

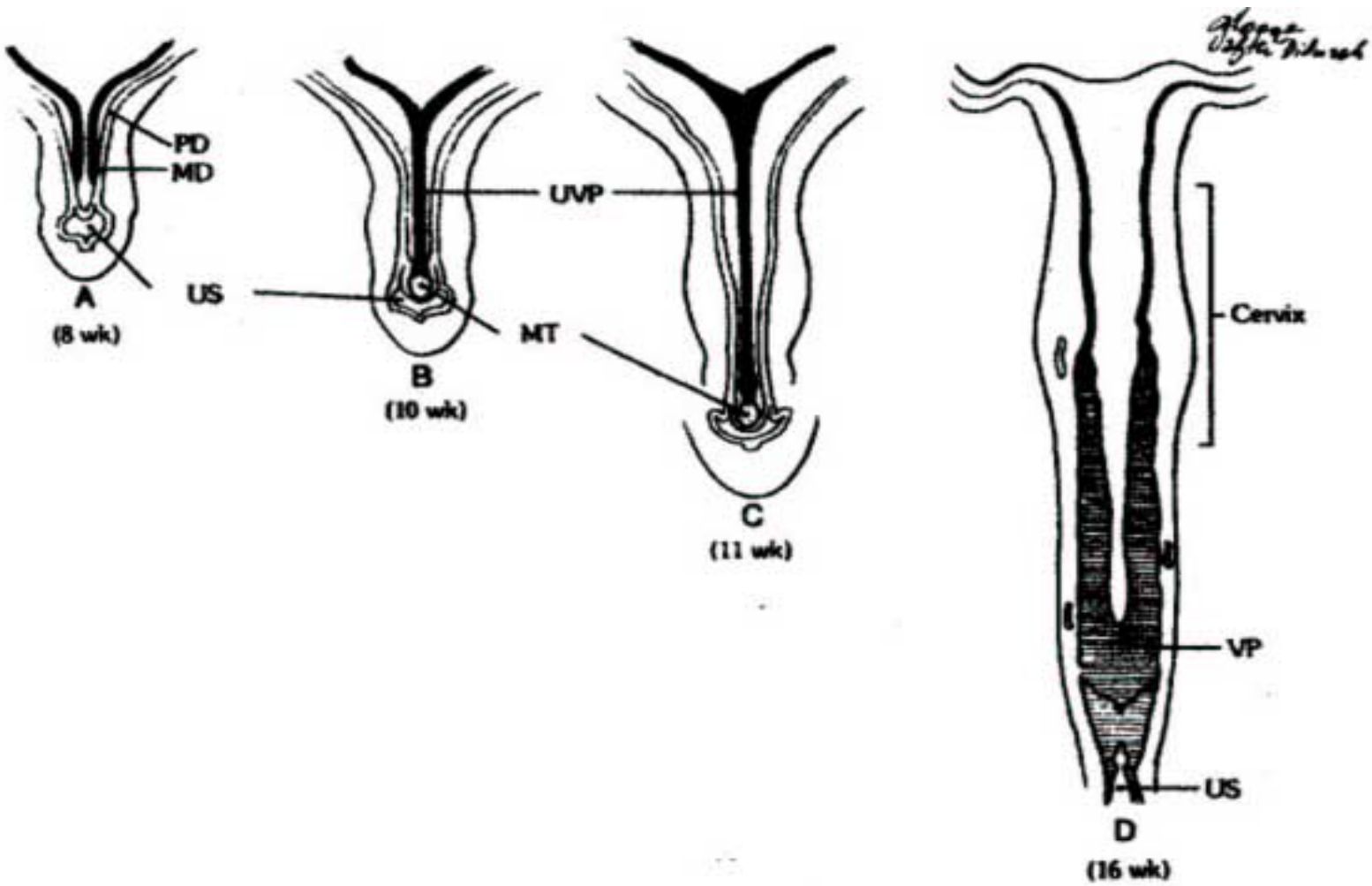
Female Reproductive Tract: With Special Focus on the Cervix

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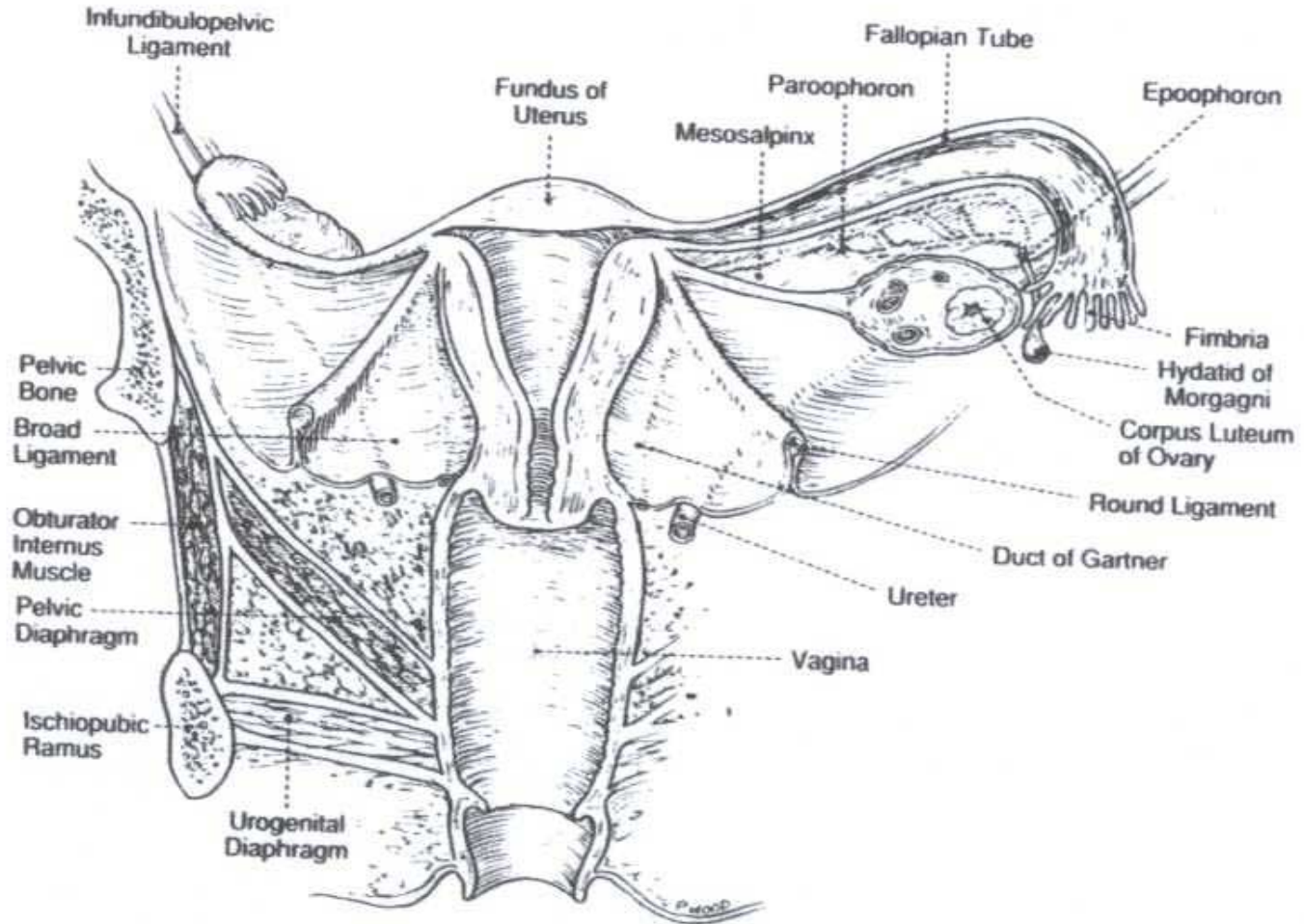
Keck School of Medicine

University of Southern California

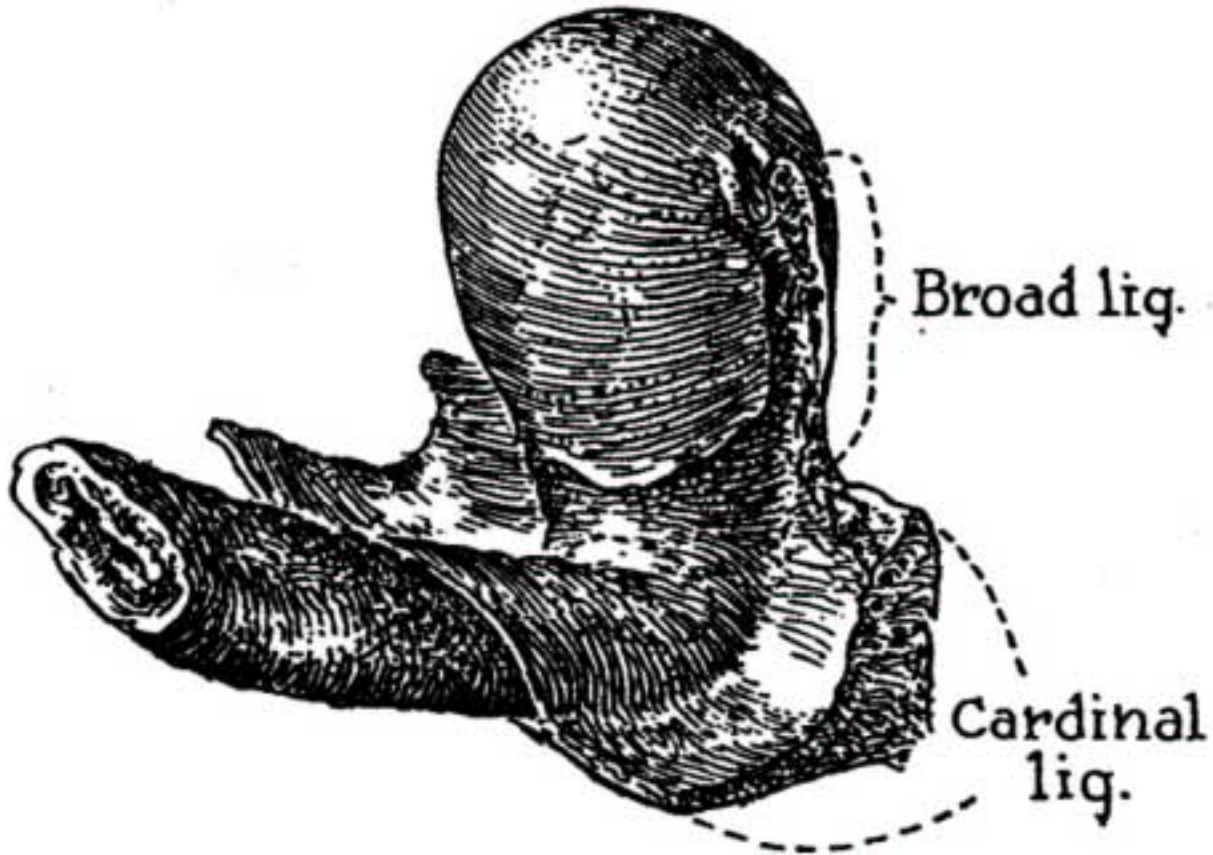
Early Embryological Development of the Female Genital Tract



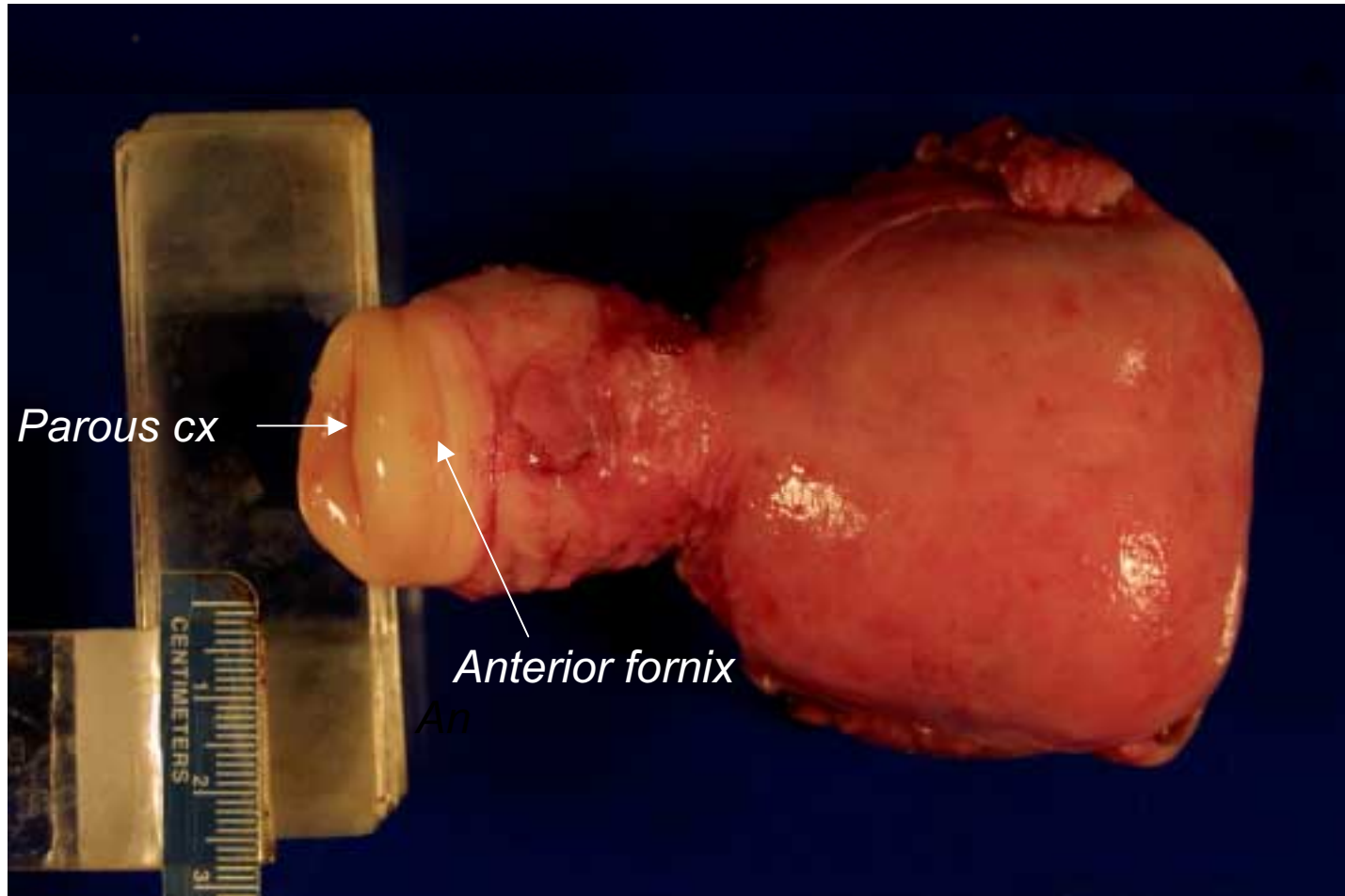
Coronal Section of the Female Genital Tract



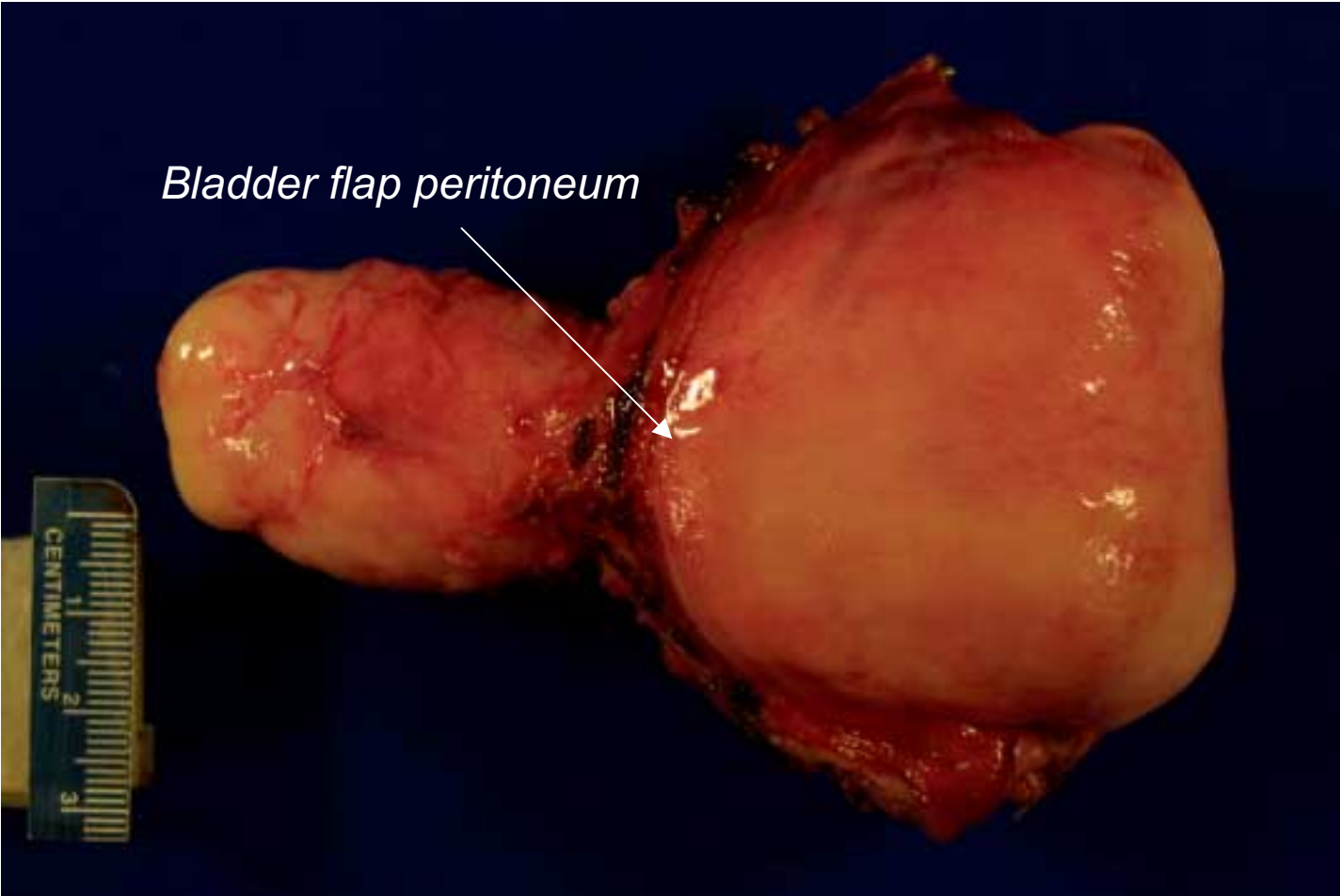
Attachments of Broad and Cardinal Ligaments



Normal Cervix & Fundus



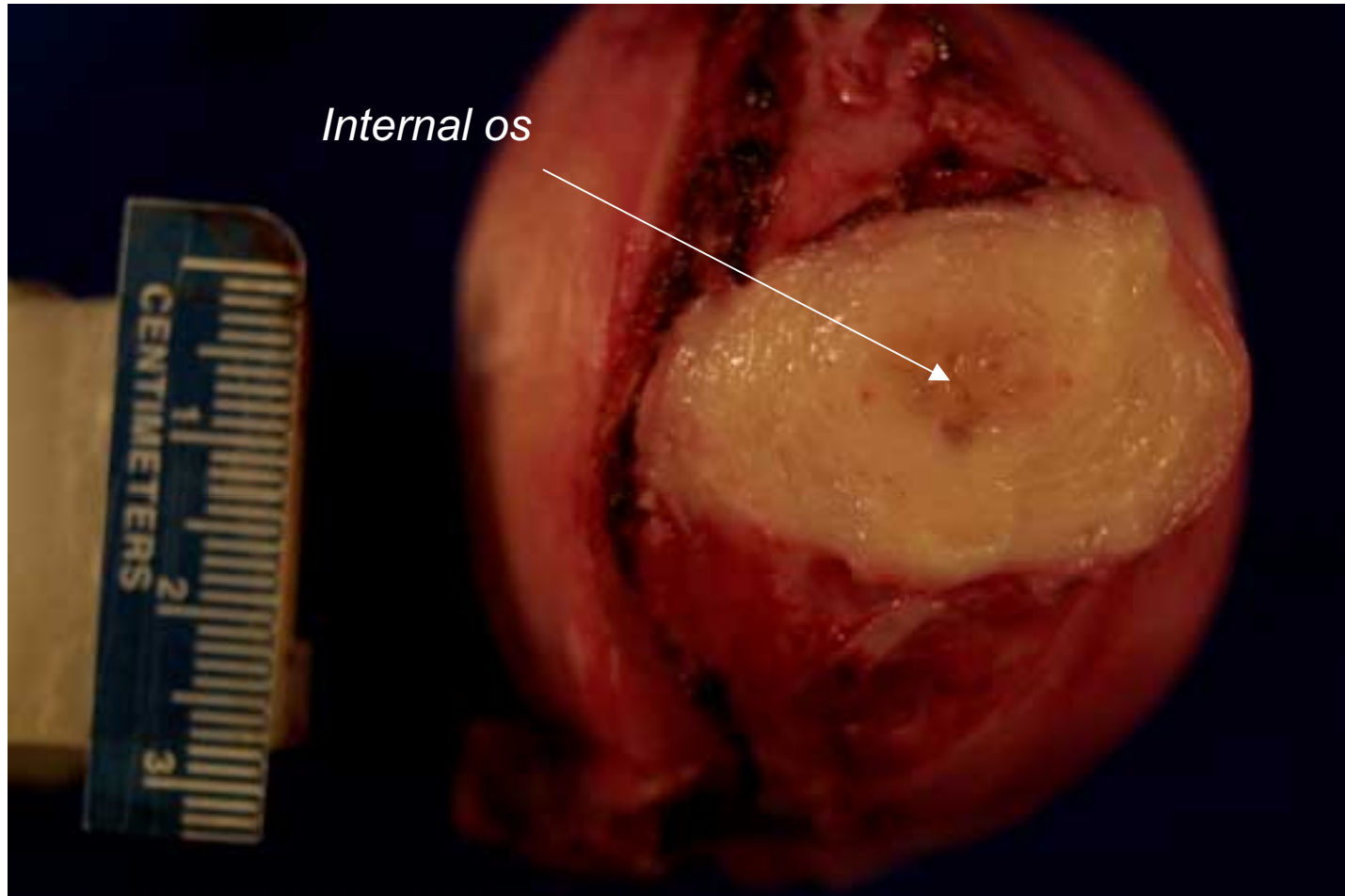
Uterus: Anterior View



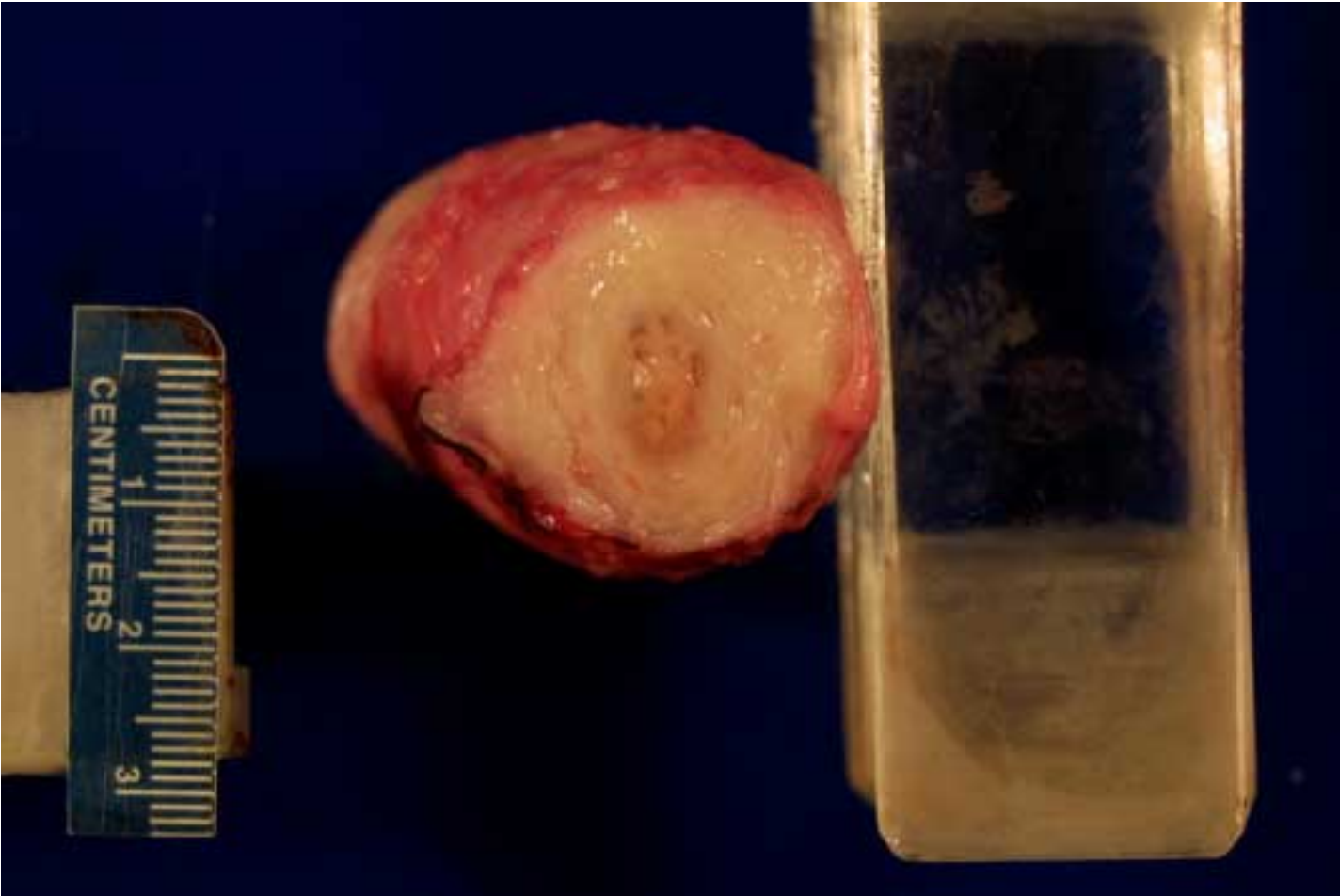
Uterus: Posterior View



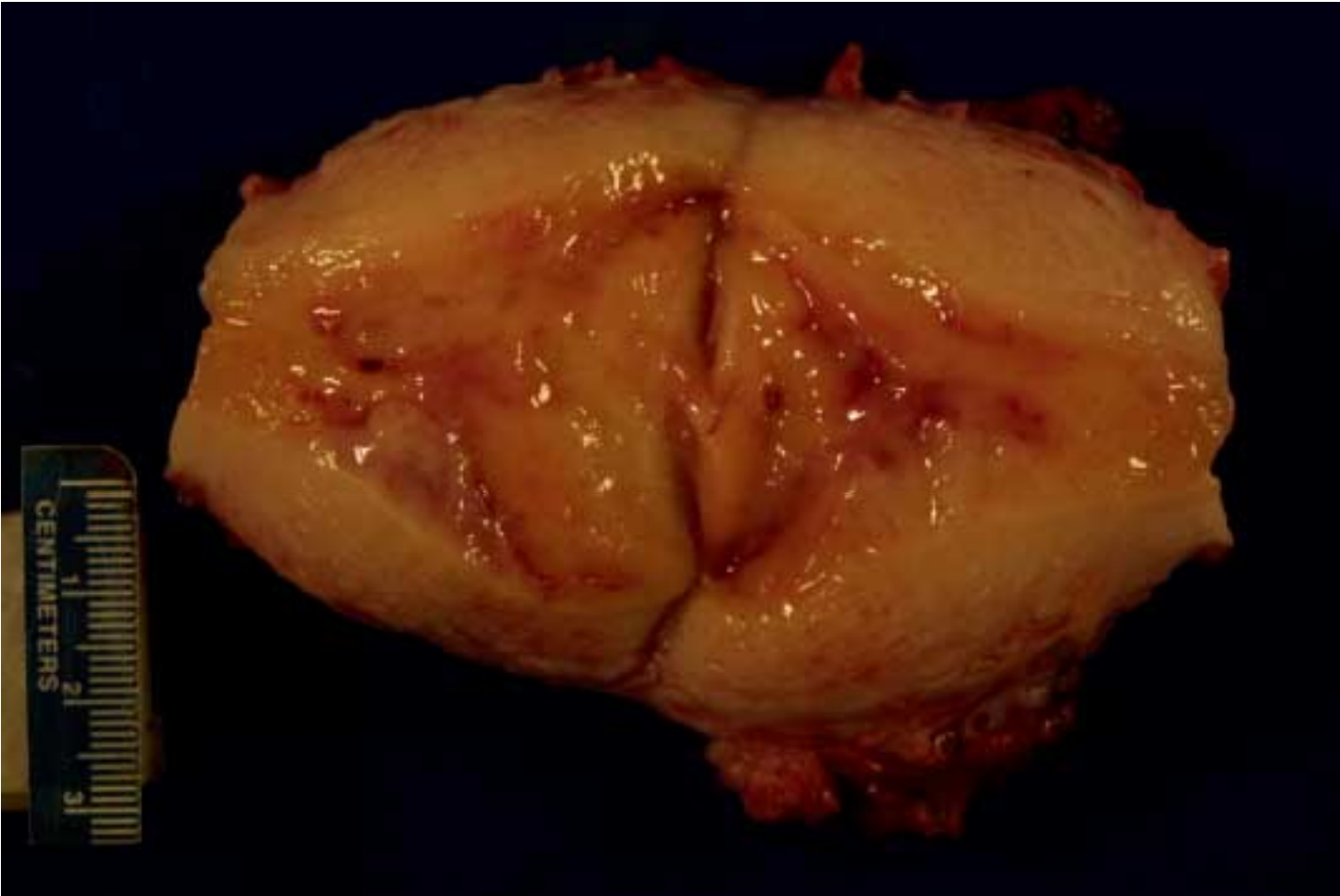
Uterine Corpus: Amputated Cervix



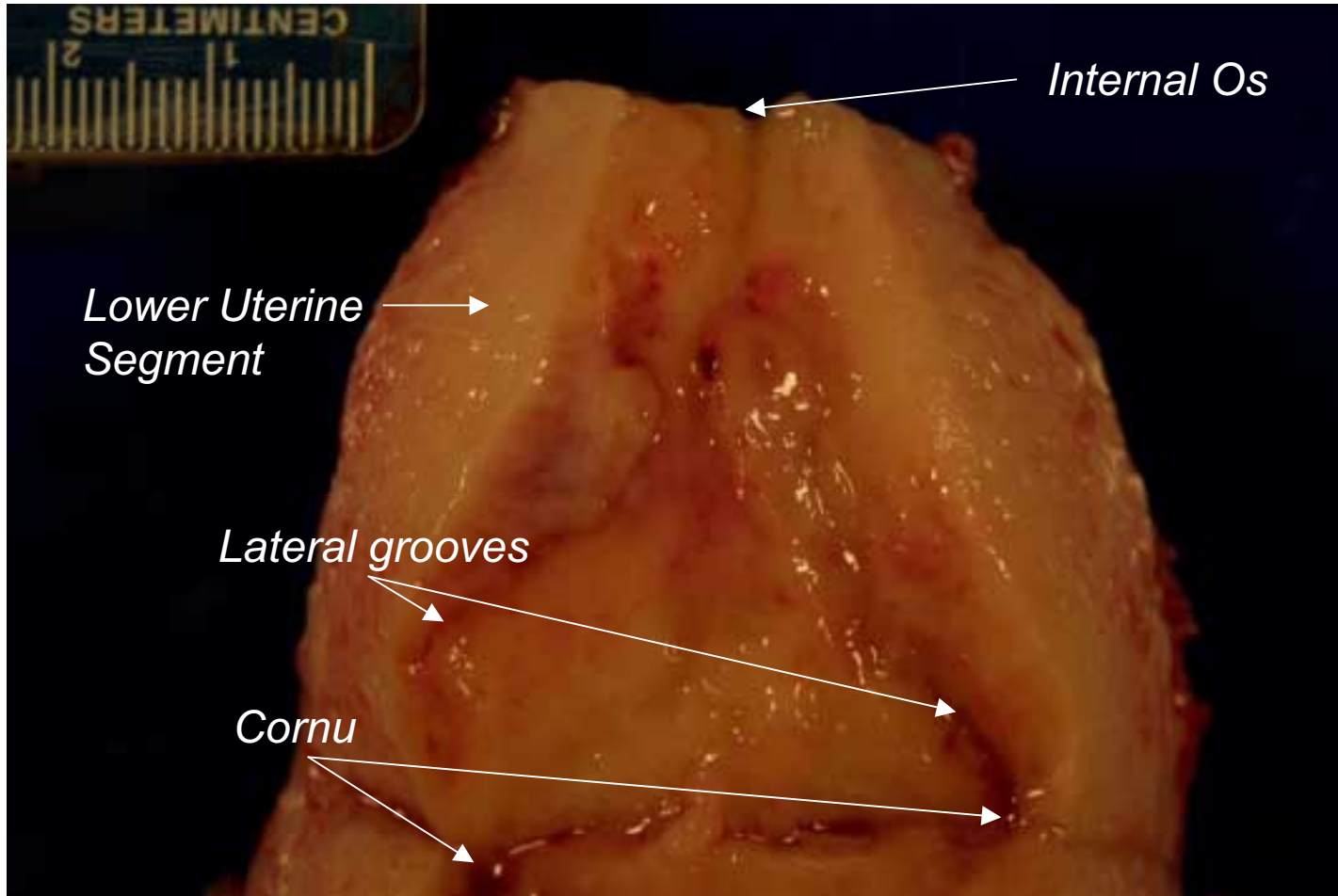
Amputated Cervix: Internal Os



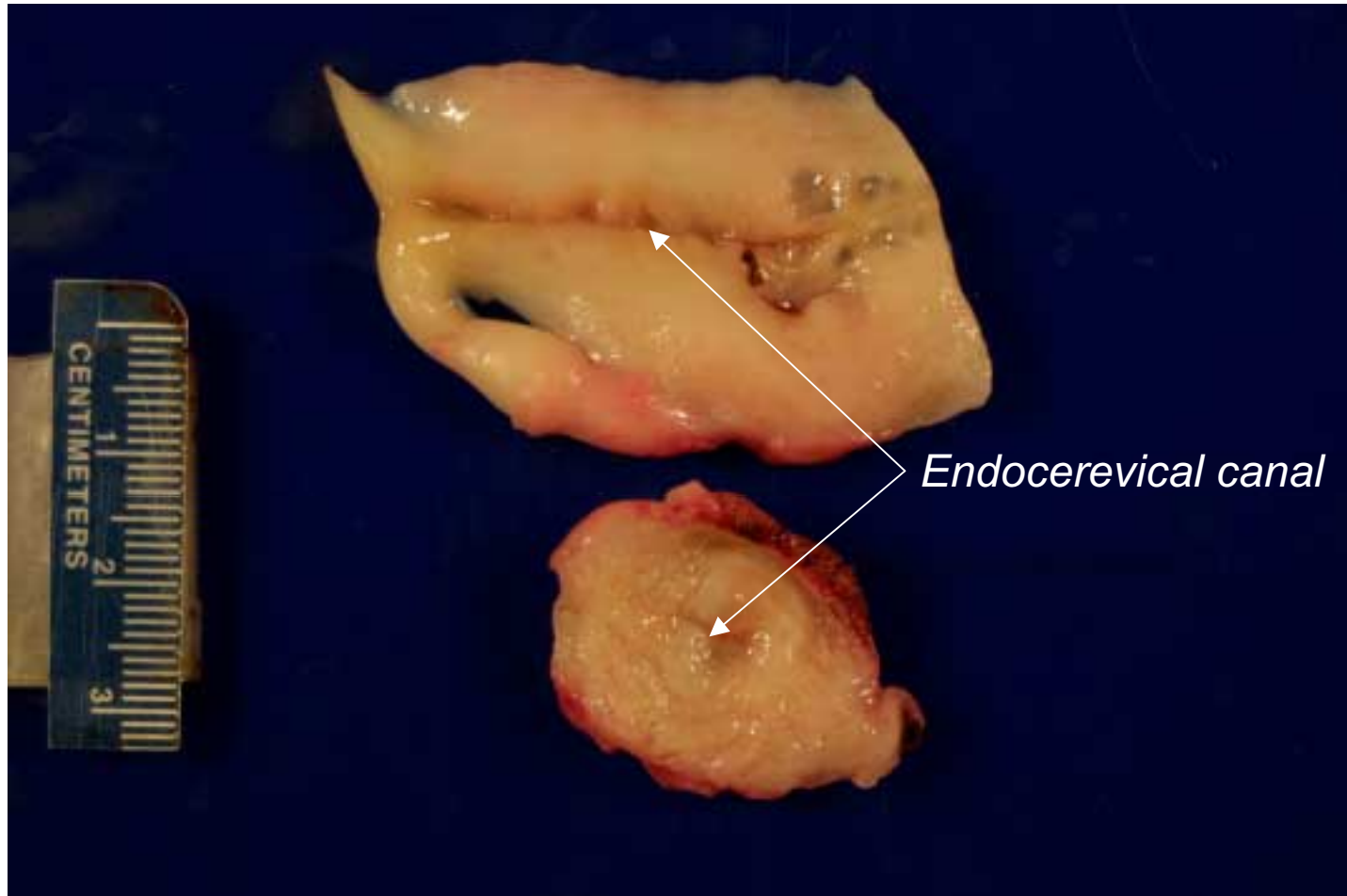
Open Corpus



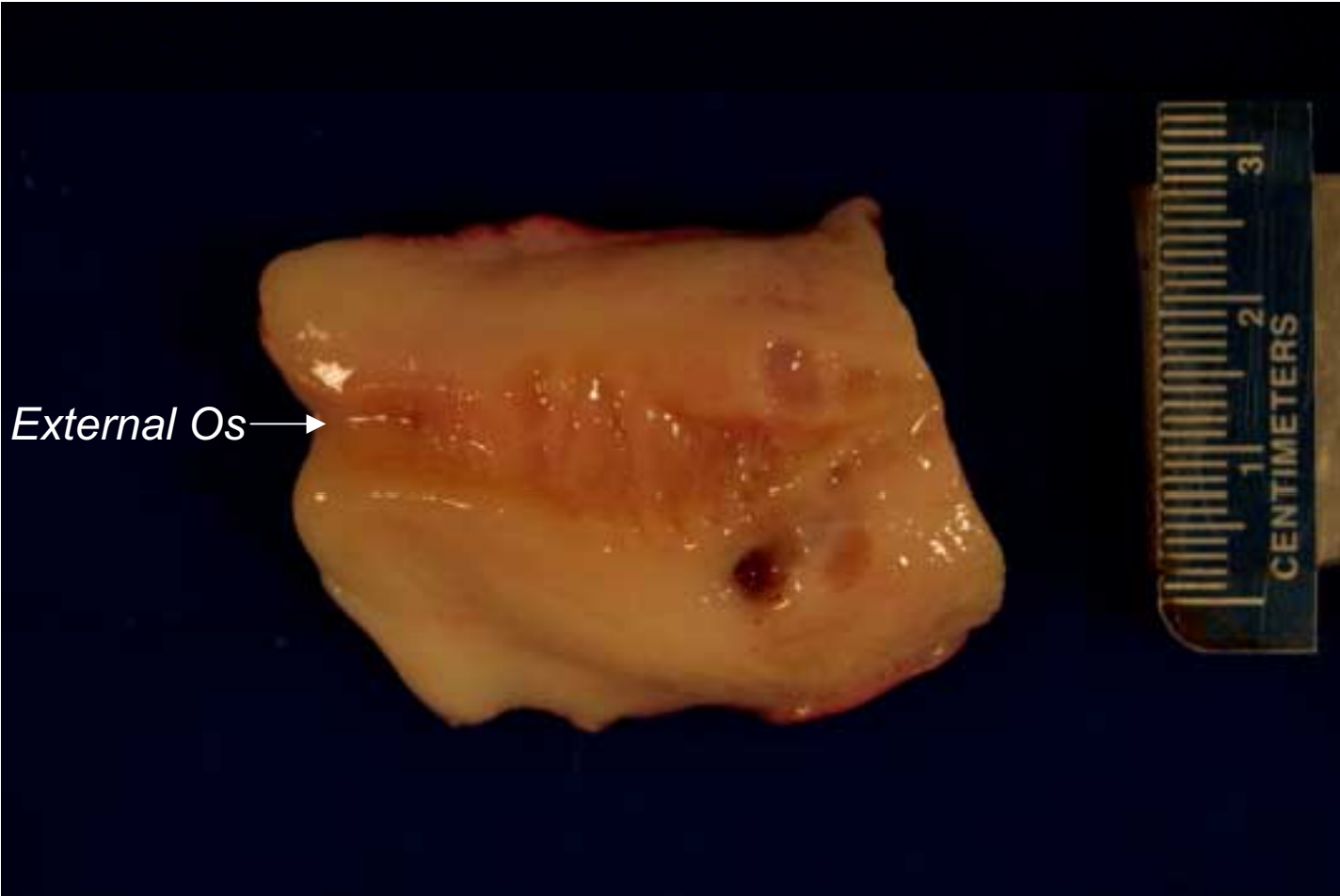
Lower Uterine Segment & Upper Cervix: Opened 3 to 9 O'clock



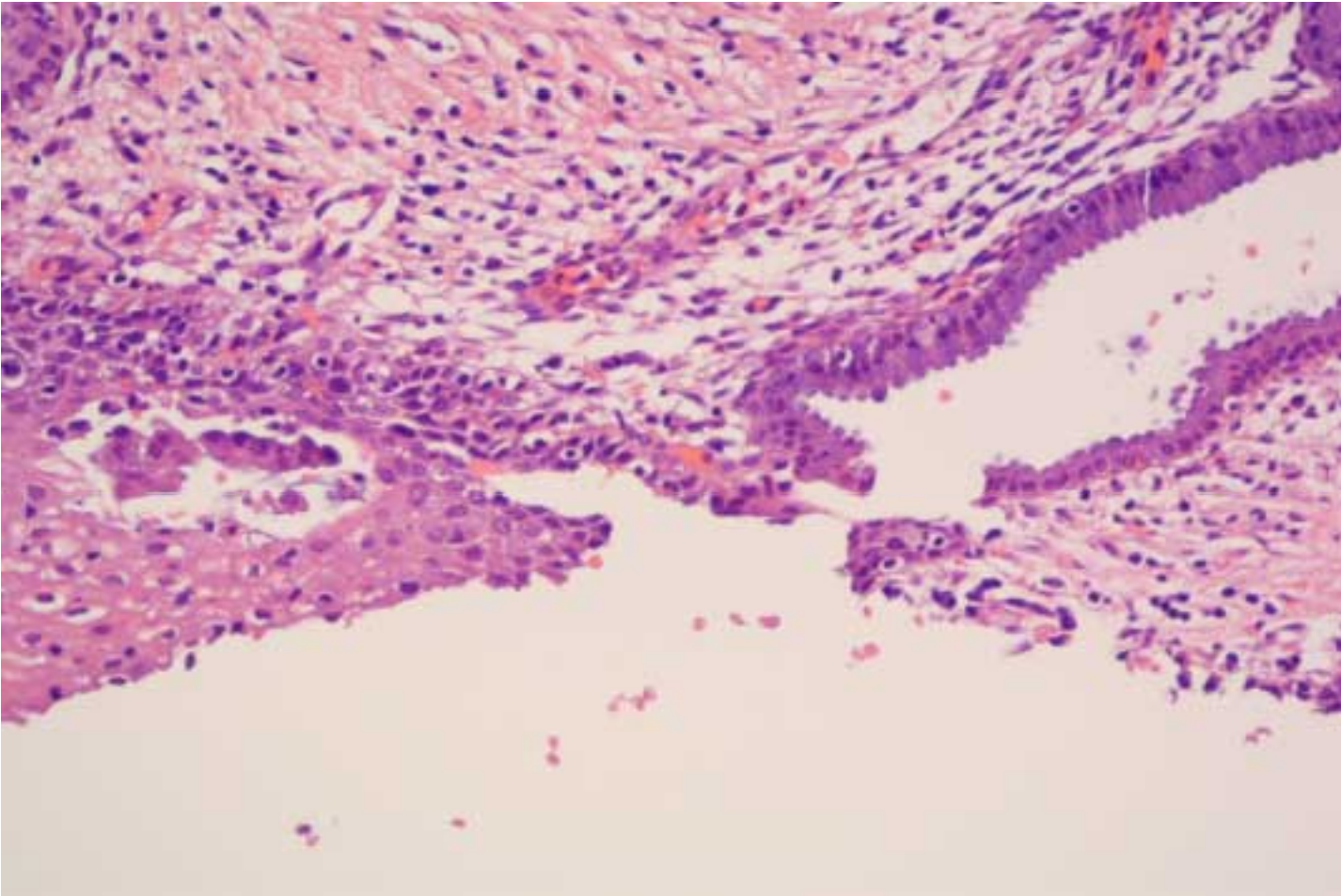
Cross & Longitudinal Sections of Cervix



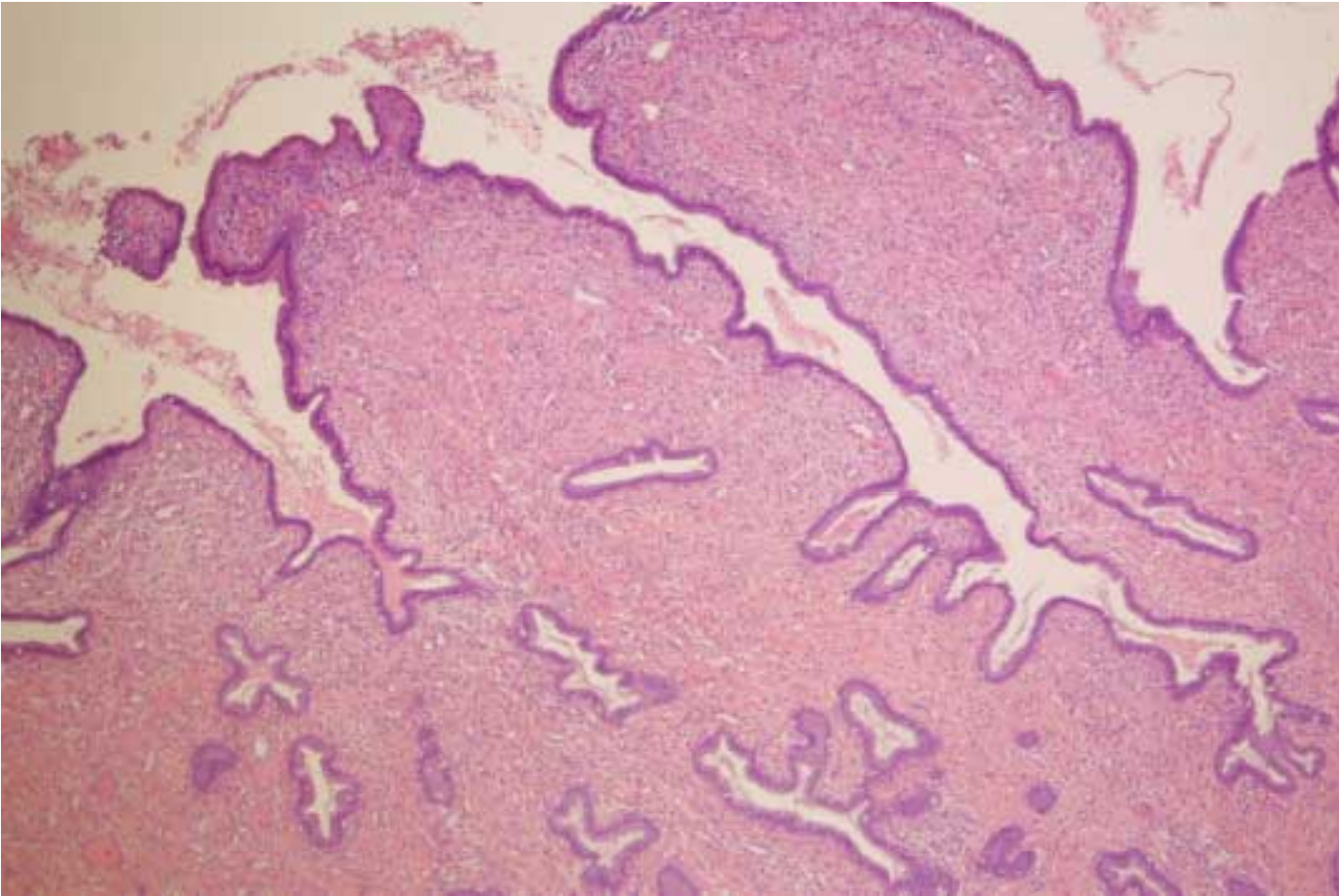
Endocervical Canal: Longitudinal



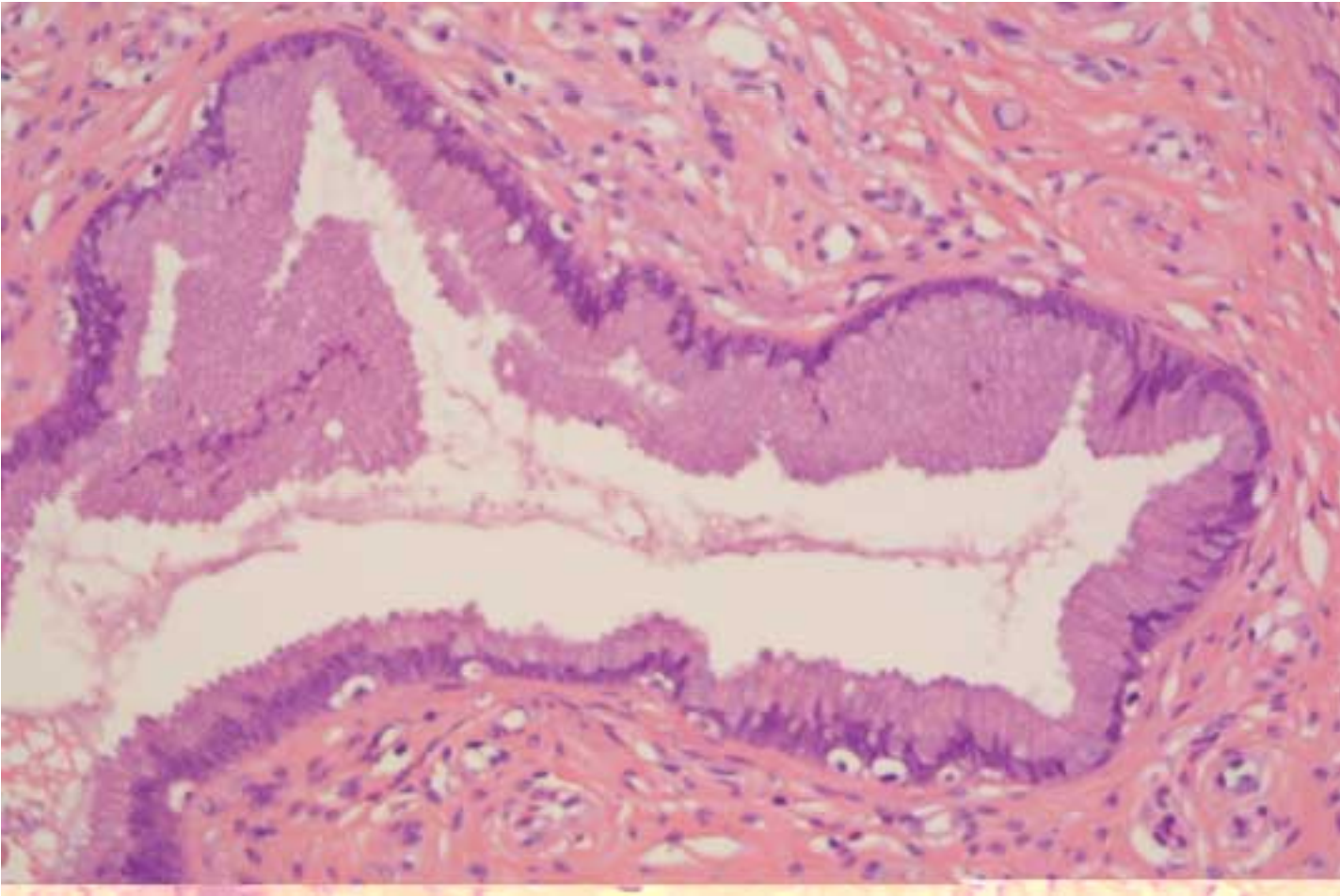
Cervix: Squamo-Columnar Junction



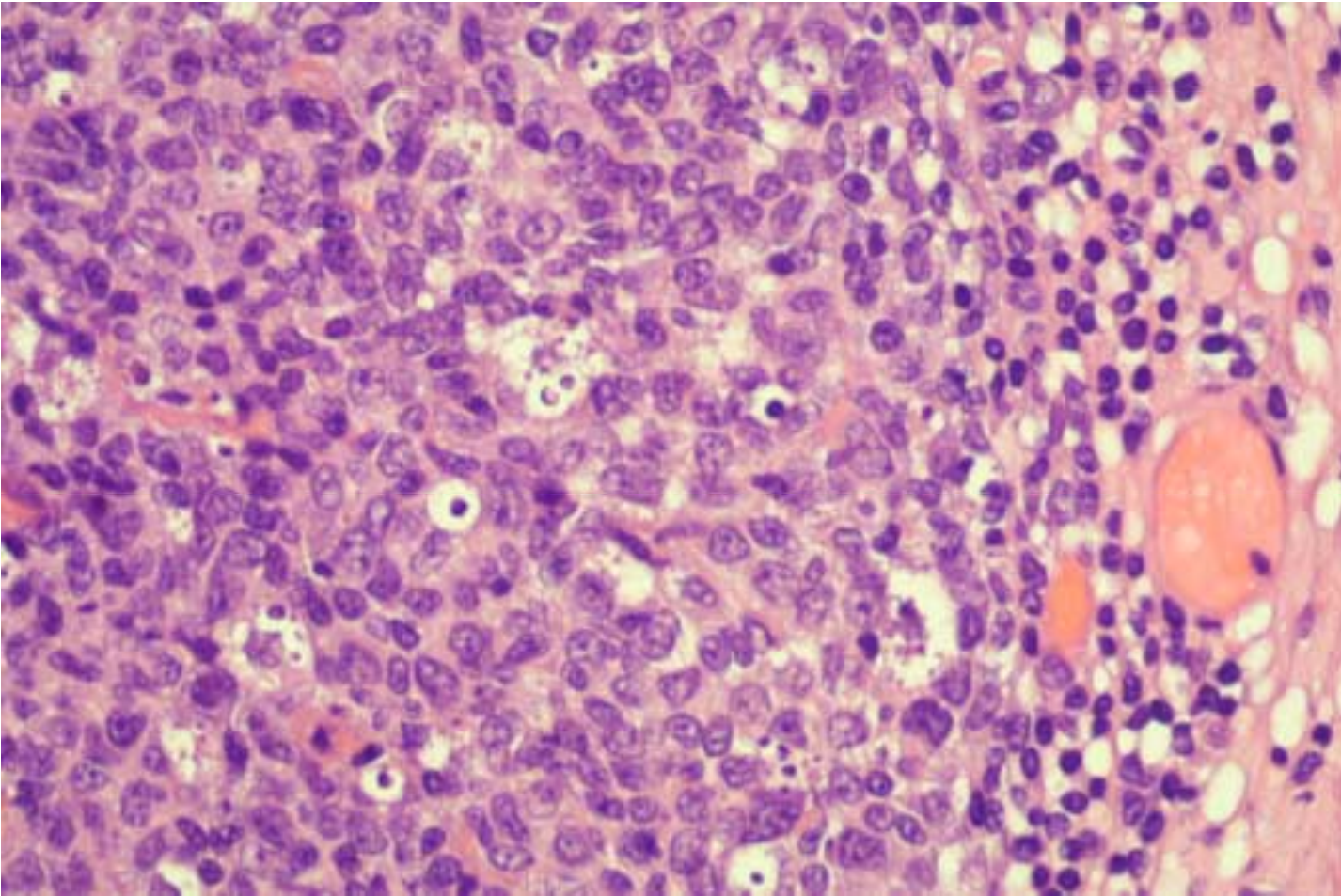
Venetian Blind Architecture of Endocervical Glands



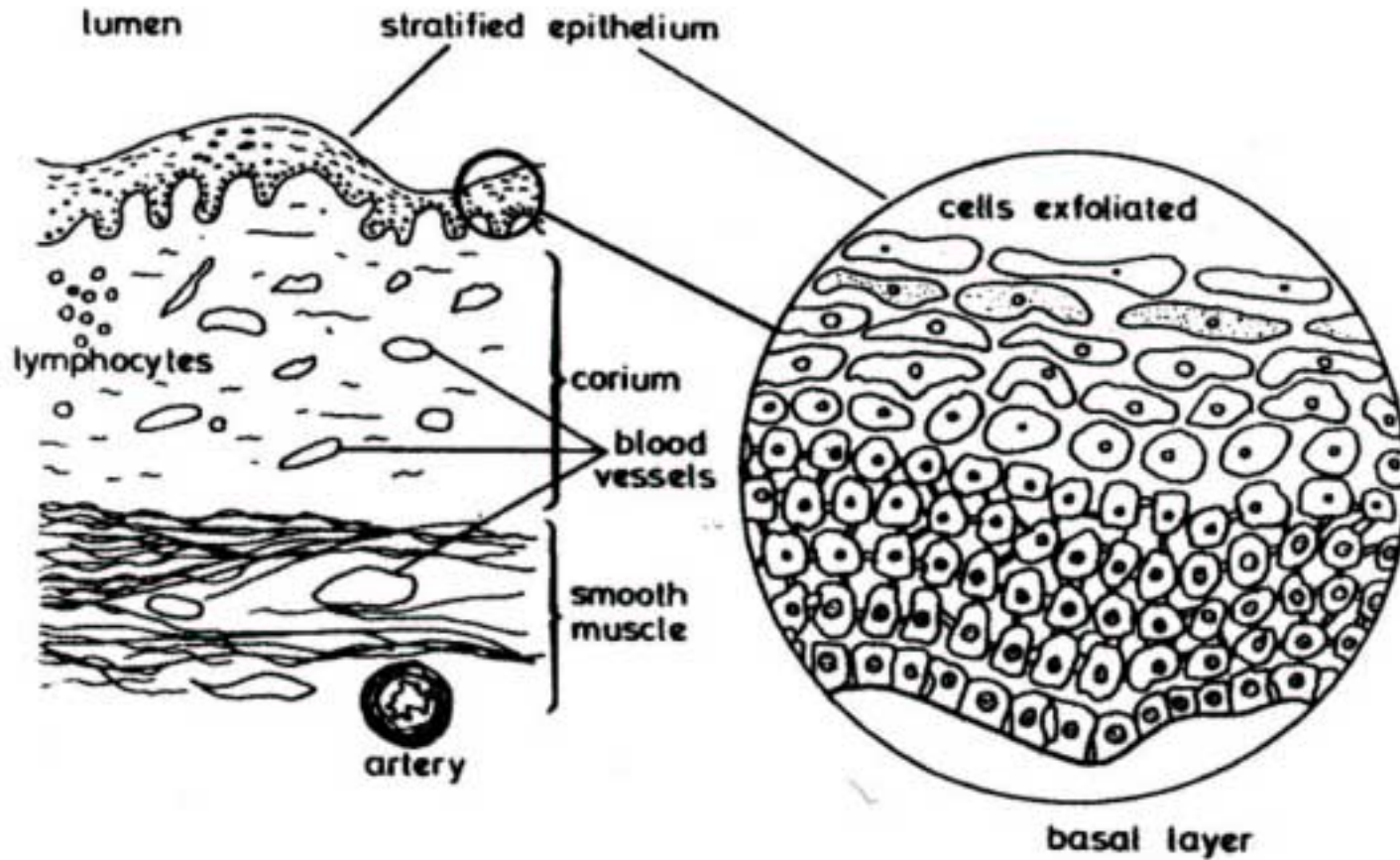
Mucus Secreting Gland



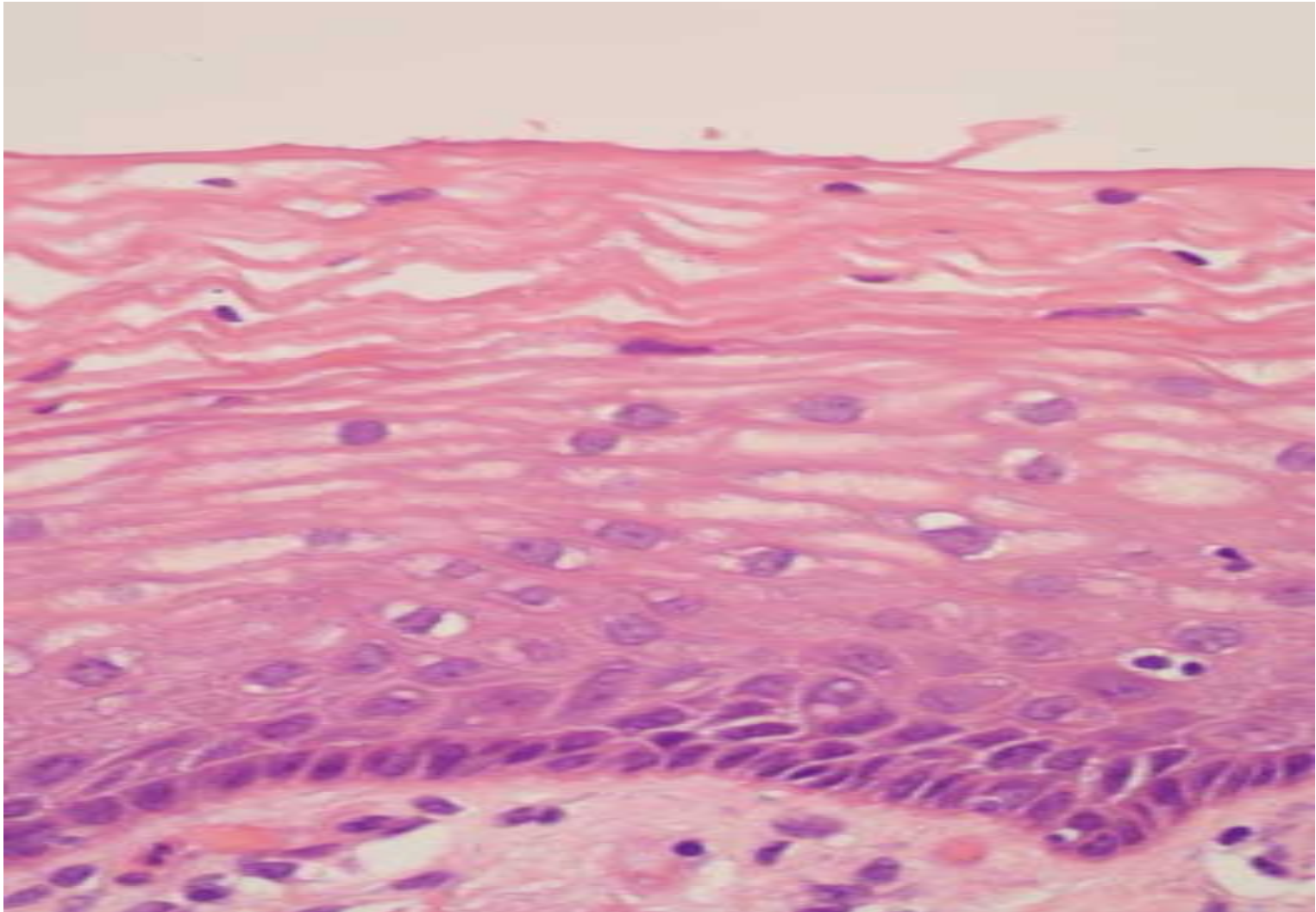
Lymphoid Follicle



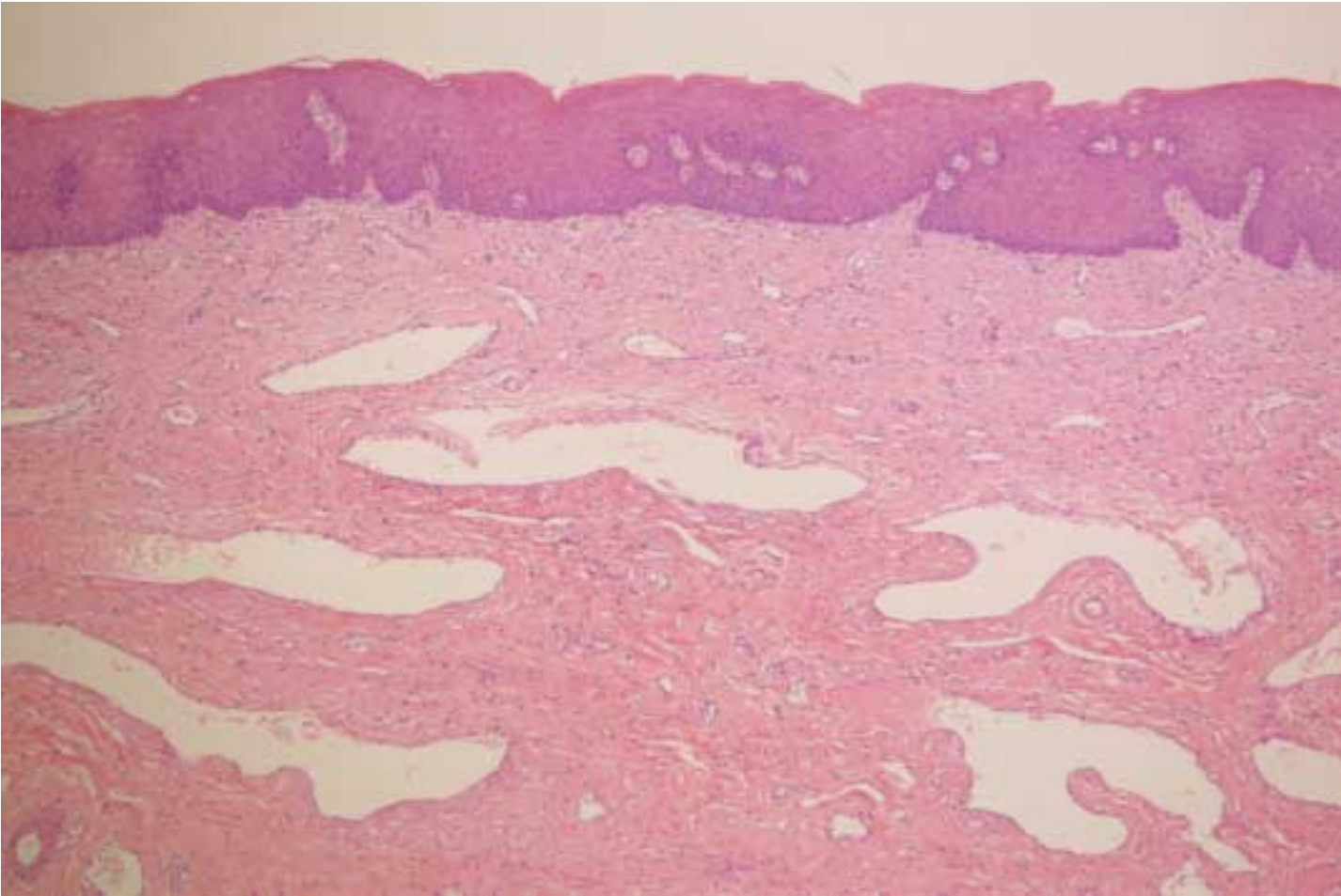
Vaginal Wall & Cytology



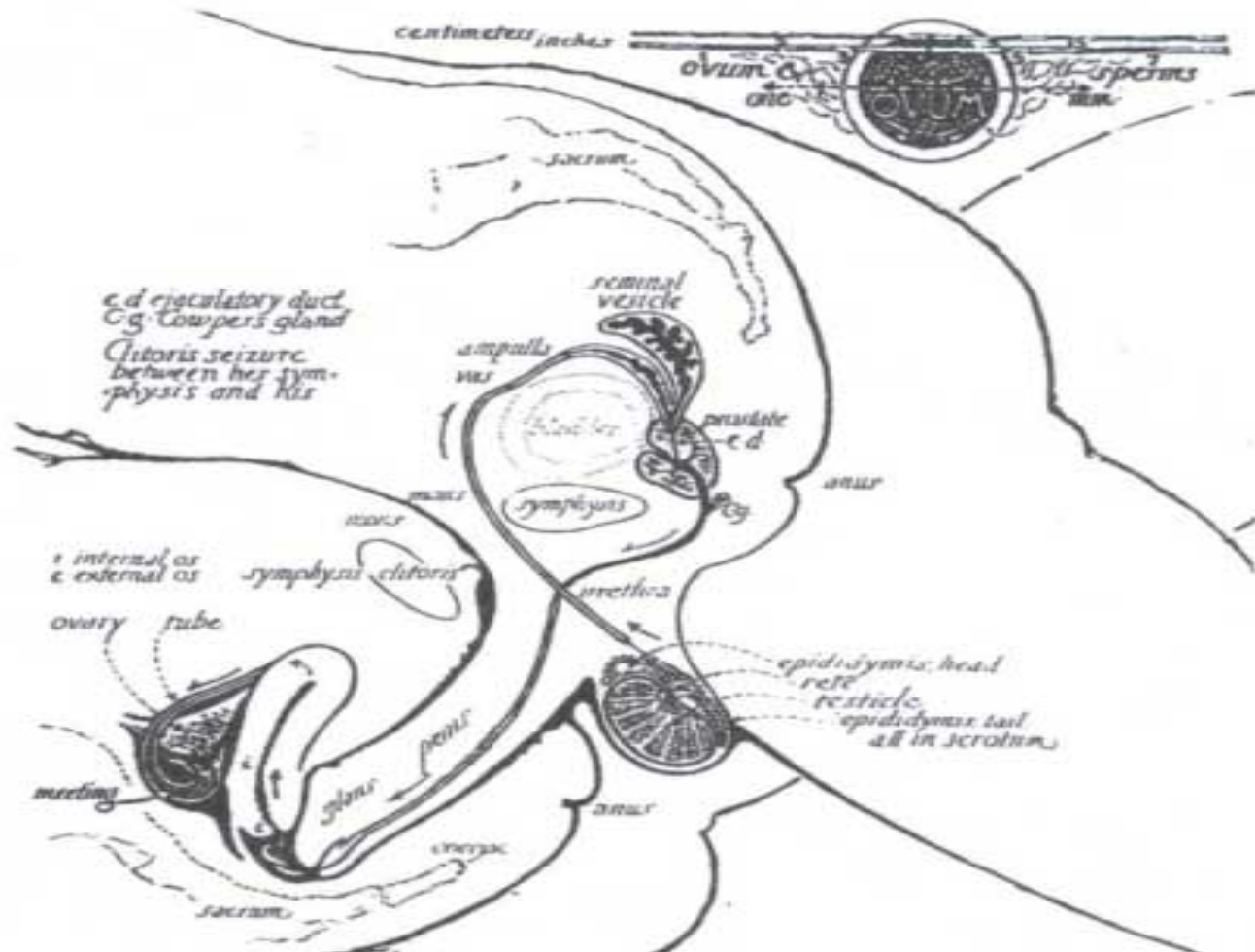
Vaginal Wall Cytology



Vaginal Vasculature



Sagittal View of Coition



Synopsis of Recent Publications

Ultrasonographic Assessment of Endocervix & Cervical Mucus

[Duijkers & Klipping Eur J Obstet Gynecol Reprod Biol 2000;93:13-7]

- *36 healthy women with normal cycles*
- *Underwent transvaginal ultrasonography q o d*
- *Conclusion: Preovulatory changes in the aspect of the endocervix and cervical mucus can be observed by TVU*

Risk Factors for Plasma Cell Endometritis

[Korn, Hessol Padian et al Am J Obstet Gynecol 1998;178:987-90]

- *111 women with cervical GC, CT or BV vs 24 women with negative tests*
- *Study group women in the proliferative phase had OR=4.5 (95% CI, 1.6-12.4) for the presence of plasma cells, as evidence of endometritis*
- *Conclusion: This observation may be due to hormonal effect or to the loss of the cervical barrier during menstruation*

Cervical Shedding of HSV, CMV in Women Infected with HIV-1

[Mostad, Kreiss, Ryncarz et al Am J Obstet Gynecol 2000;183:948-55]

- *17 women with seropositivity for above, underwent daily evaluation of cervical viral shedding*
- *Shedding of HSV did not vary with menstrual cycle*
- *Shedding of CMV was significantly greater in the luteal phase (OR 1.9, 95% CI, 1.1-3.4)*
- *Conclusion: Asymptomatic viral shedding for HSV (0% to 33%) and for CMV (20% to 97%) as percent of days, varies between patients infected with HIV-1*

The Impact of the Ovulatory Cycle on Cytokine Production

[Al-Harhi, Wright, Anderson et al J Interferon Cytokine Res 2000;20:719-24]

- *6 premenopausal women were studied during an ovulatory cycle*
- *In plasma, IL-8 was 4-fold higher in follicular phase than luteal phase ($p=0.004$)*
- *In vaginal compartment (from lavage specimens), IL-6 & IL-1 beta were both 5-fold higher in follicular than luteal phases, $p=0.0002$ and 0.03 , respectively*
- *In salivary specimens, there was no menstrual phase differences noted*
- *Conclusion: These cytokines are differentially regulated during the ovulatory cycle*

Cervical & Vaginal Shedding of HIV-1 throughout the Menstrual Cycle

[Mostad, Jackson Overbaugh et al J Infect Dis 1998;178:983-91]

- *17 women infected with HIV-1 were evaluated daily*
- *HIV-1 infected cells detected in 46% of endocervical swabs and 16% of vaginal swabs*
- *For each woman, the percentage of positive swabs varied from 4% to 100% of endocervical and from 0% to 71% of vaginal swabs*
- *The greater the plasma HIV-1 RNA load, the greater the odds of cervical and vaginal shedding*
- *Conclusion: There was no discernable pattern of genital tract shedding with phase of the menstrual cycle and with no association with serum estradiol or progesterone levels*

Mucosal Immunity in the Female Reproductive Tract

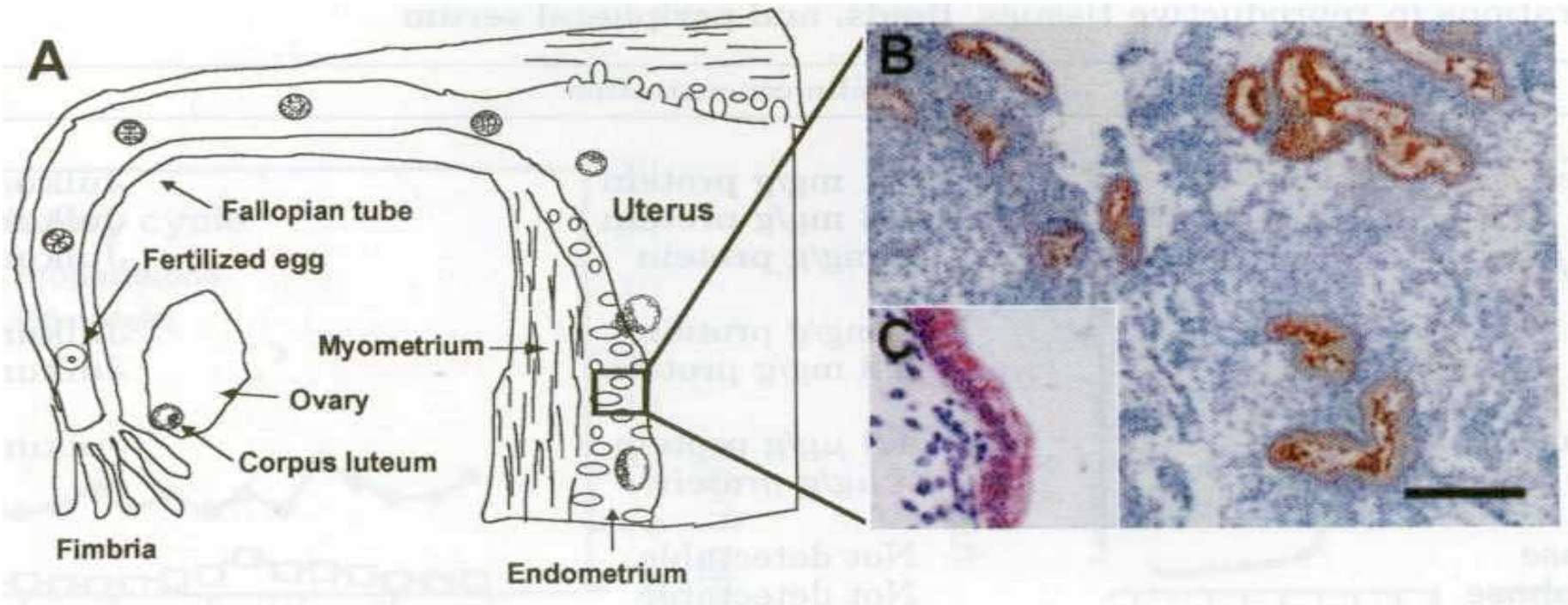
[AIDS Res Hum Retroviruses 1998;14:S51-5]

- 15 normal ovulatory women were studied*
- Cervix washed with sterile saline before aspiration of cervical mucus (50-800 microl)*
- There was a positive correlation between IgG and IgA immunoglobulin levels, interleukin 1beta and interleukin 10 and estradiol levels in circulation*
- Conclusion: These data suggest a role for cytokines and hormones in the regulation of reproductive tract immunity*

Glycodelin

[Seppala et al *Endocrine Reviews* 2002;23:401-30]

Glycodelin is a glycoprotein belonging to the lipocalin superfamily, is regulated by progesterone, appears in various isoforms, with Glycodelin-A potently and dose-dependently inhibiting sperm-egg binding, while also possessing immunosuppressive activity



A: Tissues synthesizing glycodelins; B: Localization of glycodelin in secretory endometrium by immunohistochemical staining; C: *In situ* hybridization of glycodelin mRNA in secretory endometrium

Glycodelin

[Seppala et al Endocrine Reviews 2002;23:401-30]

- *Synthesis is stimulated by progesterone, leading to inhibition of fertilization & also may modulate implantation via its immunosuppressive activity*
- *The modified 3-hydroxyphthalic anhydrides of glycodelin-A & -S dose-dependently inhibited gp120-CD4 binding at nanomolar concentrations*
- *Also, they inhibited HIV nucleocapsid p24 production and cytopathic effects of HIV-IIIB*
- *Lastly, these compounds potently inhibited infection of peripheral blood mononuclear cells by the primary HIV isolate THA/93/051 belonging to subtype E, which grows more efficiently in Langerhans' cells, suggesting that it may be preferentially spread by sexual transmission*
- *Thus, it may be possible to apply these substances locally to inhibit HIV transmission*

Uterine Peristalsis During the Follicular Phase of the Menstrual Cycle

[Kunz, Noe Herbertz et al Hum Reprod Update 1998;4:647-54]

- *Vaginal sonography was performed in the early, mid and later proliferative phases of the menstrual cycle to detect uterine peristalsis*
- *Peristaltic contractions were always confined to the subendometrial layer of the muscular wall, being lowest during menstruation & highest at midcycle*
- *They progressed from the lower to the upper segments, and to the isthmic part of the tube ipsilateral to the dominant follicle*

Sonographic Evidence for Utero-Ovarian Counter-Current System

[Kunz, Herbertz, Noe et al Hum Reprod Update 1998;4:667-72]

- *The uterine peristaltic activity involves only the stratum subvasculare of the myometrium, which exhibits a predominantly circular arrangement of muscular fibres that separate at the fundal level into the fibres of the cornua and continue into the circular muscles of the respective tubes*
- *Doppler flow of both uterine arteries and the arterial anastomoses of the uterine and ovarian arteries in the cornual region demonstrated significant lower resistance indices of the junctional vessels ipsilateral to the side of the dominant ovarian structure*

Caveats

- *The cervix changes in size during the menstrual period. Single size devices may cause ulceration if sized immediately following menses*
- *Coition may cause displacement of cervical devices*
- *Vaginal infections may be associated with upper genital tract infections because of the counter current peristalsis mechanism*
- *The follicular phase is particularly susceptible for uterine acquisition of vaginal organisms (with or without orgasm) but also associated with increased immunoglobulin and cytokine expression*
- *The hormonal influence on these mechanisms appears to be critical*