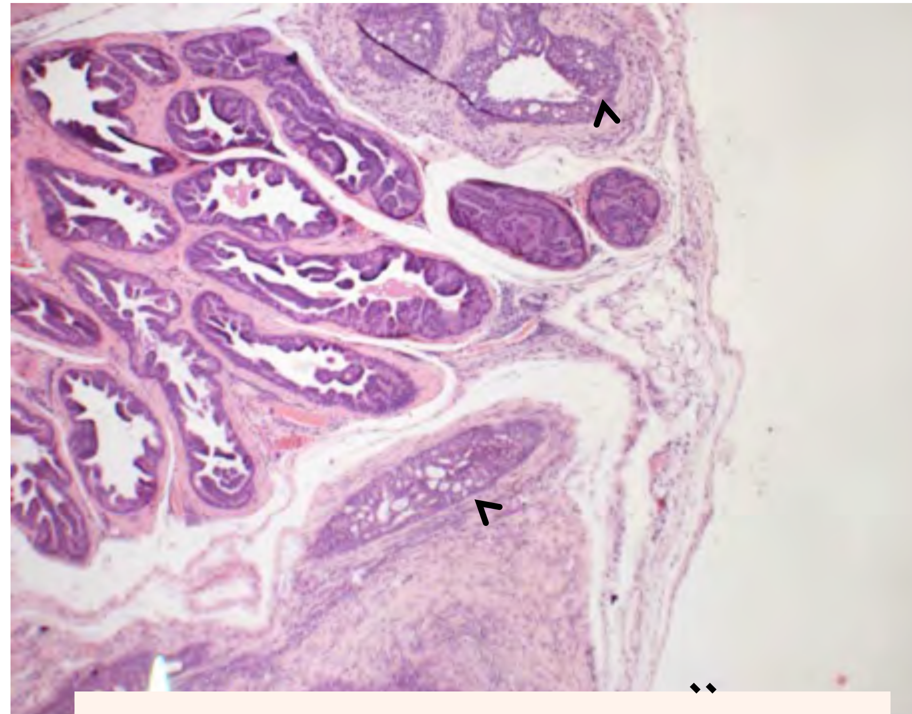


Prostate carcinoma around a normal prostate duct, with IHC (?prostate specific acid phosphatase PSA) marker http://tvmouse.ucdavis.edu/prostate/mouse/prostateindex2.htm

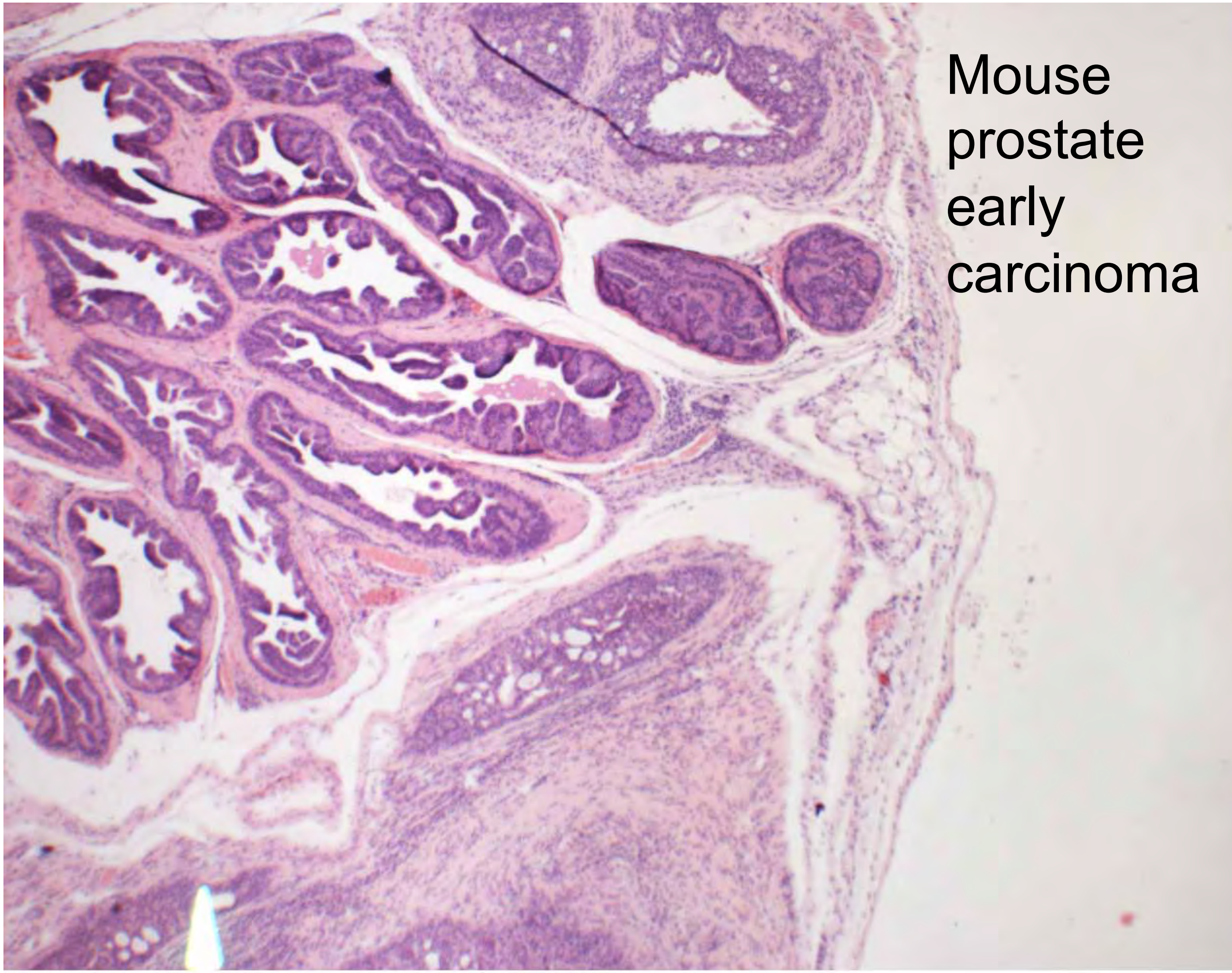

Mouse prostate

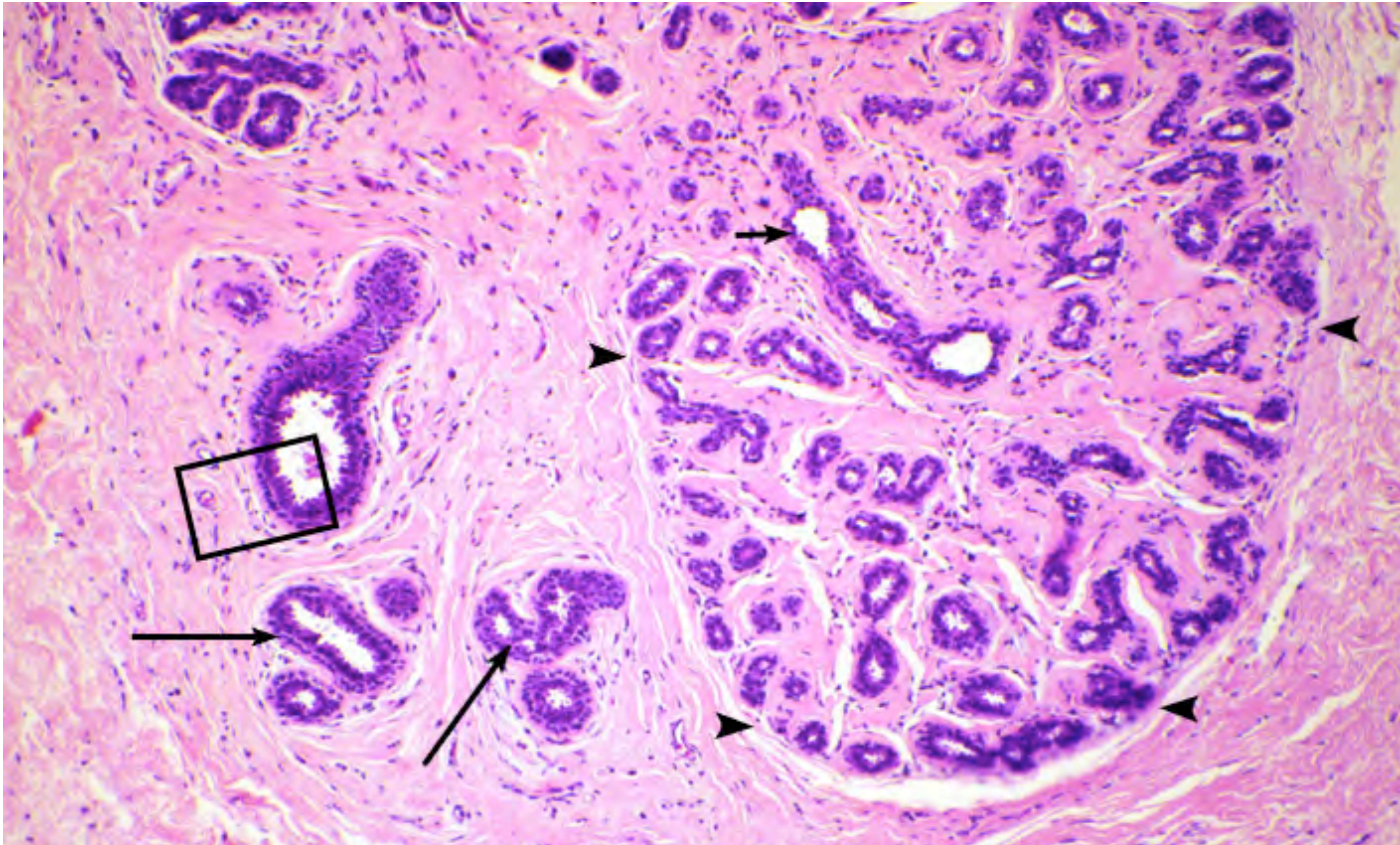


Normal mouse prostate



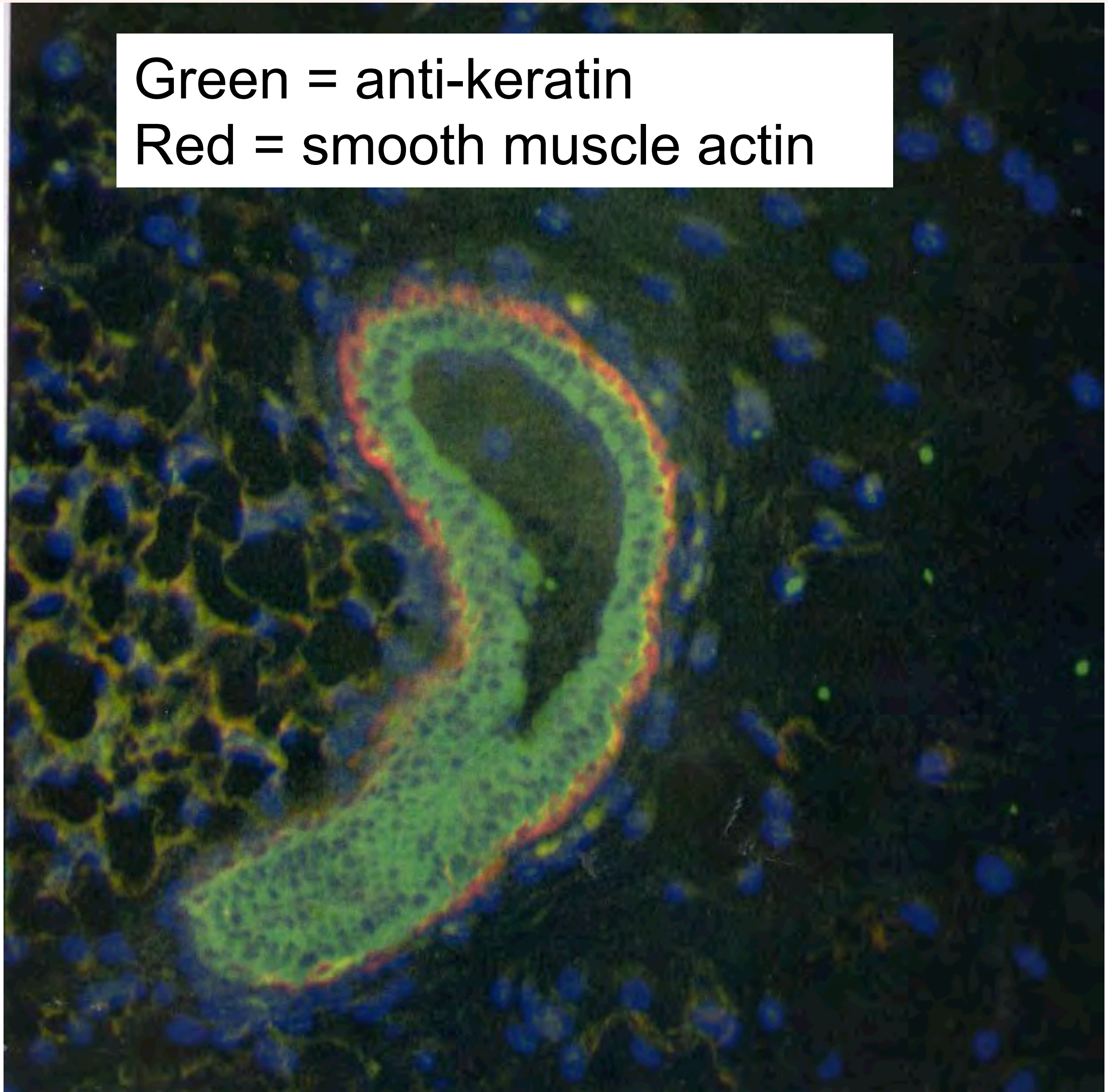
mouse prostate carcinoma in situ

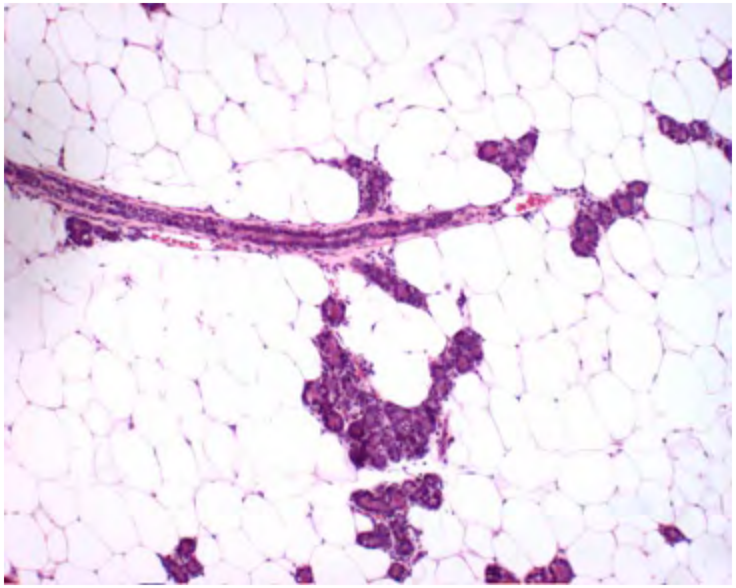

Mouse
prostate
early
carcinoma

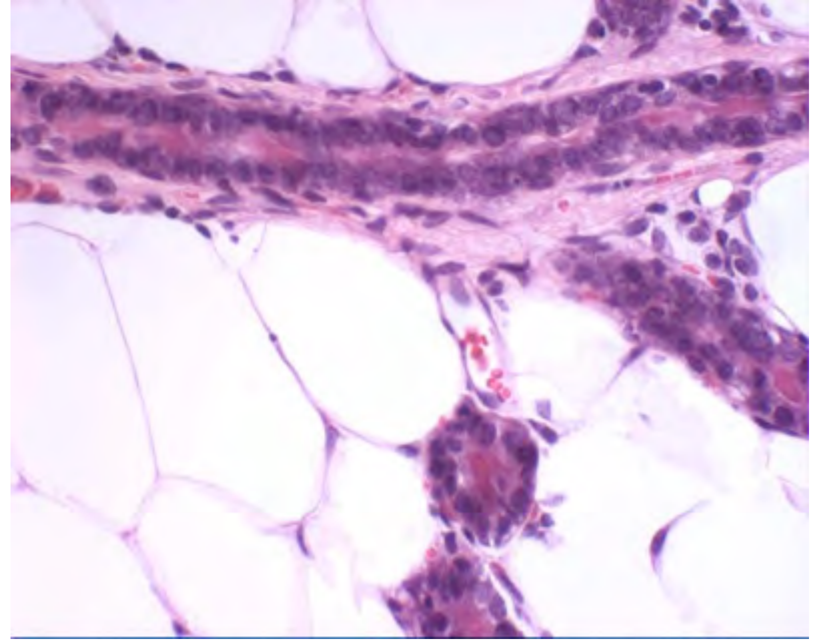


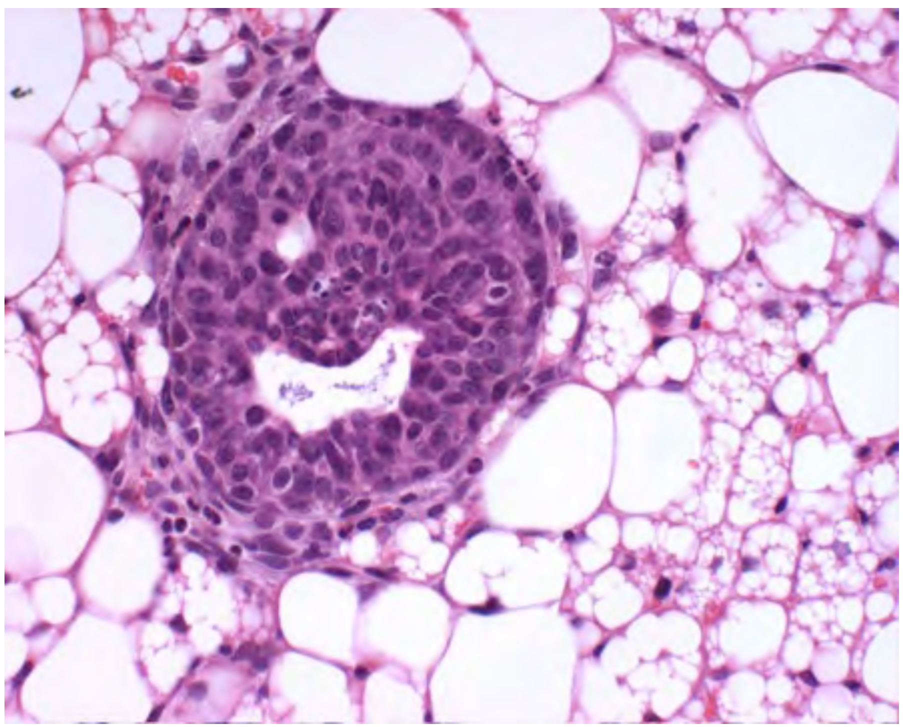
Human breast lobules and ducts
Normal with one layer of lining epithelial cells and an outer layer of myoepithelial cells

Normal breast ducts and alveoli have an Inner layer of cuboidal epithelial cells and an Outer layer of myoepithelial cells









Normal mammary gland and carcinoma in-situ