
臨床病理討論會

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2019.10.24

Clinical history

- The 73 y/o woman has history of
- 1. Left breast invasive lobular carcinoma, with left axillary LNs metastases, cT2N1M0 diagnosed in 2018/12.

s/p weekly taxol *1 + weekly herceptin, loading dose s/p Port-A revision on 2019-01-31

- 2. Right breast cancer, s/p MRM more than 30 years ago
- 3. Hx of cholecystectomy
- 4. Hx of hysterectomy

Clinical history

- S/P taxol + herceptin *1 on 20190115
- Tumor shrunk nicely after 3rd taxol + herceptin
- Postpone taxol (delay 5th taxol~) since 20190223 due to leukopenia
- Patient refuse to have taxol on 20190412 due to dizziness
- CT scan after 9TH taxol + herceptin:
- Tumor almost complete disappeared and residual axillary LN, left 0.5cm.
- T11 osteoblastic lesion, nature ?

Admission (2019-04-09)

- Patient was admitted due to carbuncle with secondary infection over left temporal area. After admission, empirical antibiotic was prescribed.
- In addition, epigastric pain was also noted.
- Panendoscopy presented GERD. PPI with Esomeprazole po was added.
- Under stable condition she was discharged.

Panendoscopy, upper GI

2019-04-09

- E-C junction. GERD la class a was considered.
- Stomach: one sessile polyp, 0.4cm, was seen over fundus. Bx was done (a).
 - Fundic-gland polyp
- Some hyperemic patches were seen over antrum, nearby pyloric ring. Bx was done(b) .
 - Chronic gastritis with focal intestinal metaplasia
- **Duodenum: hyperemic, prominent major papilla.** Bx for excluding neoplasm (c).
 - Tubular adenoma with low grade dysplasia

Panendoscopy, upper GI

2019-05-06

- This exam was done by duodenoscope.
- Esophagus: negative at visible part.
- Stomach: hyperemic mucosa and some tiny erosions with hematin coating over the antrum.
- **Duodenum:** a JPD was noted with the major papilla located at 6 o'clock. **Hyperemic mucosa** of **major papilla** was noted, but under NBI, **no obvious irregular surface and vascular pattern** was noted, and biopsy was done.
 - Compatible with Taxane(paclitaxel) effect

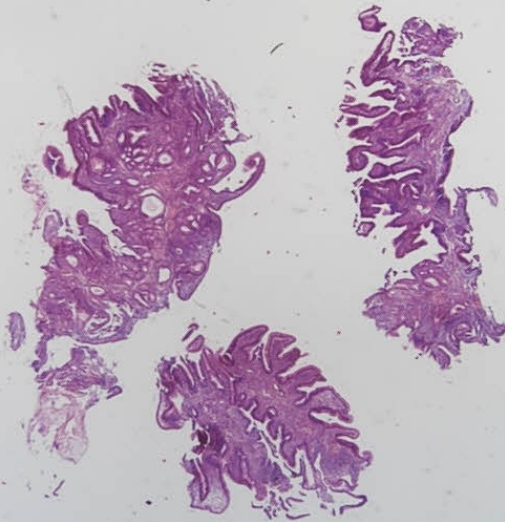
Microscopic Findings (2019-04-09)

Panendoscopy, upper GI

2019-04-09

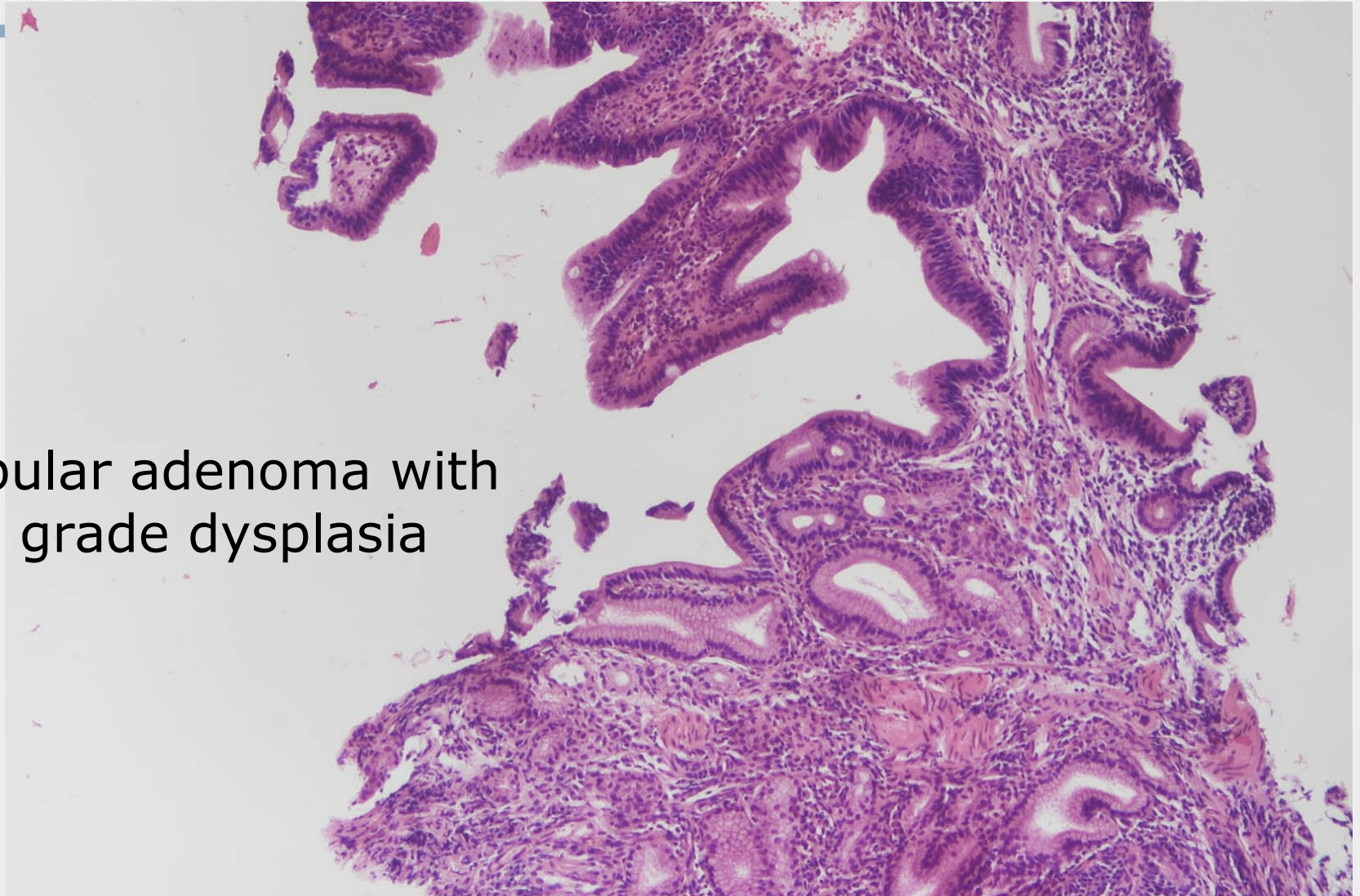
- **Duodenum: hyperemic, prominent major papilla.**

Bx → Tubular adenoma with low grade dysplasia



Panendoscopy, upper GI

2019-04-09

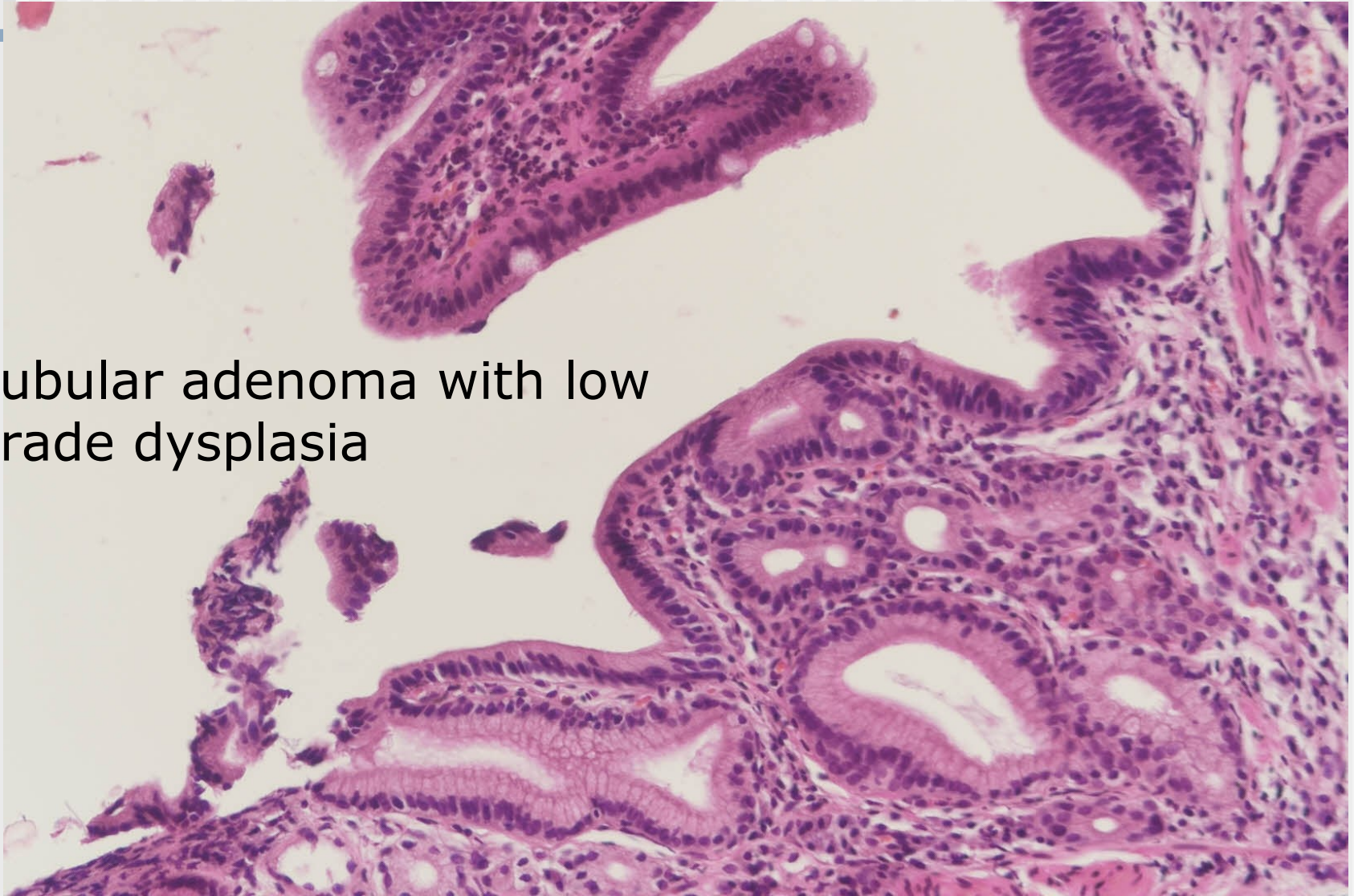


- Tubular adenoma with low grade dysplasia

Panendoscopy, upper GI

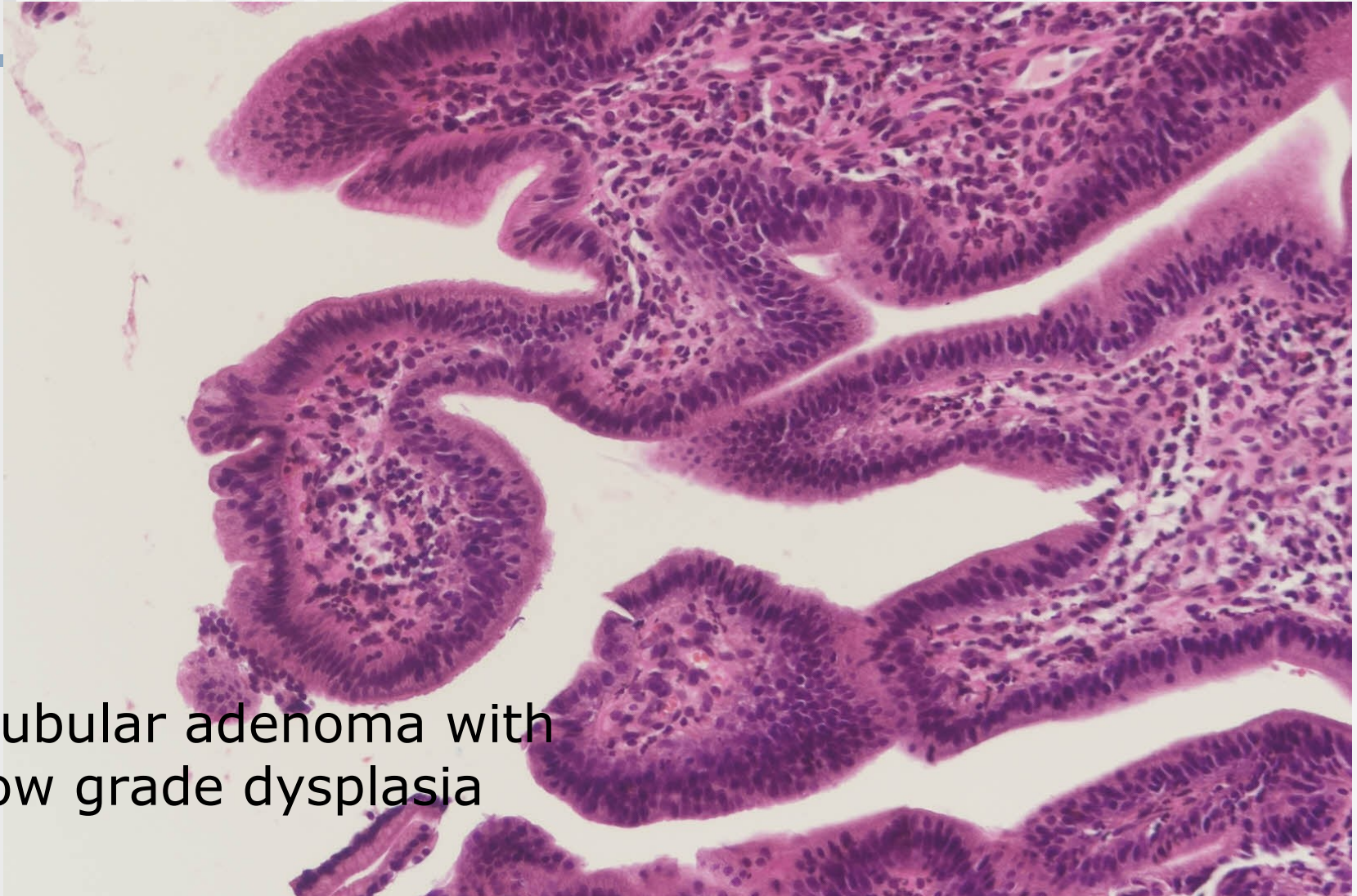
2019-04-09

■ Tubular adenoma with low grade dysplasia



Panendoscopy, upper GI

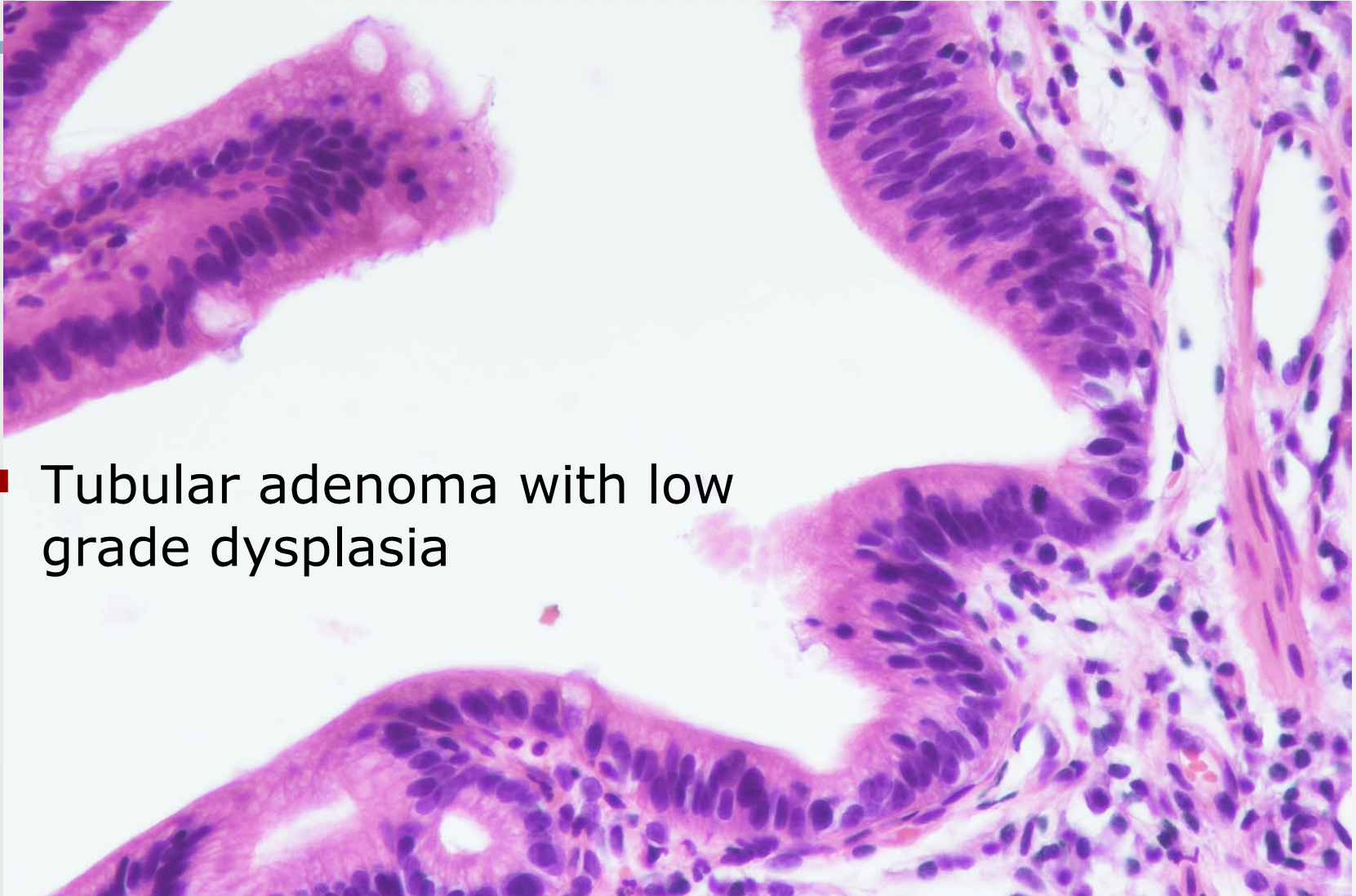
2019-04-09



- Tubular adenoma with low grade dysplasia

Panendoscopy, upper GI

2019-04-09

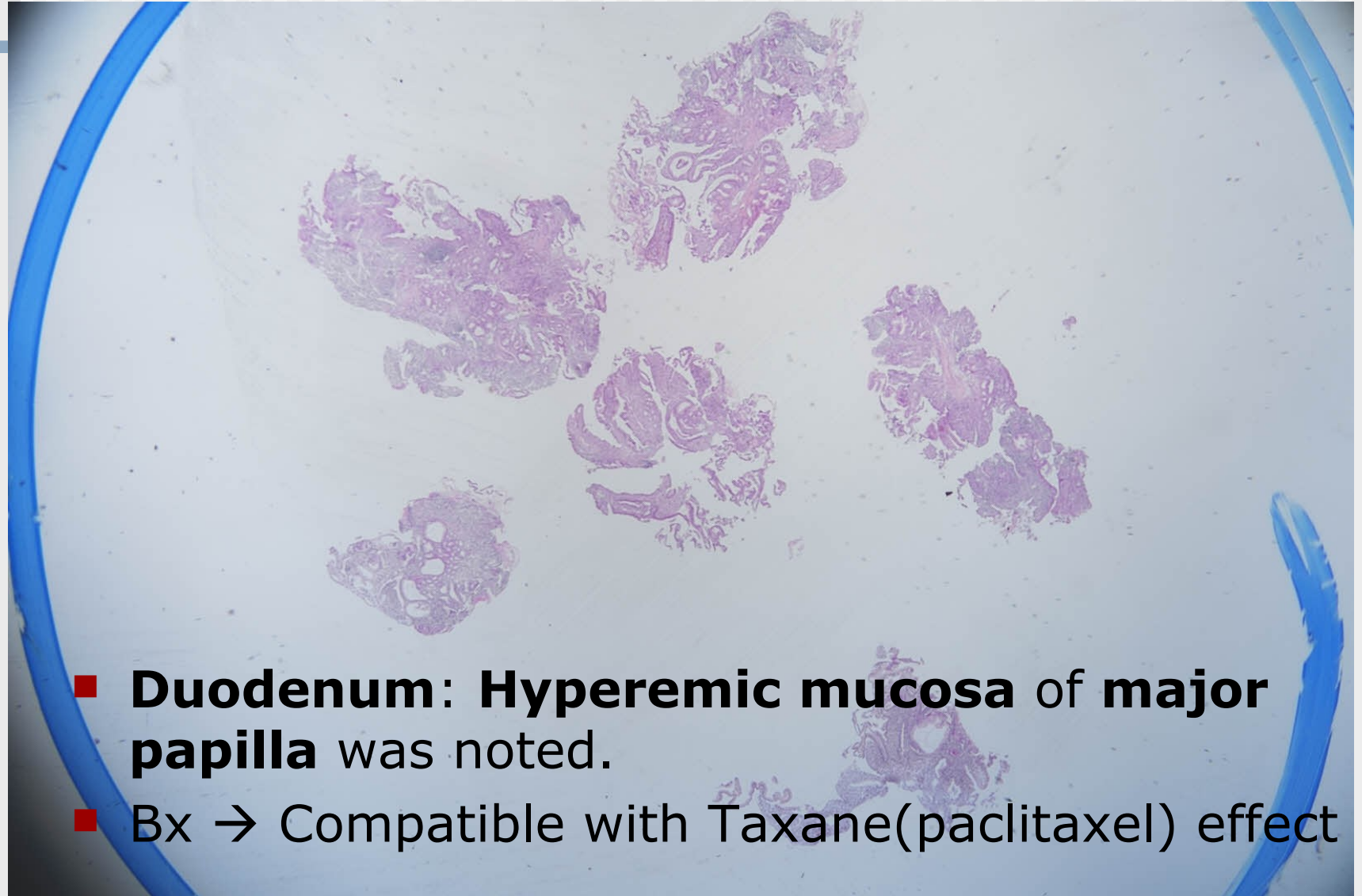


- Tubular adenoma with low grade dysplasia

Microscopic Findings (2019-05-06)

Panendoscopy, upper GI

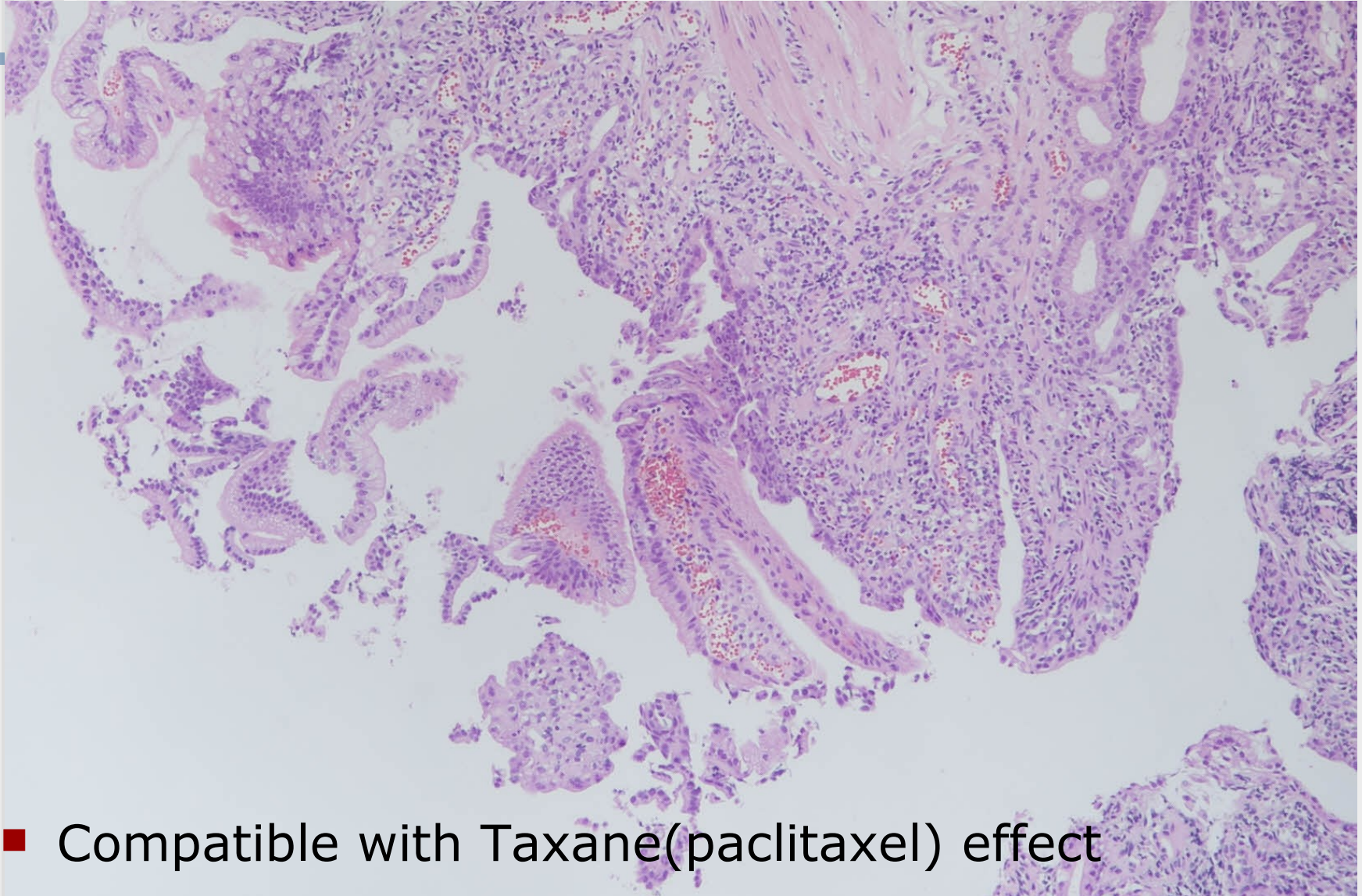
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- **Duodenum: Hyperemic mucosa of major papilla** was noted.
- Bx → Compatible with Taxane(paclitaxel) effect

Panendoscopy, upper GI

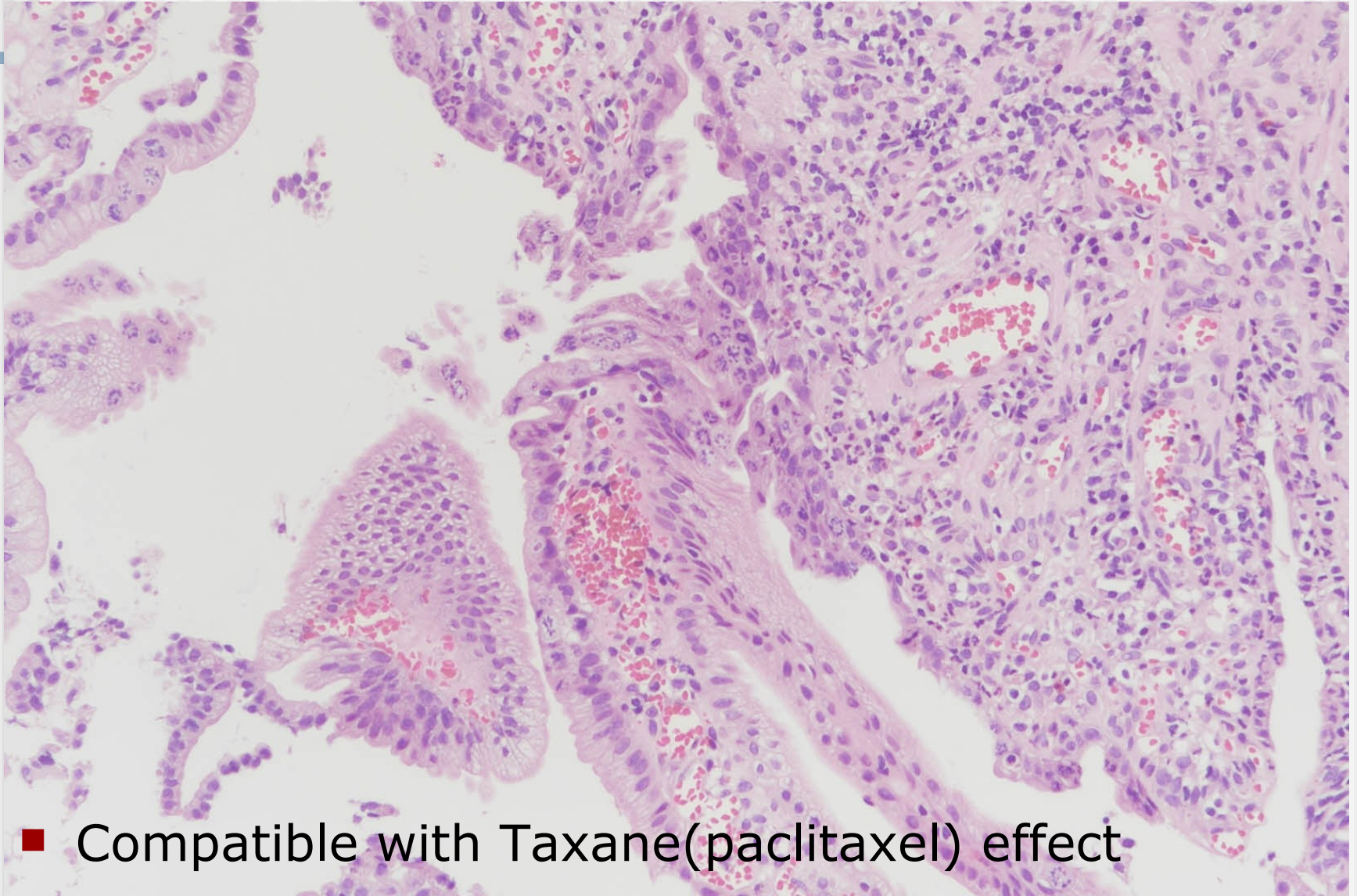
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- Compatible with Taxane(paclitaxel) effect

Panendoscopy, upper GI

2019-05-06

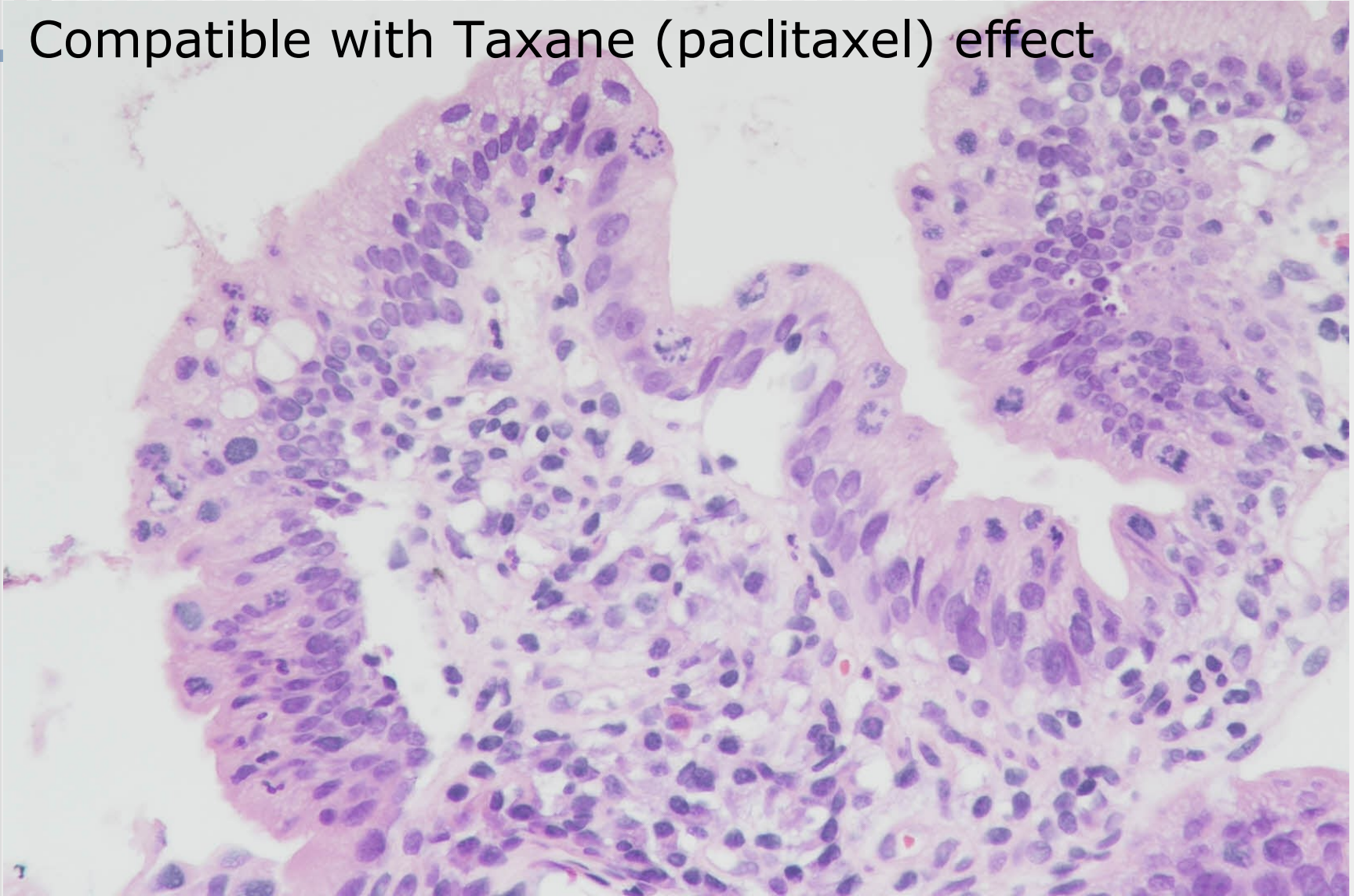


■ Compatible with Taxane(paclitaxel) effect

Panendoscopy, upper GI

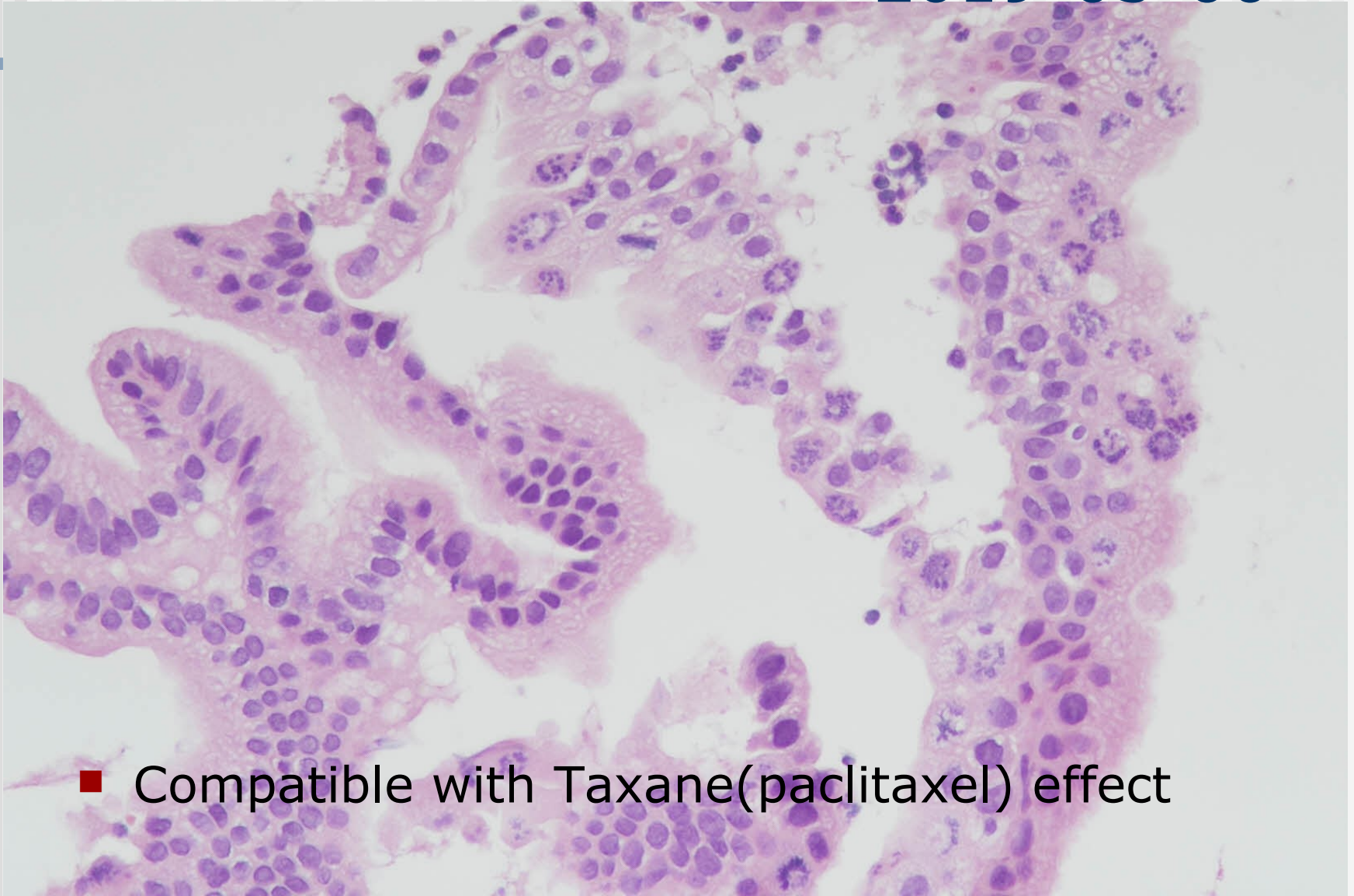
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Panendoscopy, upper GI

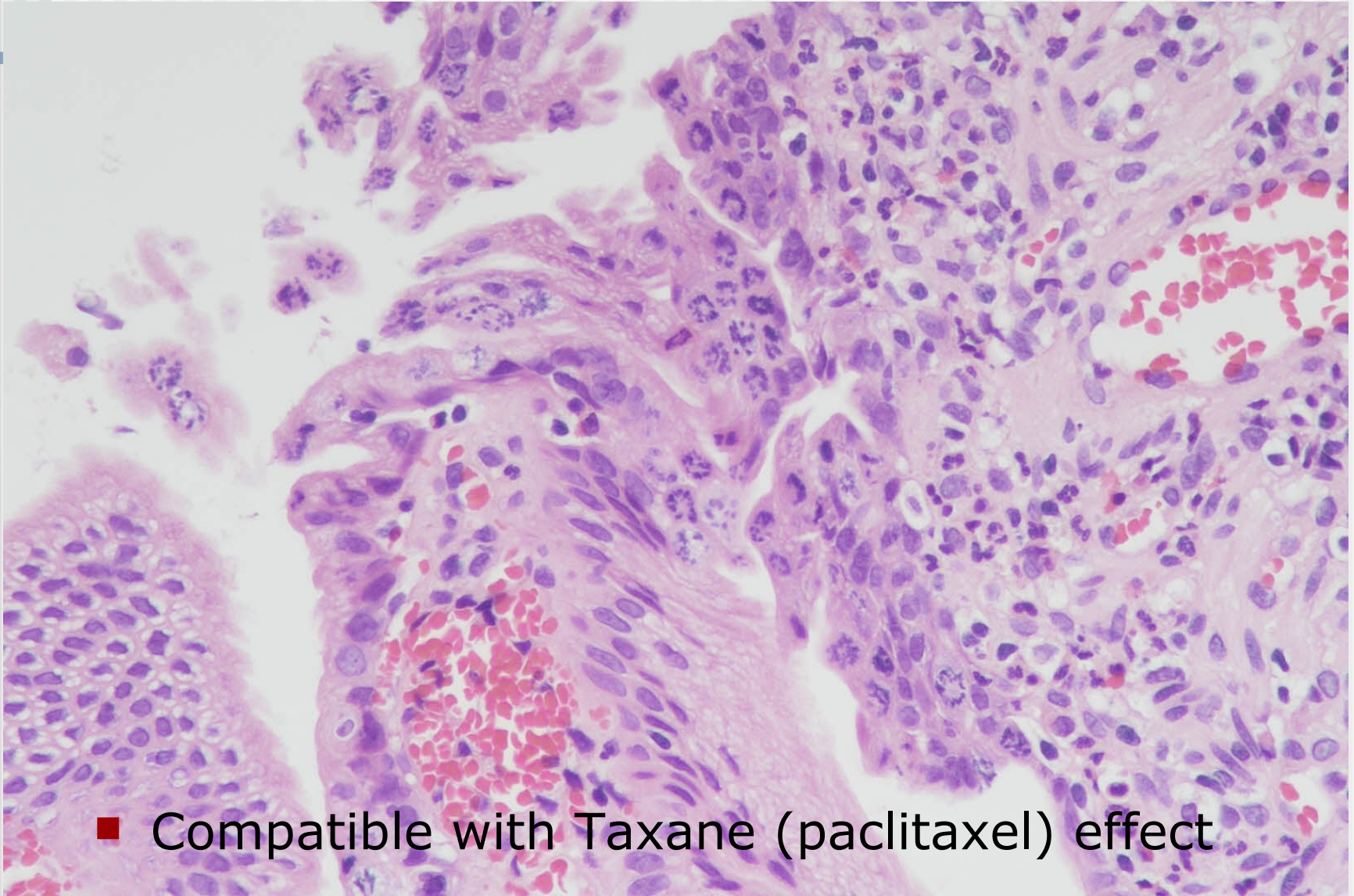
2019-05-06



- Compatible with Taxane(paclitaxel) effect

Panendoscopy, upper GI

2019-05-06



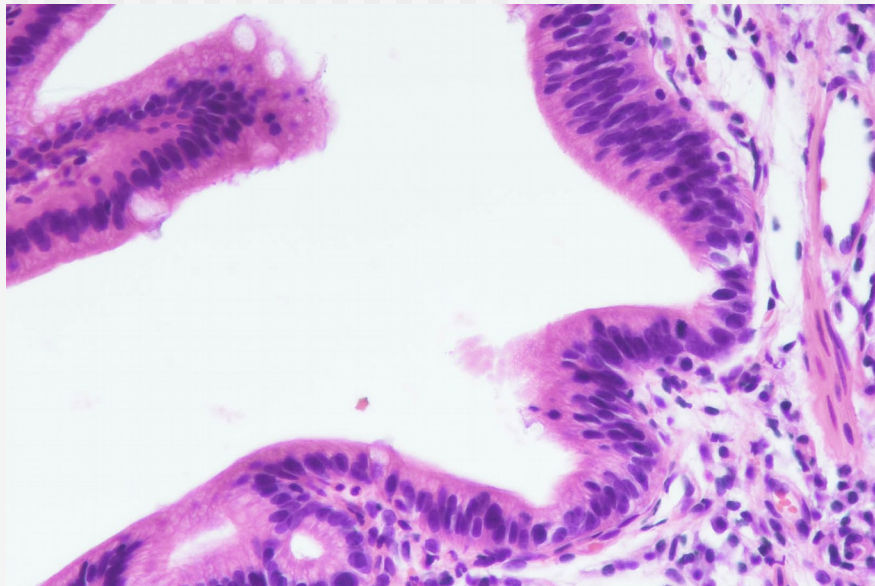
- Compatible with Taxane (paclitaxel) effect

Summary of microscopic findings

- 2019-04-09 Biopsy

Nuclear hyperchromasia, pseudostratification

→ Tubular adenoma with low grade dysplasia

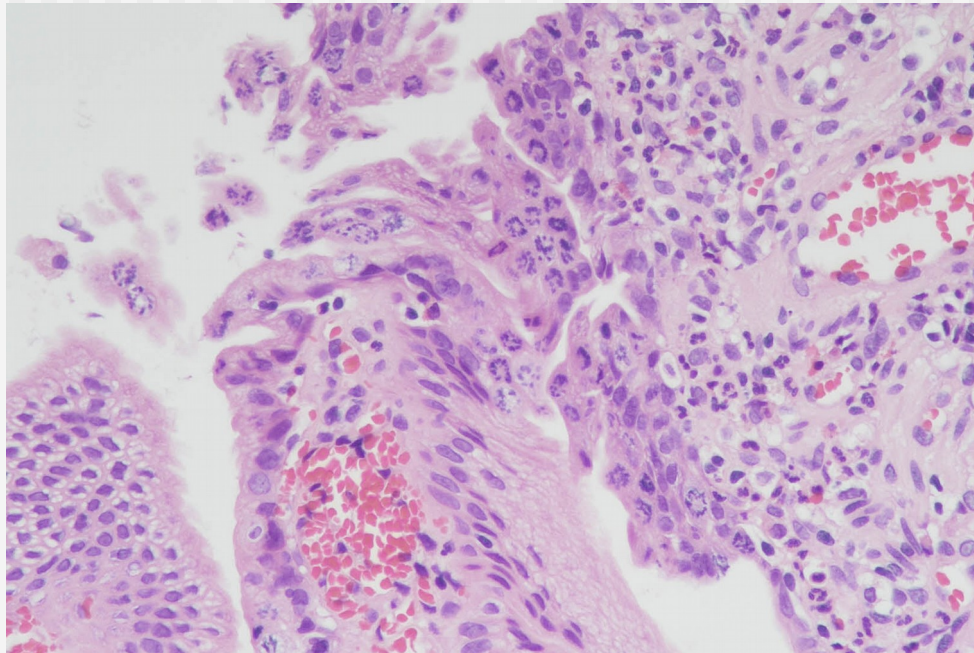


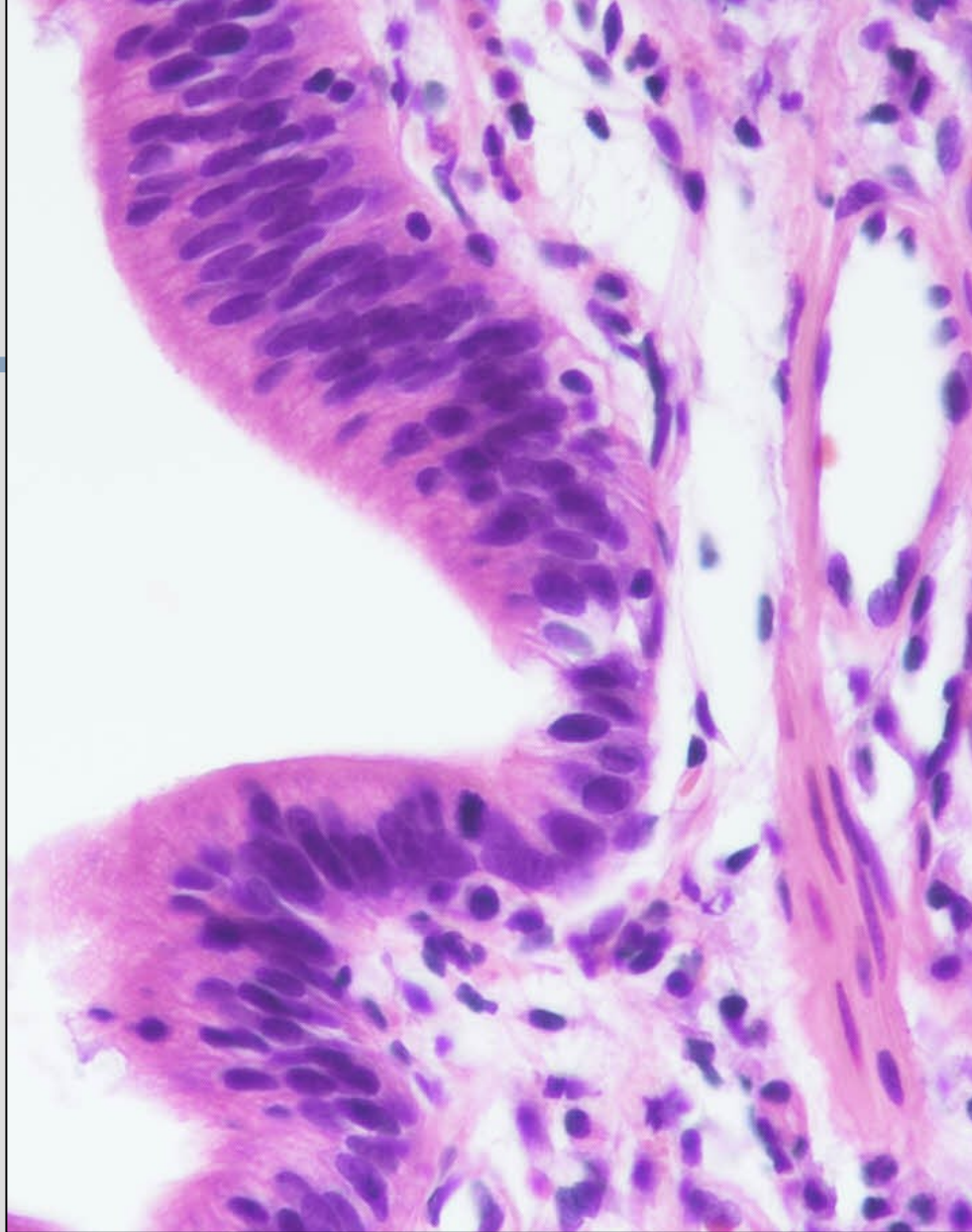
Summary of microscopic findings

- 2019-05-06 Biopsy

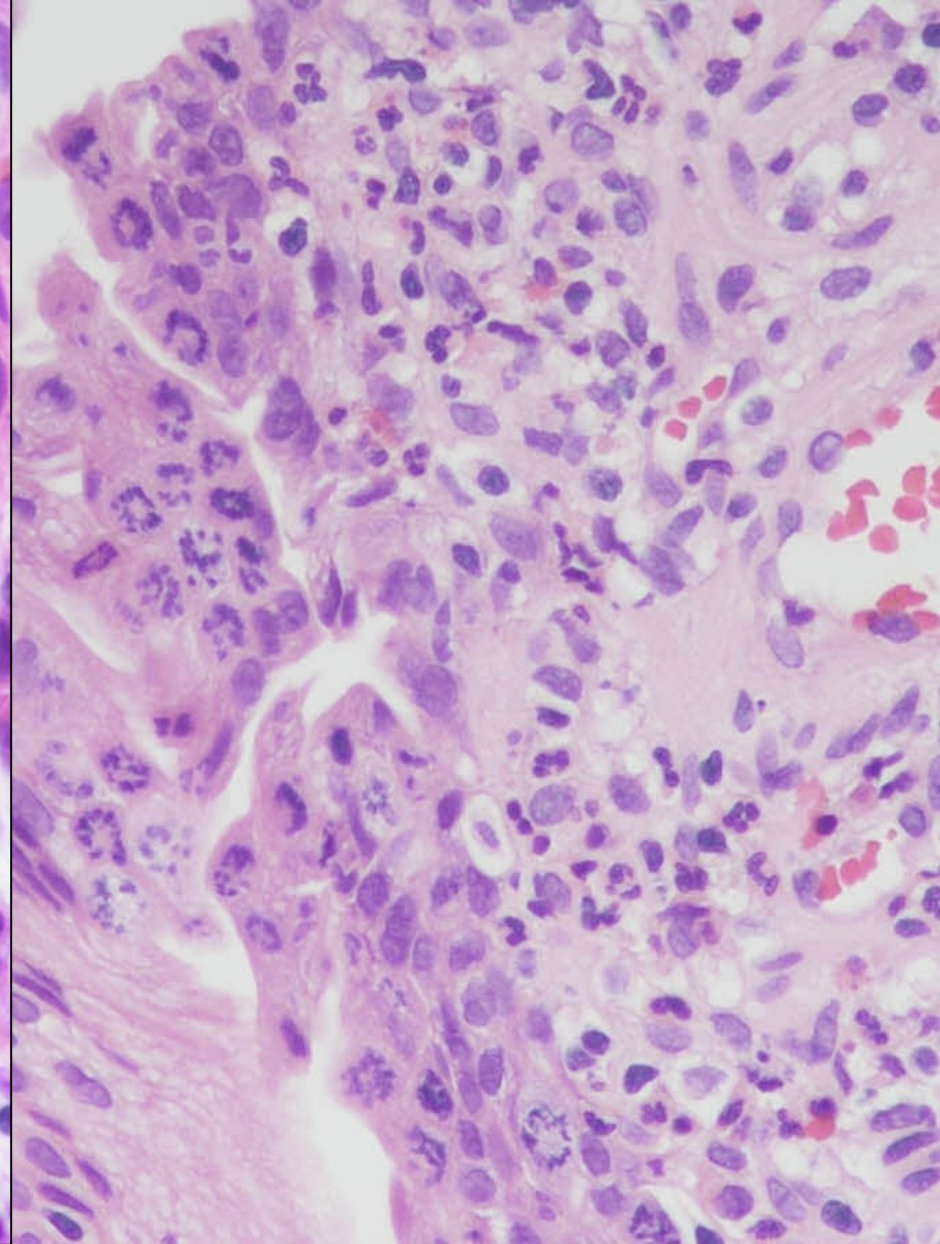
Ring mitoses and apoptosis

→ Compatible with Taxane (paclitaxel) effect





Tubular adenoma with
low grade dysplasia



Compatible with Taxane
(paclitaxel) effect

Discussion

Taxane effect (Taxol effect)

- Main drugs in class of **taxanes** are **Taxol (paclitaxel)**, docetaxel (Taxotere), and cabazitaxel (Jevtana).
- Paclitaxel originally isolated from bark of **Pacific yew tree, *Taxus brevifolia*** (短葉紅豆杉，又名太平洋紫杉)



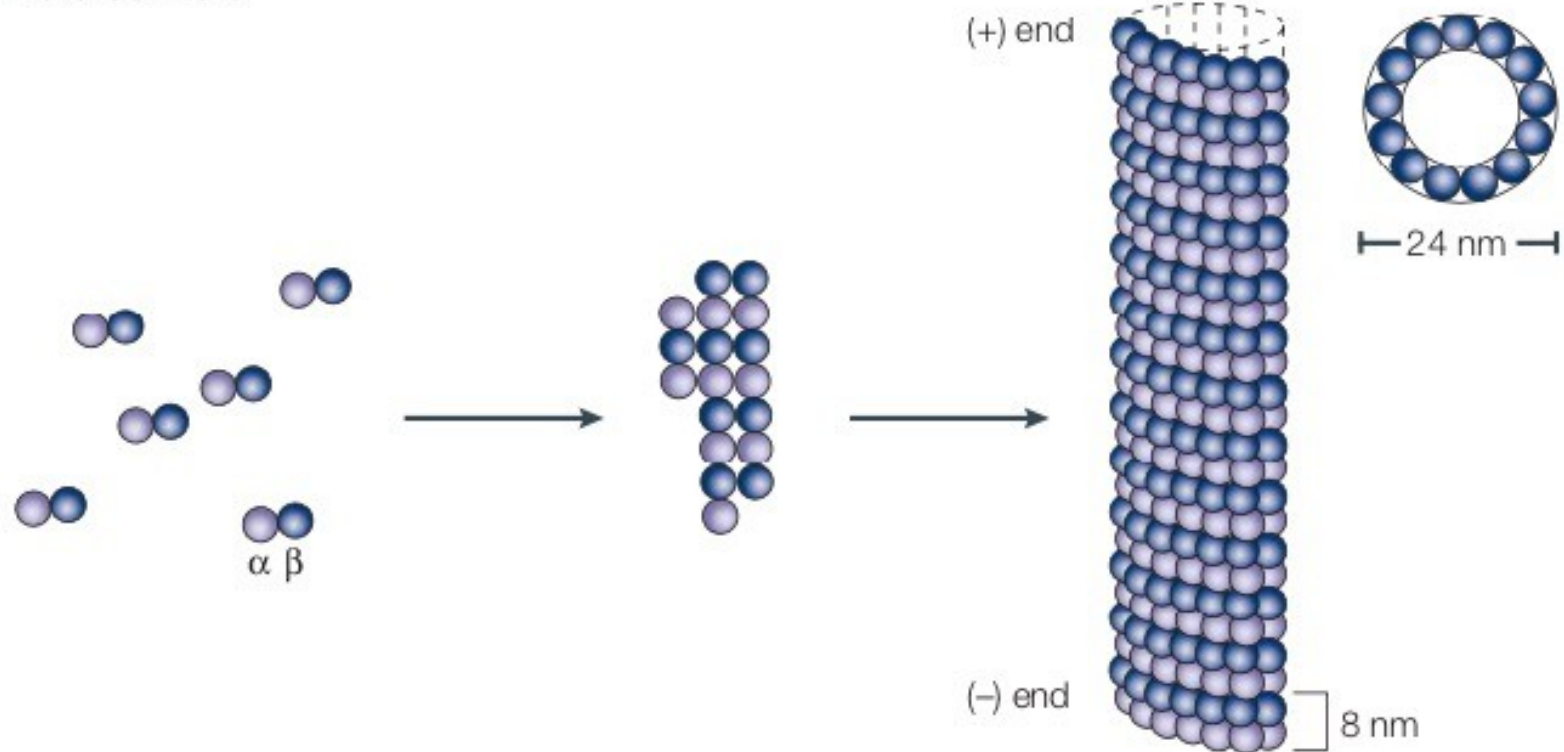
Taxane effect (Taxol effect)

- Paclitaxel works by **interfering with normal microtubule breakdown** during cell division.
- Also **activates apoptosis** by inducing Bcl-2 phosphorylation, which inhibits Bcl-2 binding to BAX, with subsequent increase in apoptosis.
- Important chemotherapeutic agents
 - Used to treat cancer of **esophagus, breast, prostate, and lung** as well as **advanced Kaposi sarcoma**

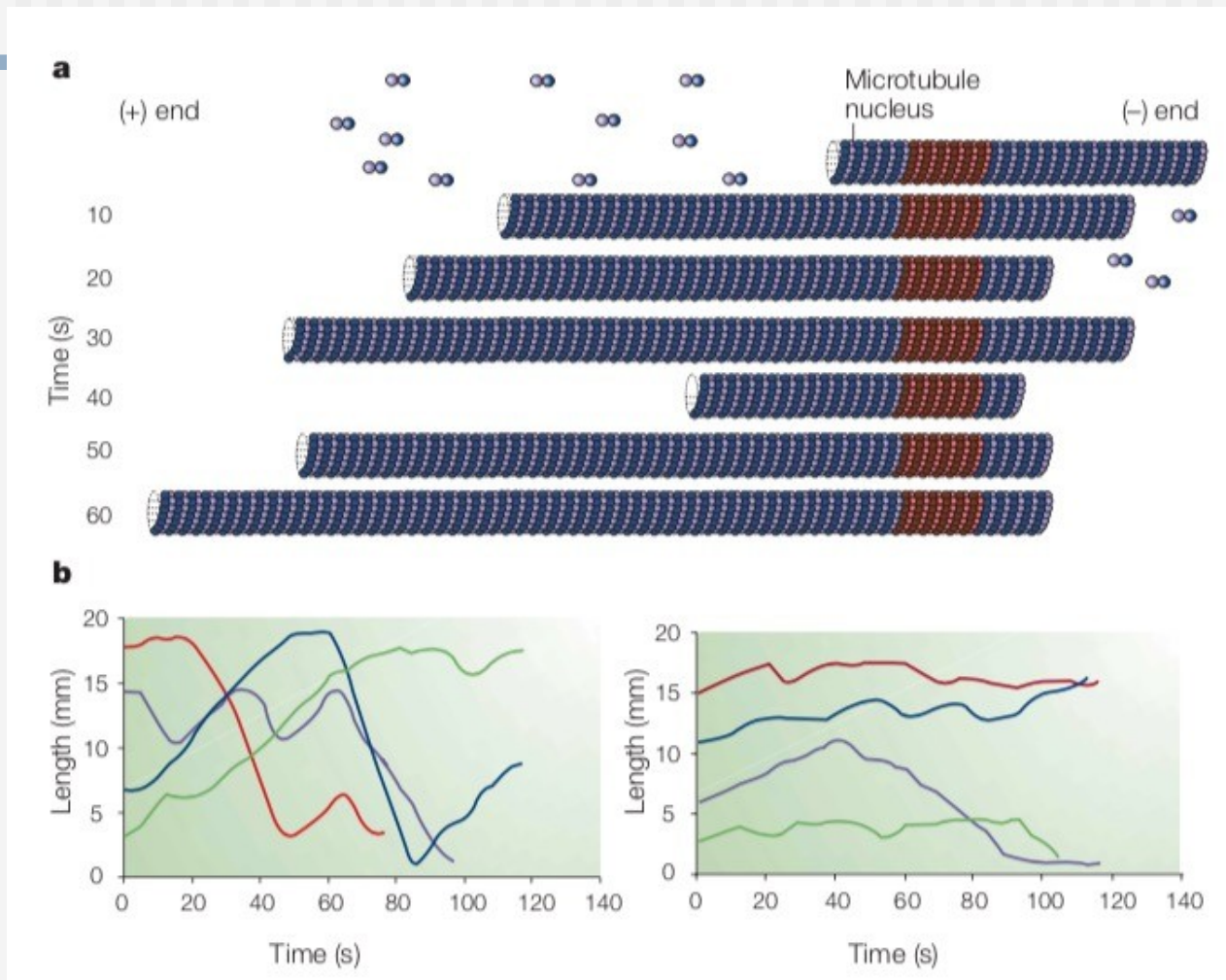
α - and β -tubulin
heterodimers

Microtubule nucleus

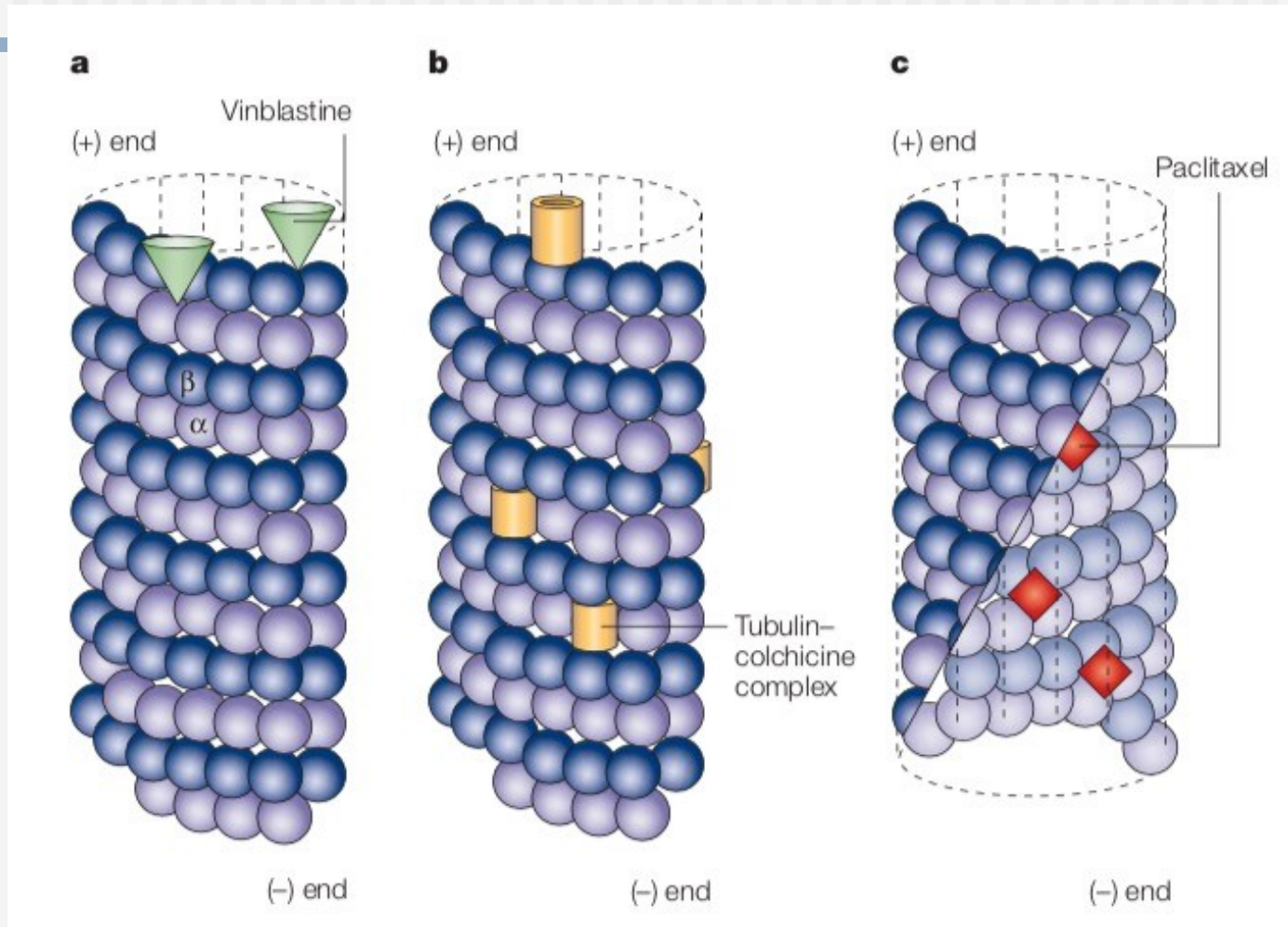
Microtubule



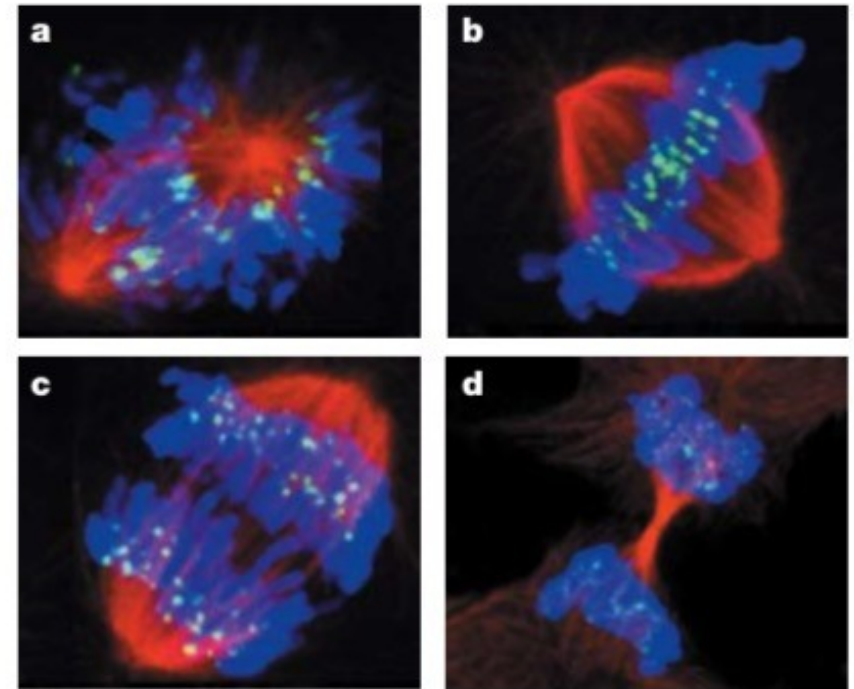
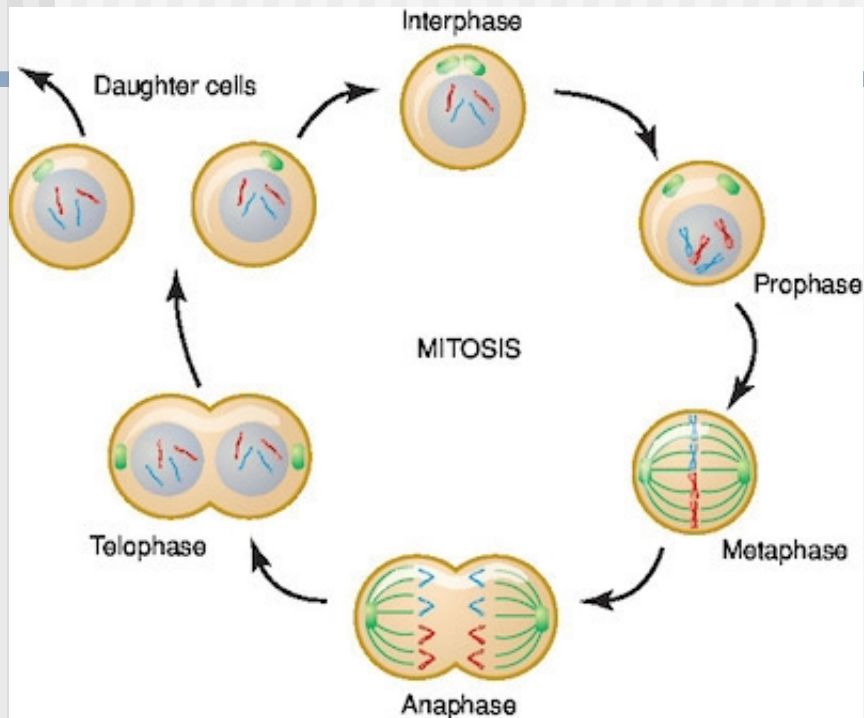
Polymerization of microtubules.



Antimitotic drugs suppress dynamic instability of microtubules.

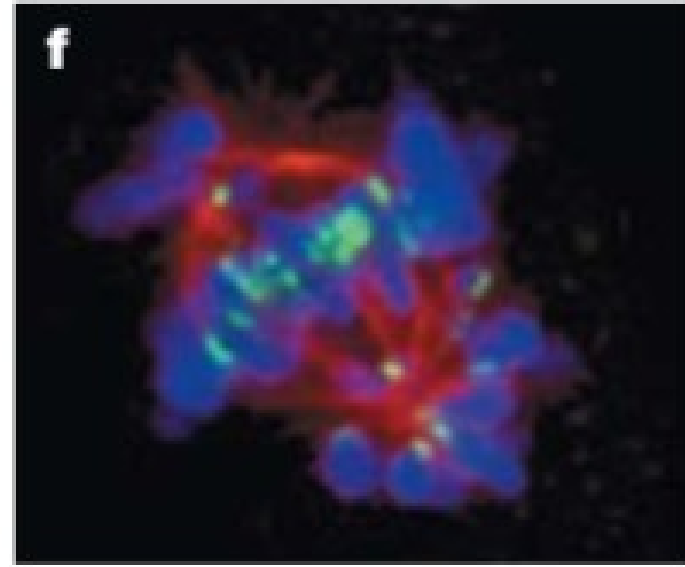
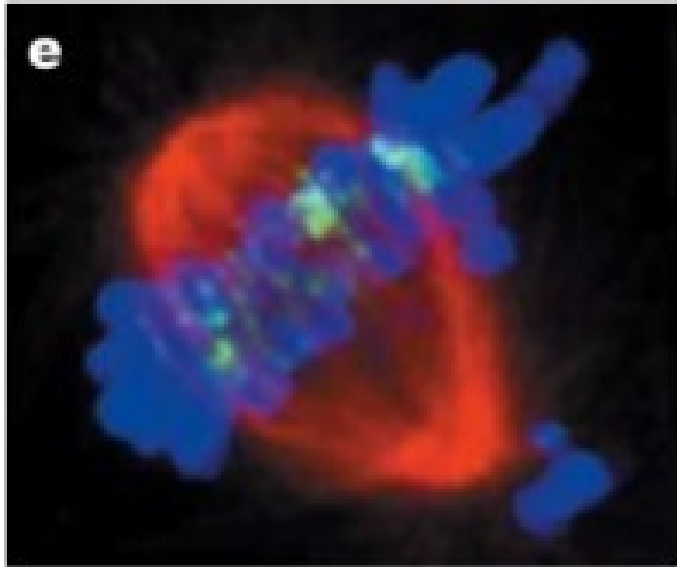


Antimitotic drugs bind to microtubules at diverse sites.



Microtubules are extremely important in the process of mitosis.

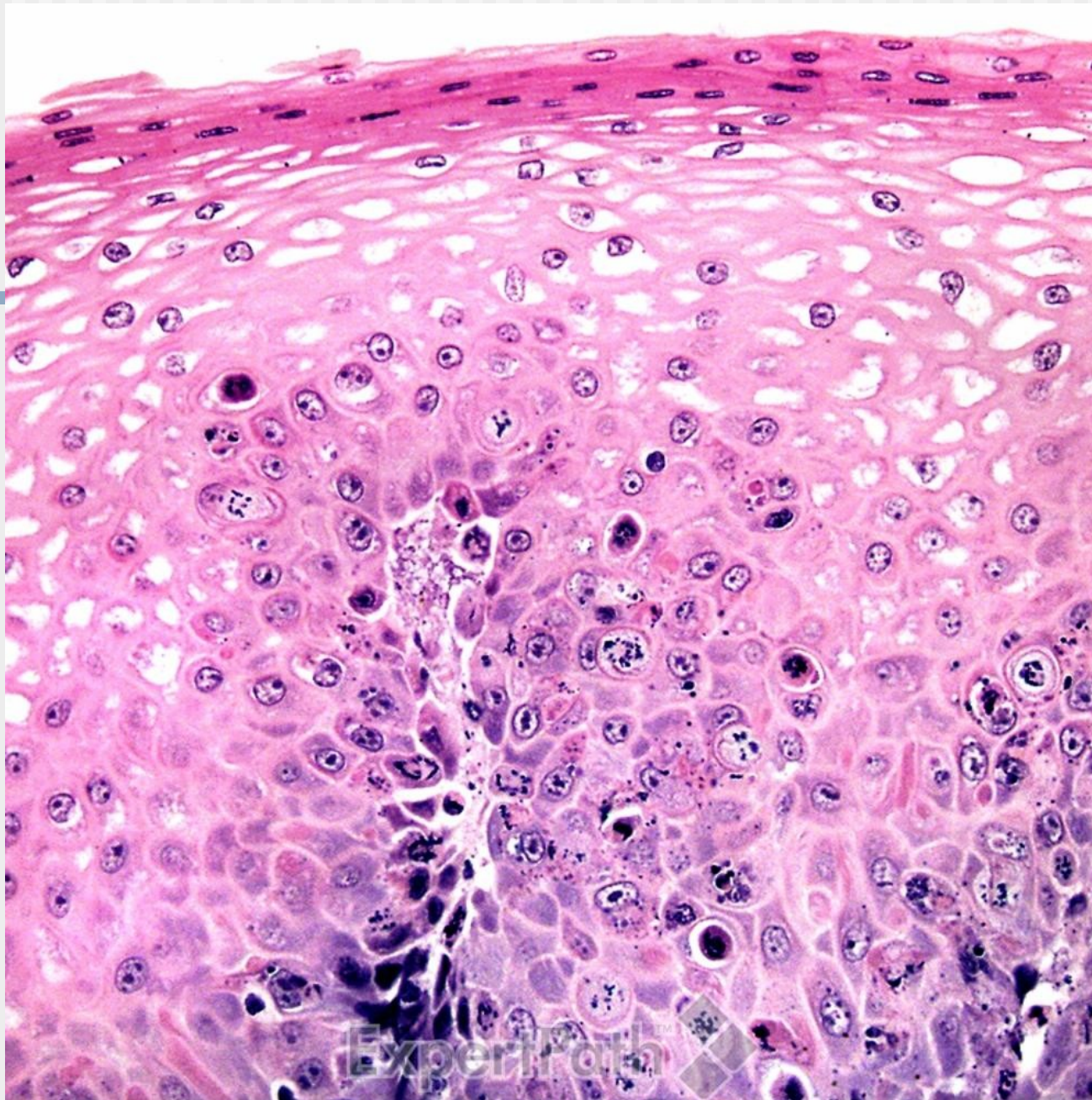
Their importance in mitosis and cell division makes microtubules an important target for anticancer drugs.

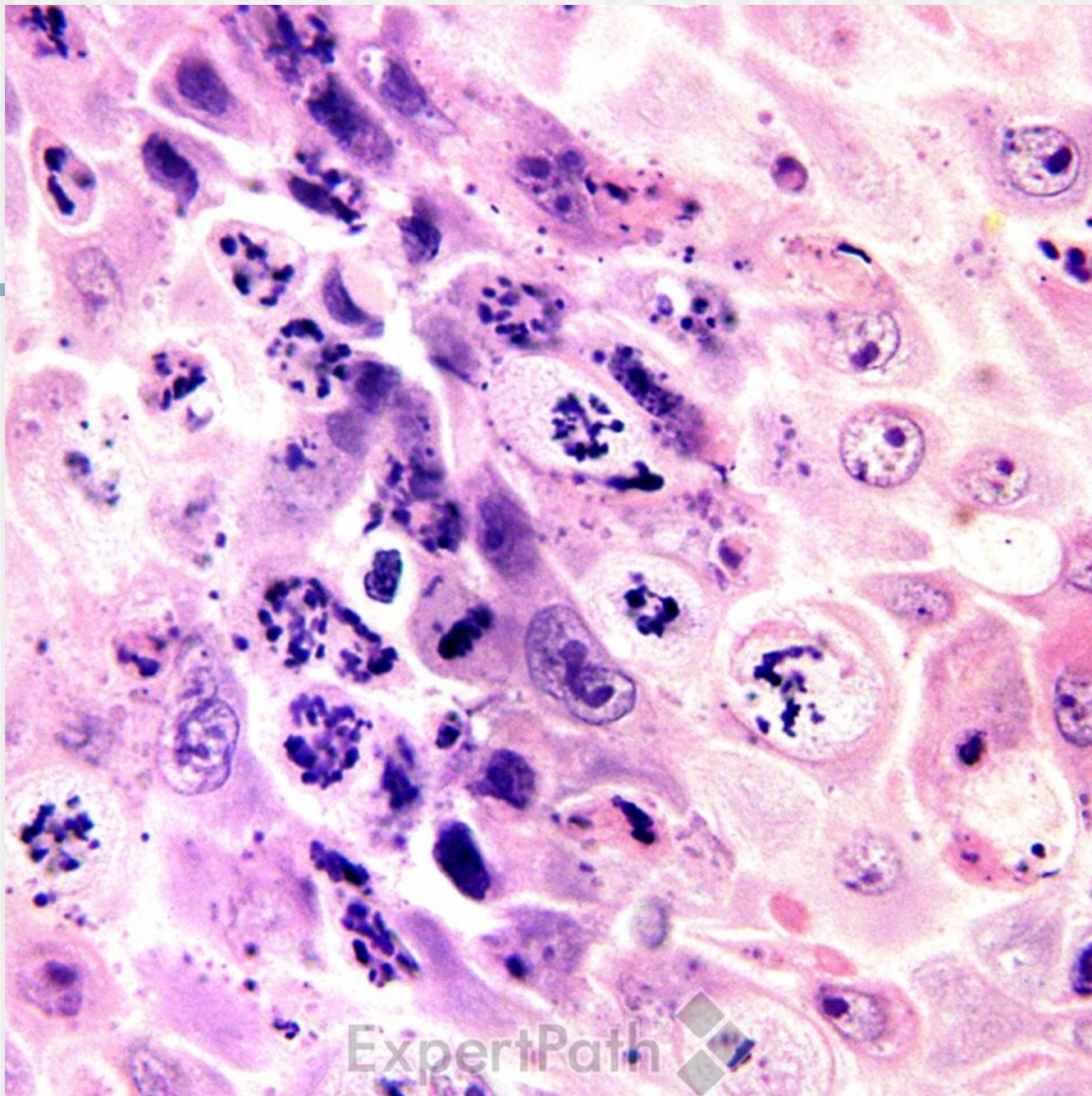


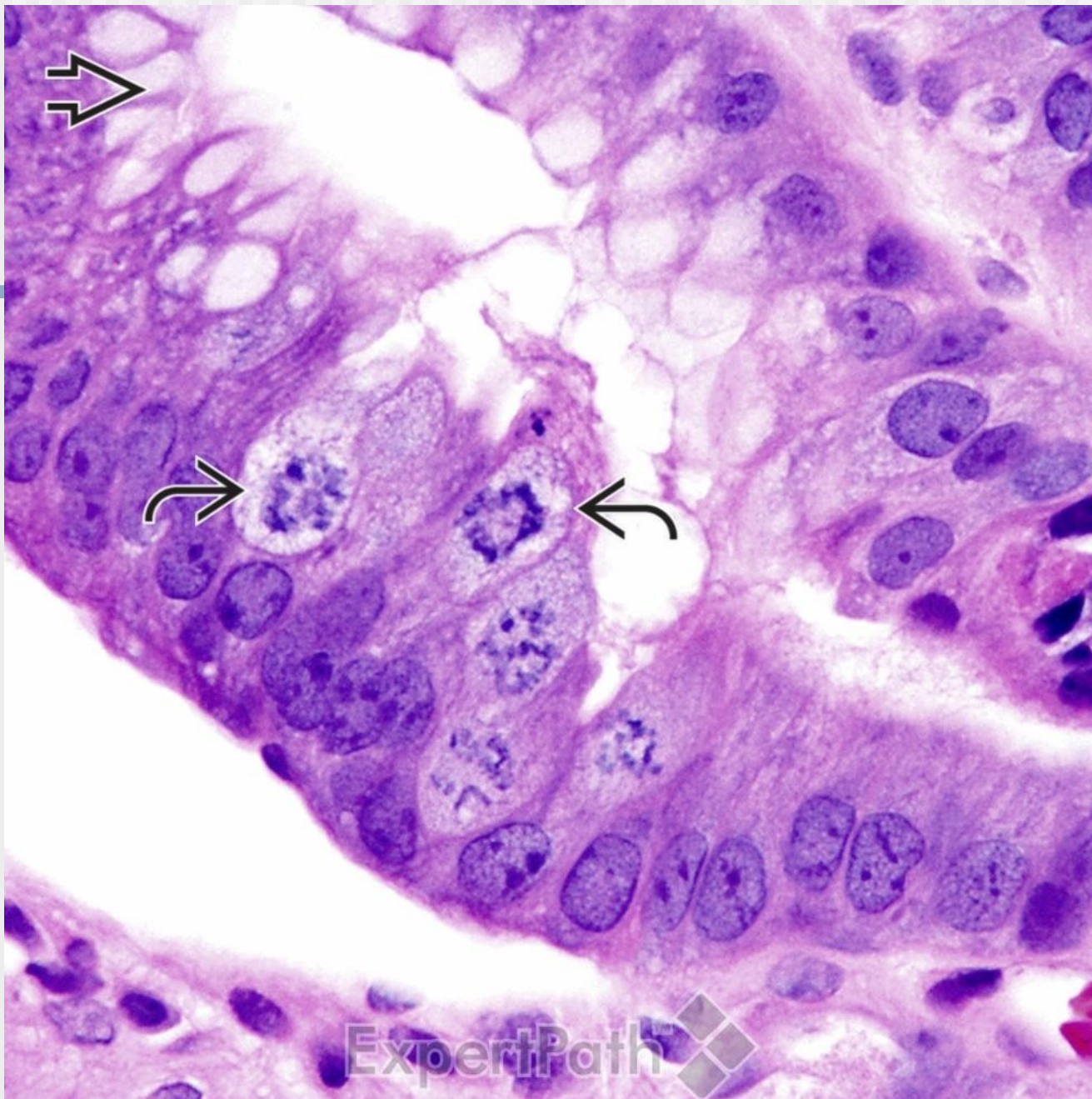
We have found that suppression of microtubule dynamics by drugs such as paclitaxel (Taxol) and Vinca alkaloids seems to be a common mechanism by which these drugs block mitosis and kill tumour cells.

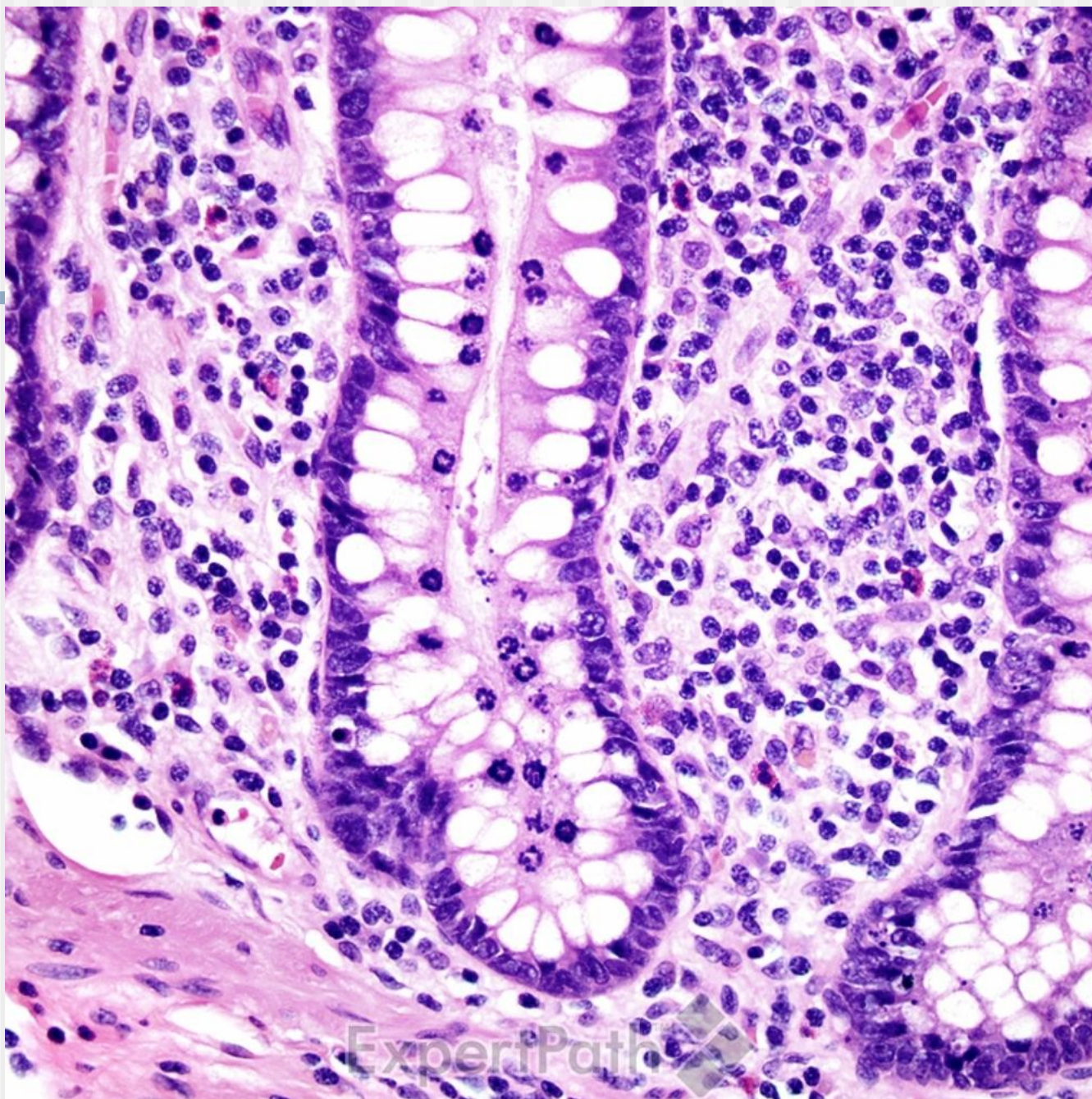
Taxane effect: Histologic Features

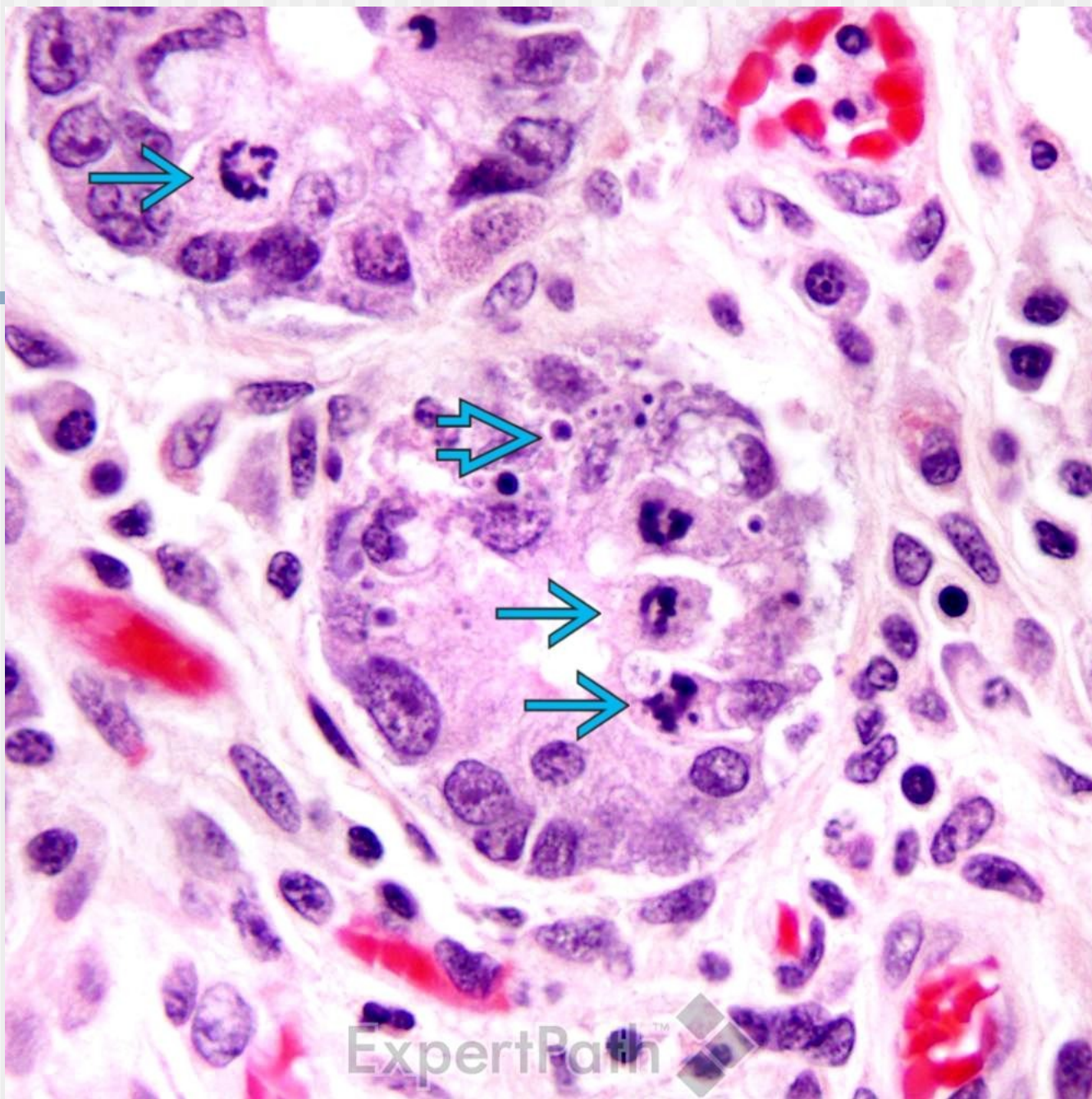
- Prominent **apoptosis** and **mitotic arrest**
- **Ring mitoses**
 - Nuclear alterations are in **proliferative compartment**
 - In esophagus, in **basal layer**
 - In intestines, just above **crypt base** to **midcrypt**
 - In stomach, **necks of glands**
 - **Surface epithelium** lacks characteristic alterations in all sites

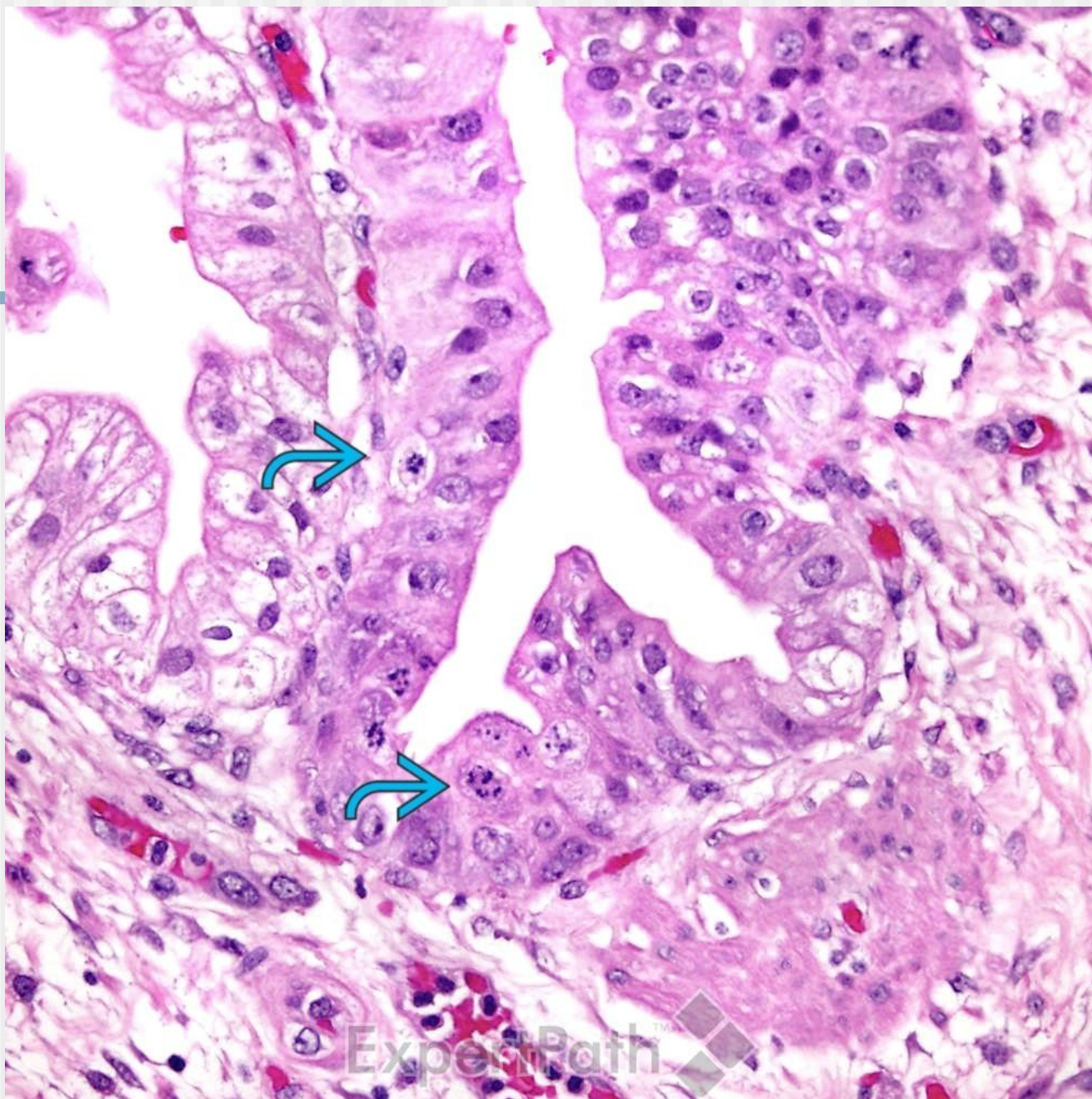












Taxane effect:

Differential Diagnosis

■ Epithelial Dysplasia

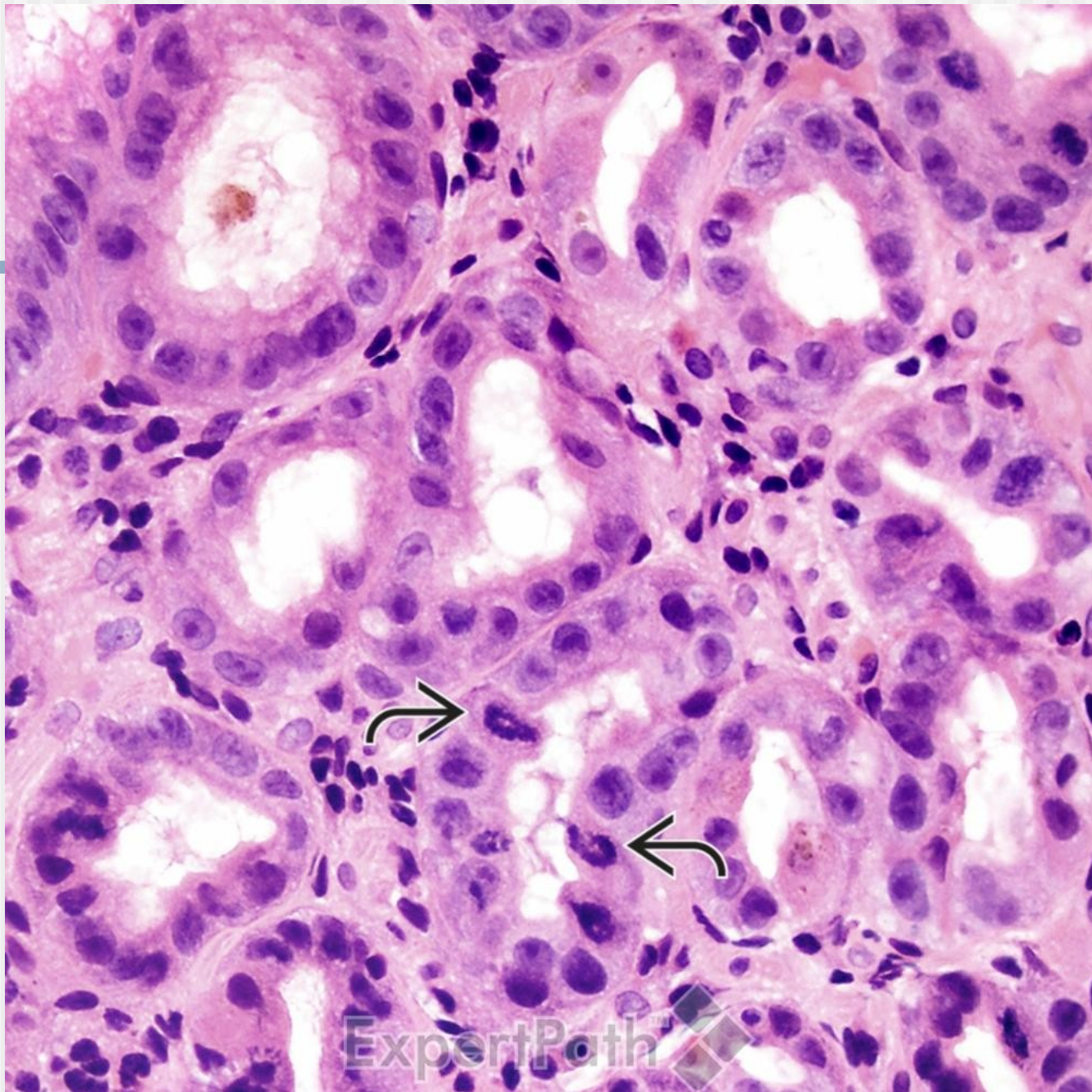
- Nuclear enlargement and hyperchromasia that extends to epithelial surface
- Apoptosis scant
- Ring mitoses rare

■ Colchicine Toxicity

- Difficult to distinguish
- Correlation with clinical information always required

Differential Diagnosis: Colchicine Toxicity

- Presence of **ring mitoses** in patient taking colchicine is diagnostic of toxicity/toxic serum drug levels
- Typically found in patients **with kidney or liver disease**
 - Colchicine has long half-life, so patients with renal or liver insufficiency at risk
 - Both organs (liver and kidney) are required for clearance of drug



Taxane effect: Presentation

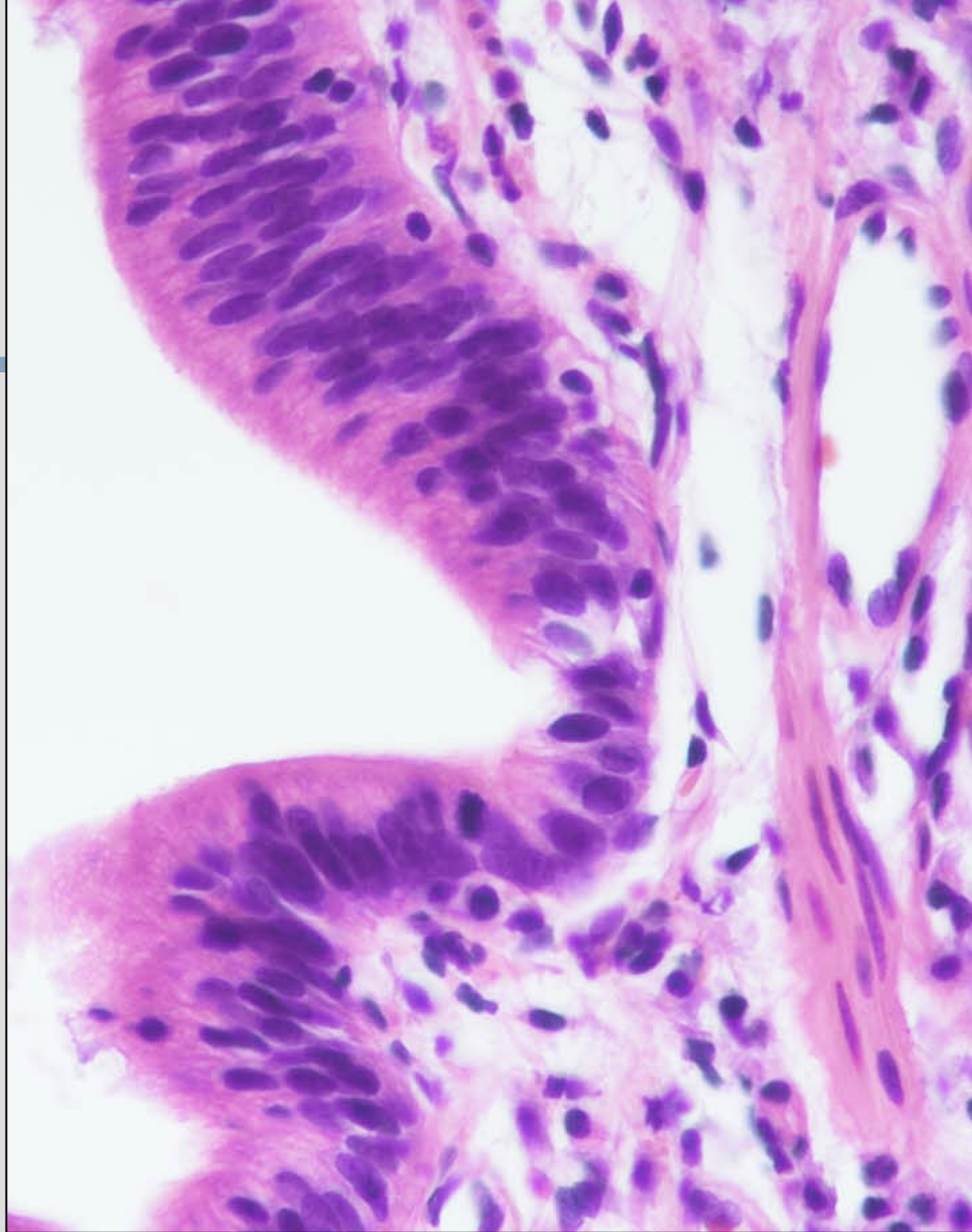
- Characteristic histologic changes can be found **incidentally** in mucosal biopsies or resections obtained **within 1-4 days** of administration of paclitaxel.
- Reported symptoms and associations
 - Vomiting
 - Diarrhea
 - Mucositis
 - Neutropenic enterocolitis
 - Colonic perforation

Taxane effect: Treatment

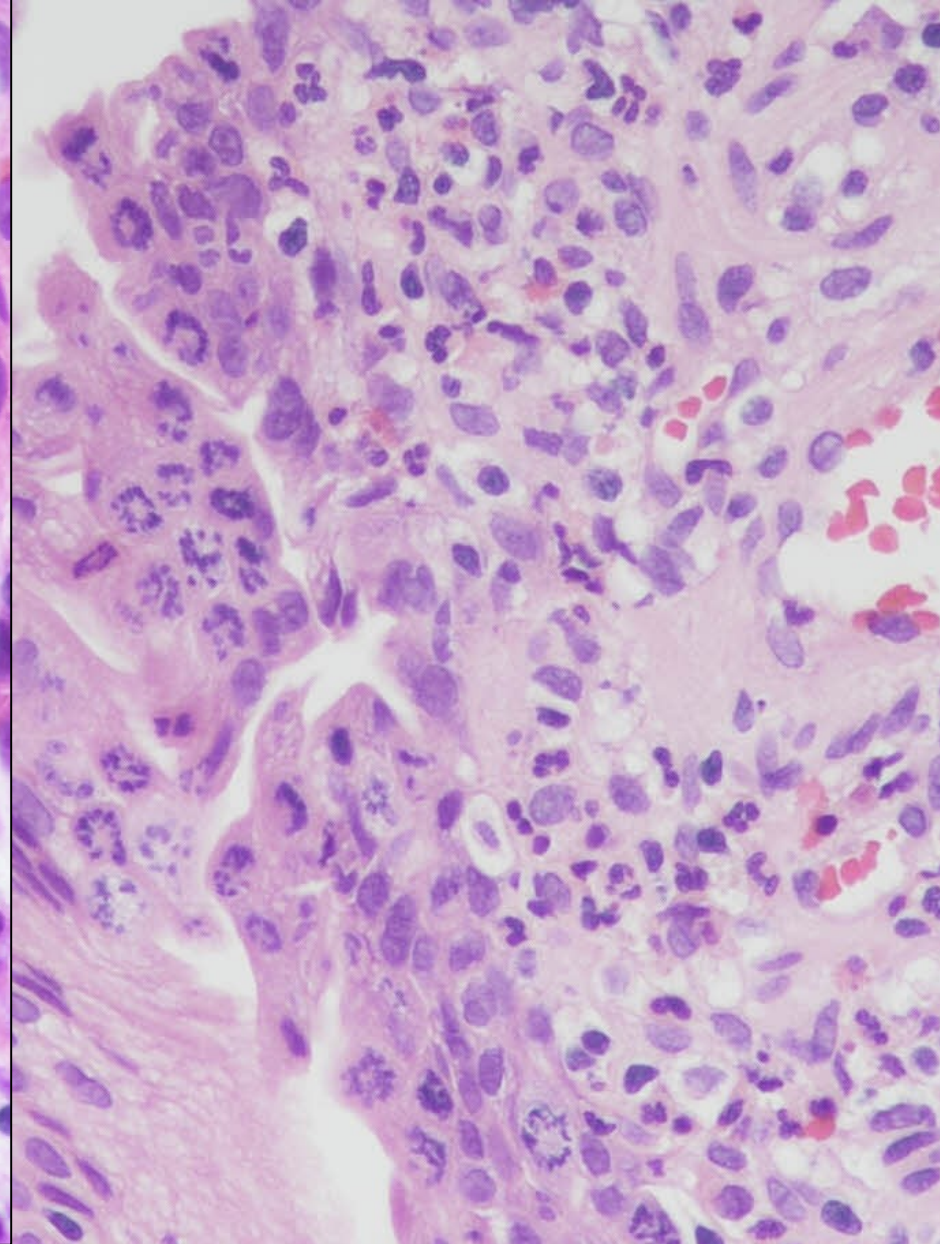
- Withdrawal of medication (for toxicity)
- No treatment necessary in most cases
- Right colon resection in cases associated with typhlitis (Neutropenic enterocolitis)

Taxane effect: Prognosis

- Excellent in most cases
 - Usually, findings are incidental rather than reflection of toxicity
- Reports of colonic perforation and acute abdomen following taxane administration



Tubular adenoma with
low grade dysplasia



Compatible with Taxane
(paclitaxel) effect

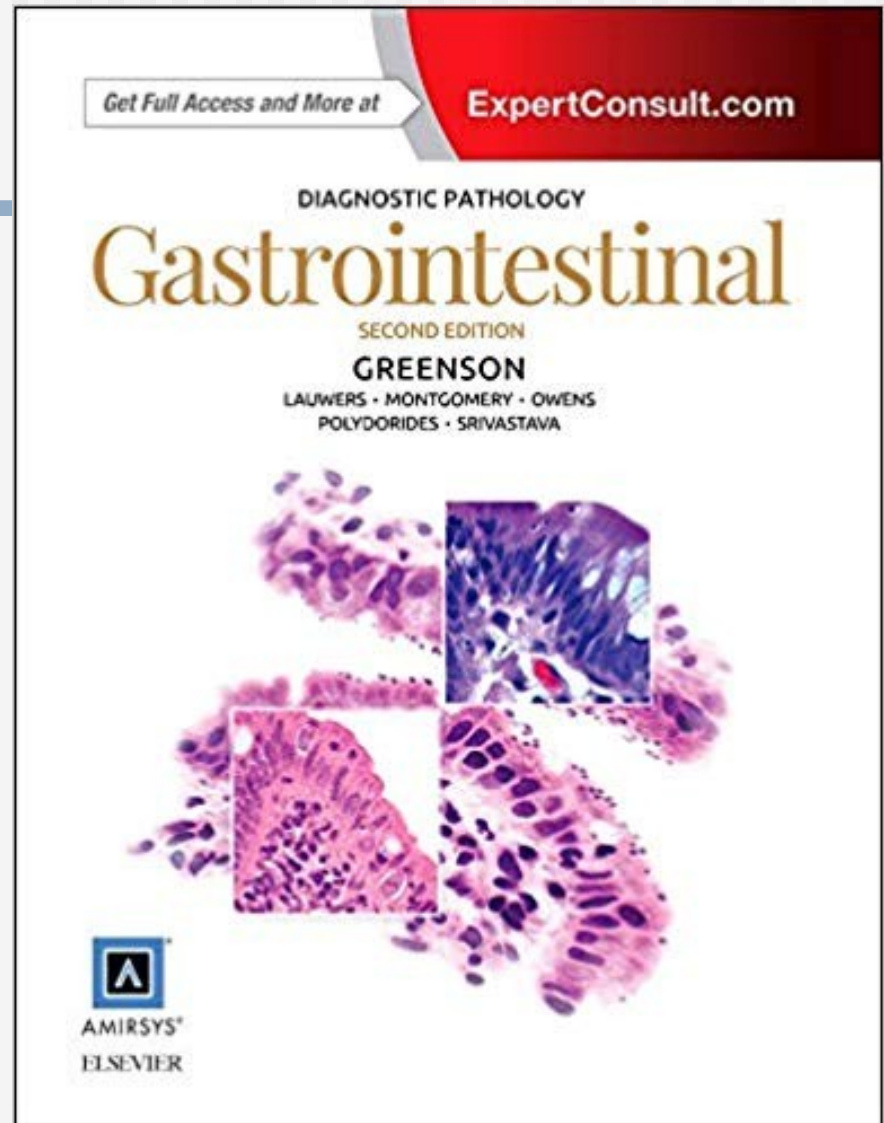
Conclusions

Taxanes effect (Taxol effect)

- Chemotherapeutic agents for esophagus, breast, prostate, and lung cancers
- **GI complication**
- Pathology: **Ring mitosis** and Apoptosis
- DDx: **Epithelial Dysplasia, Colchicine Toxicity**
- Treatment: **Withdrawal of medication**
- Prognosis: Excellent

Reference

Diagnostic Pathology: Gastrointestinal 2nd Edition (2015 ed)



Thanks for your attention !