Precancerous (Premalignant) Lesions

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Precancerous (Premalignant) Lesions

- Group of conditions which predispose to the subsequent development of cancer

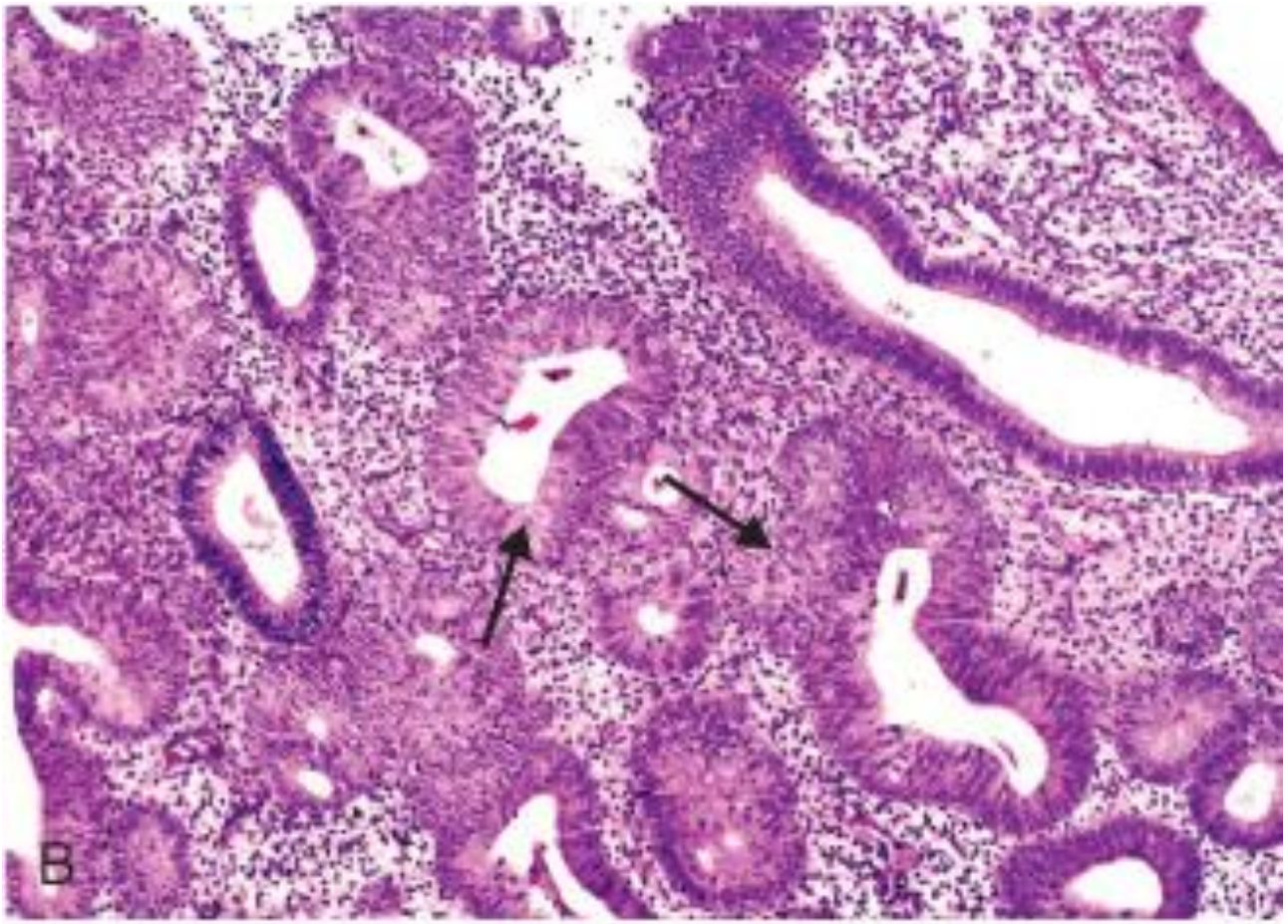
Imp to recognize to prevent progression

Many of these conditions are characterized by morphological changes

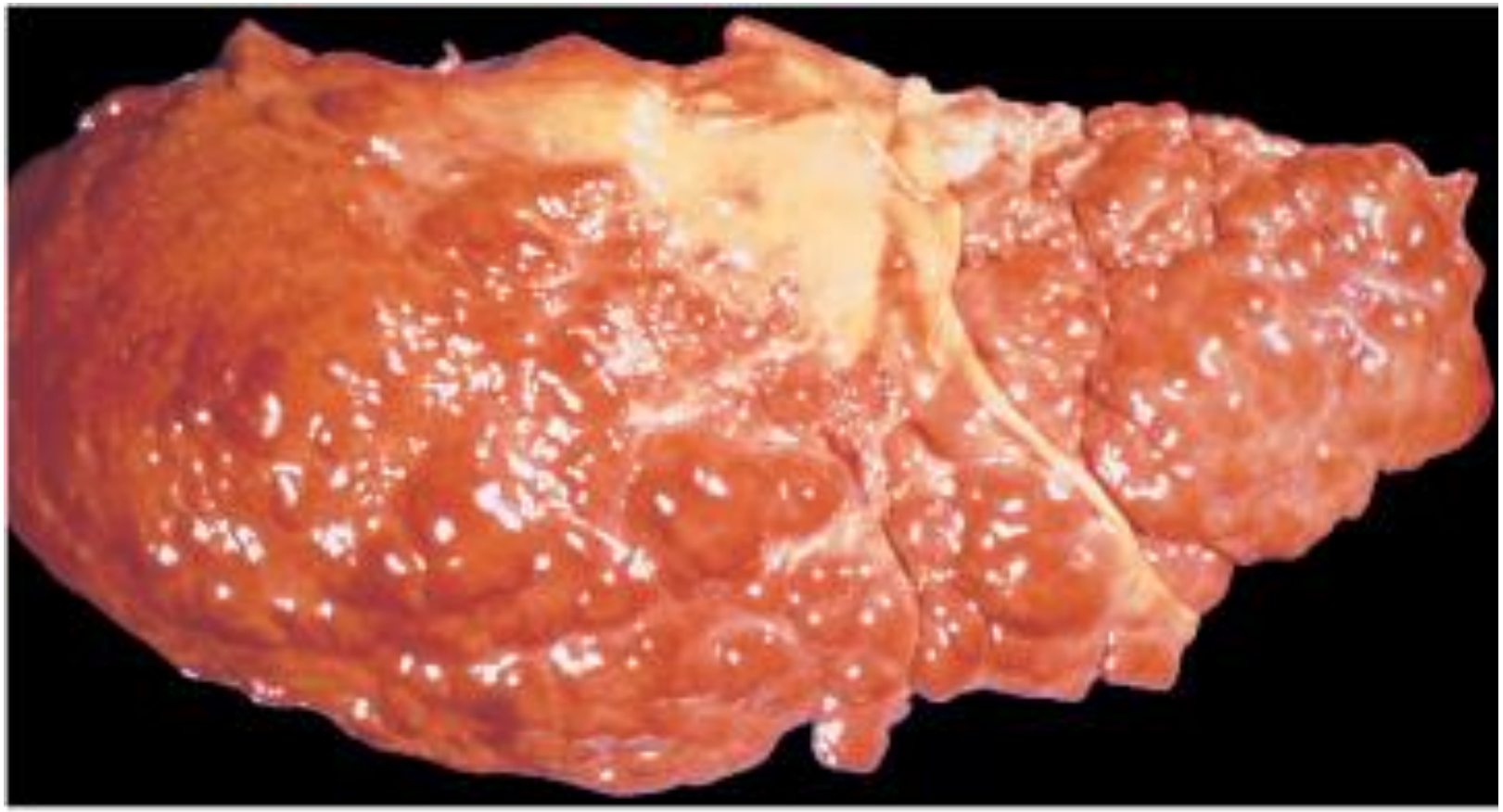
- Increased N:C,
- Pleomorphism,
- Increased mitotic activity ,
- Poor differentiation

Precancerous Lesion	Cancer
Hyperplasia	
Endometrial hyperplasia	Endometrial carcinoma
Breast—lobular and ductal hyperplasia	Breast carcinoma
Liver—cirrhosis of the liver	Hepatocellular carcinoma

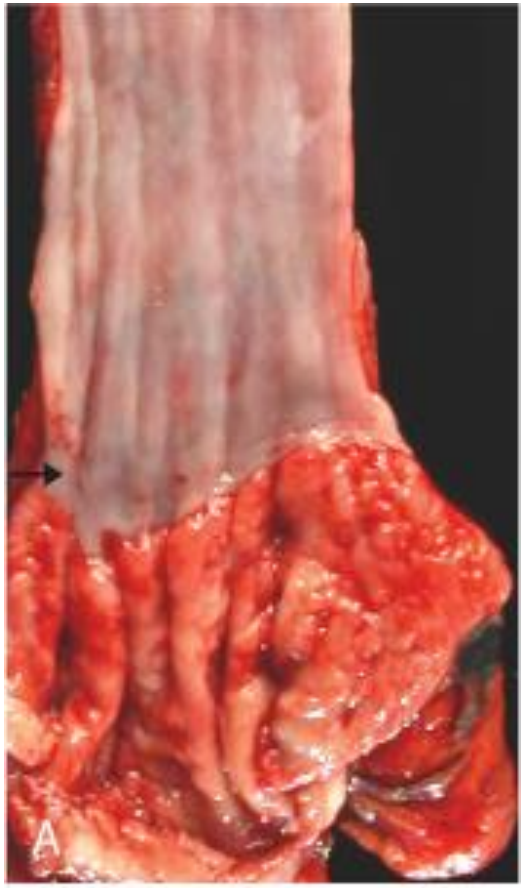
Atypical hyperplasias (endometrial intraepithelial neoplasia) exhibit increased gland/stroma ratio (gland crowding) and epithelial stratification

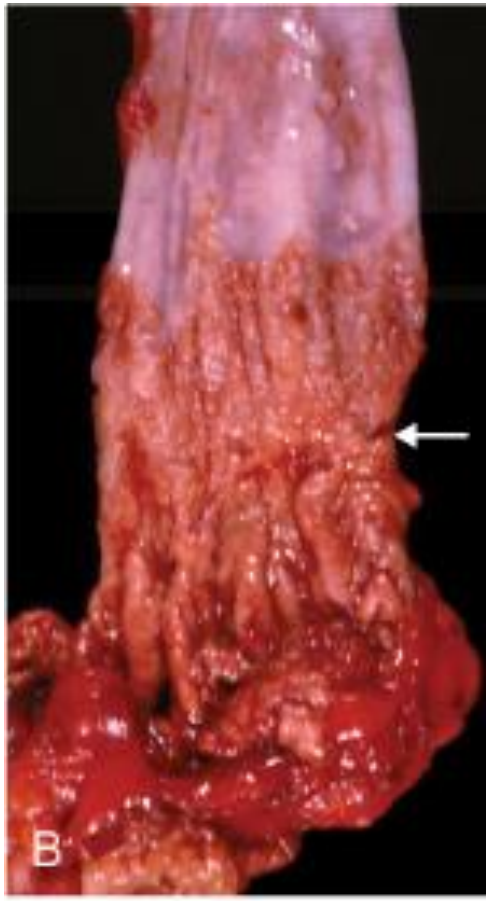


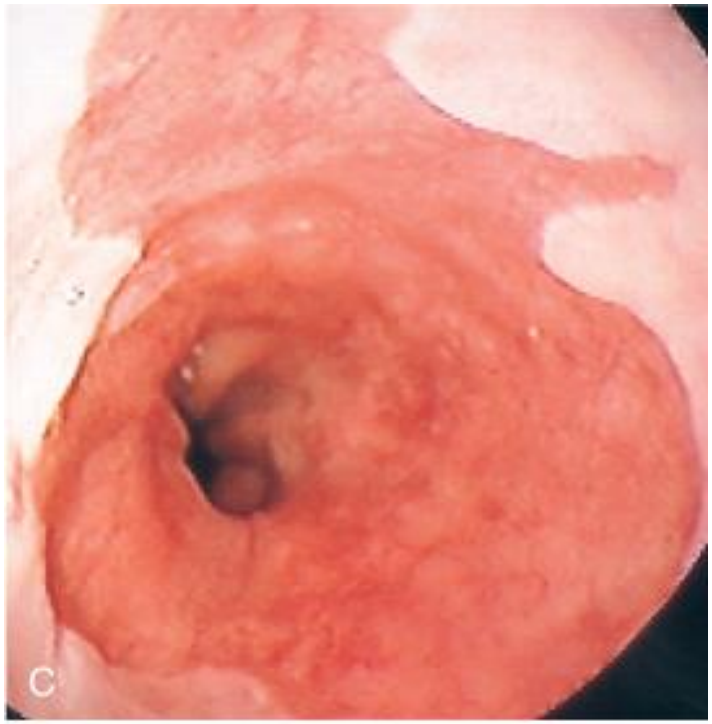
Cirrhosis :coarse nodular surface

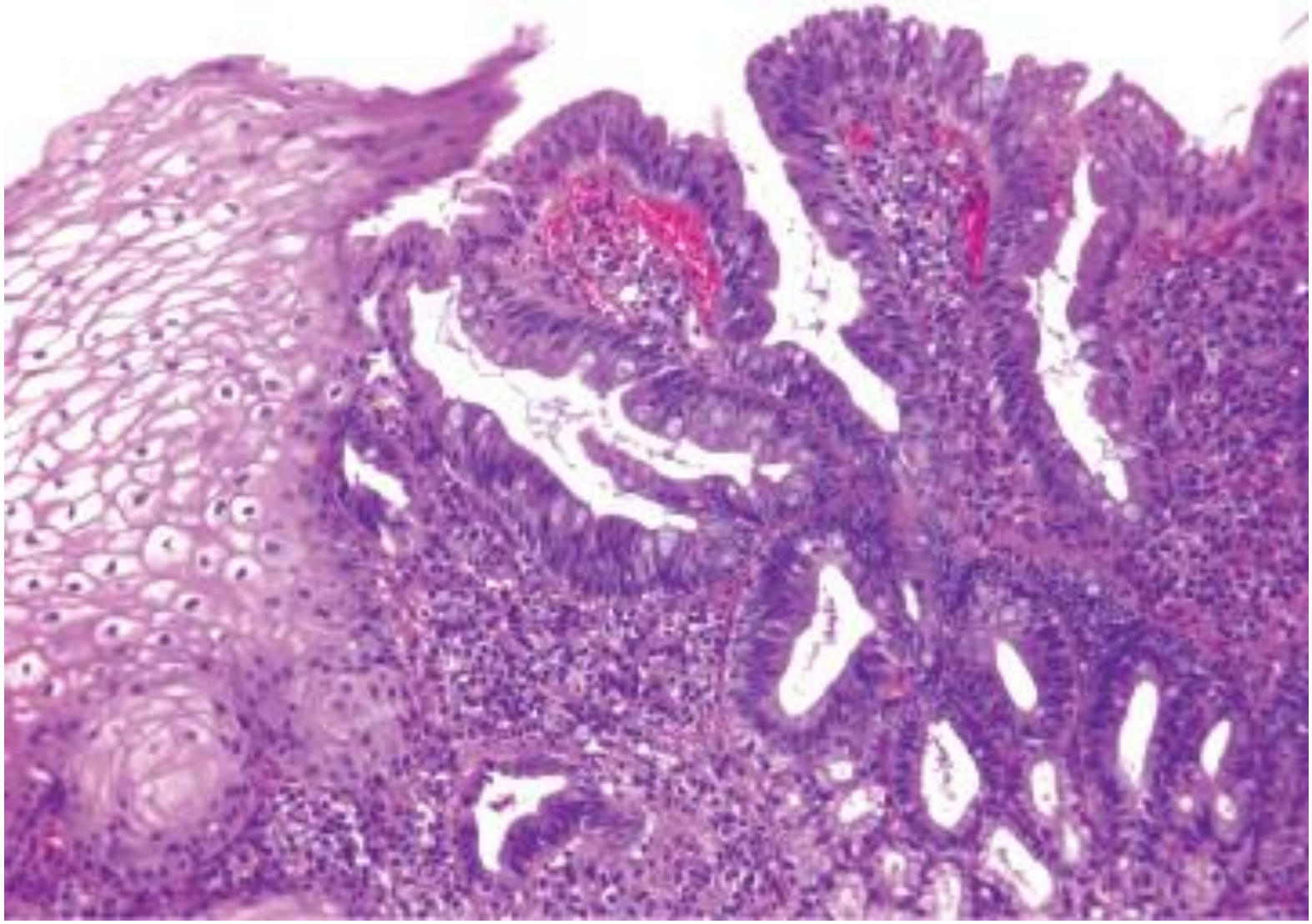


Dysplasia	
Cervix	Squamous carcinoma of cervix
Skin	Squamous carcinoma
Bladder	Transitional cell carcinoma
Bronchial epithelium	Lung carcinoma
Metaplasia	
Glandular metaplasia of esophagus	Adenocarcinoma of esophagus



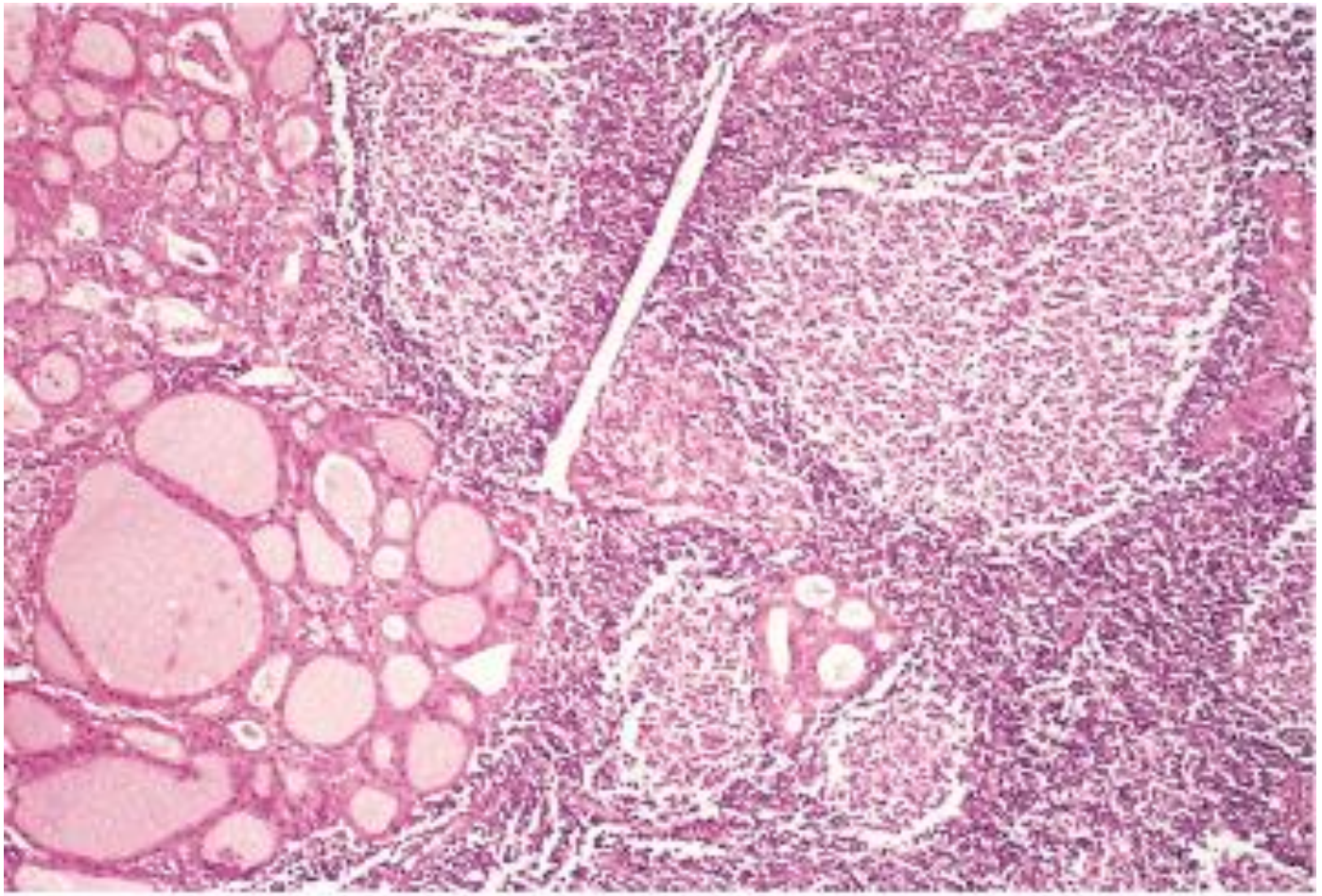






Inflammatory lesions	
Ulcerative colitis	Carcinoma of colon
Atrophic gastritis	Carcinoma of stomach
Autoimmune (Hashimoto's) thyroiditis	Malignant lymphoma, Thyroid carcinoma

Autoimmune (Hashimoto's) thyroiditis



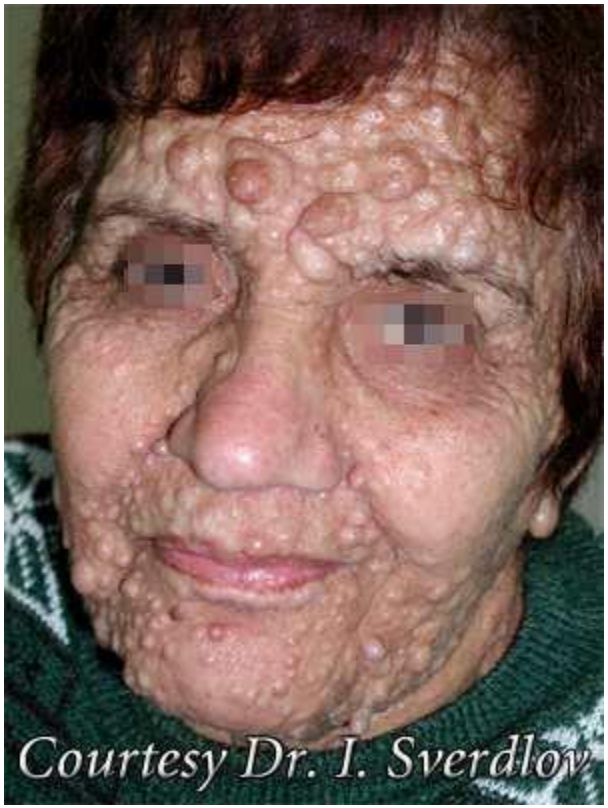
Benign neoplasms	
Colonic adenoma: Multiple Villous Adenomas of large intestine	Carcinoma of colon
Neurofibroma Multiple neurofibramotosis (von Recklinghausin's disease)	Malignant peripheral–nerve–sheath tumor (malignant schwannoma)

The malignant risk with an ADENOMATOUS POLYP is correlated with three interdependent features

- *Polyp size, histologic architecture, and severity of epithelial dysplasia, as follows*:

- Cancer is rare in tubular adenomas smaller than 1 cm
- The risk of cancer is high (approaching 40%) in sessile villous adenomas more than 4 cm in diameter.
- Severe dysplasia, when present, is often found in villous areas.

Multiple neurofibramotosis (von Recklinghausin's disease)



Cirrhosis of liver	Carcinoma liver
Chronic Bronchitis Heavy cigarette smokers	Cancer of the bronchus
Old burn scar(Marjolin's ulcer)	Sq.Cell ca
Chronic irritation from jagged teeth Ill fitting dentures	Oral cavity cancer

Inherited Predisposition to Cancer

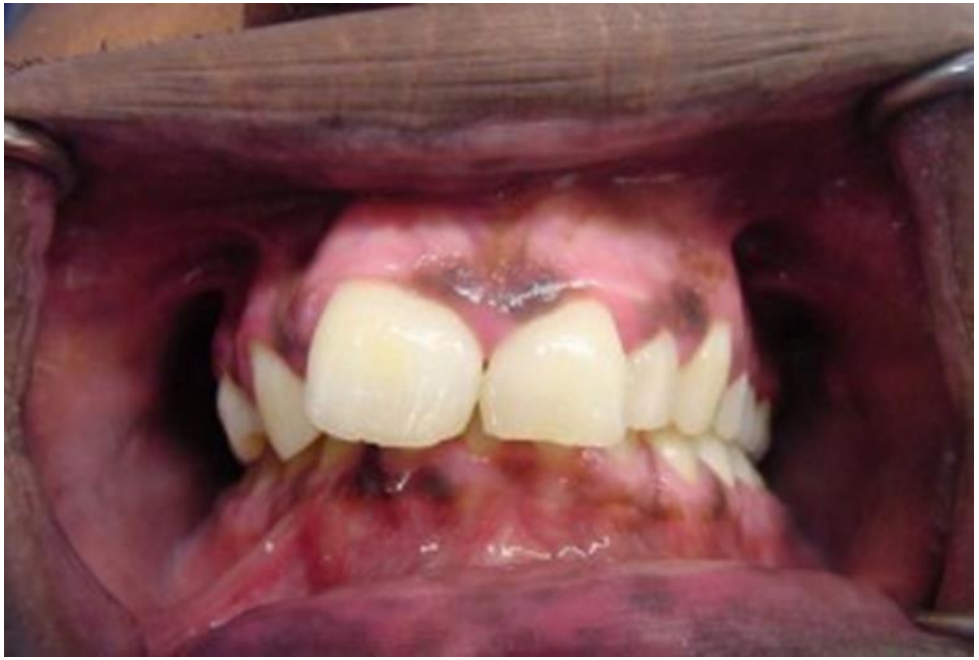
Inherited Cancer Syndromes (Autosomal Dominant)	
Gene	*Inherited Predisposition*
RB	Retinoblastoma
p53	Li-Fraumeni syndrome (various tumors)
p16INK4A	Melanoma
APC	Familial adenomatous polyposis/colon cancer
NF1, *NF2*	Neurofibromatosis 1 and 2
BRCA1, *BRCA2*	Breast and ovarian tumors
MEN1, *RET*	Multiple endocrine neoplasia 1 and 2
MSH2, *MLH1*, *MSH6*	Hereditary nonpolyposis colon cancer
PATCH	Nevoid basal cell carcinoma syndrome

Familial Cancers	
Familial clustering of cases, but role of inherited predisposition not clear for each individual	
Breast cancer	
Ovarian cancer	
Pancreatic cancer	
Inherited Autosomal Recessive Syndromes of Defective DNA Repair	
Xeroderma pigmentosum	
Ataxia-telangiectasia	
Bloom syndrome	
Fanconi anemia	

Familial Syndromes

- AD
- Peutz-Jeghers syndrome
- Characterized by Hamartomatous intestinal polyposis and Melanotic pigmentation of lips,mouth and genitalias.

- A modestly increased risk of cancer, frequently in extragastrointestinal sites
- Pancreas,lung,breast,ovary
- and uterus



Familial Adenomatous Polyposis (FAP) Syndrome

- Typically develop 500 to 2500 colonic adenomas that carpet the mucosal surface

- Occasionally as few as 150 polyps are present; a minimum of 100 polyps is necessary for a diagnosis of classic FAP

Gardner syndrome

- Intestinal polyps identical to those in classic FAP, combined with multiple osteomas ,epidermal cysts, and fibromatosis.

- Higher frequency of duodenal and thyroid cancer

Turcot syndrome

- Combination of adenomatous colonic polyposis and tumors of the central nervous system.
- Two thirds have *APC* gene mutations and develop brain medulloblastomas.
- The remaining one third have mutations in one of the genes associated with HNPCC and develop brain glioblastomas

Hereditary Nonpolyposis Colorectal Cancer (HNPCC) Syndrome

- AD
- Increased risk of colorectal cancer and extraintestinal cancer, endometrium.

- The hallmark of HNPCC is mutations in DNA REPAIR genes, leading to microsatellite instability,

Chronic Inflammation and Cancer

- In 1863 Virchow proposed that *cancer develops at sites of chronic inflammation*
- Ulcerative colitis, Crohn disease, *Helicobacter pylori* gastritis, viral hepatitis, and chronic pancreatitis.
- The precise mechanisms that link inflammation and cancer development have not been established

- Production of cytokines=> stimulate the growth of transformed cells.

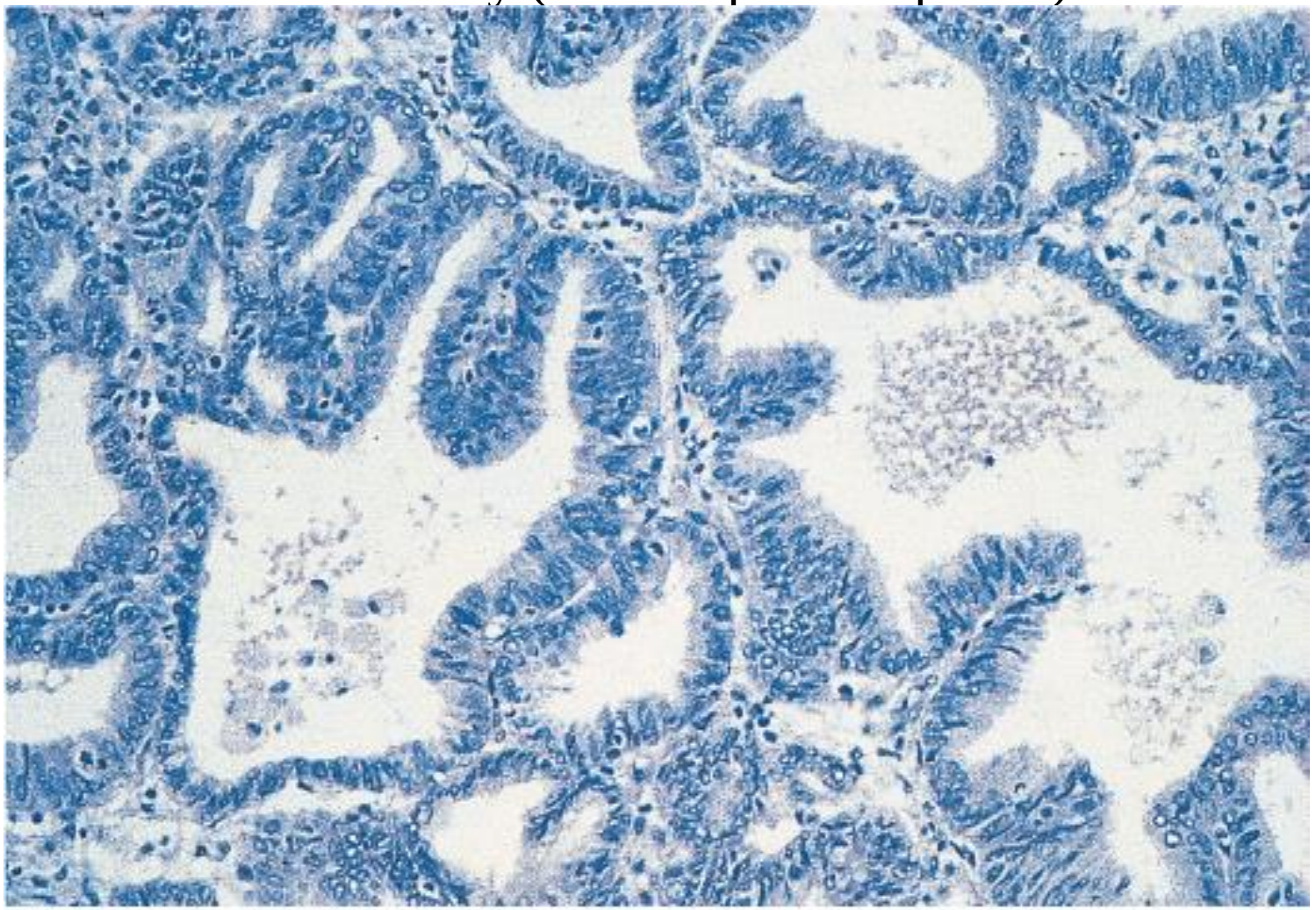
- In some cases, chronic inflammation may increase the pool of tissue stem cells, which become subject to the effect of mutagens.

Endometrial Complex hyperplasia with atypia
(severe hyperplasia)

- Gland crowding with back-to-back glands and marked cytologic atypia characterized by pleomorphism, hyperchromatism, and abnormal nuclear chromatin pattern.

- Carries a high risk of endometrial carcinoma.

Atypical hyperplasia of the endometrium. There is a combination of architectural abnormality and cytological abnormality (nuclear pleomorphism).

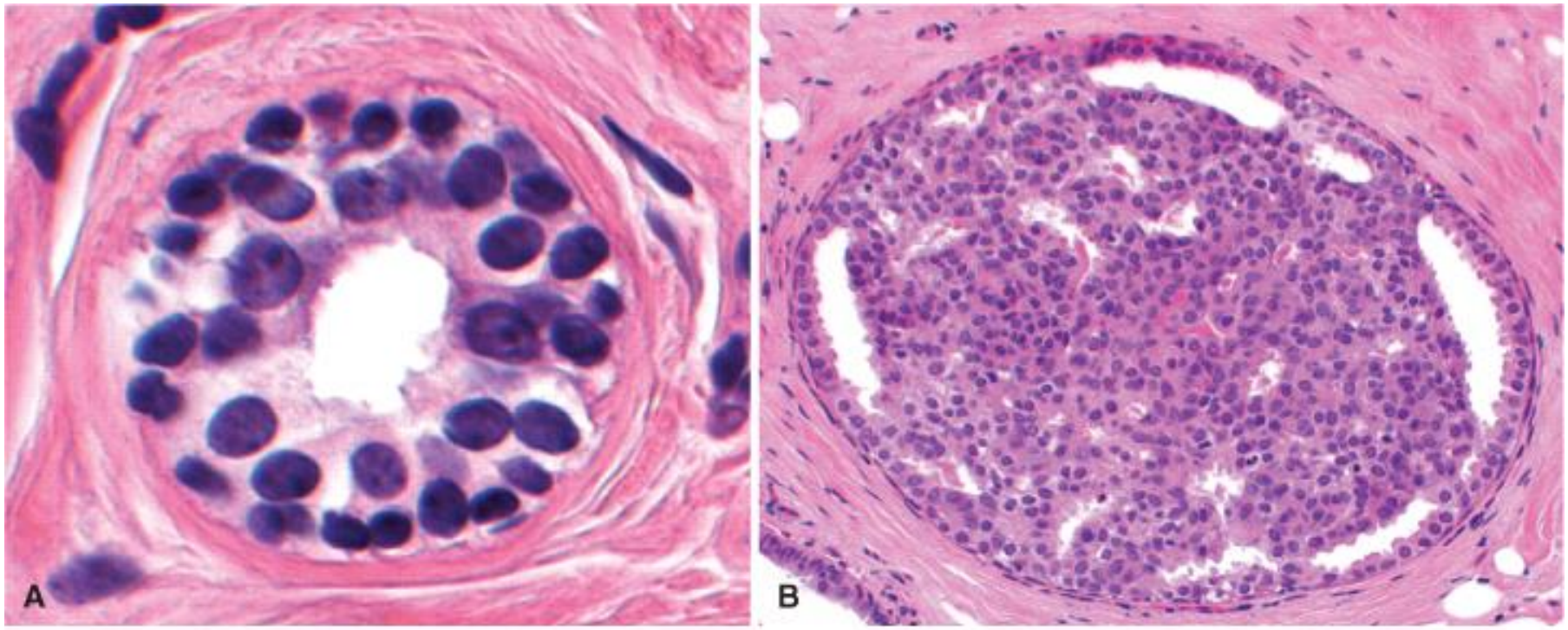


Atypical ductal hyperplasia (ADH) & Atypical lobular hyperplasia (ALH)

- Atypical hyperplasia is a cellular proliferation resembling ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS) but lacking sufficient qualitative or quantitative features for a diagnosis of carcinoma in situ.

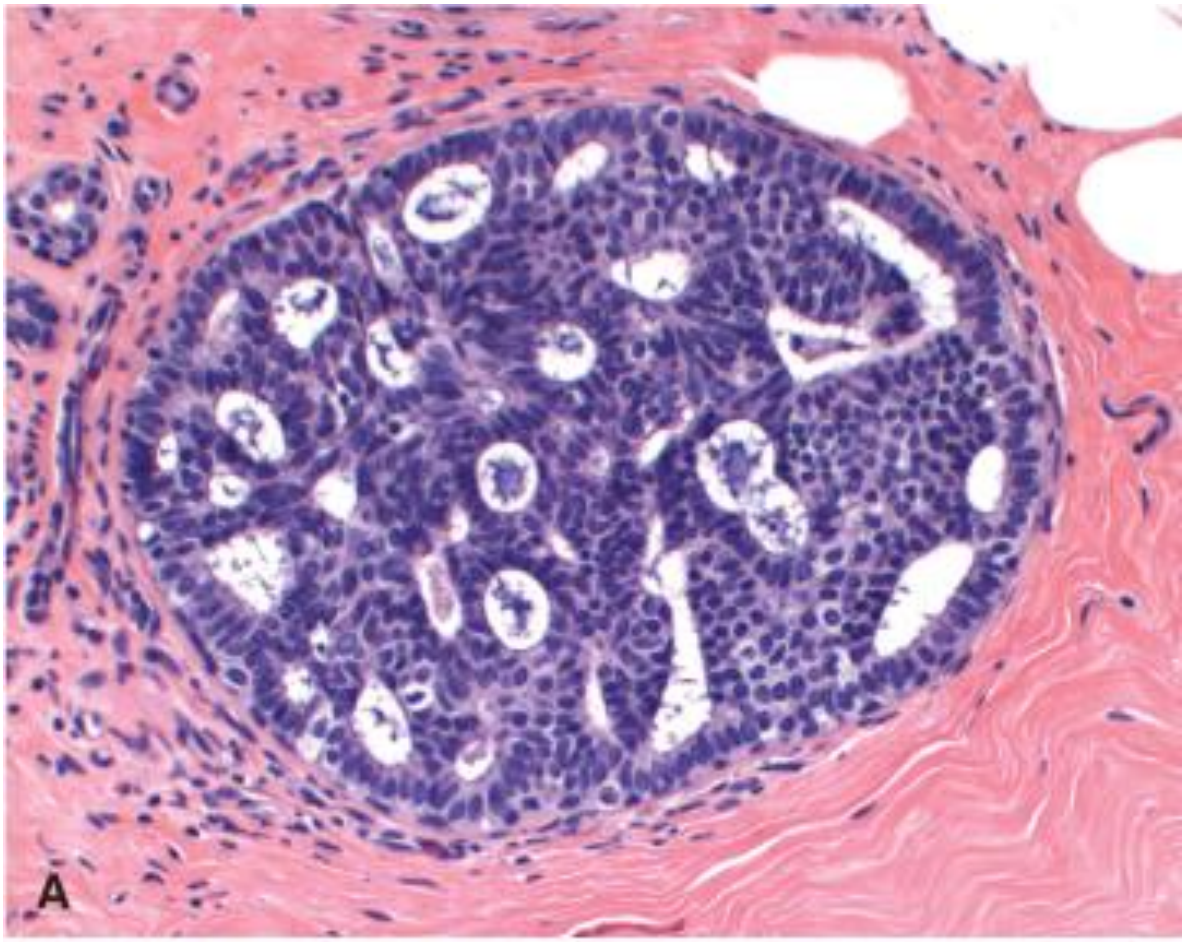
- ADH is recognized by its histologic resemblance to ductal carcinoma in situ, including a monomorphic cell population, regular cell placement, and round lumina.

- ALH refers to a proliferation of cells identical to those of LCIS, but the cells do not fill or distend more than 50% of the acini within a lobule.

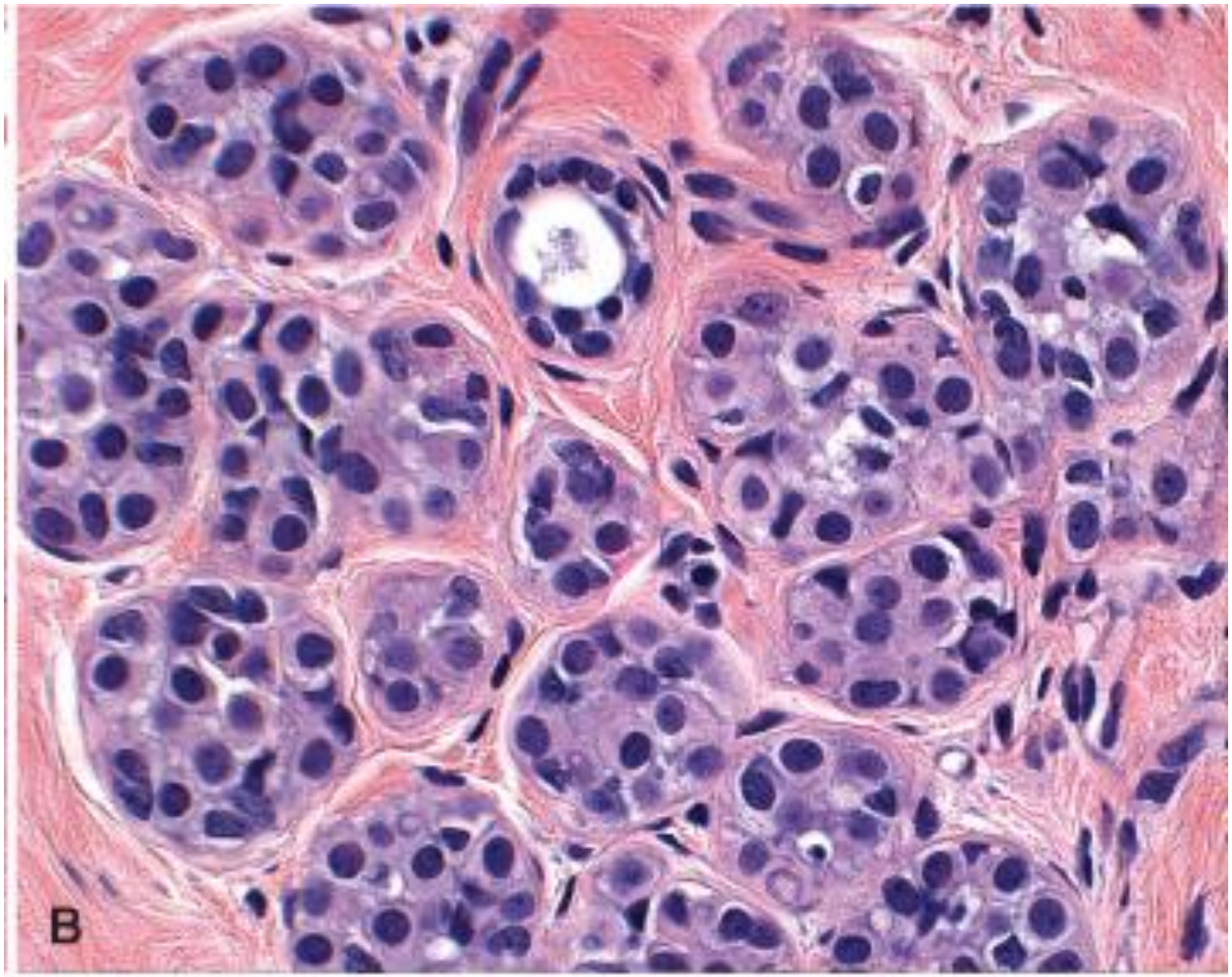


Atypical ductal hyperplasia

A duct is filled with a mixed population of cells consisting of oriented columnar cells at the periphery and more rounded cells within the central portion



Atypical lobular hyperplasia.
A population of monomorphic small, rounded, loosely cohesive cells partially fill a lobule



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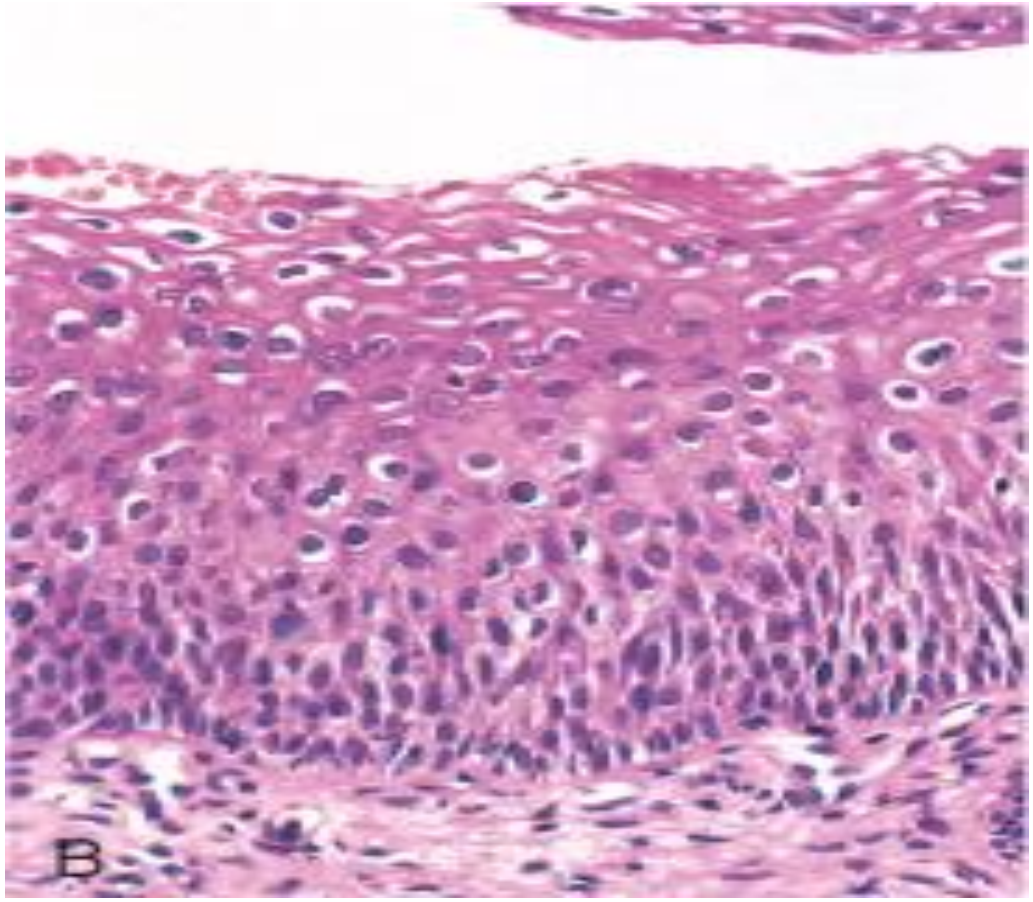
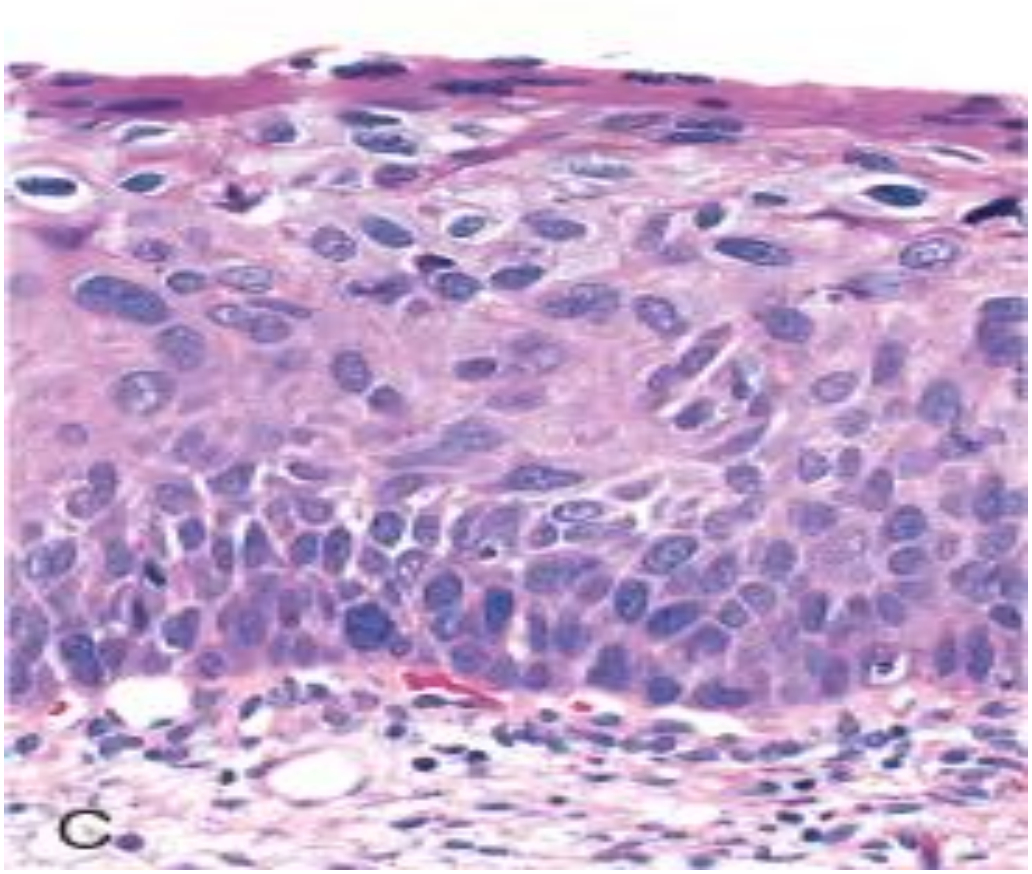
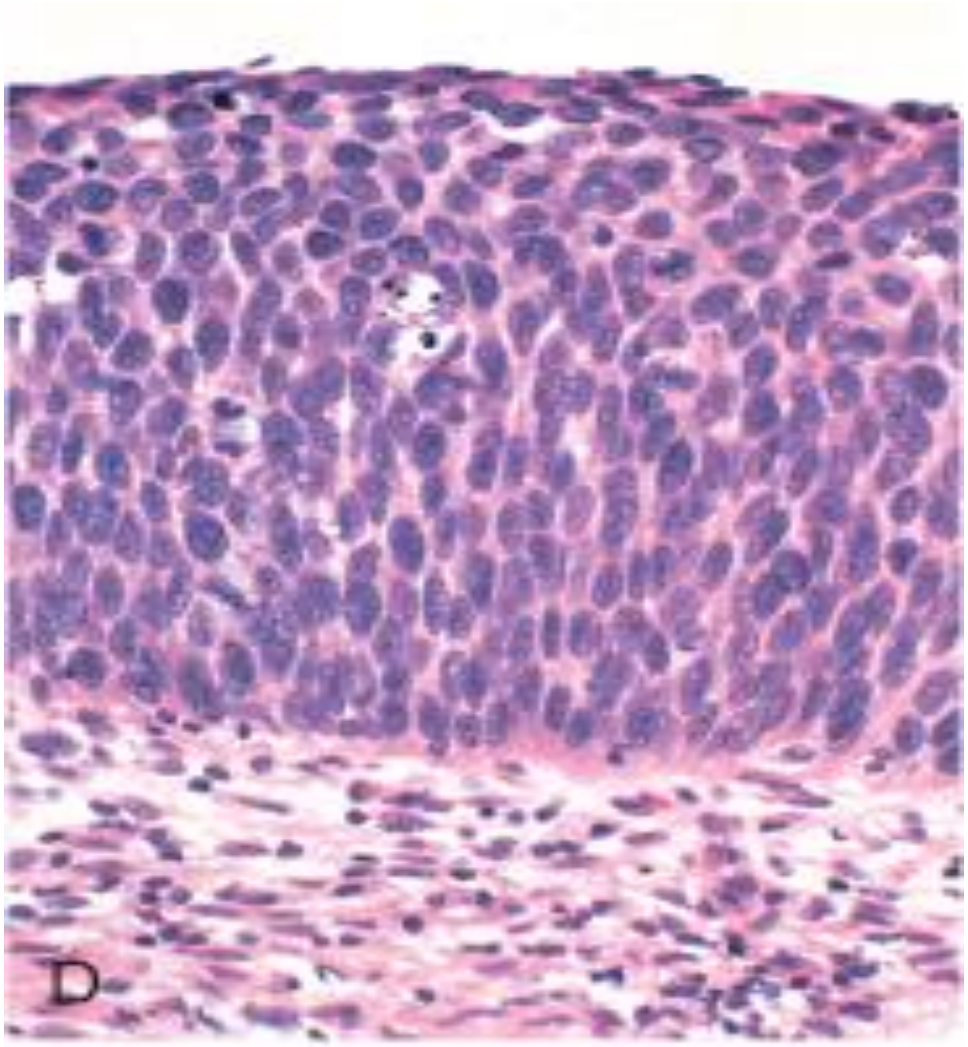
Dysplasia



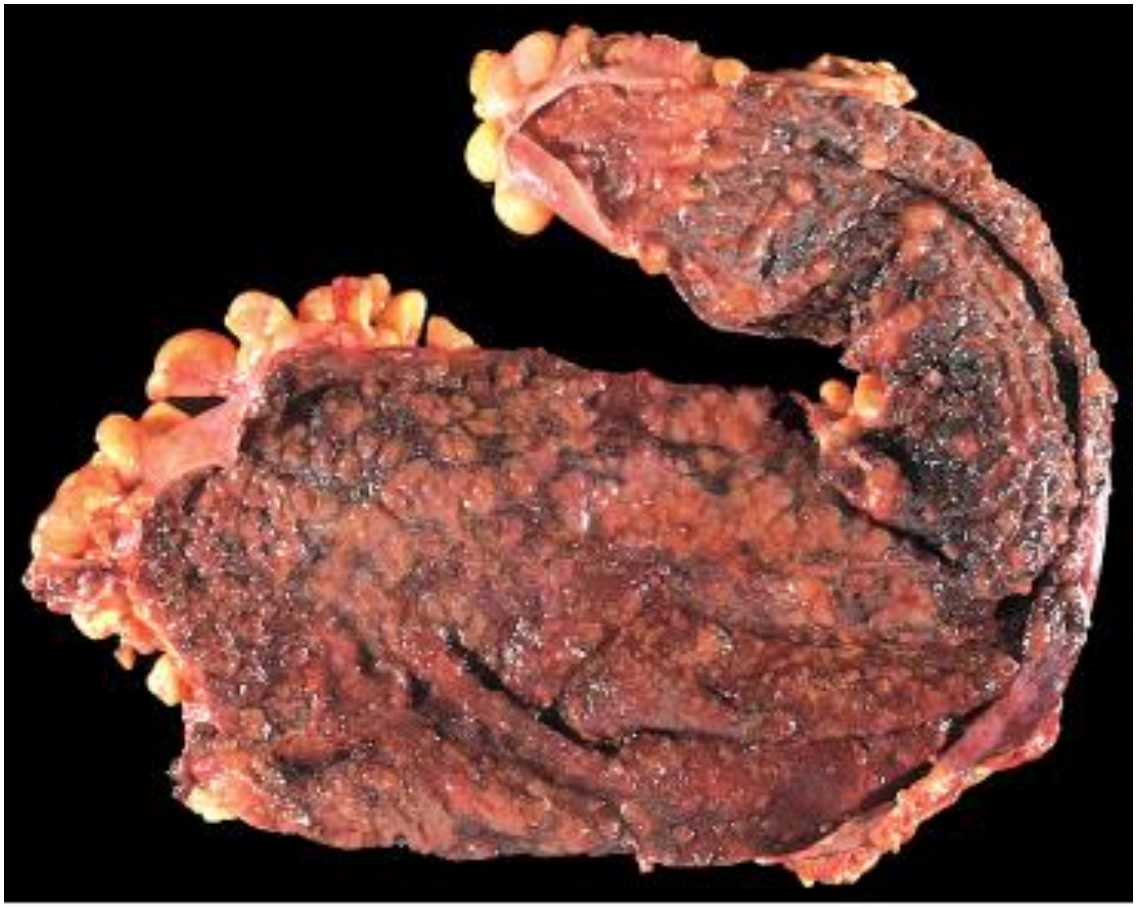
Dysplasia with progressive atypia in all layers of the epithelium



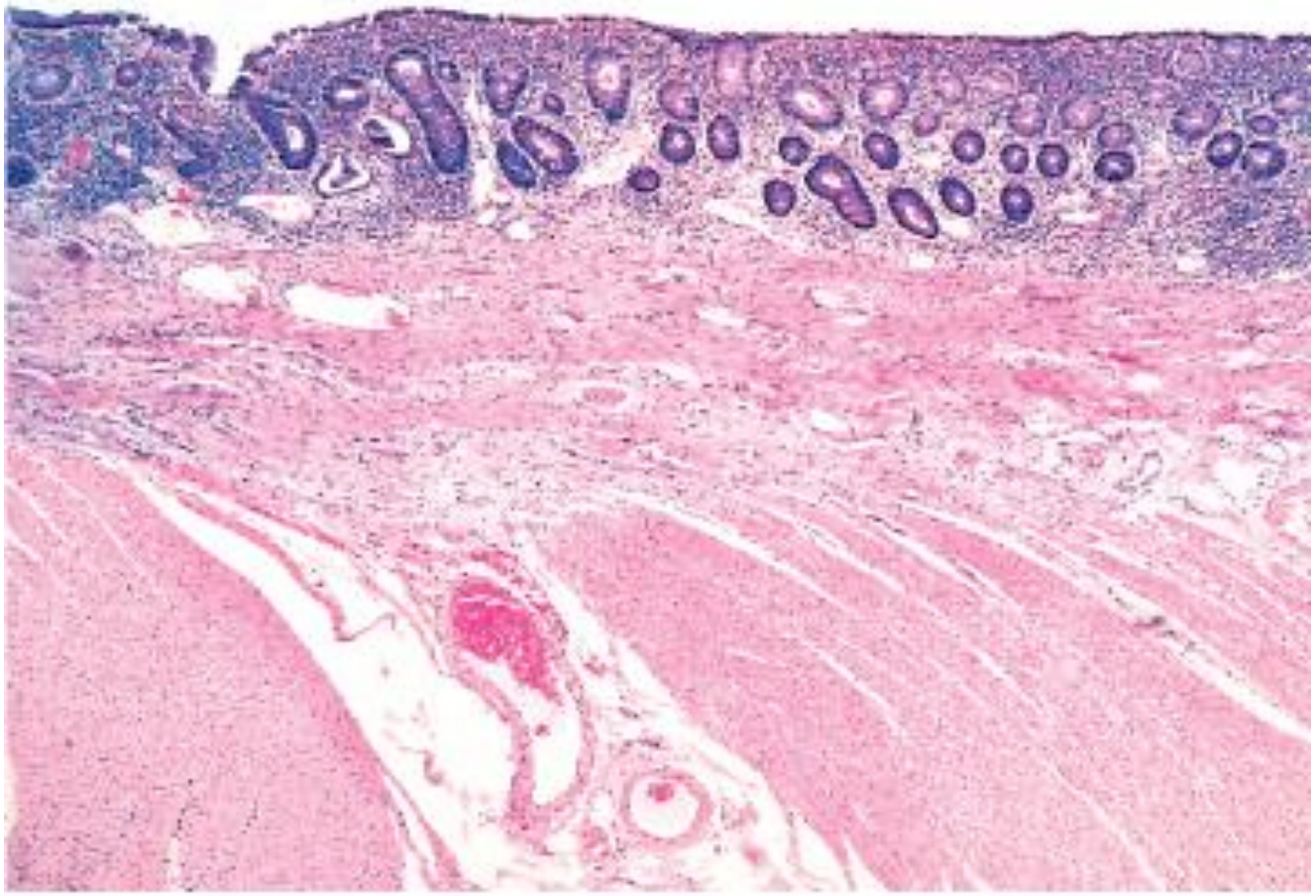
Dysplasia, CIN III (carcinoma in situ) with diffuse atypia and loss of maturation

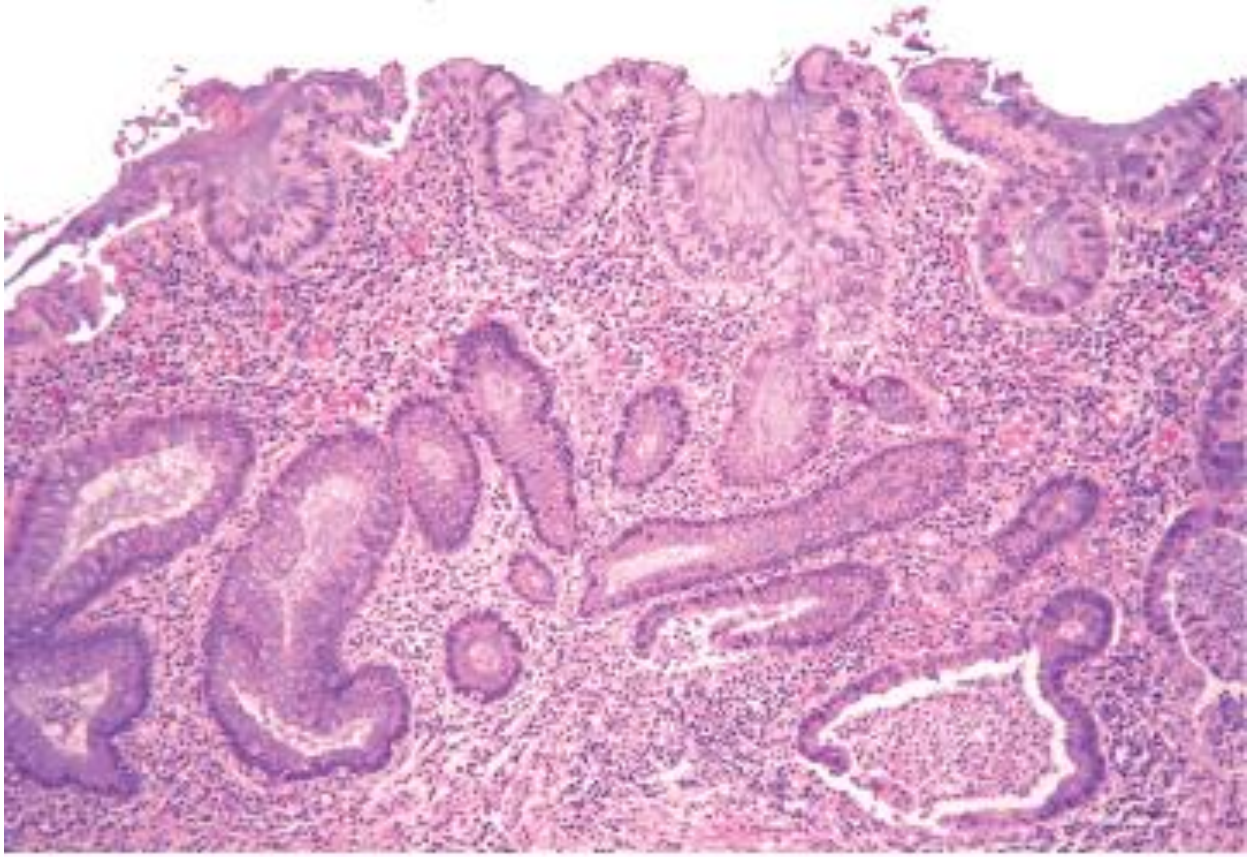


Ulcerative colitis. Ulcerated hemorrhagic surface with knobby pseudopolyps



Ulcerative colitis. Low-power micrograph showing marked chronic inflammation of the mucosa with atrophy of colonic glands, moderate submucosal fibrosis, and a normal muscle wall.





The real voyage of discovery consists not in seeking new lands but seeing with new eyes.
—Marcel Proust