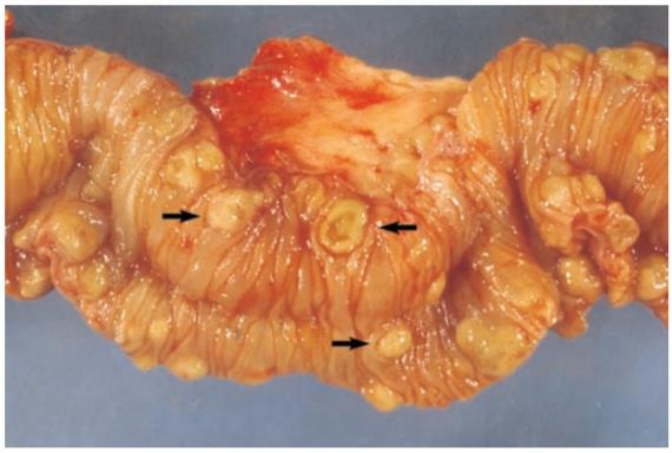
1) A 45-year-old woman presents with sudden attacks of wheezing, shortness of breath, and episodic hot flashes. She also reports abdominal cramps and diarrhea. Physical examination shows facial redness, pitting edema of the lower legs, and a murmur of tricuspid regurgitation. A 24-hour urine specimen contains elevated levels of 5-hydroxyindoleacetic acid (5-HIAA). A CT scan of the abdomen demonstrates multiple 1- to 2-cm nodules in distal ileum. A small bowel resection is performed (shown in the image). The arrows point to submucosal tumors. Microscopic examination shows nests of cells with round and uniform nuclei. Which of the following is the most likely diagnosis?

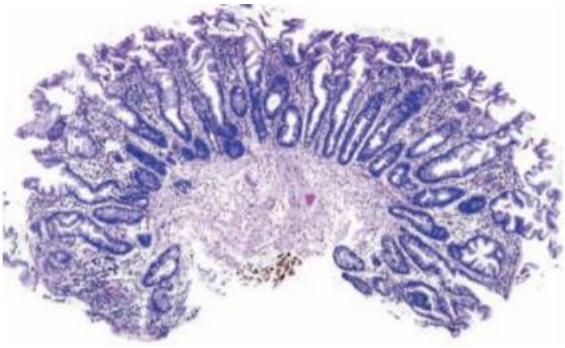


(A) Carcinoid tumor
(B) Mediterranean intestinal lymphoma
(C) MALT lymphoma
(D) Peutz-Jeghers syndrome
(E) Whipple disease

2) A 5-year-old girl is brought to the physician after her parents noticed red blood in her stool. Physical examination reveals mucocutaneous pigmentation. Small bowel radiography discloses multiple, small- to medium-sized polyps that are diagnosed pathologically as hamartomas. Which of the following is the most likely diagnosis?

(A) Congenital teratoma
(B) Hyperplastic polyp
(C) Peutz-Jeghers polyp
(D) Tubular adenoma
(E) Villous adenoma

3) A 55-year-old man undergoes routine colonoscopy. A small, raised, mucosal nodule measuring 0.4 cm in diameter is identified in the rectum and resected. The surgical specimen is shown in the image. Microscopic examination reveals goblet cells and absorptive cells with exaggerated crypt architecture, but no signs of nuclear atypia. Which of the following is the most likely diagnosis?



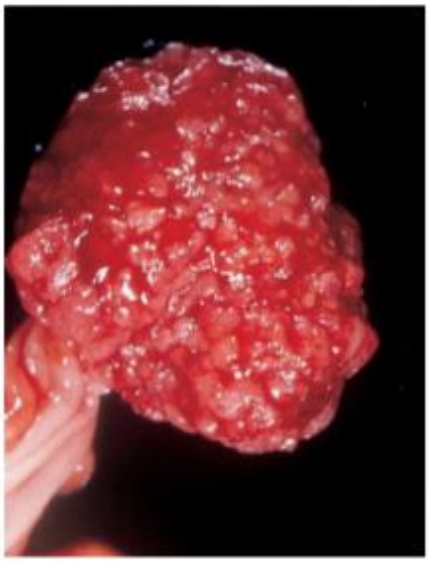
(A) Adenocarcinoma
(B) Hyperplastic polyp
(C) Inflammatory polyp
(D) Peutz-Jeghers polyp
(E) Villous adenoma

1)**The answer is A: Carcinoid tumor.** Carcinoid tumors are low-grade malignant neoplasms composed of neuroendocrine cells, which usually show considerable nuclear uniformity. They are most commonly located in the submucosa of the intestines (appendix, terminal ileum, and rectum). Carcinoids are distinguished from intestinal carcinomas based on their location, histologic features, malignant potential, endocrine activity, and clinical features. Carcinoid syndrome is a systemic paraneoplastic disease caused by the release of hormones from carcinoid tumors into venous blood. Clinical features of carcinoid tumors (e.g., flushing, bronchial wheezing, watery diarrhea, and abdominal colic) are presumably caused by the release of serotonin, bradykinin, and histamine. Release of tumor secretions from hepatic metastases leads to the formation of fibrous plaques in the tricuspid and pulmonic valves and may result in tricuspid insufficiency or pulmonic stenosis. The other choices are not associated with secretion of 5-HIAA acid or other neuroendocrine peptides. Diagnosis: Carcinoid syndrome

2) **The answer is C: Peutz-Jeghers polyp.** Peutz-Jeghers syndrome is an autosomal dominant, hereditary disorder characterized by intestinal hamartomatous polyps and mucocutaneous melanin pigmentation, which is particularly evident on the face, buccal mucosa, hands, feet, and perianal and genital regions. The polyps seen in Peutz-Jeghers syndrome are hamartomatous, characterized by a branching network of smooth muscle fibers continuous with the muscularis mucosa that support the glandular epithelium of the polyp. Congenital teratoma (choice A) does not involve the intestine. The other choices are principally colonic polyps that derive from the luminal epithelium.
Diagnosis: Gastrointestinal polyp, Peutz-Jeghers polyp

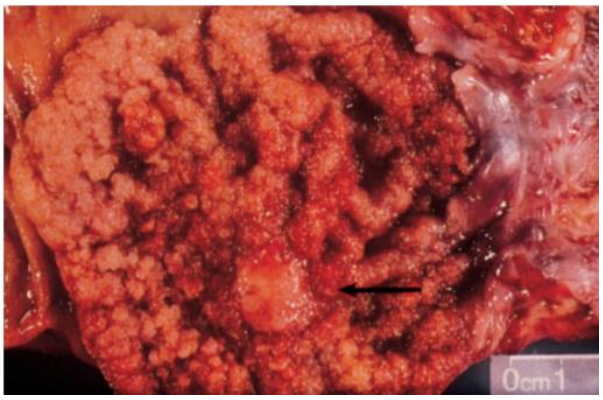
3) **The answer is B: Hyperplastic polyp.** Hyperplastic polyps are small, sessile mucosal excrescences that display exaggerated crypt architecture. They are the most common polypoid lesions of the colon and are particularly frequent in the rectum. The crypts of hyperplastic polyps are elongated and may exhibit cystic dilations. The epithelium is composed of goblet cells and absorptive cells, without any dysplasia. There are no dysplastic features indicative of adenocarcinoma (choice A). Villous adenomas (choice E) are considerably larger and exhibit prominent thin, tall, fingerlike processes. Peutz- Jeghers polyps (choice D) are hamartomatous. Diagnosis: Gastrointestinal polyp, hyperplastic polyp

4) A 65-year-old woman undergoes routine colonoscopy. During the procedure, a 2-cm mass is identified in the rectosigmoid region and resected. The surgical specimen is shown in the image. Microscopic examination shows irregular crypts lined by pseudostratified epithelium with hyperchromatic nuclei, without dysplastic features. Which of the following is the most likely diagnosis for this patient's colonic lesion?



(A) Adenocarcinoma
(B) Carcinoid tumor
(C) Hyperplastic polyp
(D) Tubular adenoma
(E) Villous adenoma

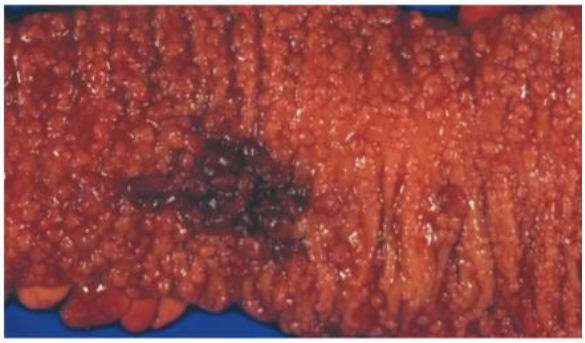
5) A 63-year-old woman complains of rectal bleeding of 1 week in duration. Laboratory studies show hypochromic, microcytic anemia (hemoglobin = 7.6 g/dL and MCV = 70 µm3). Colonoscopy reveals a large polypoid mass, which is removed (surgical specimen shown in the image). The arrow points to a malignant tumor. The patient asks about the relative risk of cancer arising in various types of gastrointestinal polyps. Which of the following types of colonic polyps is most likely to undergo malignant transformation?



(A) Hyperplastic polyp
(B) Lymphoid polyp
(C) Peutz-Jeghers polyp
(D) Tubular adenoma
(E) Villous adenoma

6) A portion of the large bowel was removed from a 34-year-old man with a familial disease that affects his gastrointestinal tract. The surgical specimen is shown in the image. This patient most likely carries a germline mutation in which of the following genes?

(A) APC
(B) C-myc
(C) DCC
(D) p53
(E) Ras

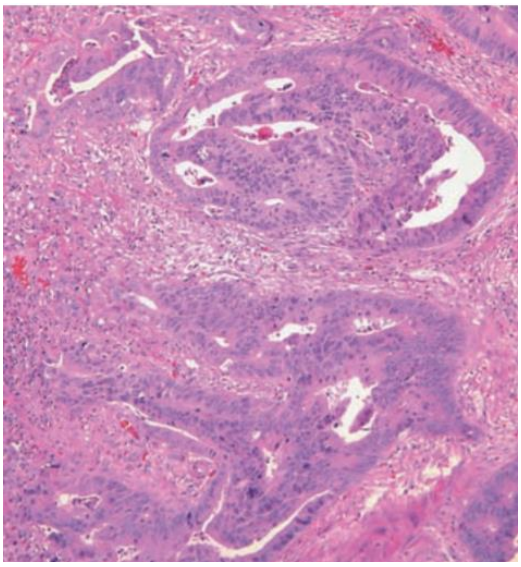


4) **The answer is D: Tubular adenoma.** Tubular adenomas constitute two thirds of benign colonic adenomas. They are typically smooth-surface lesions, usually less than 2 cm in diameter, and often have a stalk. Microscopically, tubular adenomas exhibit closely packed epithelial tubules, which may be uniform or irregular with excessive branching. Dysplasia and carcinoma often develop in tubular adenomas. As long as dysplastic foci remain confined to the polyp mucosa, the lesion is almost always cured by resection. Adenocarcinoma (choice A) is incorrect because the lesion does not have dysplastic features. Pseudostratified epithelium is not a feature of carcinoid tumor (choice B) or hyperplastic polyp (choice C). The incorrect choices do not typically exhibit a stalk. Diagnosis: Gastrointestinal polyp, tubular adenoma

5) **The answer is E: Villous adenoma.** These polyps comprise one third of colonic adenomas and are found predominantly in the rectosigmoid region. They are typically large, broadbased, elevated lesions that display a shaggy, cauliflower-like surface. Microscopically, villous adenomas are composed of thin, tall, fingerlike processes, which superficially resemble the villi of small intestine. Compared to tubular adenomas (choice D), villous adenomas more frequently contain foci of carcinoma. Hyperplastic polyps (choice A) have a much lower risk for malignant transformation. Diagnosis: Gastrointestinal polyp, villous adenoma

6) **The answer is A: APC.** The photograph shows numerous adenomas of the colon, consistent with familial adenomatous polyposis (FAP), also termed adenomatous polyposis coli (APC). This autosomal dominant inherited disease accounts for about 1% of colorectal cancers. It is characterized by the progressive development of innumerable adenomatous polyps of the colorectum, particularly in the rectosigmoid region. Germline mutations in the APC gene, a putative tumor suppressor gene, are responsible for FAP. Carcinoma of the colon and rectum is inevitable in these patients, and the mean age of onset is 40 years. The DCC gene ("deleted in colon cancer"— choice C) is a putative tumor suppressor gene that is often missing in colorectal cancers. Activating mutations of the ras protooncogene (choice E) occur early in tubular adenomas of the colon. Diagnosis: Adenomatous polyposis coli

7) A 59-year-old man complains of progressive weakness. His friends have noticed that he has become pale, and he reports that his stools are tinged with blood. On abdominal palpation, there is fullness in the right lower quadrant. Laboratory studies show iron-deficiency anemia, with a hemoglobin level of 7.4 g/dL. Stool specimens are positive for occult blood. Colonoscopy reveals an elevated and centrally ulcerated lesion of the sigmoid colon. The biopsy is shown in the image. Which of the following is the most likely diagnosis?



(A) Adenocarcinoma
(B) Carcinoid tumor
(C) Gastrointestinal stromal tumor
(D) Lymphoma
(E) Mucinous cystadenoma

8) A 65-year-old woman presents with a 3-month history of diarrhea and abdominal pain. She has lost 9 kg (20 lb) in the past 6 months. The patient had two benign colonic polyps removed 3 years ago. Laboratory studies reveal mild iron-deficiency anemia, and stool specimens are positive for occult blood. Sigmoidoscopy demonstrates an ulcerated mass, and a biopsy shows malignant glands. A segment of the colon is resected, and the surgical specimen is shown in the image. Based on current models of colonic carcinogenesis, which of the following genes was most likely mutated in the transition from benign adenoma to carcinoma in this patient?

(A) BRCA1
(B) C-myc
(C) p53
(D) Ras
(E) VHL

7) **The answer is A: Adenocarcinoma.** Adenocarcinoma of the rectum or sigmoid colon often presents as a circumferential mass narrowing the intestinal lumen. The gross appearance of the colorectal cancer is similar to that seen elsewhere in the gastrointestinal tract. The most important risk factors associated with the development of colonic adenocarcinoma are age, prior colorectal cancer, ulcerative colitis, genetic factors, and perhaps diet. Colorectal cancer invades lymphatic channels and initially involves the lymph nodes immediately underlying the tumor. As the tumor grows, the most common sign is occult blood in feces. Bright red blood more often occurs in distal lesions. In either case, bleeding typically causes iron-deficiency anemia. Choices B, C, and D are principally lesions of the intestinal wall. Choice E (mucinous cystadenoma) is an ovarian tumor. Diagnosis: Colorectal cancer, adenocarcinoma of colon

8) **The answer is C: p53.** In most cases of colorectal carcinoma, it has been estimated that a minimum of eight to ten mutational events must accumulate before the development of invasive cancer. This process is initiated in morphologically normal mucosa, proceeds through an adenomatous precursor, and terminates as invasive adenocarcinoma. The APC gene is considered to play an important role in the early development of most colorectal neoplasms, whereas mutations in the p53 tumor suppressor gene are thought to participate in the late transition from adenoma to carcinoma. BRCA1 (choice A) has been implicated in the pathogenesis of breast and ovarian cancers. VHL (choice E) has been incriminated in the pathogenesis of clear cell renal cell carcinoma. Diagnosis: Adenocarcinoma of colon