



CONTINUING EDUCATION IN TOXICOLOGIC PATHOLOGY REPRODUCTIVE SYSTEM

Third Conference

ORGANIZED BY SOCIETY FOR TOXICOLOGIC PATHOLOGY IN INDIA (STPI)

OCTOBER 29-31, 2010

The Atria Hotel, # 1, Palace Road, Bangalore - 560 001



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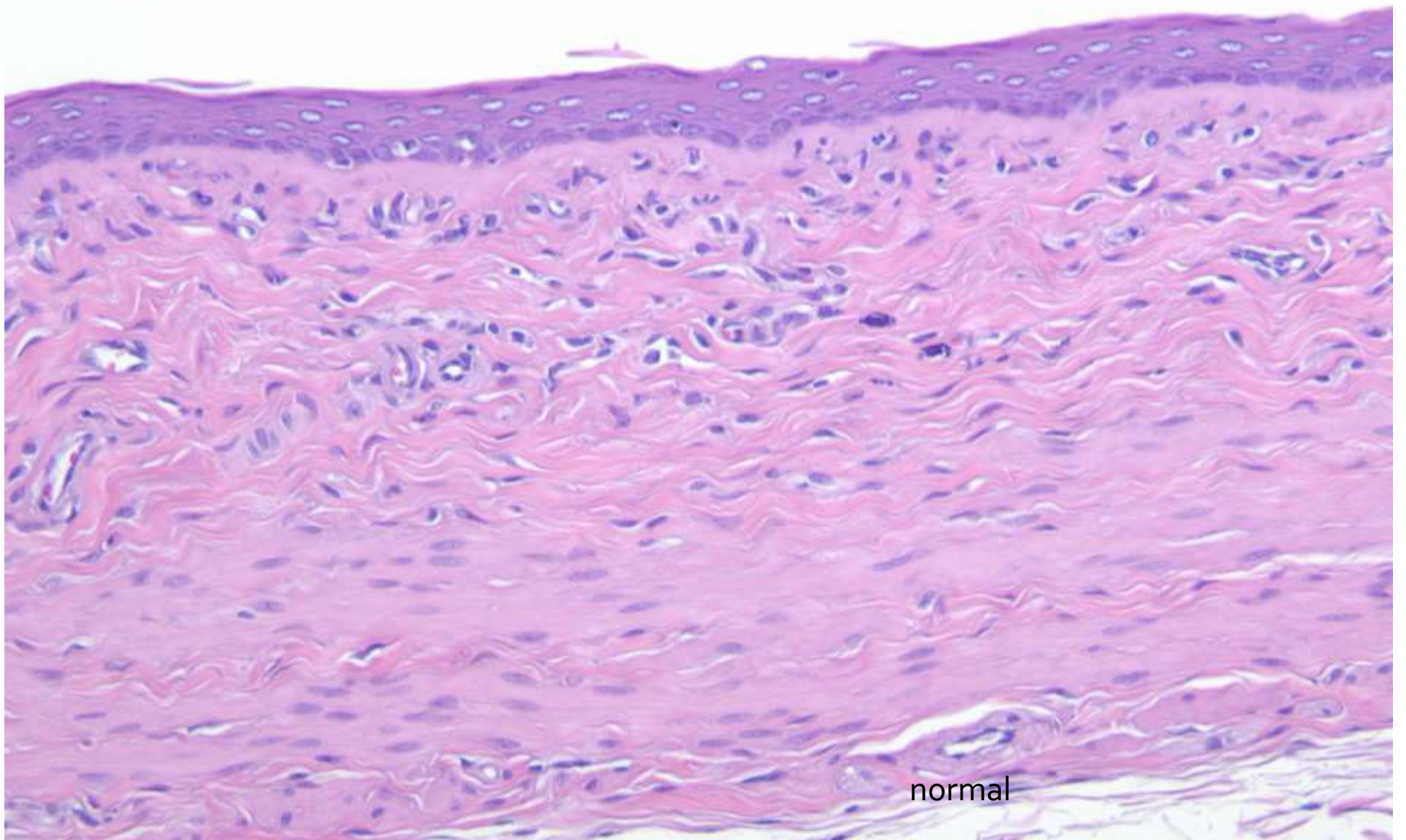
Vishnu Traders



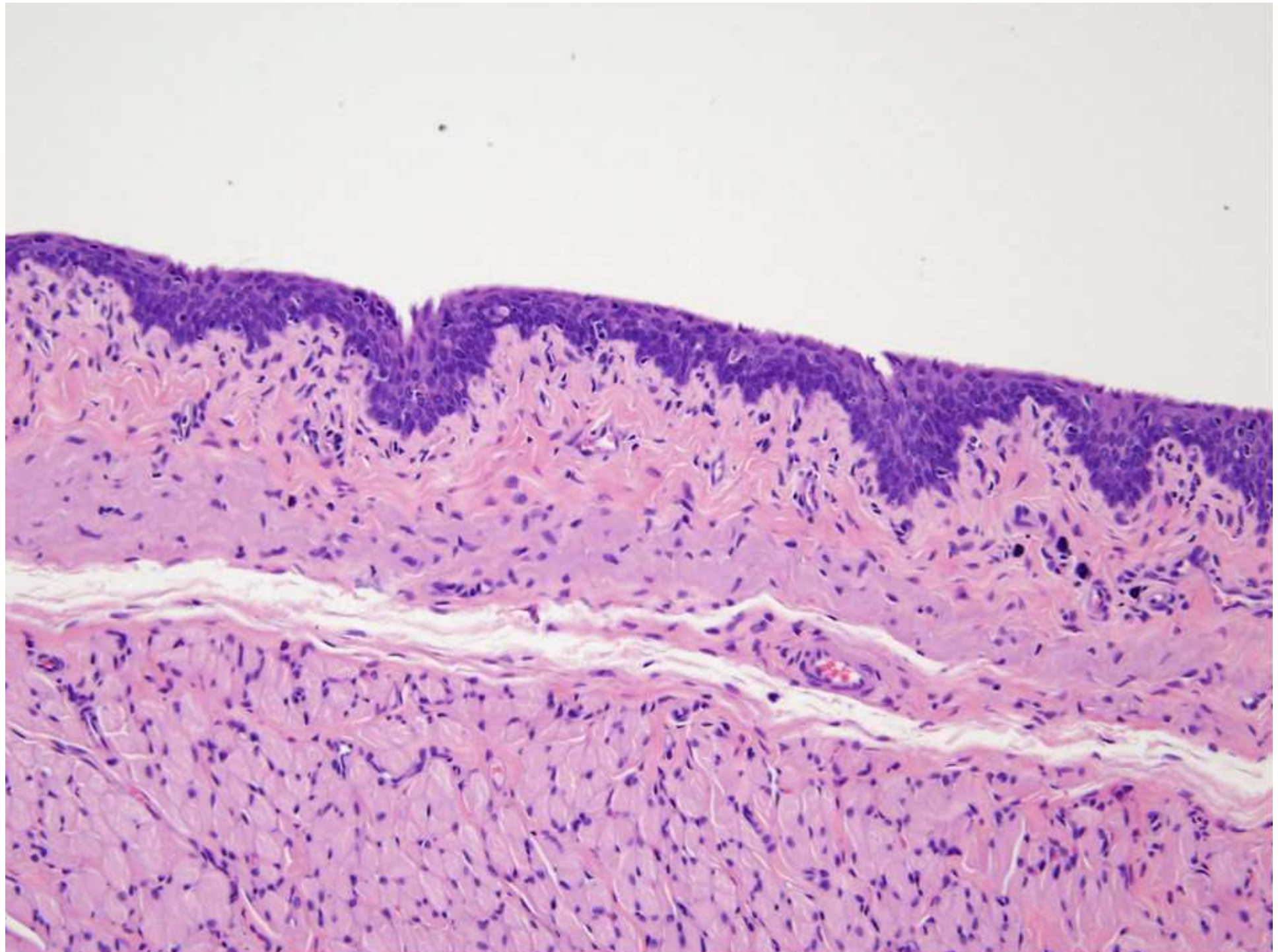
RCC
Linking science to progress

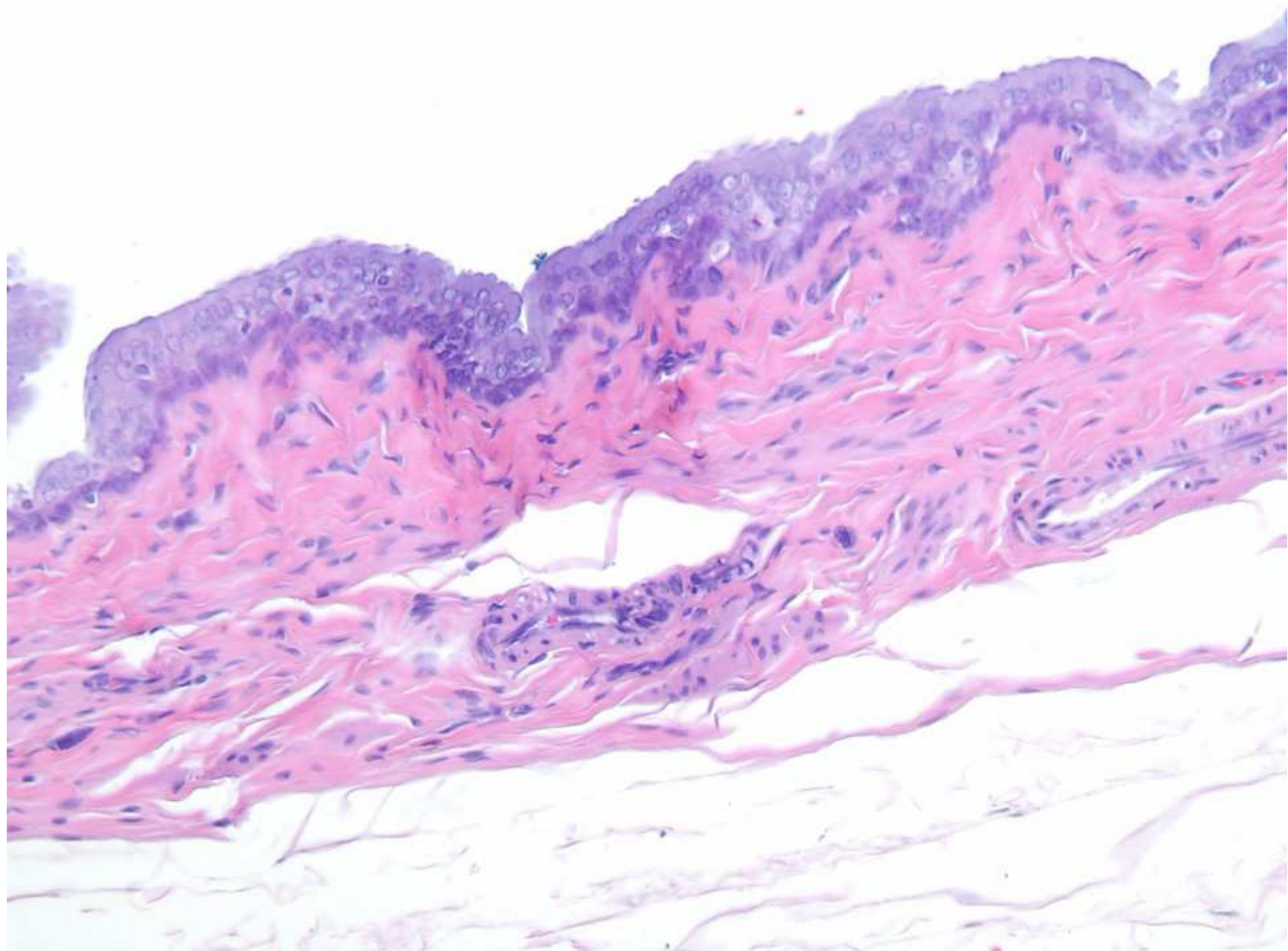
Female Reproductive Tract Evaluation

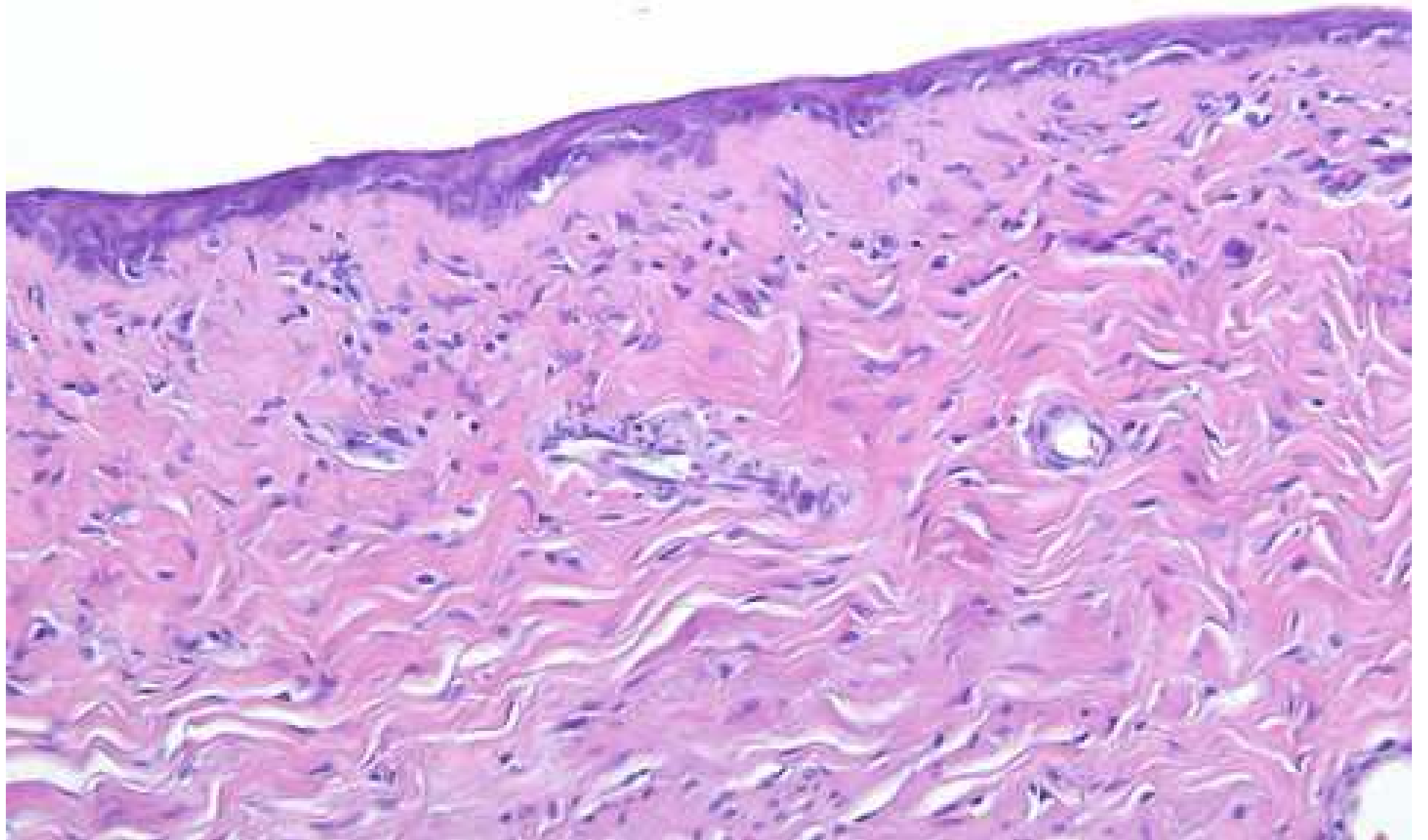
- Uterus and Vagina
 - Easiest in which to identify effects
 - Relatively simpler morphology
 - Sensitive to perturbations in sex steroids
 - Vagina in particular responds to changes in sex steroids in specific manner
 - Estrogen - proliferation, hypertrophy, squamous metaplasia, cornification, leukocyte infiltration
 - Lack of estrogen – epithelial or whole organ atrophy, lack of cornification and/or leukocyte infiltration
 - Progesterone/prolactin (indirect) – mucification, epithelial subnuclear vacuolation



normal

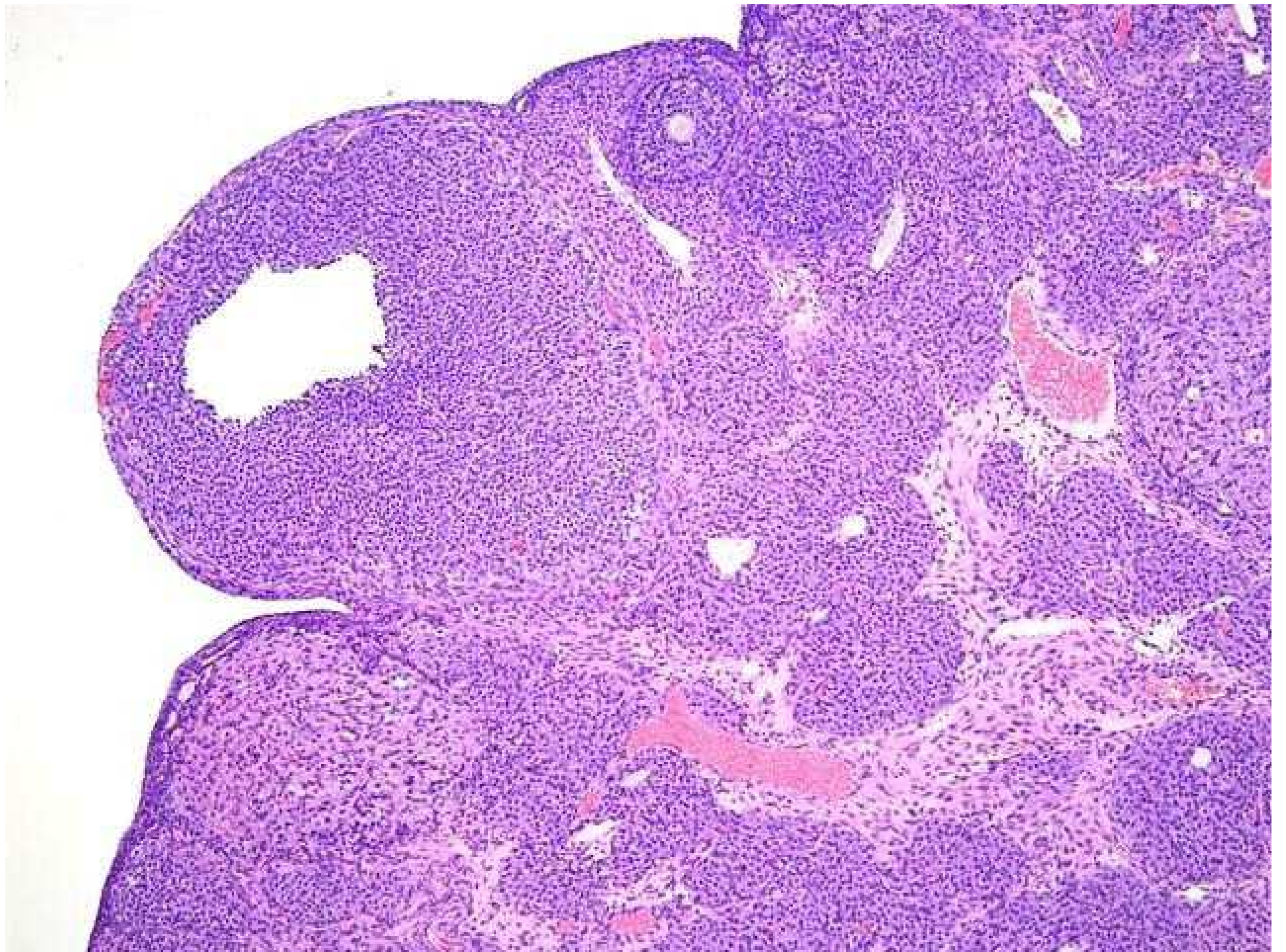


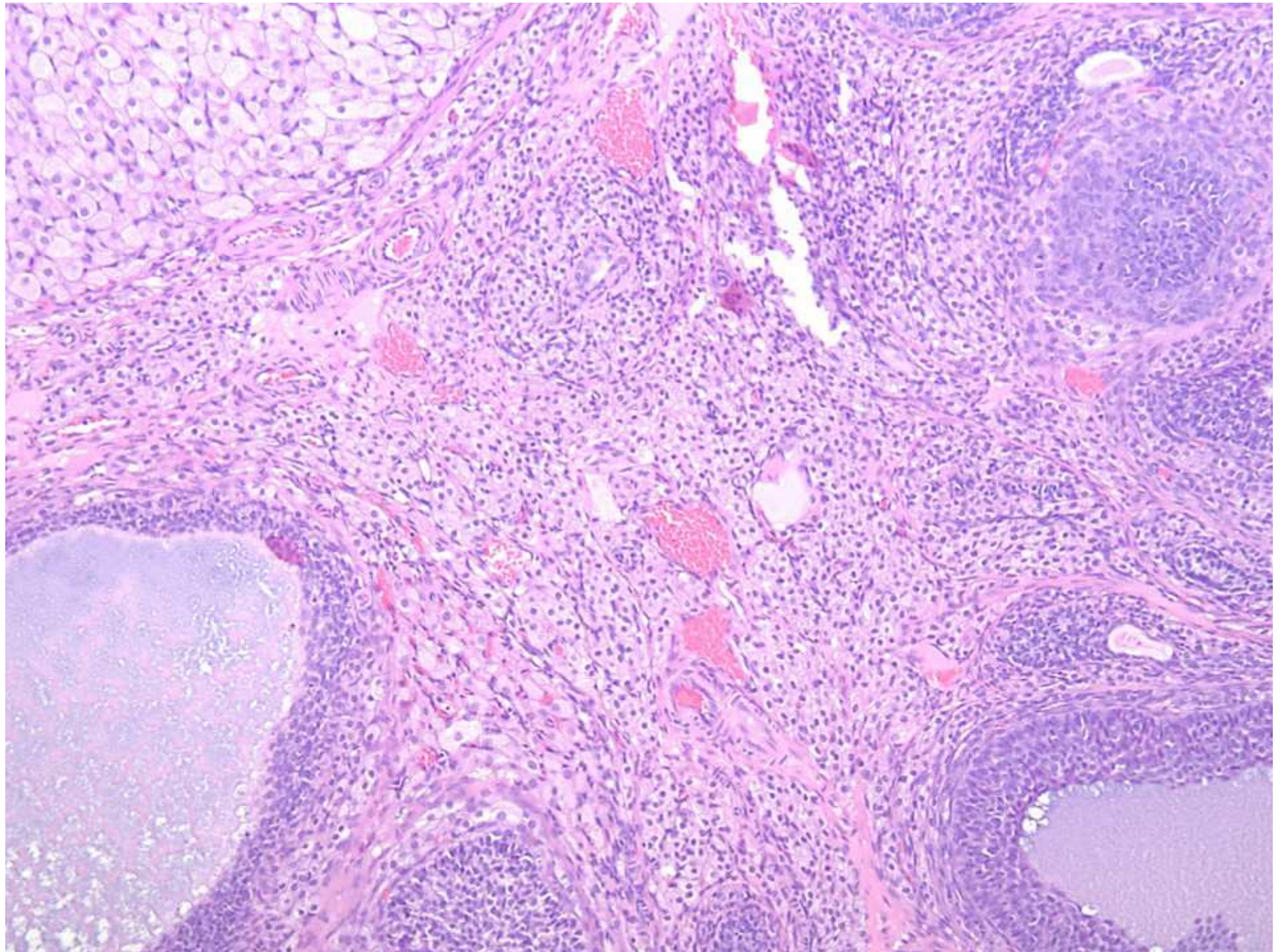


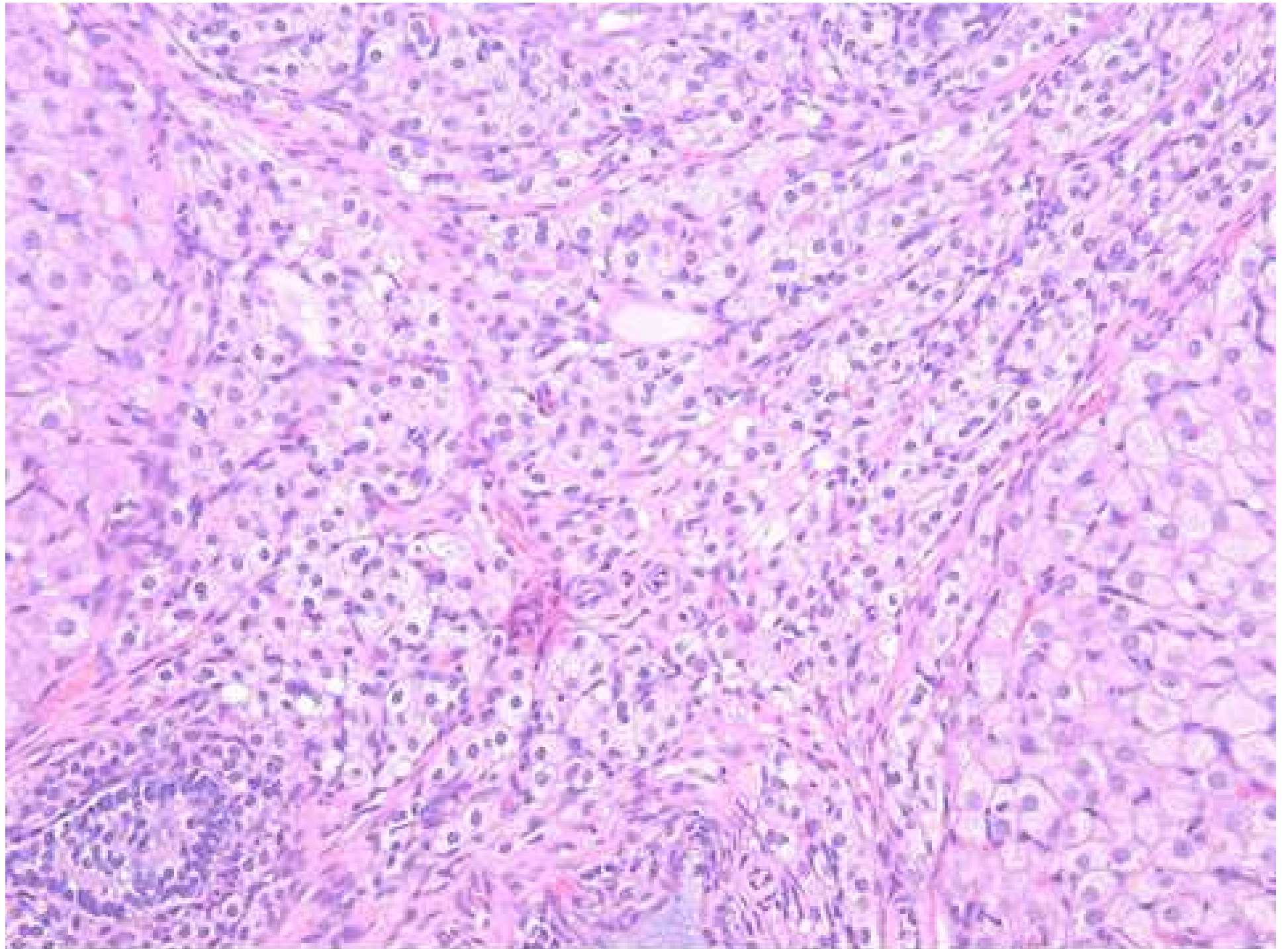


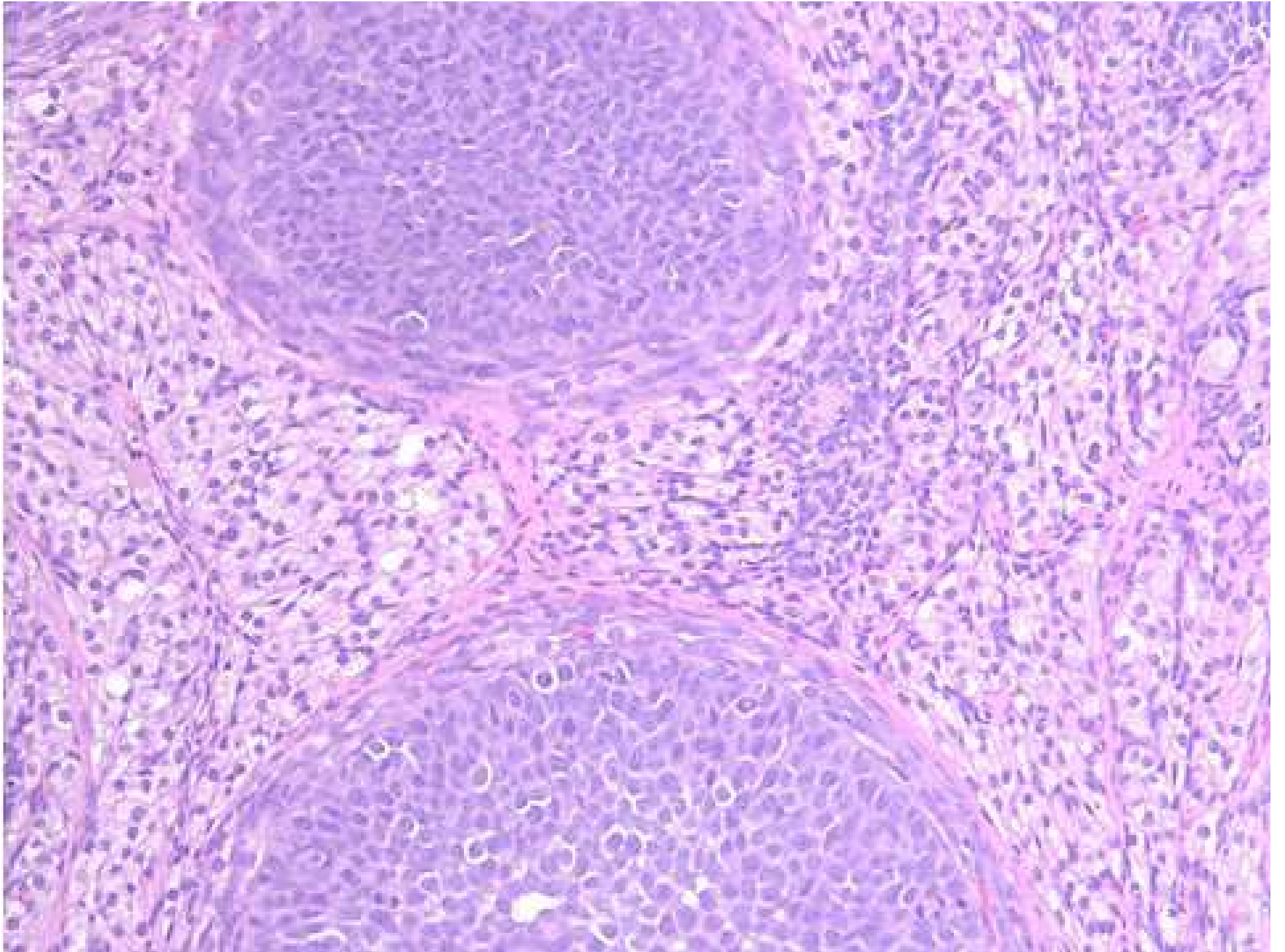
Female Reproductive Tract Evaluation

- Ovary
 - Diverse cell populations respond differently to insult
 - Primordial oocyte – non-dividing, non-growing pool often resistant to injury
 - Growing oocyte – non-dividing, metabolically active
 - Granulosa , luteal and thecal cells of growing follicles or new CLs – dividing, highly metabolically active
 - Interstitial cells- steroidogenically active









Rodent Female Pubertal Onset Assay

- 1996 - US EPA mandated by law to develop strategy to ensure the safety of food and water with regard to endocrine-disrupting chemicals
- US EPA formed EDSTAC (endocrine disruptor screening and testing advisory committee)
- 1998 – EDSTAC recommended list of Tier 1 screening assays to detect chemicals that alter estrogen, androgen and thyroid systems

Rodent Female Pubertal Onset Assay

- Female rats dosed starting PND 21 for 20 days
- Age at vaginal opening recorded
- Daily vaginal lavages from VO to end of study to determine estrous cyclicity
- Weights: body, uterus, ovaries, thyroid
- Hormone assessments: TSH, T₄, +/- E₂, PRL, T₃
- Histopathology: uterus, vagina, ovary, thyroid

Rodent Female Pubertal Onset Assay

- Detects estrogenic and antiestrogenic/androgenic activity
 - Estrogen - accelerates vaginal opening
 - Antiestrogen/androgen or altered steroid synthesis – delays vaginal opening
- Good overall assessment of endocrine and neuroendocrine function since rats are intact

Female Pubertal Onset Assay

- Phenolic compound administered via oral gavage
- Results
 - Decreased age of vaginal opening
 - Decreased body weight
 - Decreased weights of ovary and uterus
 - No effect on thyroid weight, TSH or T₄
 - Altered estrous cyclicity (extended estrus and/or diestrus)

