University of Baghdad
College of Medicine
2024-2025

Title: Pathology of the Gastro Intestinal Tract

Grade: 4

Module: Systemic Pathology

Speaker:

Date: 7/11/2024

/

PATHOLOGY OF THE Alimentary Tract

Pathology of GIT
Part Three

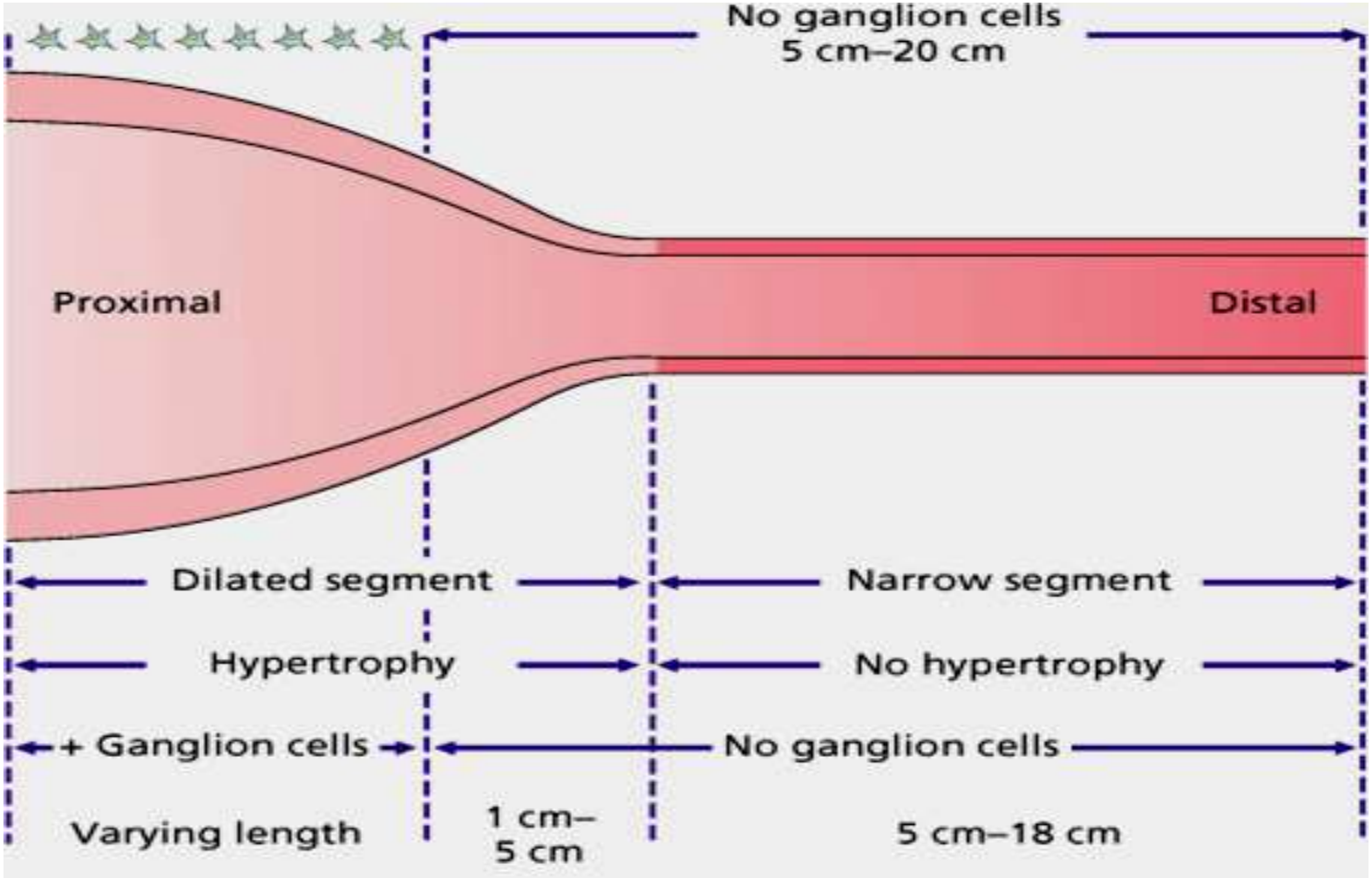
Congenital Aganglionic Megacolon (Hirschsprung Disease)

- **This congenital disorder is characterized by the absence of ganglia of the submucosal and myenteric neural plexuses, within a portion of the intestinal tract.**
- **The outcome is contraction and functional obstruction of the aganglionic segment with secondary proximal dilation.**
- **The rectum is always affected and most cases involve the rectum and sigmoid colon only (*short-segment disease*).**
- **In some cases longer segments, and rarely the entire colon may be aganglionic (*long-segment disease*).**

- **Proximal to the aganglionic segment, the ganglionic colon undergoes progressive dilation and hypertrophy, sometimes massively so (*megacolon*). When distention overruns hypertrophy, the colonic wall becomes markedly thinned and may rupture.**
- **Diagnosis of Hirschsprung is made histologically by failure to detect ganglion cells in intestinal biopsy samples of the contracted (agnaglionic) segment.**

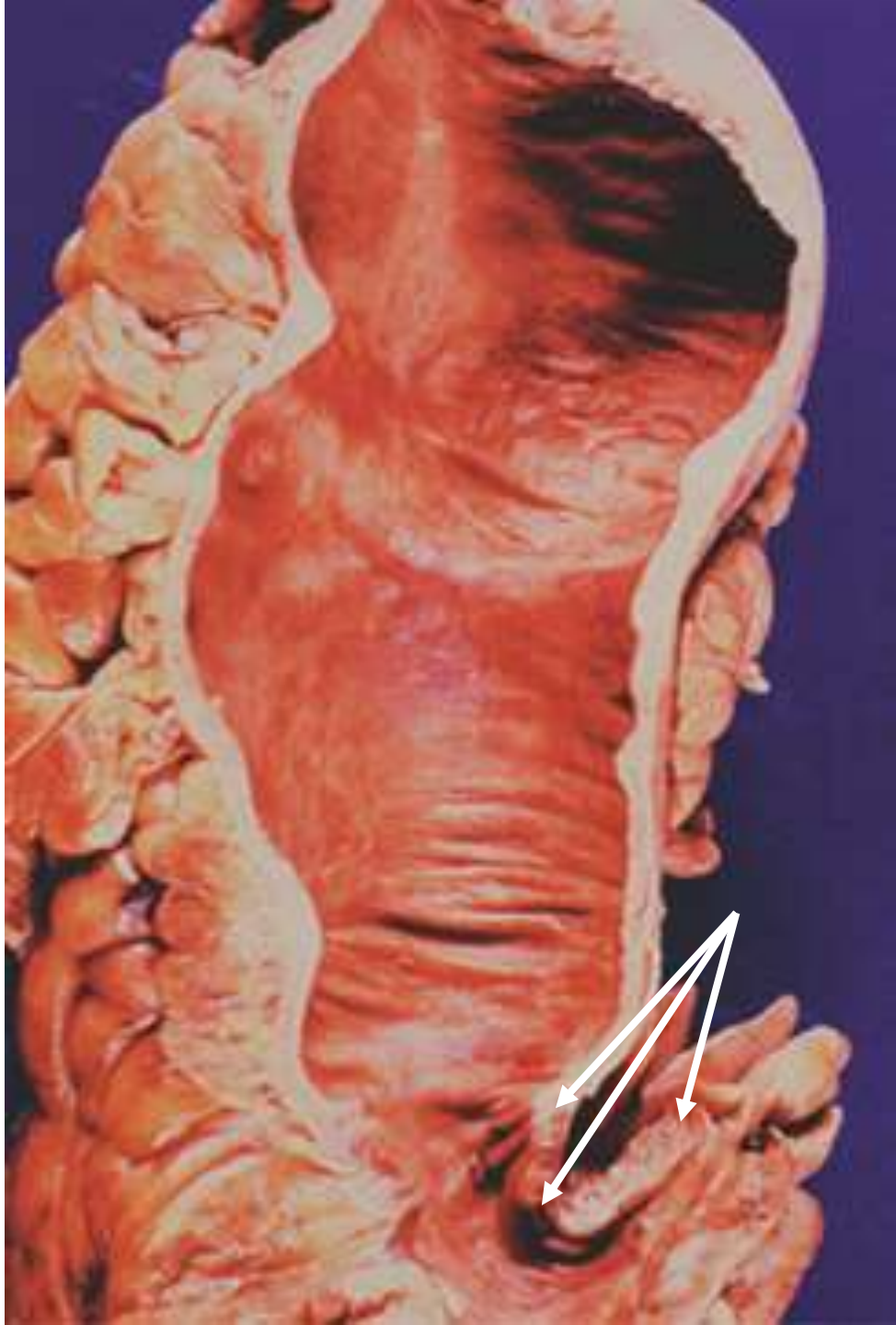
- **The disease usually manifests itself in the immediate neonatal period by failure to pass meconium, followed by obstructive constipation. Abdominal distention may secondarily develop. The major threats to life are superimposed enterocolitis with fluid and electrolyte disturbances and perforation with peritonitis.**

Hirschsprung's disease colon



Hirschsprung's disease colon

In this congenital disorder there is absence of ganglia of the submucosal and myenteric neural plexuses, within a portion of the intestinal tract. The outcome is contraction and functional obstruction of the aganglionic segment (arrows) with secondary proximal dilation.



IDIOPATHIC INFLAMMATORY BOWEL DISEASE (IBD)

- Crohn's disease (CD) and ulcerative colitis (UC).
- These diseases have distinctly different clinical and pathological features.
- Both CD and UC are chronic, relapsing inflammatory disorders of obscure origin.

- **CD** is an autoimmune disease that may affect any portion of the gastrointestinal tract from mouth to anus, but most often involves the distal small intestine and colon.

- **UC** is a chronic inflammatory disease limited to the rectum and colon. Both exhibit extra-intestinal inflammatory manifestations.

Etiology and Pathogenesis

- **In the normal GIT, the mucosal immune system is always ready to respond against ingested pathogens but is unresponsive to normal intestinal microflora.**
- **In IBD, this state of homeostasis is disrupted, leading to two key pathogenic abnormalities**
  - **Strong immune responses against normal microflora**
  - **Defects in epithelial barrier that cause microflora to reach the lymphoid tissue of the intestine**
- **The exact cause (s) leading to the above is still not established, hence the designation idiopathic. It is postulated that IBD result from exaggerated local immune responses to microflora in the gut, in genetically susceptible individuals.**

The pathogenesis of IBD

1. **Failure of immune regulation**
2. **Genetic susceptibility**
3. **Environmental triggers specifically microbial flora.**

- **CD appears to be the result of a chronic delayed-type hypersensitivity reaction induced by IFN-γ- producing T_H1 cells. This is supported by the presence of granulomas in this disease.**
- **Experiments on animals suggest that UC is caused by excessive activation of $T_H2$cells.**

Diagnosis of IBD

- **Since the exact etiology of IBD is not known, the diagnosis of IBD and the distinction between CD and UC depend on:**
- **clinical history, radiographic examination, laboratory findings, and pathologic examination of tissues involved.**
- **Pathologic appearances, both macroscopic and microscopic, play a central role in establishing a definitive diagnosis.**

CROHN DISEASE (CD)

- This disease may involve any level of the alimentary tract.
- CD occurs at any age, but the peak age of incidence is between 10 and 30 years.
- Smoking has been found to be a strong risk factor.

Pathological features

When fully developed, Crohn disease is characterized pathologically by

1. Sharply segmental and typically transmural involvement of the bowel by an inflammatory process with mucosal damage
2. The presence of
   - Small noncaseating granulomas
   - Deep fissures that may eventuate in the formation of fistulae

- there is involvement of the small intestine alone in about 40% of cases,
- small intestine and colon in 30%
- the colon alone in about 30%. Other portions of the GIT may also be uncommonly involved.

Gross features

- **Segments of the small bowel involved by the disease show granular and dull gray serosa (normally transparent and glistening).**

- **Often the mesenteric fat wraps around the bowel.**

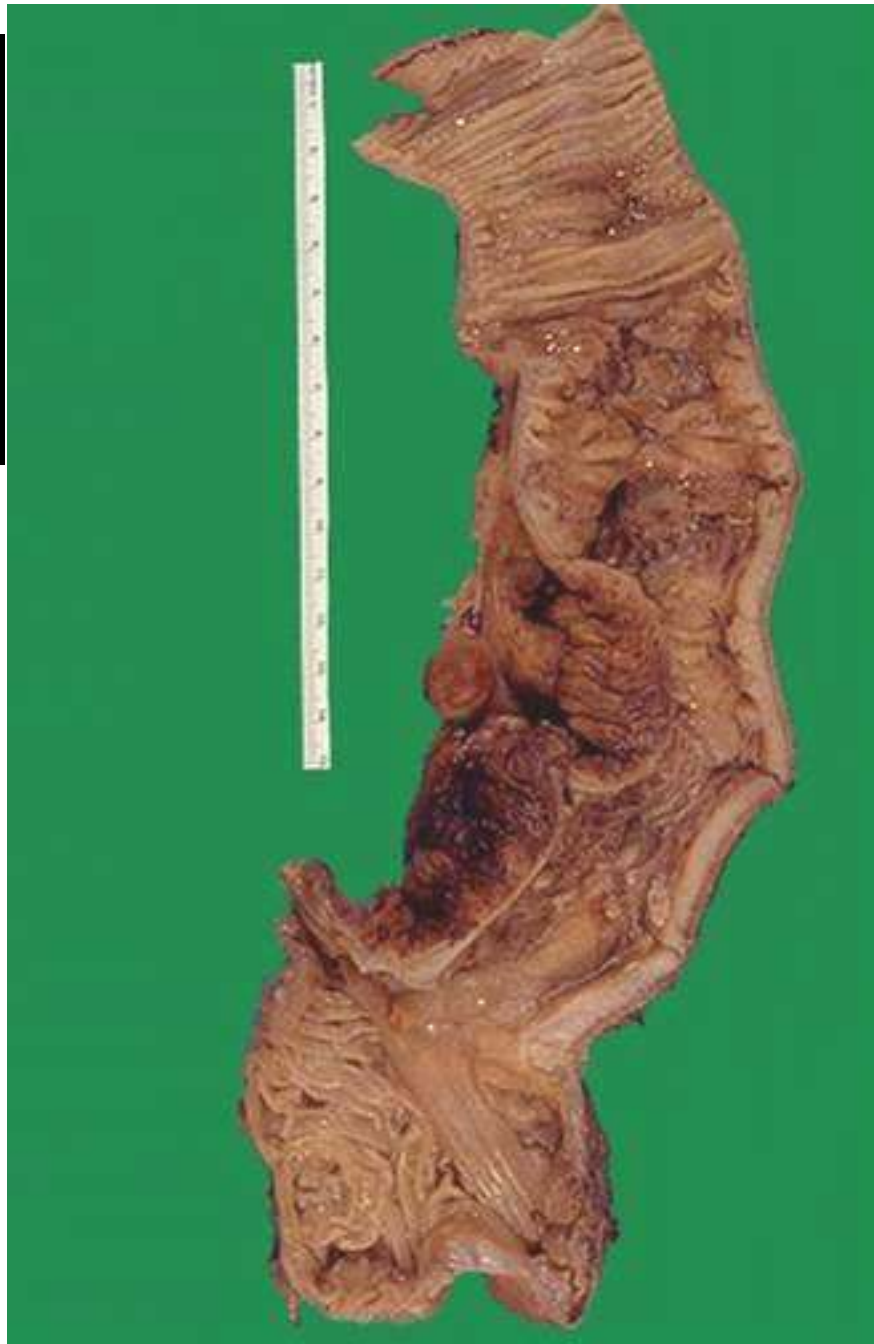
- **The involved bowel wall is thick and rubbery (because of edema, inflammation, and fibrosis). As a result, the lumen is narrowed.**

- **A classic feature of CD is the sharp demarcation of diseased bowel segments from adjacent uninvolved, essentially normal bowel (skip lesions).**

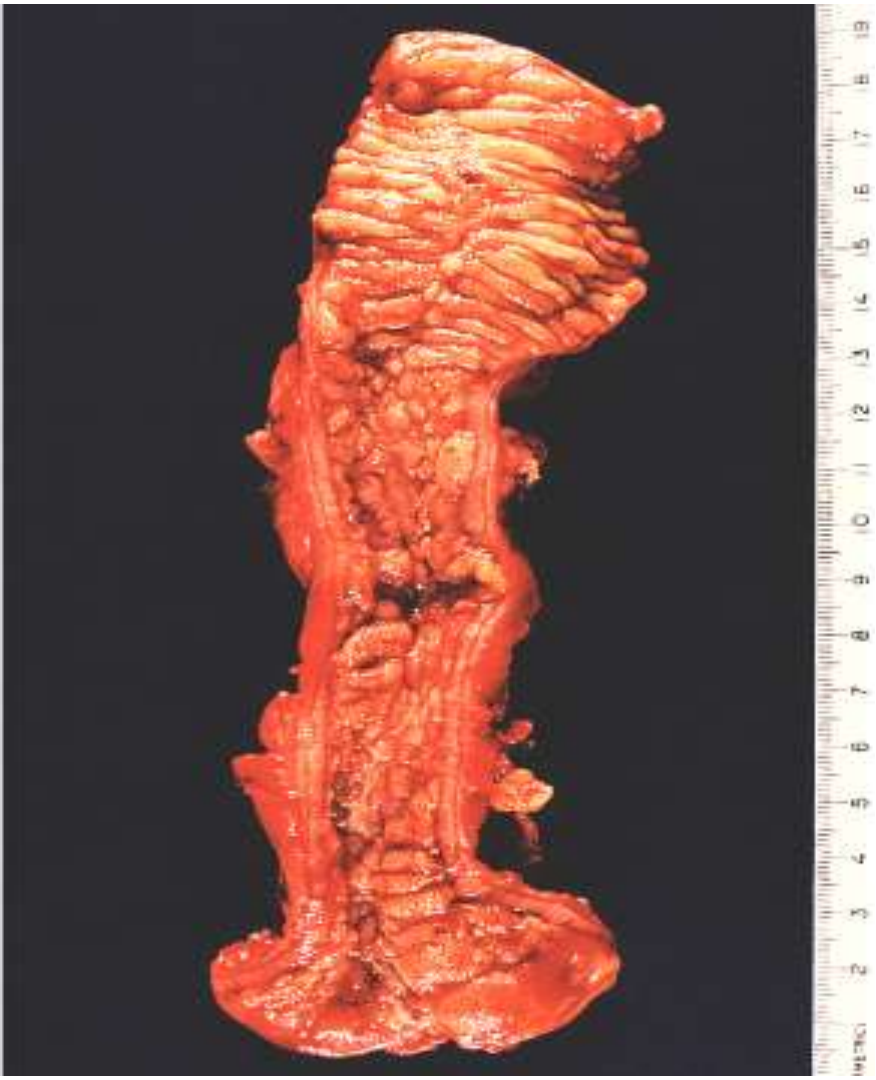
- **Early disease shows small mucosal ulcers that coalesce to form long, serpentine linear ulcers (i.e. long and twisted or sinuous).**
- **As the intervening mucosa (between the ulcers) tends to be accentuated by inflammation and edema, it acquires a *cobblestone appearance*. (*Cobble-stone*, is a rounded stone, esp. of the size used for paving).**
- **Narrow fissures develop between the mucosal folds, often penetrating deeply through the bowel wall. Further extension of these fissures leads to fistulae or sinus tracts formation, between the diseased intestinal segment and adherent structures (bowel loops, vagina, urinary bladder, skin of the abdomen) or the sinuses may end blindly within the abdominal cavity.**
- **Free perforation or localized abscesses may develop.**

Crohn's disease, terminal ileum, G

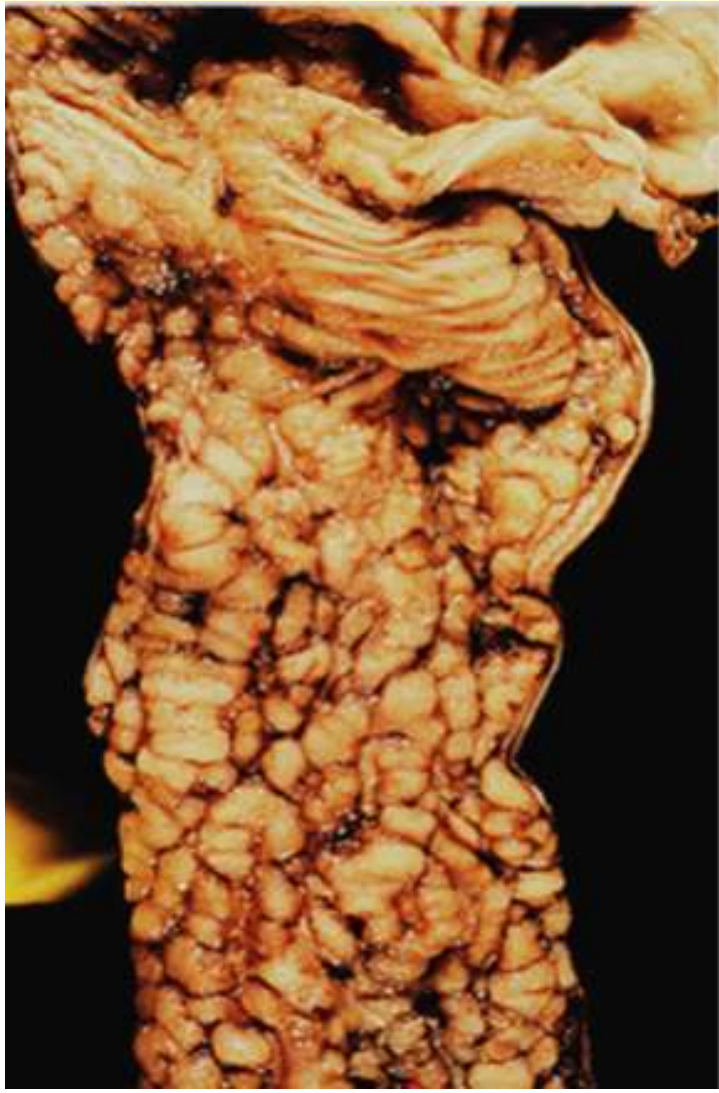
This portion of terminal ileum demonstrates the gross findings with Crohn's disease. The middle portion has a thickened wall and the mucosa has lost the regular folds. The serosal surface demonstrates reddish indurated adipose tissue that creeps over the surface. Serosal inflammation leads to adhesions. The areas of inflammation tend to be discontinuous throughout the bowel.



Crohn's disease Small intestine

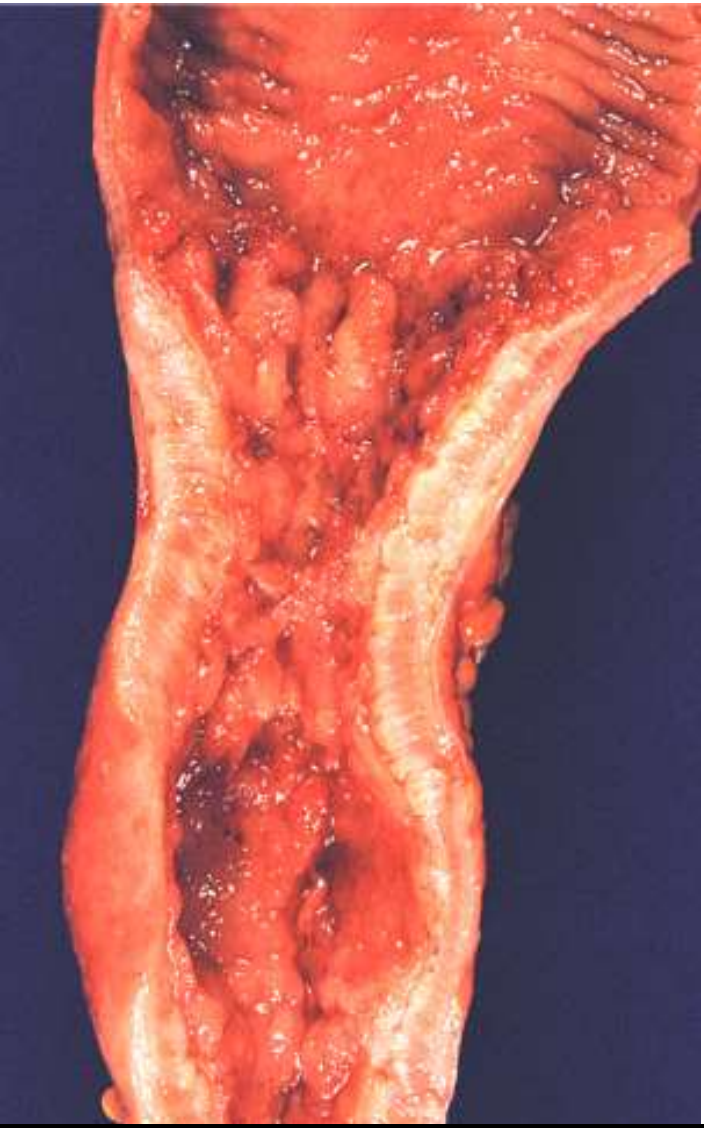


Gross appearance of Crohn's disease. Note the segmental nature of the inflammation, and rigidity of the wall, and cobble-stoning of the mucosa are characteristic.

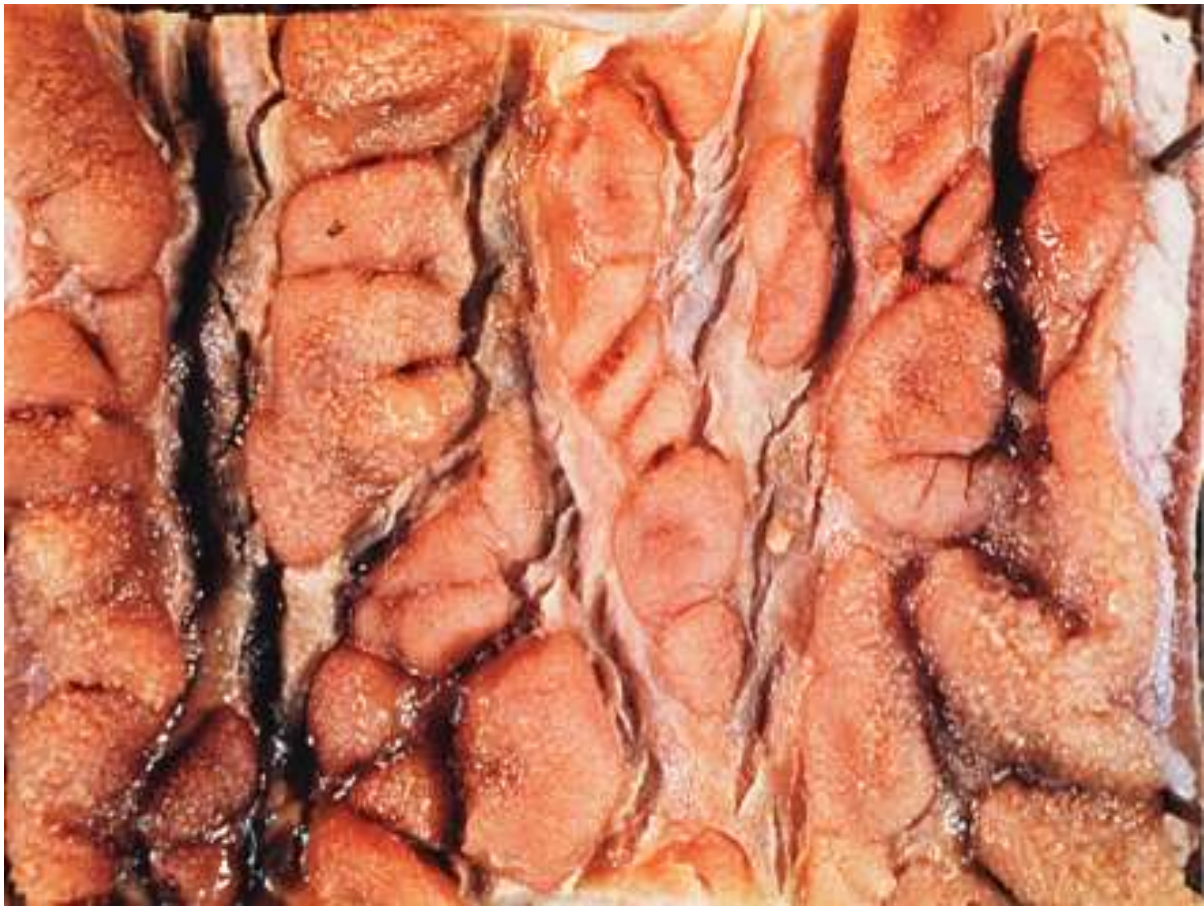


Another example of cobblestone appearance.

Crohn’s disease colon gross



Gross appearance of Crohn's disease of large bowel; segmental distribution



Gross appearance of Crohn’s disease of large bowel showing typical cobblestone appearance.

Microscopic features

1. ***Acute mucosal inflammation*: there is neutrophilic infiltration of the surface & crypt epithelium that eventually collects within the lumen of the crypts forming crypt abscesses.**

2. ***Chronic mucosal damage*:**

This is the hallmark of chronicity of CD (and UC). It manifests as architectural distortion (in the small intestine as villus blunting; in the colon, the crypts exhibit irregularity, and branching). Crypt destruction leads to progressive mucosal atrophy.

3. ***Ulcerations* are the usual outcome of severe active disease; these may be superficial, or may penetrate deeply (as fissures) into underlying tissue layers.**

4. ***Transmural chronic inflammation affecting all layers*: chronic inflammatory cells (lymphocytes and plasma cells) fill the affected mucosa and, to a lesser extent, all underlying intestinal layers. Lymphoid aggregates are usually scattered throughout the bowel wall.**

5. *Noncaseating granulomas*: in about 50% of the cases, noncaseating small granulomas may be present in all tissue layers. Because they are not always present; the absence of granulomas does not rule out the diagnosis of CD.

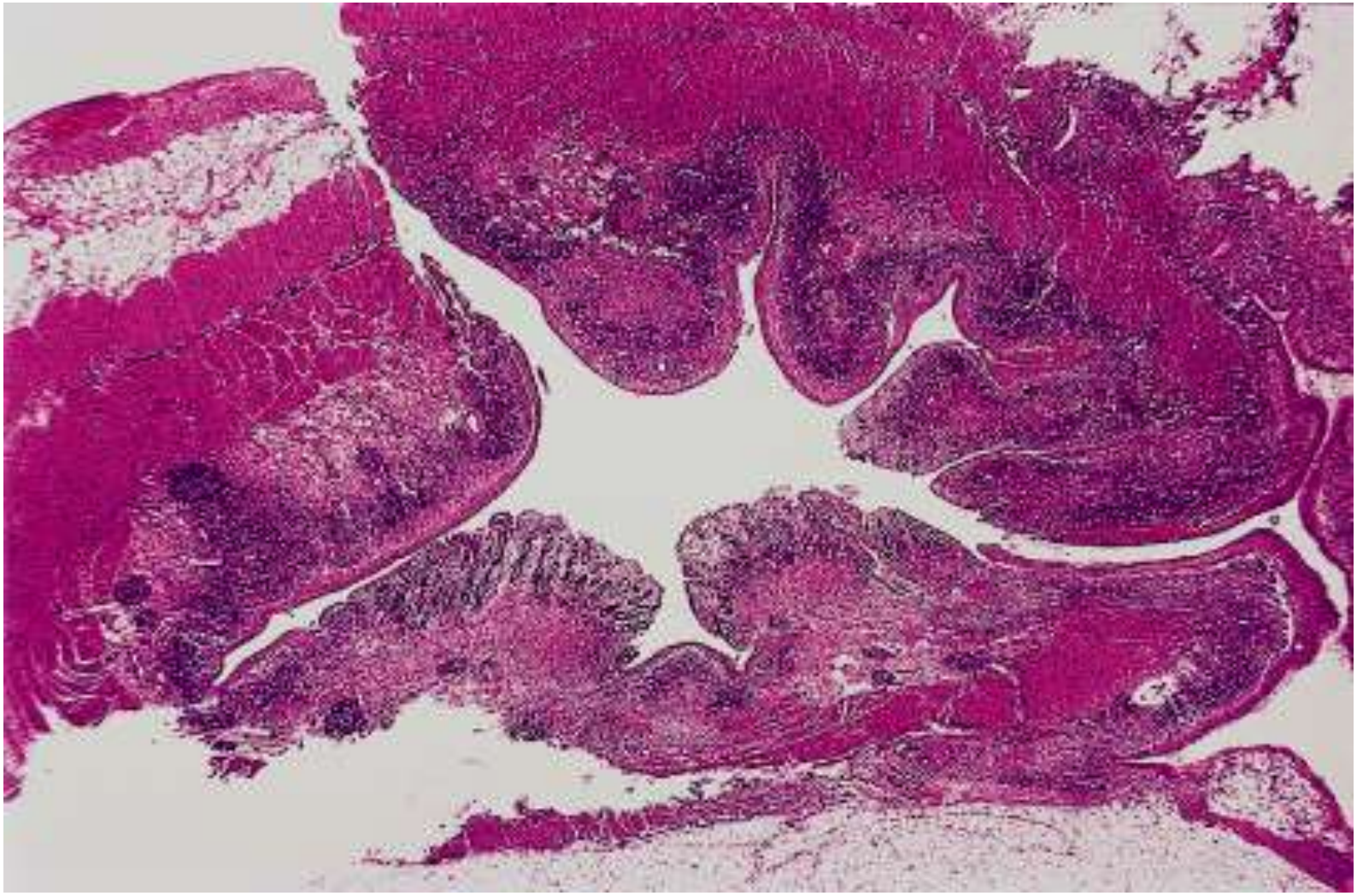
6. *Other mural changes*: in diseased segments, the muscularis mucosae usually exhibits duplication & thickening.

- **There is also fibrosis of the submucosa, muscularis propria, and serosa that eventually leads to stricture formation.**

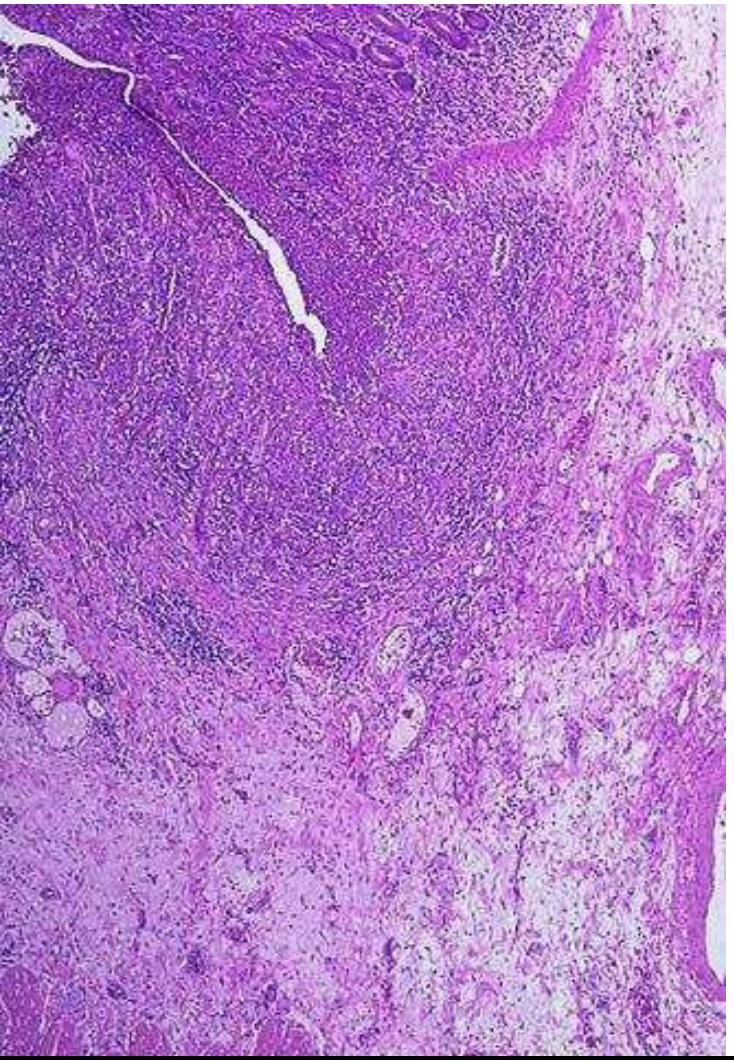
7. *Dysplastic changes of the mucosal epithelial cells* are particularly important in persons with long-standing chronic disease are.

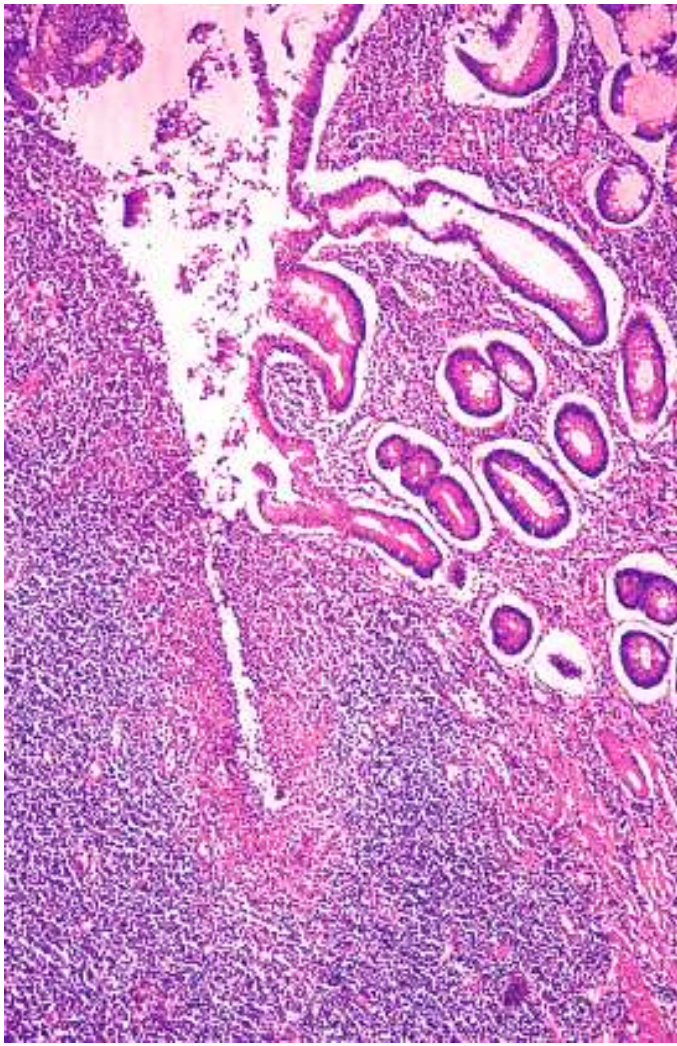
- **These may be focal or widespread, tend to increase with time, and are thought to be related to increased risk of carcinoma, particularly of the colon.**

Crohn's disease appendix



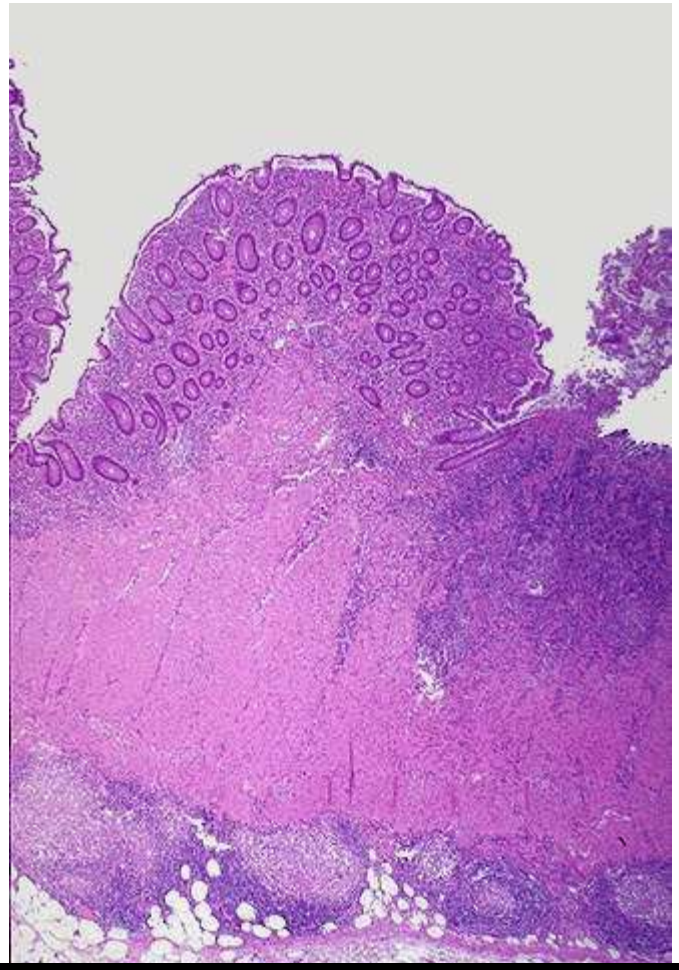
Crohn’s disease colon



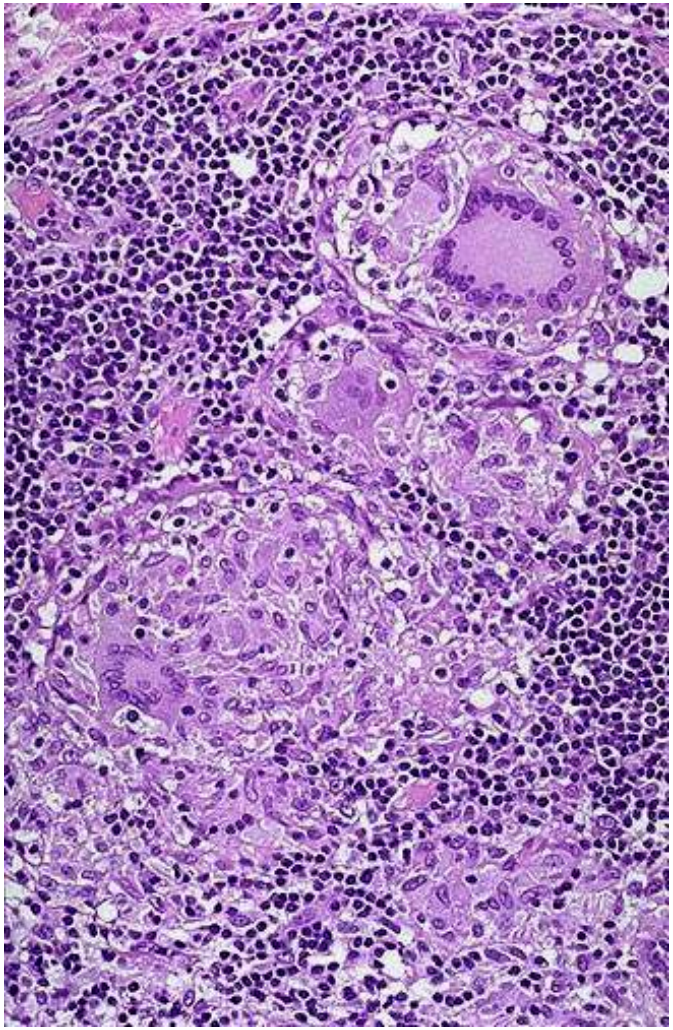


One complication of Crohn's disease is fistula formation. Seen here is a fissure extending through mucosa at the left into the submucosa toward the muscular wall, which eventually will form a fistula· Fistulae can form between loops of bowel, bladder, and skin. With colonic involvement, perirectal fistulae are common. There is also intense inflammation of the mucosa and submucosa.

Crohn’s disease colon



Microscopically, Crohn's disease is characterized by transmural inflammation. Here, inflammatory cells (the bluish infiltrates) extend from mucosa through submucosa and muscularis and appear as nodular infiltrates on the serosal surface with pale granulomatous centers.



At high magnification the granulomatous nature of the inflammation of Crohn's disease is demonstrated here with epithelioid cells, giant cells, and many lymphocytes. Special stains for organisms are negative.

Clinical Features

The disease usually begins with intermittent attacks of diarrhea, fever, and abdominal pain, spaced by asymptomatic periods lasting for weeks to many months. In those with colonic involvement, occult or overt fecal blood loss may lead to anemia. During this lengthy, chronic disease, *complications* may arise from

1. **Fibrosing strictures, particularly of the terminal ileum (intestinal obstruction)**
2. **Fistulas formed to other loops of bowel, urinary bladder, vagina, or perianal skin, or into a peritoneum. In the latter focal abscesses may occur.**
3. **Extensive involvement of the small bowel, including the terminal ileum, may cause**

   a. marked loss of albumin (protein-losing enteropathy)

   b. generalized malabsorption

   c. specific malabsorption of vitamin B_{12} (pernicious anemia), or malabsorption of bile salts, leading to steatorrhea.

Extraintestinal manifestations of this disease

include

1. **Arthritis & finger clubbing**
2. **Red nodules of the skin (Erythema nodosum)**
3. **Primary sclerosing cholangitis, (but the association is not as strong as in UC).**
4. **Renal disorders secondary to trapping of the ureters in the inflammatory process sometimes develop and leading to hydronephrosis and pyelonephritis.**
5. **Systemic amyloidosis (rare late consequence).**
6. **An increased incidence of cancer of the GIT in patients with long-standing progressive CD; however, the risk of cancer in CD is considerably less than in patients with chronic UC.**

Ulcerative Colitis

- **In contradistinction to CD, ulcerative colitis is a chronic ulcero-inflammatory disease limited to the colon and affecting only the mucosa and submucosa; it extends in a continuous fashion proximally from the rectum.**
- **Well-formed granulomas are absent.**
- **However, like CD, UC is a systemic disorder associated in some patients with arthritis, uveitis, hepatic involvement (primary sclerosing cholangitis), and skin lesions.**
- **The onset of disease peaks between ages 20 and 25 years.**
- **Nonsmoking is associated with UC; ex-smokers are at higher risk for developing UC than never-smokers.**

Pathological features

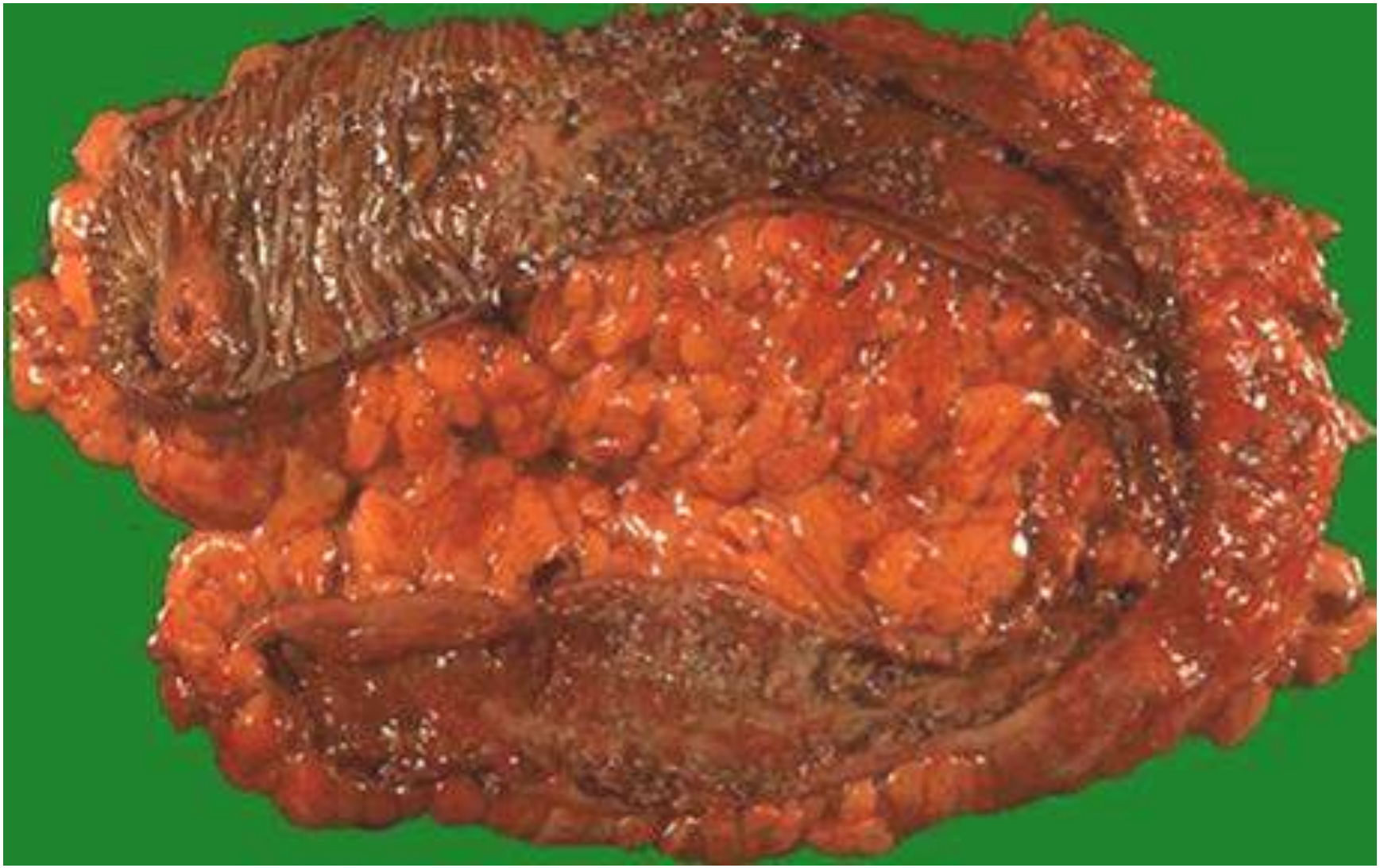
Ulcerative colitis involves the rectum and extends proximally in a retrograde fashion to involve the entire colon ("*pancolitis*") in the more severe cases. It is a disease of continuity, and "skip" lesions are not found (cf. CD).

Gross features

- **A key feature of UC is that the mucosal damage is continuous from the rectum and extending proximally.**
- **The mucosa may exhibit reddening and granularity with easy bleeding.**
- **With fully developed severe, active inflammation, there may be *extensive ulcerations* of the mucosa.**
- **Isolated islands of regenerating mucosa bulge upward to create *polypoid projections (pseudopolyps).***

- **With chronicity or healing of active disease, progressive *mucosal atrophy* occurs.**
- **Unlike CD, thickening of the bowel wall does not occur in UC, and the serosal surface is usually completely normal (cf. CD).**
- **Only in the most severe cases of ulcerative disease (UC, CD, and other severe inflammatory diseases) does toxic damage to the muscularis propria and neural plexus lead to complete shutdown of neuromuscular function. In this instance the colon progressively swells and becomes gangrenous, a life-threatening condition called *toxic megacolon.***

Extensive ulcerative colitis (pancolitis)

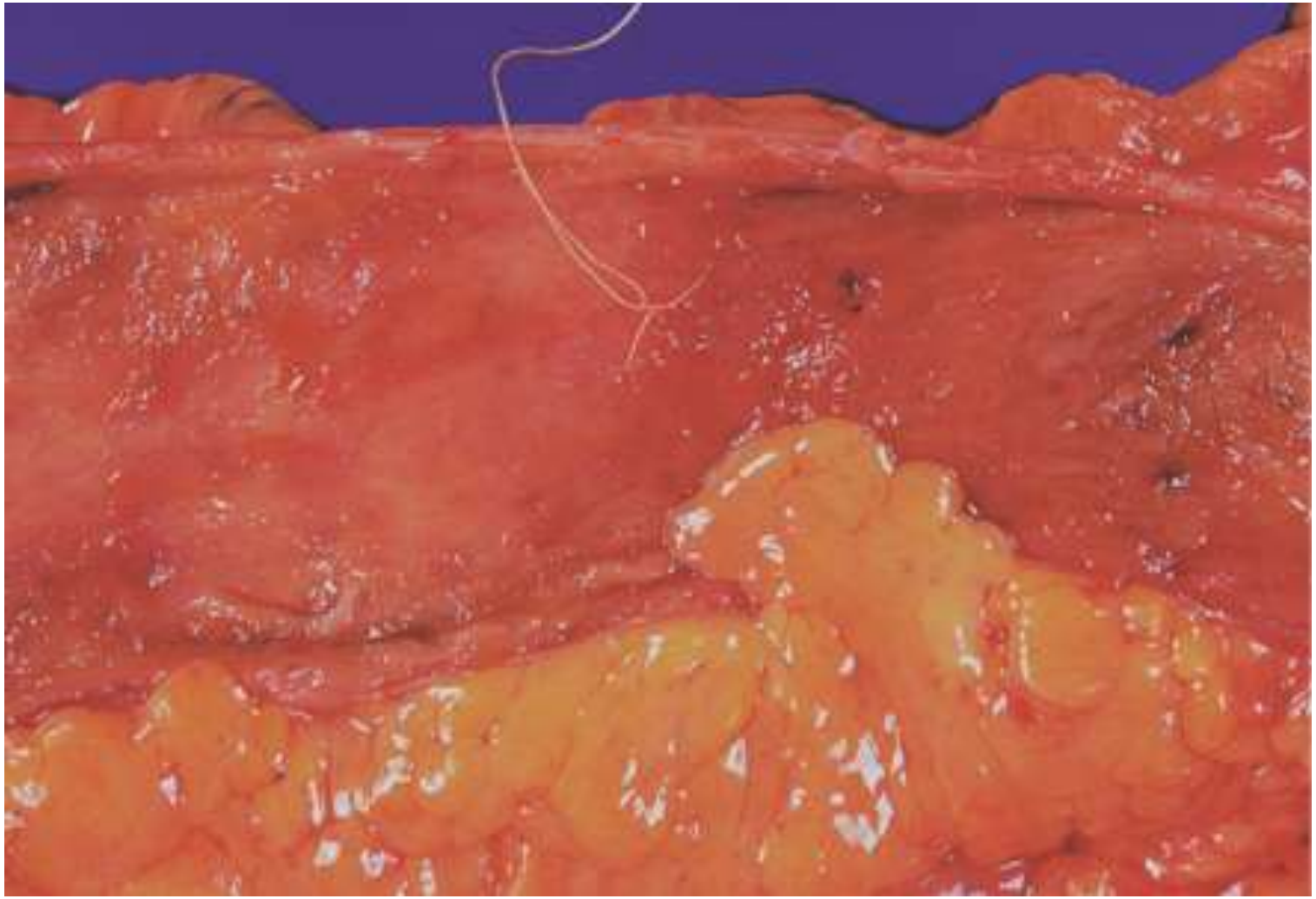


The ileocecal valve is seen at the upper left. Just distal to this begins increasing mucosal inflammation. There is diffuse mucosal hyperemia with large, irregular, rather superficial ulcers.

Active ulcerative colitis

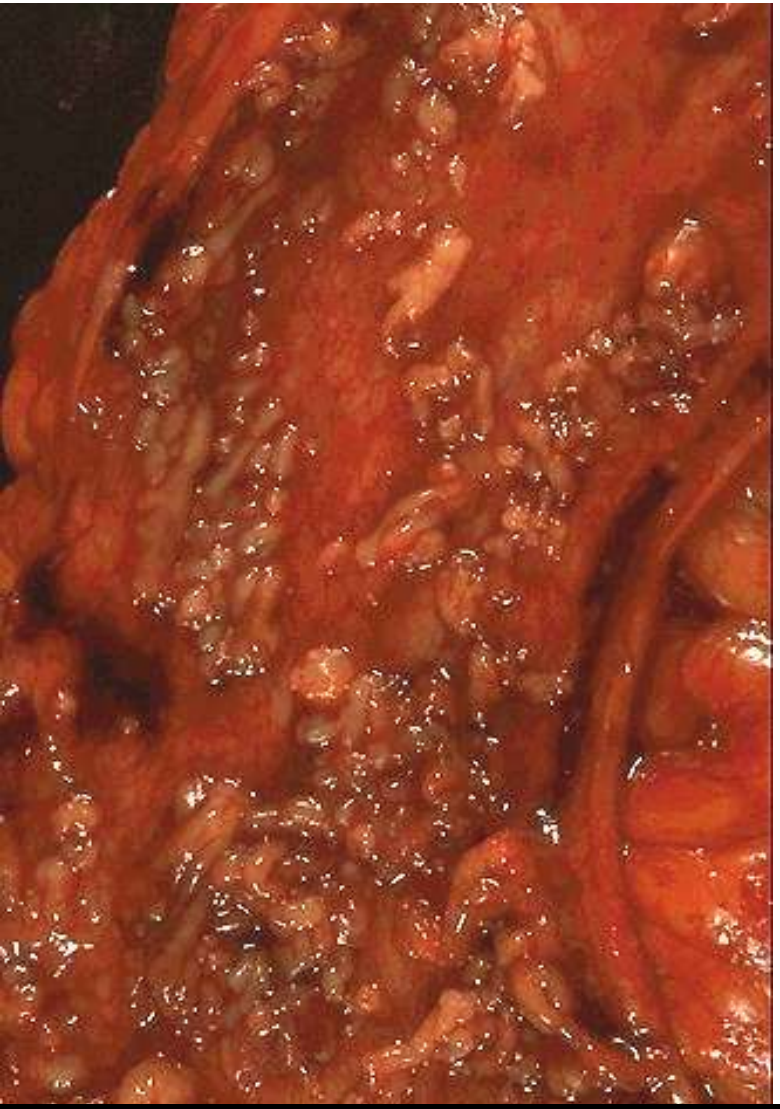
There is diffuse, marked mucosal hyperemia and sanguineous exudate.

Late stage of chronic ulcerative colitis,

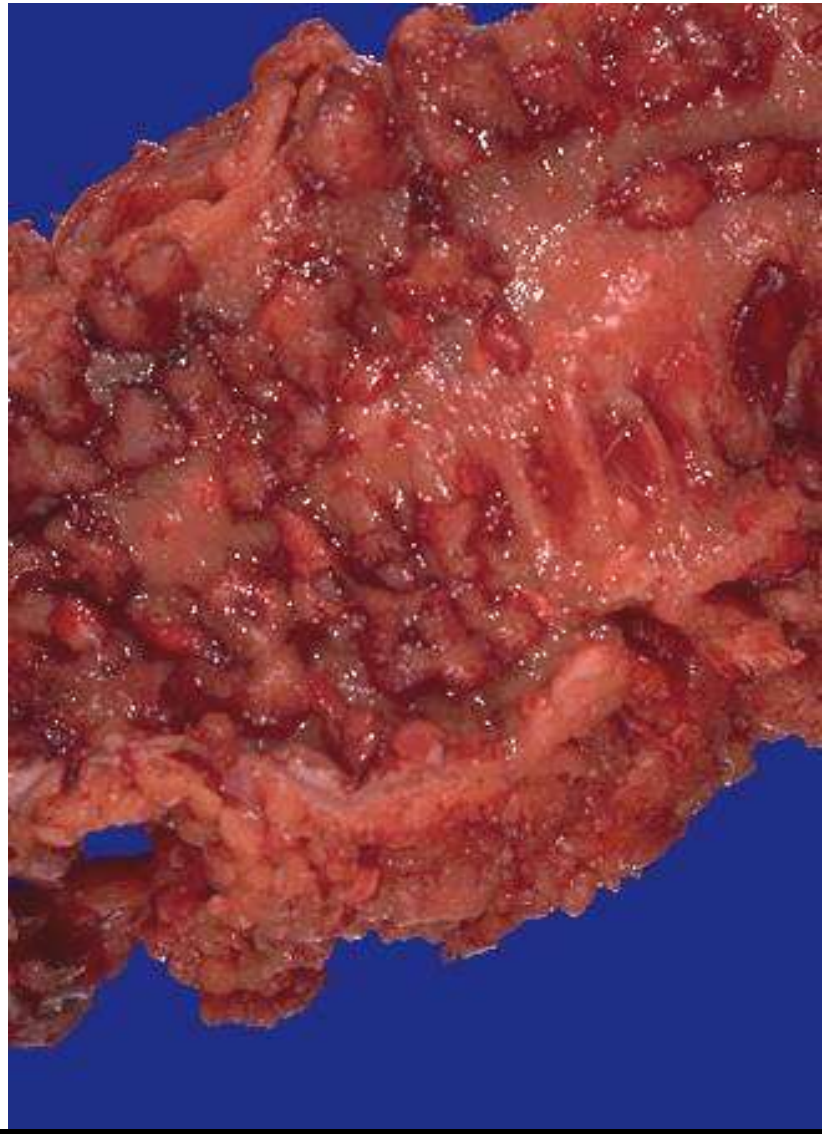


There is total mucosal atrophy; there is total absence of mucosal folds

Pseudopolyps in ulcerative colitis

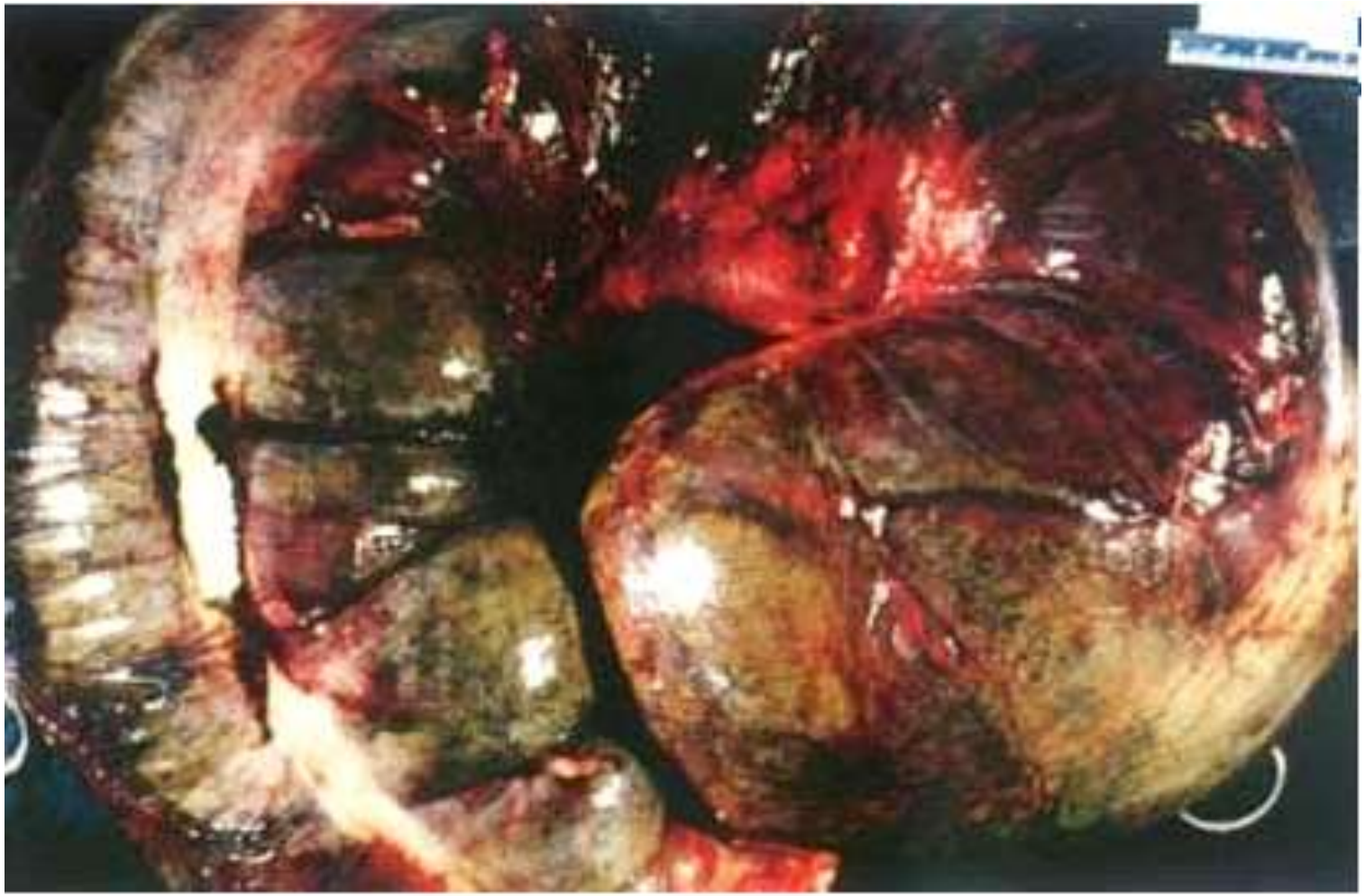


Pseudopolyps are seen here. The remaining mucosa has been ulcerated away and is hyperemic.



At higher magnification, the pseudopolyps can be seen clearly as raised red islands of inflamed mucosa. Between the pseudopolyps is only remaining muscularis.

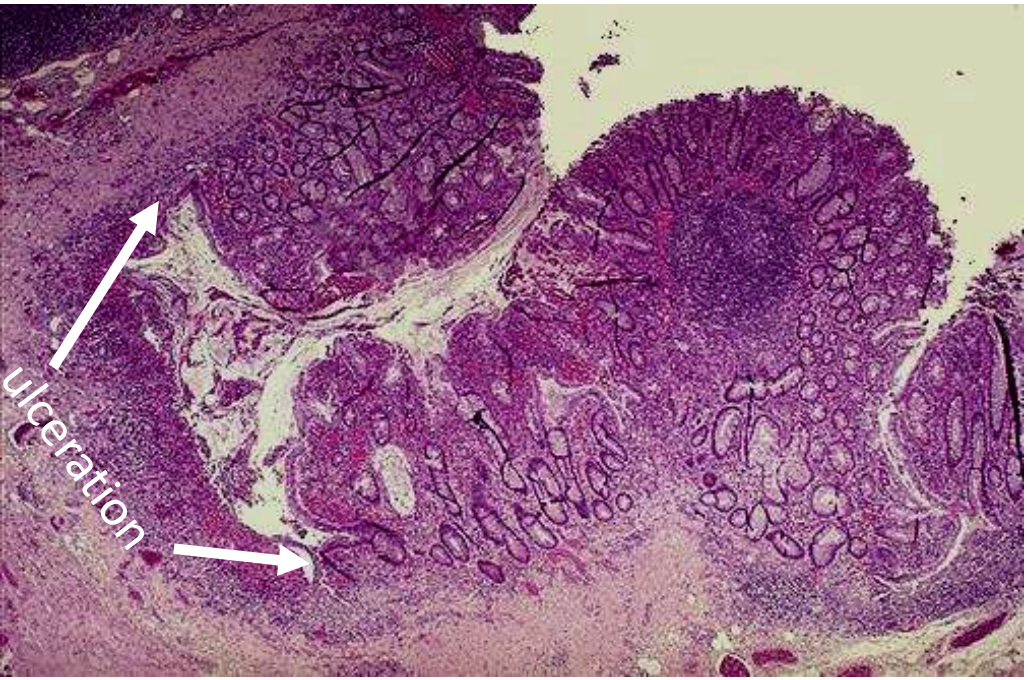
Toxic megacolon



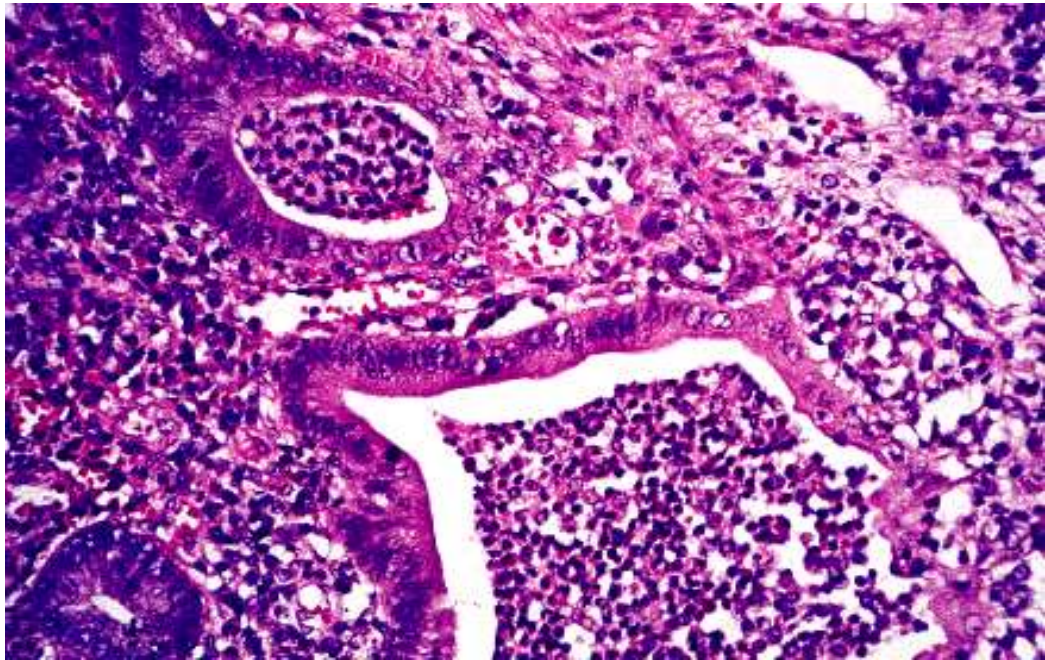
Microscopic features

- **The basic mucosal alterations in UC are similar to those of colonic CD, with inflammation, chronic mucosal damage, and ulceration.**
- **There is diffuse, predominantly chronic inflammatory infiltrate in the lamina propria.**
- **Neutrophilic infiltration of the epithelial layer may produce crypt abscesses. The latter are not specific for UC and may be observed in CD or any active inflammatory colitis.**
- **Unlike CD, there are no granulomas.**
- **Destruction of the mucosa leads to broad-based ulcerations that are superficial i.e. extending at most into the submucosa.**
- **Isolated islands of regenerating mucosa bulge upward to create pseudopolyps.**
- **Features of chronic but healed (inactive) disease include submucosal fibrosis; mucosal architectural distortion and atrophy.**
- **Particularly significant is the spectrum of epithelial dysplasias, which are divided into low-grade and high-grade depending on the severity.Invasive carcinoma is the ultimate lesion arising from dysplasia.**

Active chronic ulcerative colitis



the inflammation is confined primarily to the mucosa. The mucosa is eroded by an ulcer that undermines surrounding mucosa



Ulcerative colitis featuring crypt abscesses.

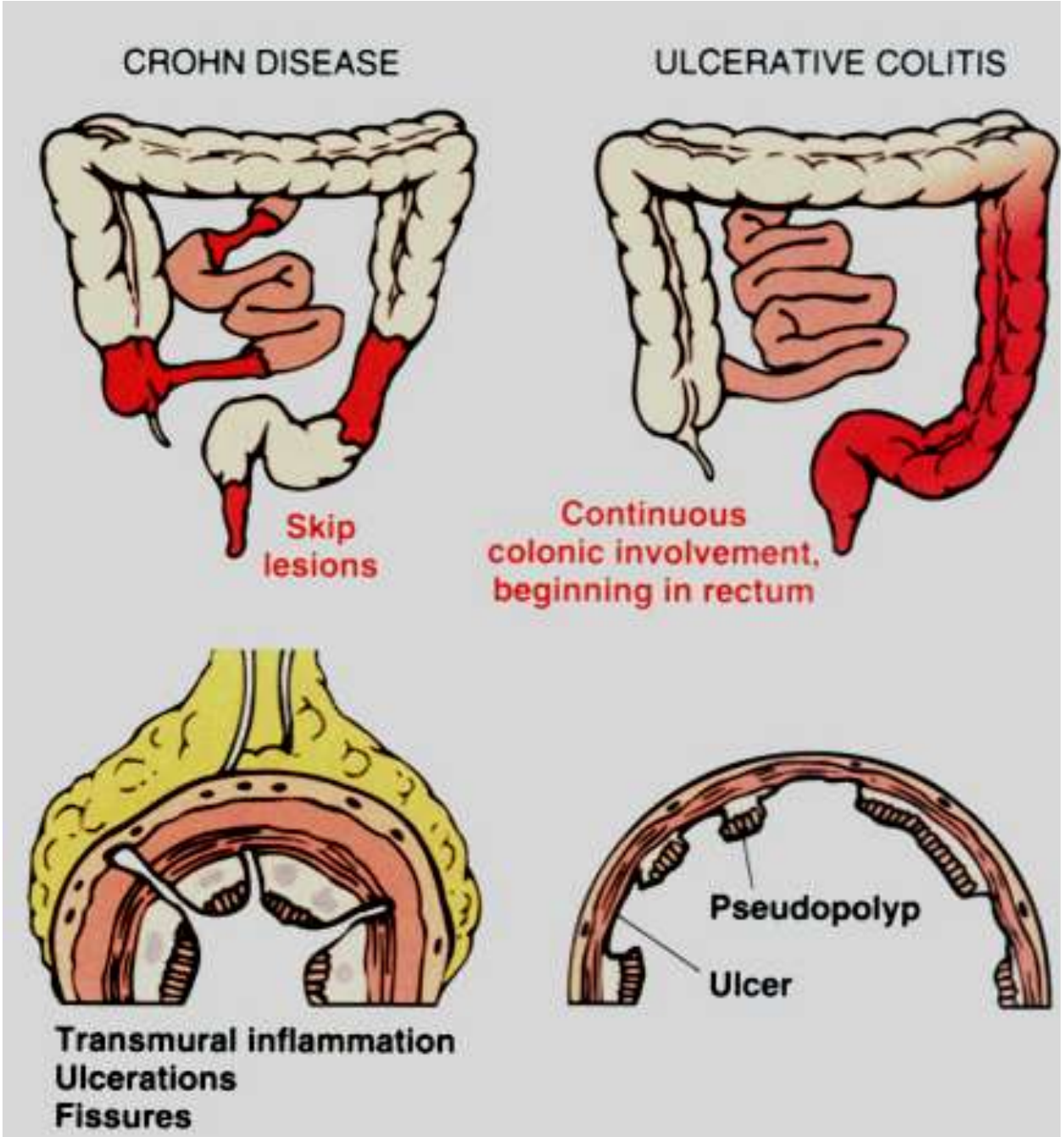
To summarize UC differs pathologically from CD in the following

- **Well-formed granulomas are absent.**
- **There are no skip lesions.**
- **The mucosal ulcers rarely extend below the submucosa, and**
- **There is surprisingly little fibrosis.**
- **Mural thickening does not occur, and the serosal surface is usually completely normal.**
- **There appears to be a higher risk of carcinoma development.**

Course & prognosis

- **Ulcerative colitis typically presents as a recurrent attacks of bloody mucoid diarrhea that may persist for days, weeks, or months and then subside, only to recur after an asymptomatic interval of months to years.**

Crohn disease Vs Ulcerative colitis



INTESTINAL OBSTRUCTION

- **The small intestine is most often involved due to its narrow lumen. Tumors and infarction, although the most serious, account for only up to 20% of small-bowel obstructions.**
- **The remaining 80% are due to**

1. Hernias

2. Intestinal adhesions

3. Intussusception

4. Volvulus

<u>The clinical manifestations include:</u>

abdominal pain and distention,

vomiting,

constipation,

and in complete obstruction failure to pass flatus.

Intussusception

- This occurs when one segment of the intestine, constricted by a wave of peristalsis, suddenly becomes telescoped into the immediately distal segment of bowel. Once trapped, the invaginated segment is propelled by peristalsis farther into the distal segment, pulling its mesentery along with it.
- When encountered in infants and children, there is usually no underlying anatomic lesion or defect in the bowl, but some cases of intussusception are associated with rotavirus infection, suggesting that localized intestinal inflammation may serve as a traction point for the intussusception.
- However, intussusception in adults signifies an intraluminal mass or tumor as the point of traction. In both settings, intestinal obstruction ensues, and trapping of mesenteric vessels leads to infarction.

Volvulus

- This signifies complete twisting of a loop of bowel about its mesenteric base of attachment.
- It produces intestinal obstruction and infarction. This lesion occurs most often in large redundant loops of sigmoid, followed in frequency by the cecum, and small intestine.

Tumors of the Small Intestine and Large Intestine

TUMORS OF THE SMALL AND LARGE INTESTINE

Tumors of the small intestine

The most common benign tumors in the small intestine are *adenomas* and *mesenchymal tumors*. Of malignant tumors *adenocarcinomas and carcinoids* have roughly equal incidence, followed in order by *lymphomas and sarcomas.*

Tumors of the Colon and Rectum

***Non-neoplastic and benign neoplastic lesions of the colo-rectum are collectively known as polyps*, which are common in the older adult population.**

Epithelial polyps that arise as the result of proliferation and dysplasia are termed *adenomatous polyps* (adenomas). They are precursors of carcinoma.

Non-Neoplastic Polyps include

hyperplastic polyp

hamartomatous polyp

inflammatory polyp

lymphoid polyp

Hyperplastic Polyps

- **These are the most common polyps of the colon and rectum.**
- **They are small (usually <5 mm in diameter) and appear as smooth protrusions of the mucosa.**
- **They are often multiple and consists of well-formed glands and crypts lined by non-neoplastic epithelial cells.**

Hamartomatous Polyps

1. *Juvenile polyps*

- are essentially hamartomatous proliferations, mainly of the lamina propria, enclosing widely spaced, dilated cystic glands.
- They occur most frequently in children younger than 5 years old but also are found in adults of any age; in the latter group they may be called *retention polyps.*
- The lesions are usually large in children (1-3 cm in diameter) but smaller in adults; they are rounded, smooth, or slightly lobulated and sometimes have a stalk as long as 2 cm.
- In general, they occur singly and in the rectum, and have no malignant potential.
- Juvenile polyps may be the source of rectal bleeding and in some cases become twisted on their stalks to undergo painful infarction.

2. Peutz-Jeghers polyps

- are also hamartomatous polyps that involve the mucosal epithelium, lamina propria, and muscularis mucosae.
- They may occur sporadically or in the setting *Peutz-Jeghers syndrome (PJS).*
- *PJS* is a rare autosomal dominant syndrome characterized by

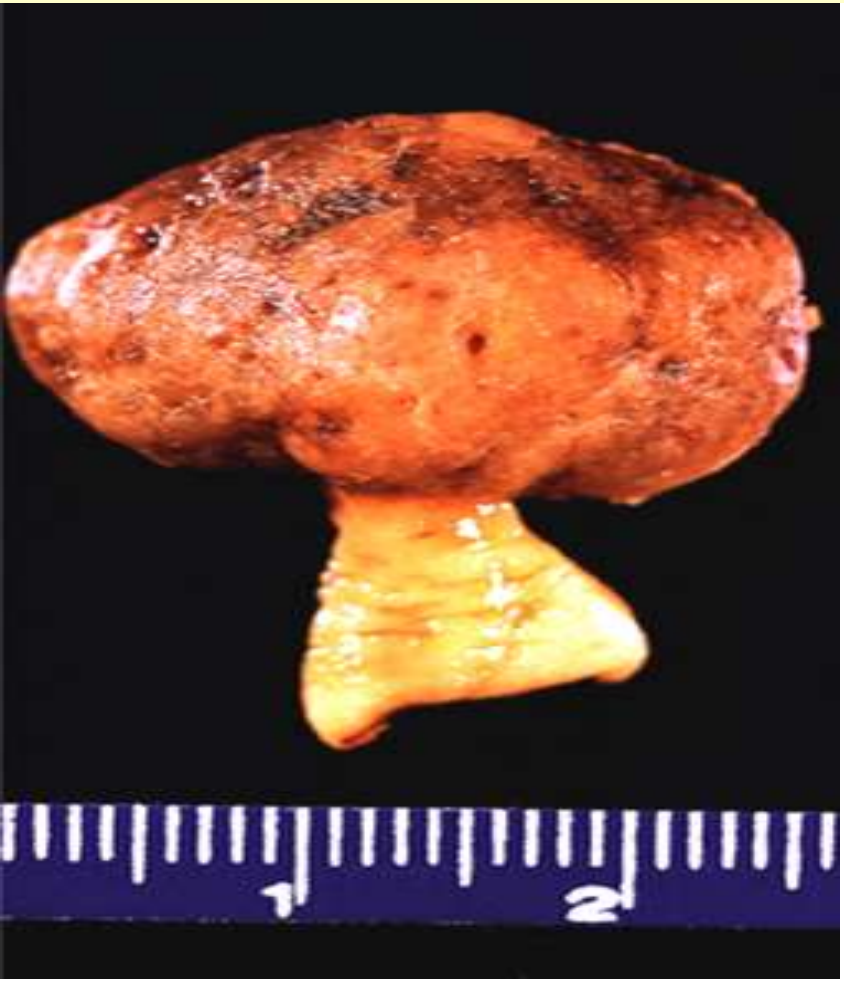
a. multiple hamartomatous polyps scattered throughout the entire GIT

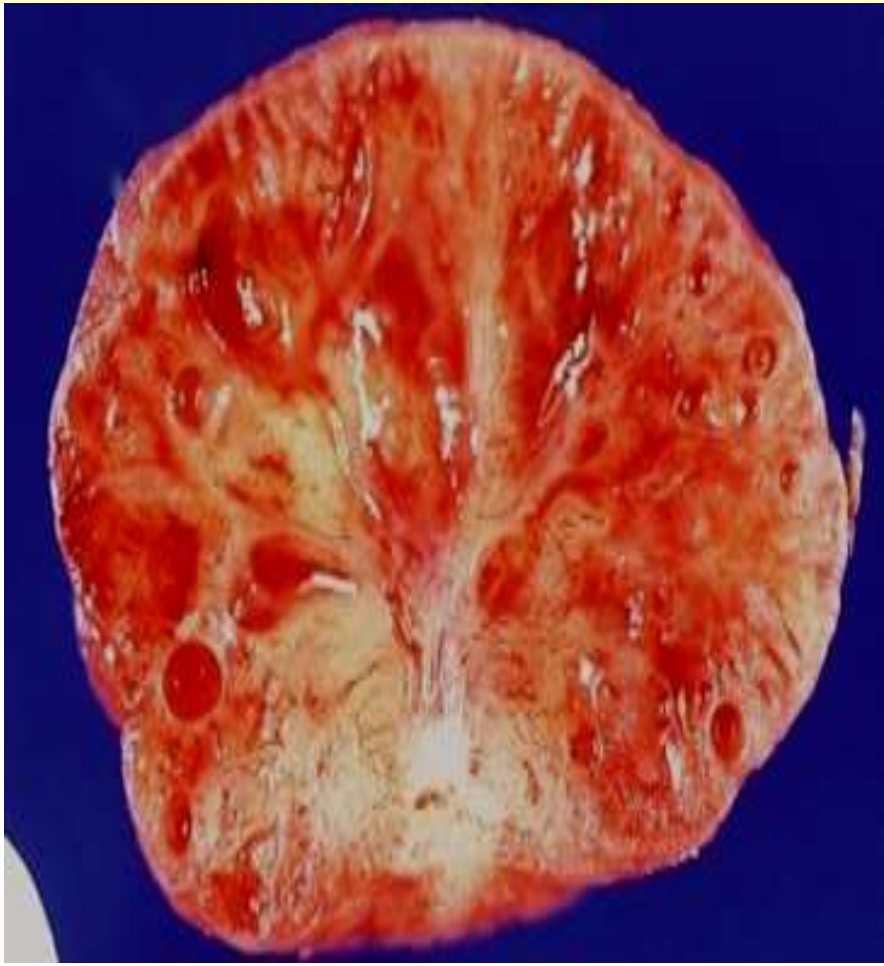
b. melanotic mucosal and cutaneous pigmentation especially around the lips & in the oral mucosa.

Patients with this syndrome are at risk for intussusception, which is a common cause of mortality.

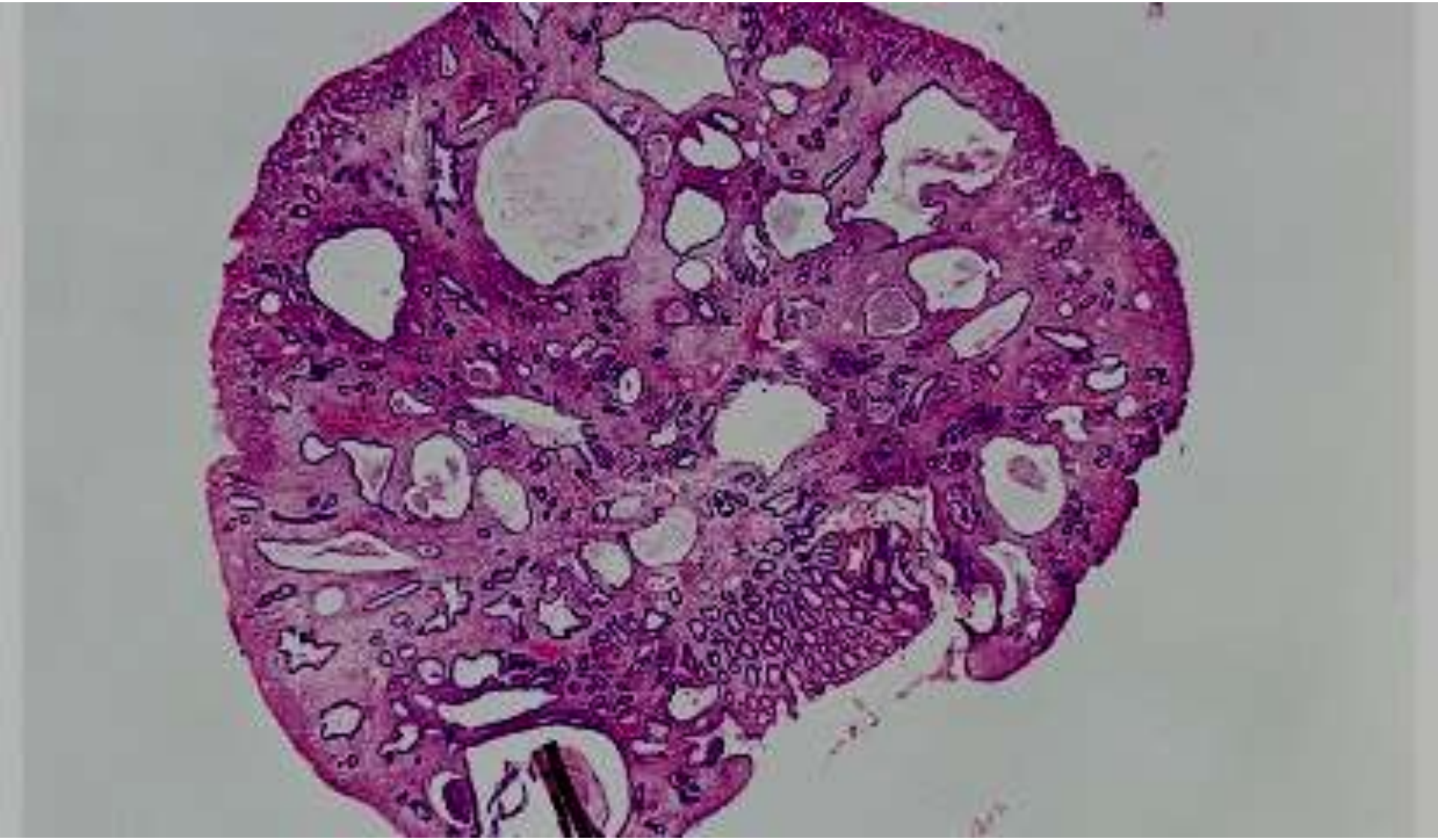
The polyps are present most frequently in the small intestine.

Juvenile polyp Large intestine





Juvenile polyp Large intestine

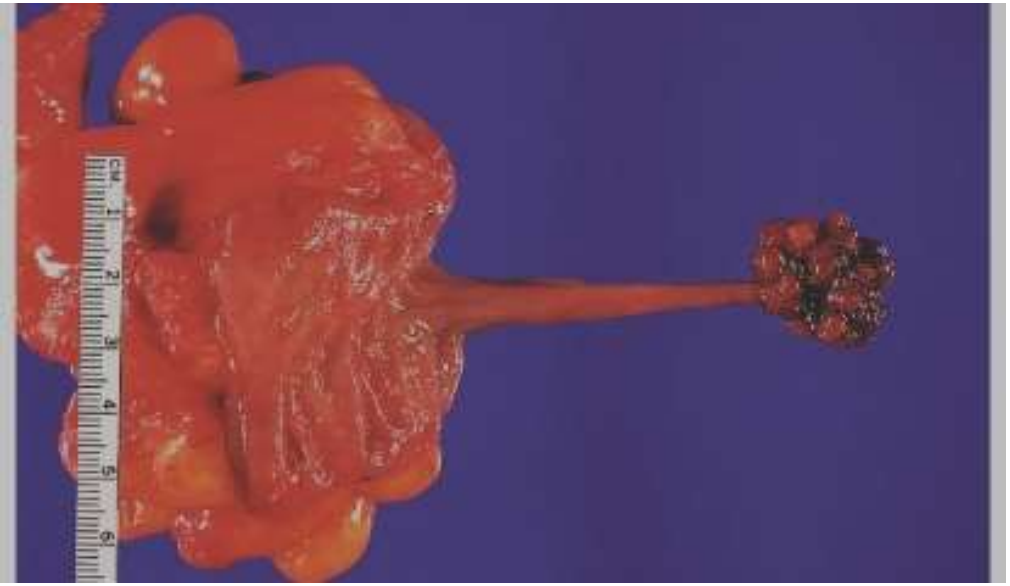


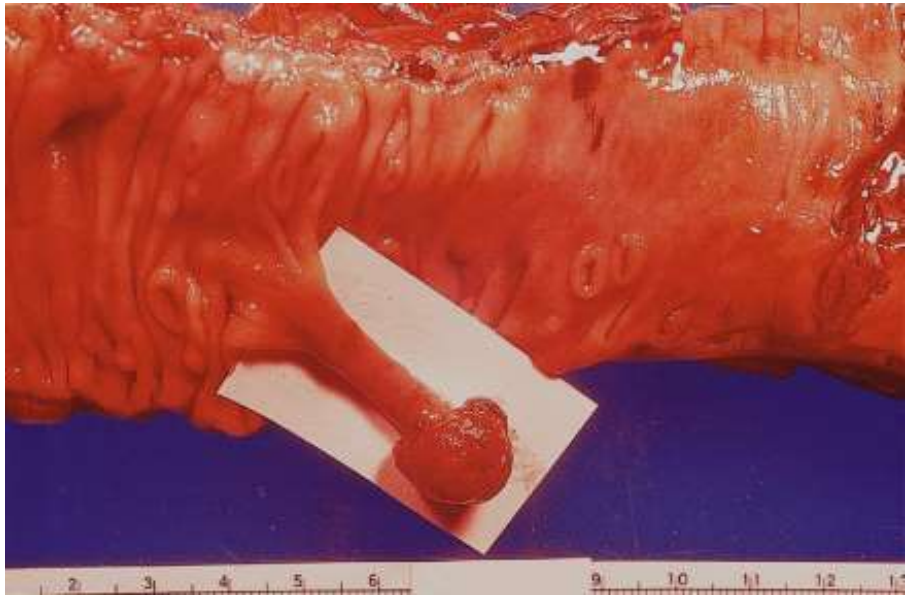
Adenomas (Adenomatous polyps)

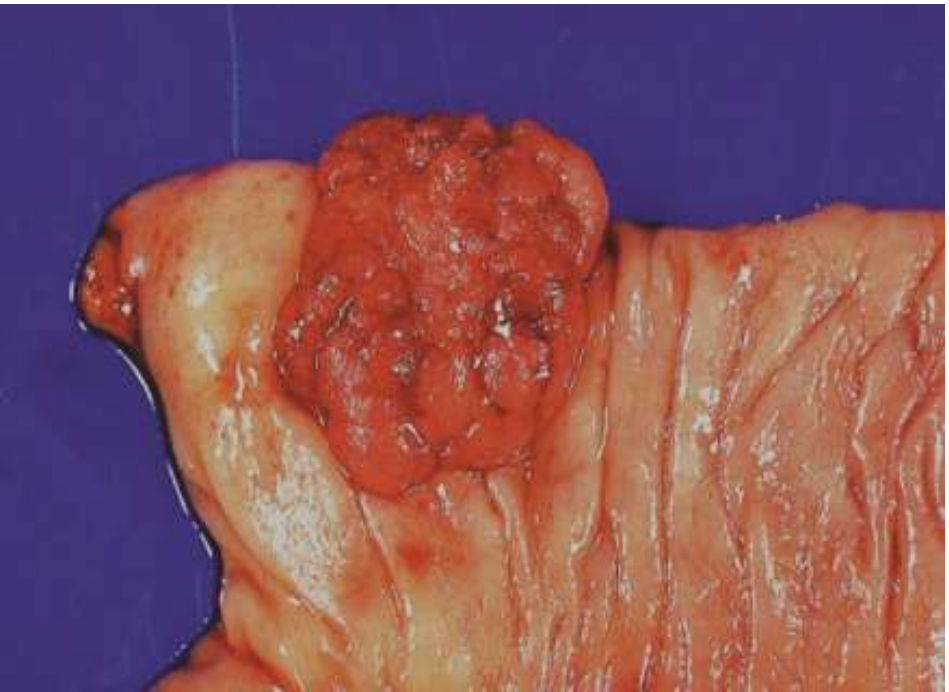
- **Adenomas are intraepithelial neoplasms that range from small, often pedunculated lesions to large neoplasms that are usually sessile.**
- **The prevalence of colonic adenomas increases progressively with age.**
- **Males and females are affected equally.**
- **Adenomatous polyps are divided into three subtypes on the basis of the epithelial architecture :**
  - **Tubular adenomas: compose of tubular glands**
  - **Villous adenomas: composed of villous projections**
  - **Tubulovillous adenoma: composed of a mixture of the above two.**

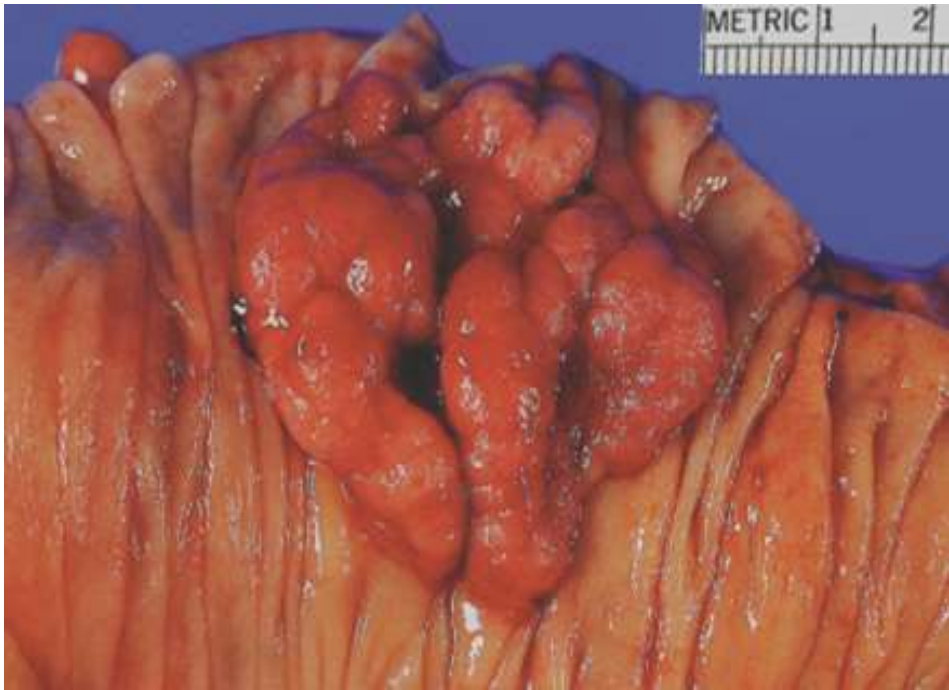
- **All adenomas by definition arise as the result of dysplastic epithelial proliferation.**
- **The dysplasia ranges from low-grade to high-grade.**
- **There is *strong evidence that adenomas are precursors for invasive colorectal adenocarcinomas.***
- **The risk of cancer is high (approaching 40%) in villous adenomas more than 4 cm in diameter.**
- **Adenomas may be single or multiple, may be asymptomatic, and many are discovered during evaluation of anemia (due to occult bleeding) through endoscopy.**
- **Villous adenomas are often are discovered because of overt rectal bleeding.**
- **The most distal villous adenomas may secrete sufficient amounts of mucoid material rich in protein and potassium to produce hypoproteinemia or hypokalemia.**
- **The only adequate treatment for adenomas is complete resection.**

Pedunculated adenomatous polyps.

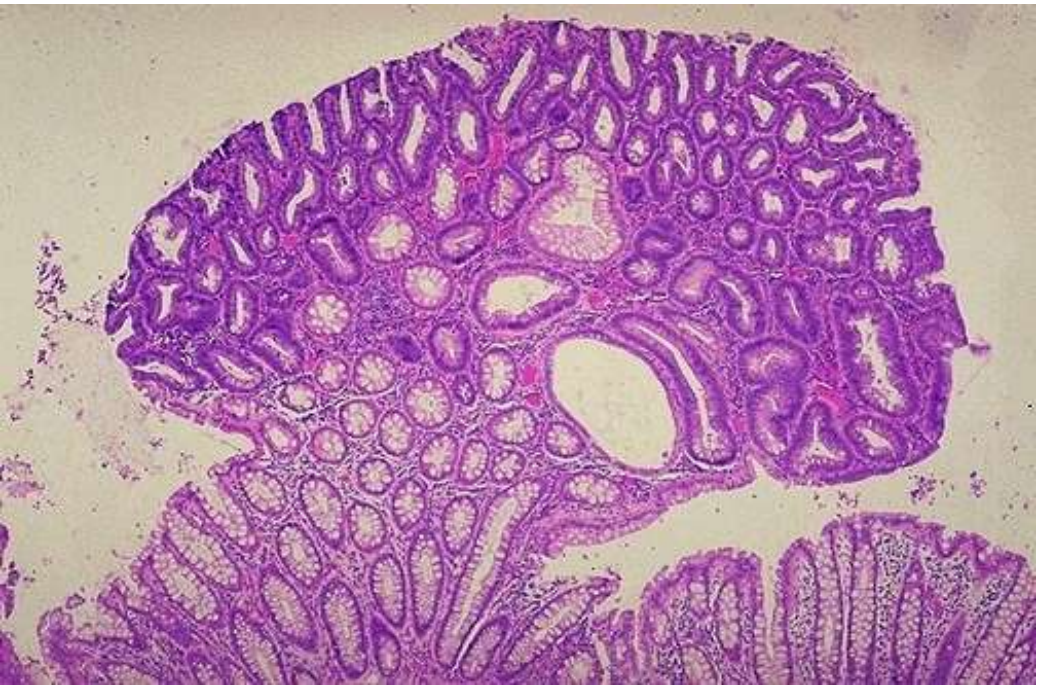


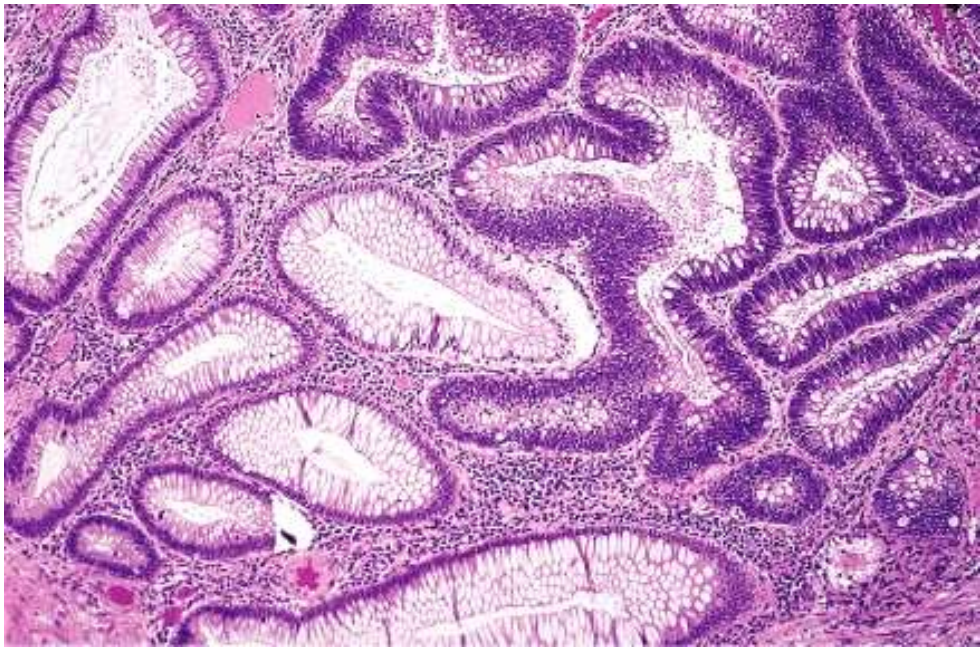




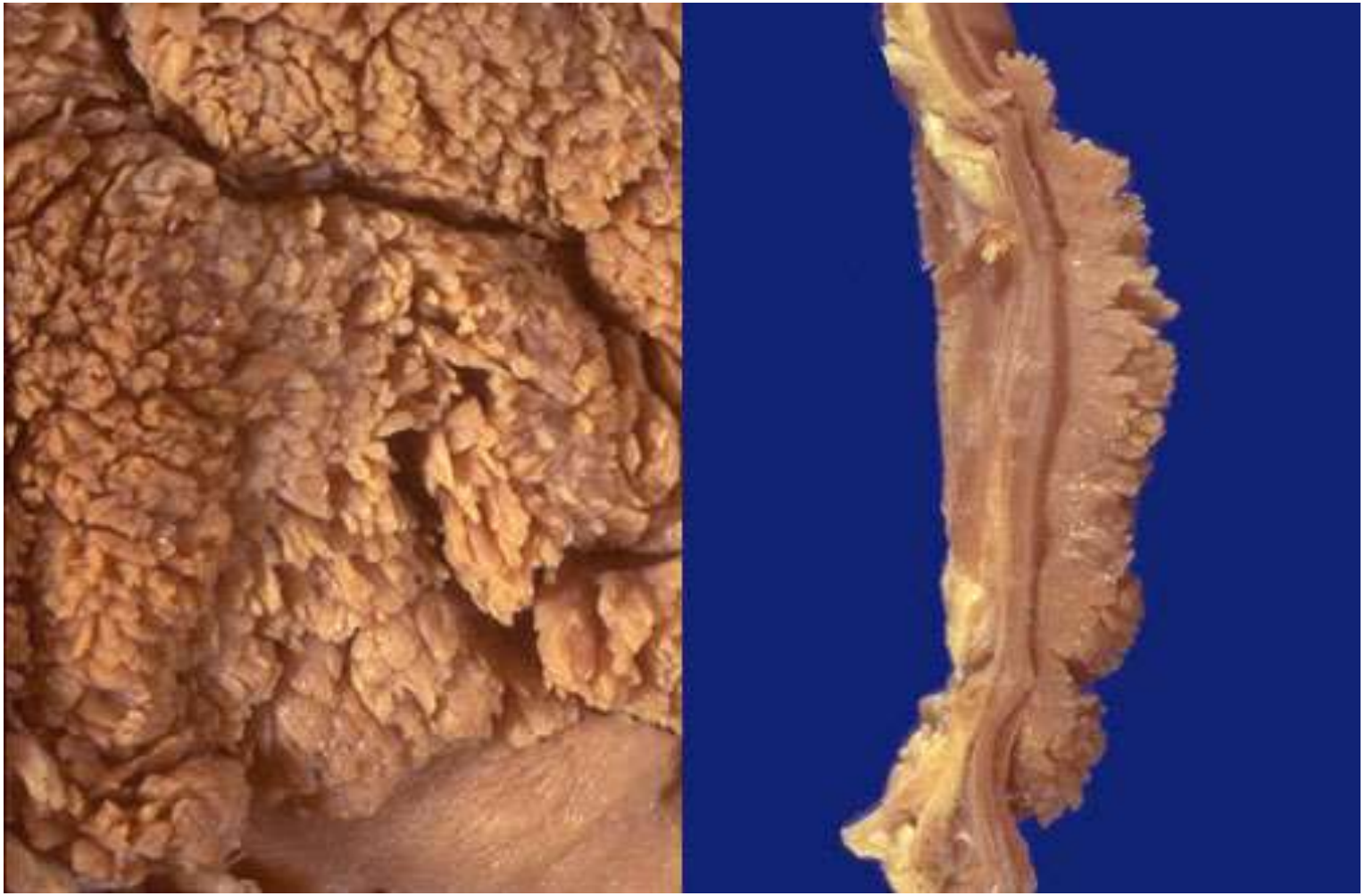


Adenomatous polyp (tubular adenoma), LP

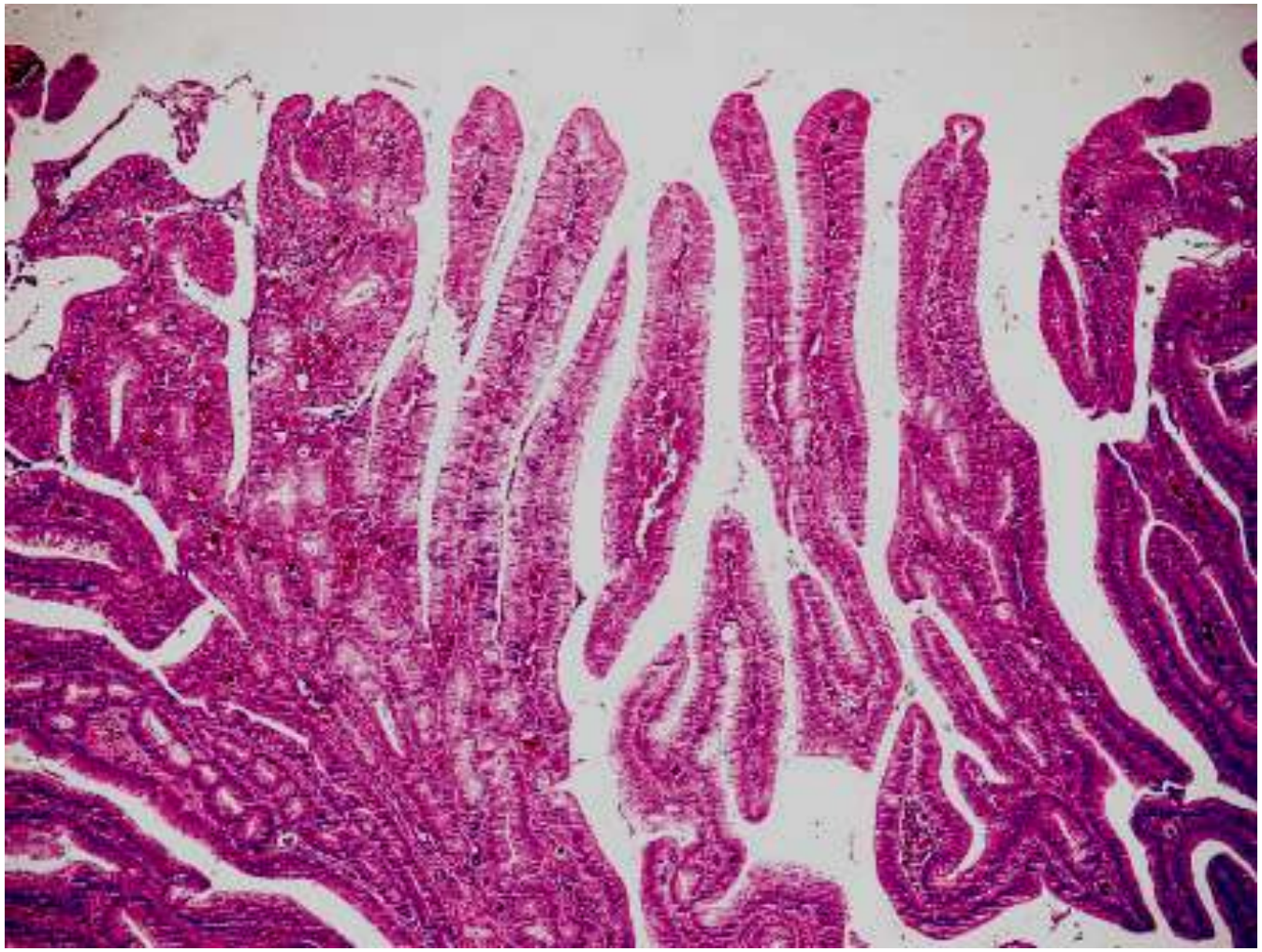




Villous adenoma colon

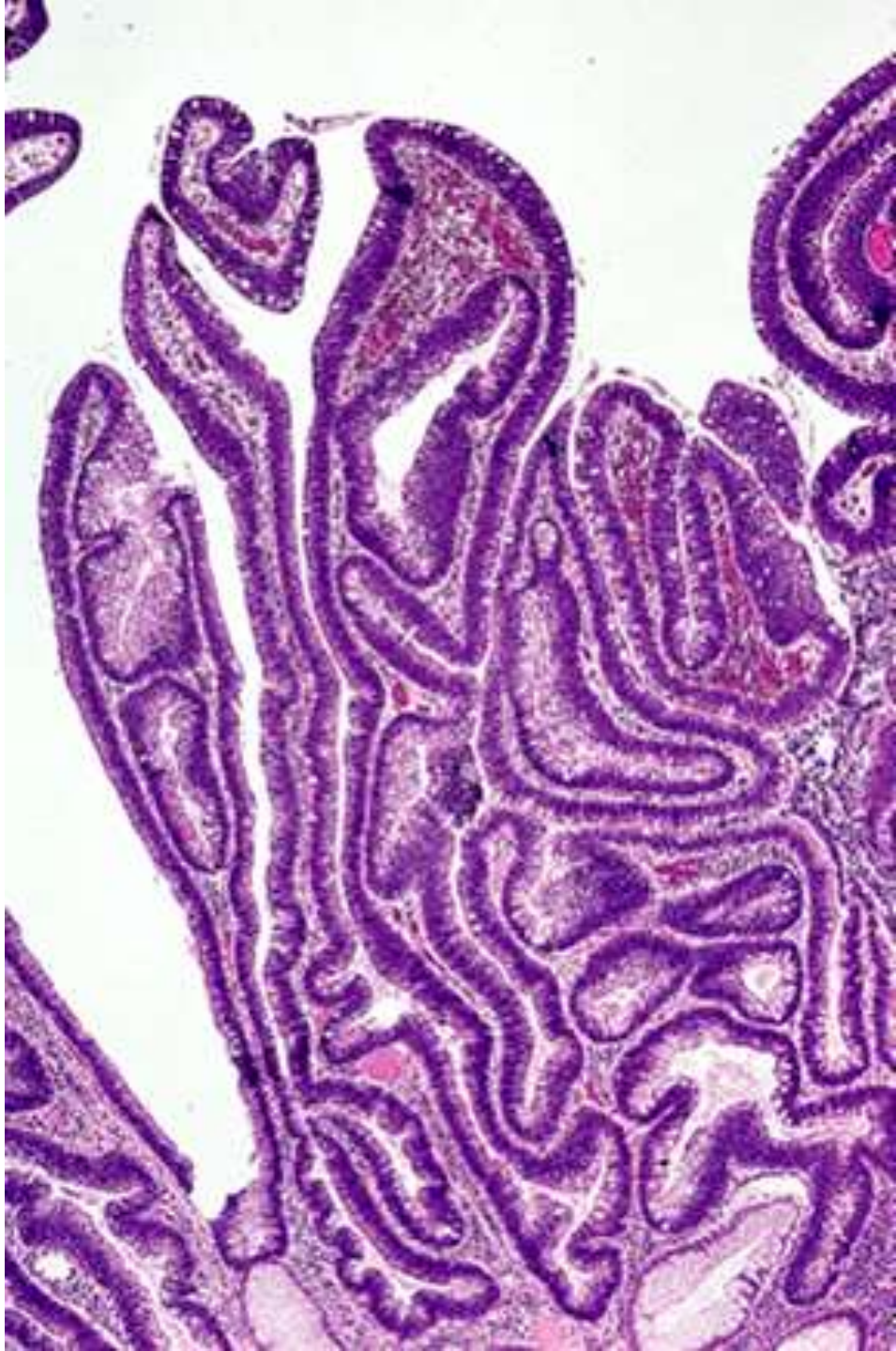


Villous adenoma



Villoglandular polyp.

There is an admixture of villous and glandular structures.



FAMILIAL POLYPOSIS SYNDROMES

These are uncommon autosomal dominant disorders. Their importance lies in their tendency for malignant transformation.

1. ***Peutz-Jeghers syndrome***
2. ***Juvenile polyposis syndrome***
3. ***Familial adenomatous polyposis (FAP)***

Another hereditary condition in this context but is not associated with polyp formations is:

the *hereditary nonpolyposis colorectal cancer syndrome (Lynch syndrome).*

Familial Adenomatous Polyposis (FAP) Syndrome

- **This is caused by *mutations of the adenomatous polyposis coli (APC) gene* on chromosome 5.**
- **In the *classic FAP syndrome*, affected patients typically develop 500 to 2500 colonic adenomas that carpet the mucosal surface; the presence of *a minimum of 100 polyps is necessary for a diagnosis.***
- **The lifetime risk of cancer development is 100%. Some patients already have cancer of the colon or rectum at the time of diagnosis.**
- **Cancer-prevention measures include early detection of the condition and *prophylactic colectomy.***

Adenomatous Familial Polyposis (AFP)

Polyposis with numerous small polyps covering the colonic mucosa. 18-year-old woman. The mucosal surface is carpeted by innumerable polypoid adenomas.

Gross appearance of familial polyposis. The entire large bowel was involved. Note the fact that practically all of the polyps are small and sessile.

Colorectal Carcinoma

A widely accepted proposal of carcinogensis is *the adenoma-carcinoma sequence* i.e. most carcinomas arise from preexisting adenomas. This has been supported by the following observations:

1. **Populations that have a high prevalence of adenomas have a high prevalence of colorectal cancer.**
2. **The distribution of adenomas parallel that of colorectal cancer.**
3. **The peak incidence of adenomas precedes that of carcinoma by some years.**
4. **When invasive carcinoma is identified at an early stage, a related adenoma is often present**
5. **The risk of cancer is directly related to the number of adenomas, that is why carcinoma complicates all those with FAP syndrome.**
6. **Removal of all adenomas that are suspicious reduces significantly the incidence of carcinoma.**

- **98% of all cancers in the large intestine are adenocarcinomas.**
- **They usually arise in polyps and produce symptoms relatively early and at a stage generally curable by surgical resection. Yet, it is responsible for *10% of all cancer-related deaths.***
- **The peak incidence for colorectal carcinoma is between ages *60 and 79.***
- **When colorectal carcinoma is found in a *young person, pre-existing ulcerative colitis or one of the polyposis syndromes must be suspected.***
- ***Environmental factors*, *particularly dietary practices*, are implicated in the striking geographic variations in incidence. Japanese families that have migrated from their low-risk areas to the United States (high-risk areas) have acquired, over the course of 20 years, the rate prevailing in the new environment; mainly because the immigrants adopted the common dietary practices of the U.S. population.**

The dietary factors receiving the most attention as predisposing to a higher incidence of cancer are

1. Excess dietary caloric intake relative to requirements

2. Low content of unabsorbable vegetable fibers & high content of refined carbohydrates

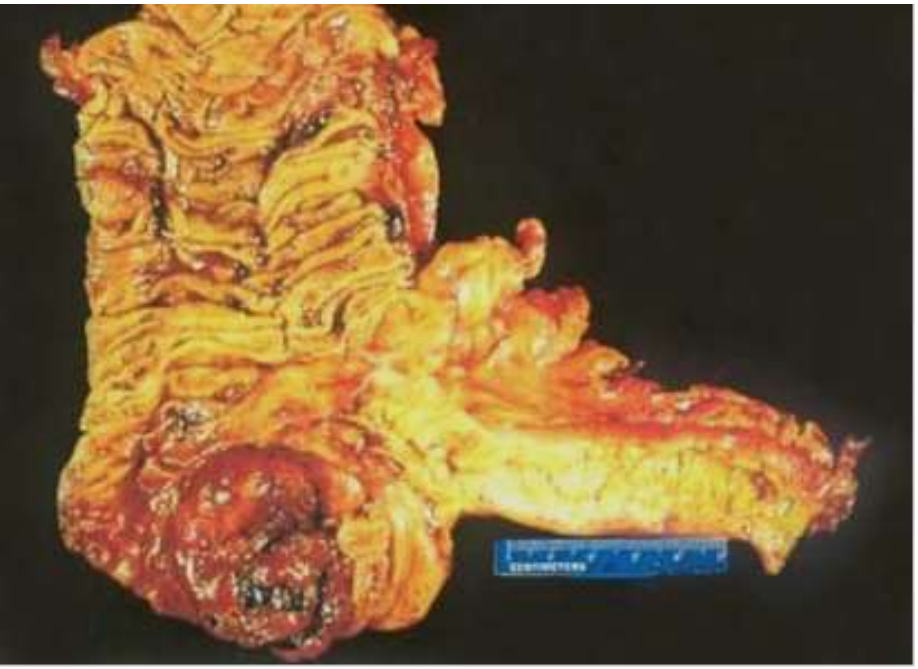
3. Intake of red meat

Several epidemiological studies suggest that the use of aspirin and other nonsteroidal anti-inflammatory drugs exerts a protective effect against colon cancer.

Gross features

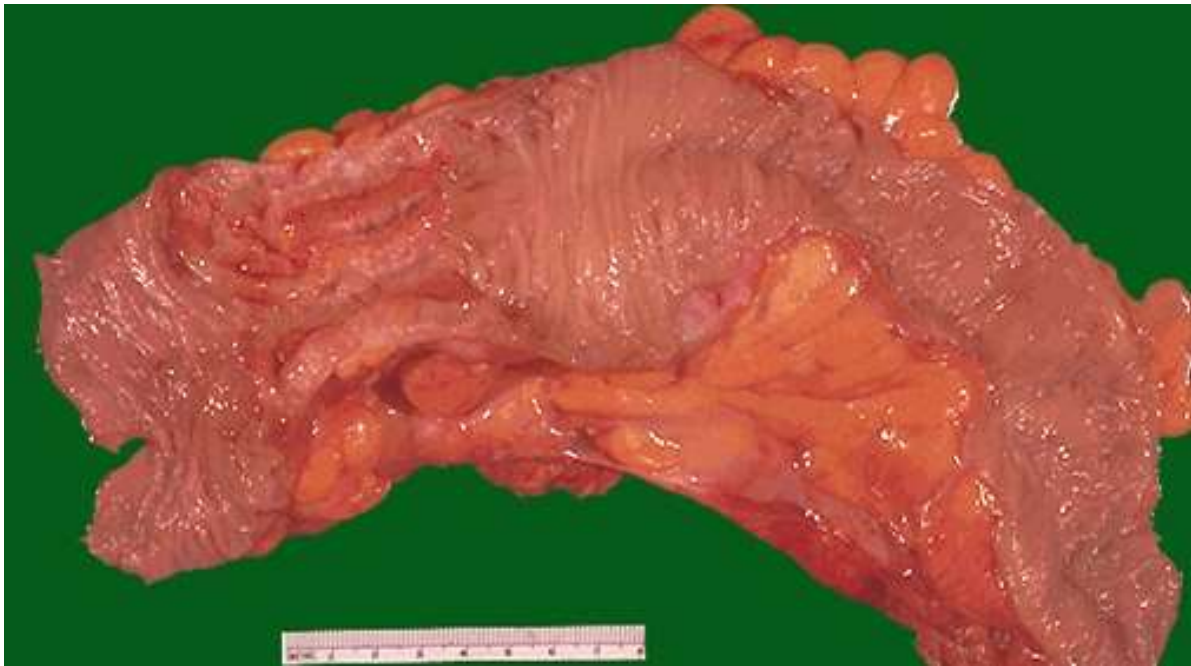
- **The rectosigmoid colon is the most frequent location (60%), followed by cecum/ascending colon (20%).**
- **Tumors in the *proximal colon tend to grow as polypoid, exophytic masses*; obstruction is uncommon.**
- **In the *distal colon, they tend to be annular*, encircling lesions that produce napkin-ring constrictions. The lumen is markedly narrowed leading to obstruction with secondary proximal distention.**
- **Both forms (polypoid and annular) directly penetrate the bowel wall over the course of time (probably years) and may appear as subserosal and serosal white, firm masses.**

Carcinoma large intestine



Carcinoma of the cecum. The fungating carcinoma projects into the lumen but has not caused obstruction.

Adenoca descending colon
The encircling mass of firm adenocarcinoma in this colon at the left is typical for adenocarcinomas arising in the descending Colon.



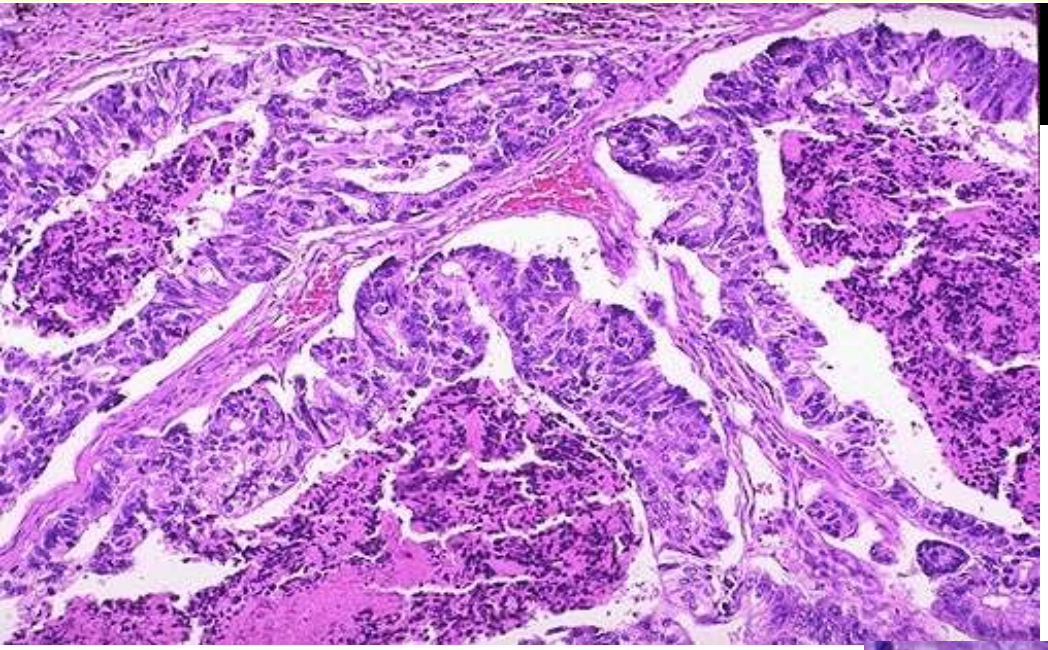
Microscopic features

- **The features of right- and left-sided colonic adenocarcinomas are similar.**
- **Differentiation (grade) may range from well-differentiated tumors to undifferentiated, frankly anaplastic masses.**
- **Invasive tumor provokes a strong desmoplastic (fibrotic) stromal response (responsible for the characteristic firm, hard consistency of most carcinomas).**
- **Carcinomas arising in the anal canal are mostly of squamous cell type.**

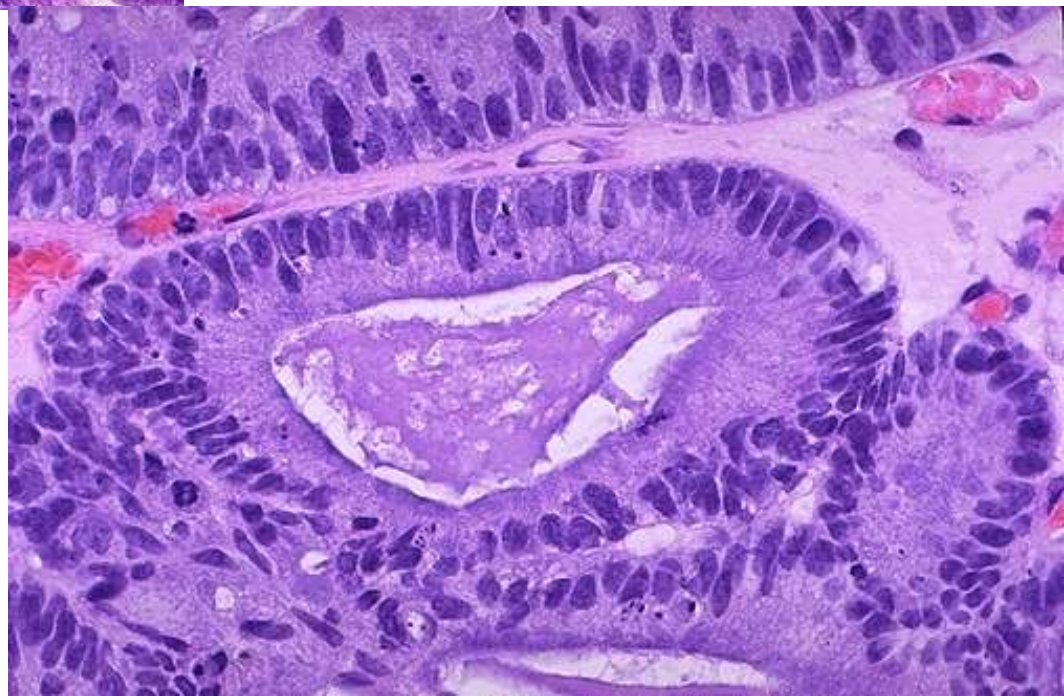
Clinical features

- **Colorectal cancers remain asymptomatic for years; symptoms develop insidiously and frequently have been present for months, sometimes years, before diagnosis.**
- **Patients with cecal and right colonic cancers are most often presented with iron-deficiency anemia (due to insidious blood loss).**
- **Left-sided lesions come to attention by producing occult bleeding and changes in bowel habit.**
- ***Iron-deficiency anemia in an older male means gastrointestinal cancer until proved otherwise.* In females the situation is less clear, since menstrual losses, multiple pregnancies, or abnormal uterine bleeding may underlie such an anemia.**

Adenocarcinoma colon



MP: the glands are large and filled with necrotic debris.

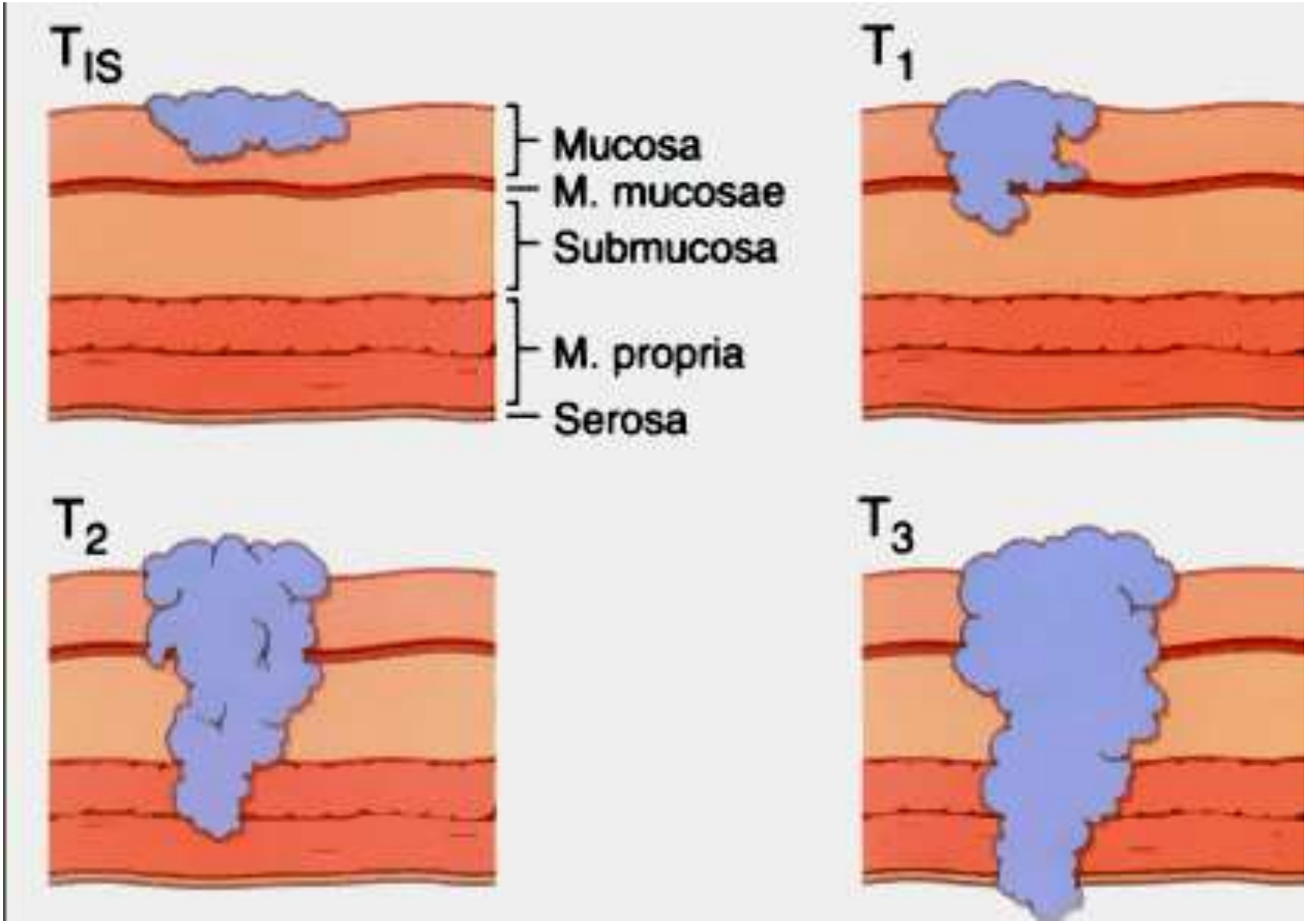


HP, the neoplastic glands of adenocarcinoma have crowded nuclei with hyperchromatism and pleomorphism. No normal goblet cells are seen.

Spread & metastsis

- **All colorectal tumors spread by direct extension into adjacent structures and by metastasis through the lymphatics and blood vessels.**
- **The favored sites of metastatic spread are the *regional lymph nodes, liver, lungs, and bones.* In general, the disease has spread beyond the range of curative surgery in 25% of patients.**
- **The single most important prognostic factor of colorectal carcinoma is the extent of the tumor at the time of diagnosis (stage).**
- ***Currently, the staging system most widely used is the tumor-nodes-metastasis (TNM).***
- **The principal aim is to discover these neoplasms when curative resection is possible. Indeed, each death from colonic cancer must be viewed as a preventable tragedy.**

H



CARCINOID TUMORS

- Carcinoid means carcinoma-like lesion because it shows a much more indolent clinical course than genuine carcinoma.
- Carcinoid tumor is derived from resident endocrine cells, with the gastrointestinal tract and lung as the predominant sites of occurrence.
- less than 2% of colorectal malignancies, 50% of small intestinal malignant tumors.
- Confined to the mucosa and submucosa or may be deeply invasive with metastatic spread to regional lymph nodes and the liver.
- Appendiceal and rectal carcinoids almost never metastasize.

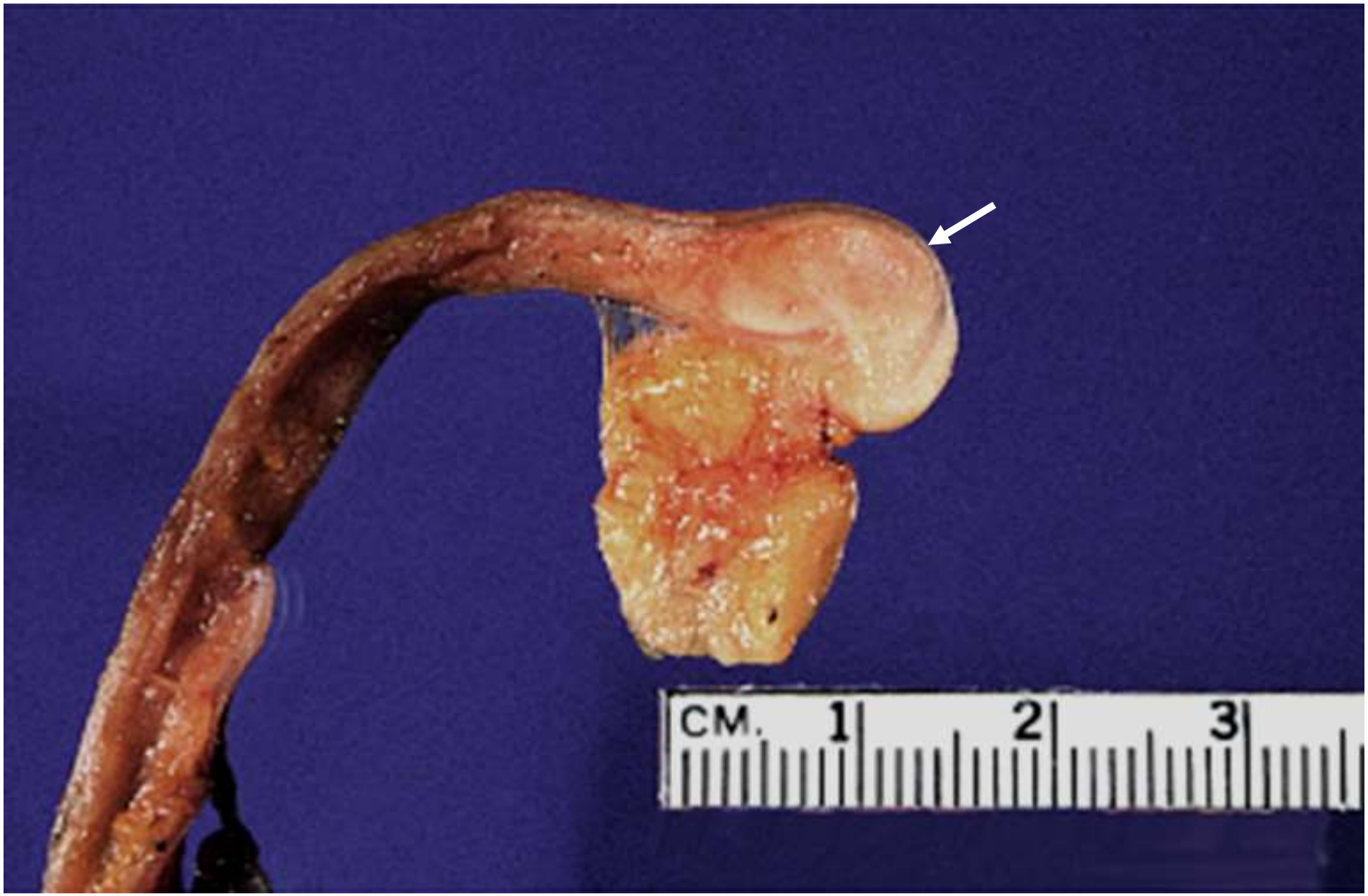
Gross features

- The appendix is the most common site of gut carcinoid tumors.
- In the appendix, they appear as rounded swellings of the tip.
- A characteristic feature is a solid, yellow-tan appearance on transection.

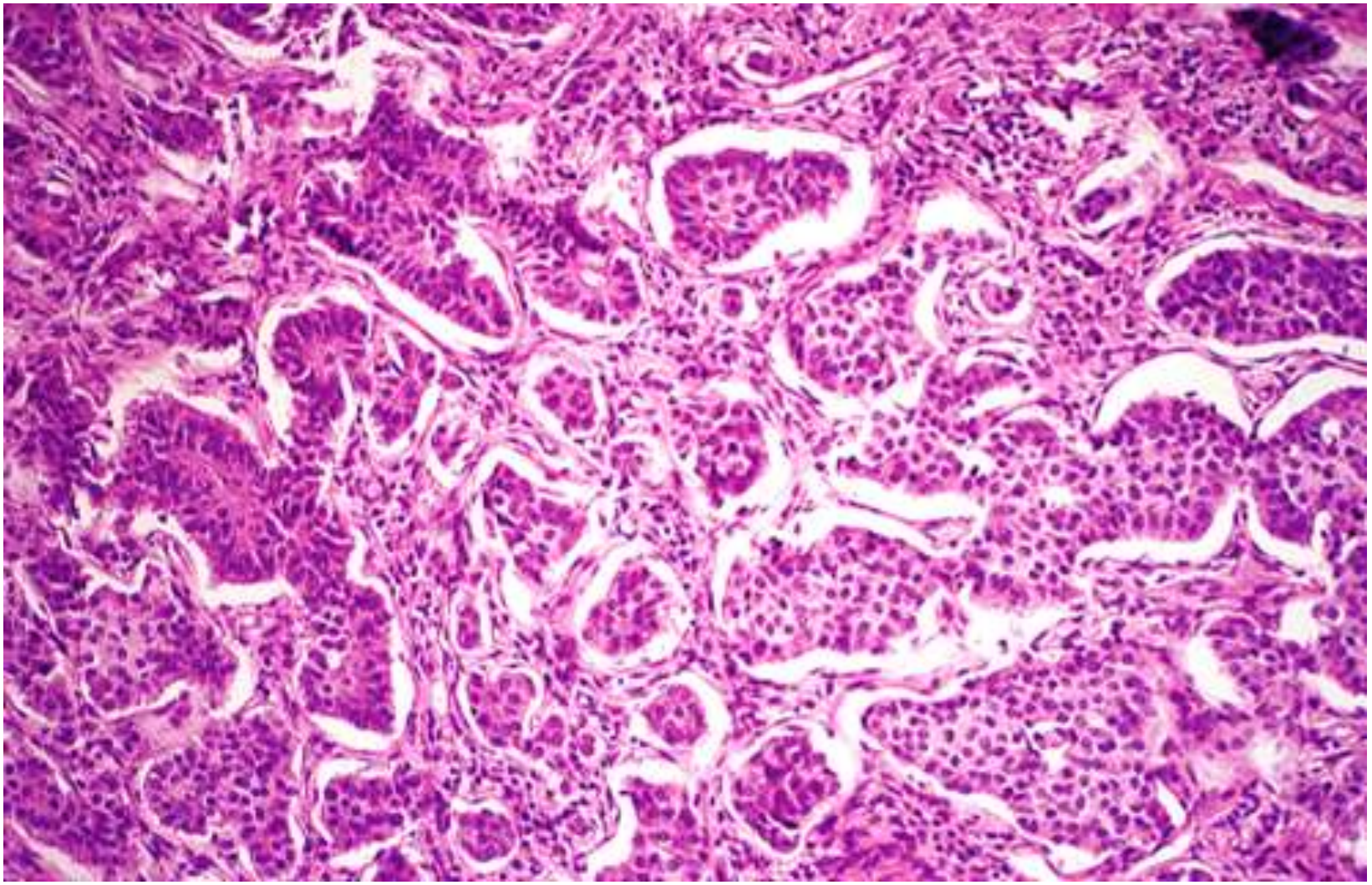
Microscopic features

- The neoplastic cells may form islands, trabeculae, glands, or sheets.
- The tumor cells show very little if any variation in cell and nuclear size, having a scant, pink granular cytoplasm and a round to oval nucleus.
- Mitoses are infrequent or absent.

Carcinoid appendix



Carcinoid tumor classic type appendix



GASTROINTESTINAL LYMPHOMAS

- Any segment of the gastrointestinal tract may be secondarily involved by systemic dissemination of nodal-based non-Hodgkin lymphomas.
- Up to 40% of lymphomas arise in sites other than lymph nodes (extra-nodal lymphomas), and the gut is the most common location.
- Primary gastrointestinal lymphomas usually arise without an obvious predisposing factor but they also occur more frequently in certain patient groups:

1. Chronic gastritis caused by H. pylori
2. Chronic celiac disease
3. Natives of the Mediterranean region (Mediterranean lymphoma)
4. Congenital immunodeficiency states, infection with HIV or following organ transplantation with immunosuppression

- Most gut lymphomas are of B-cell type (over 95%) and are either low- or high-grade tumors.
- Early discovery is the key to survival.
- The depth of local invasion, size of tumor and its histologic grade as well as extension into adjacent viscera are important determinants of prognosis.