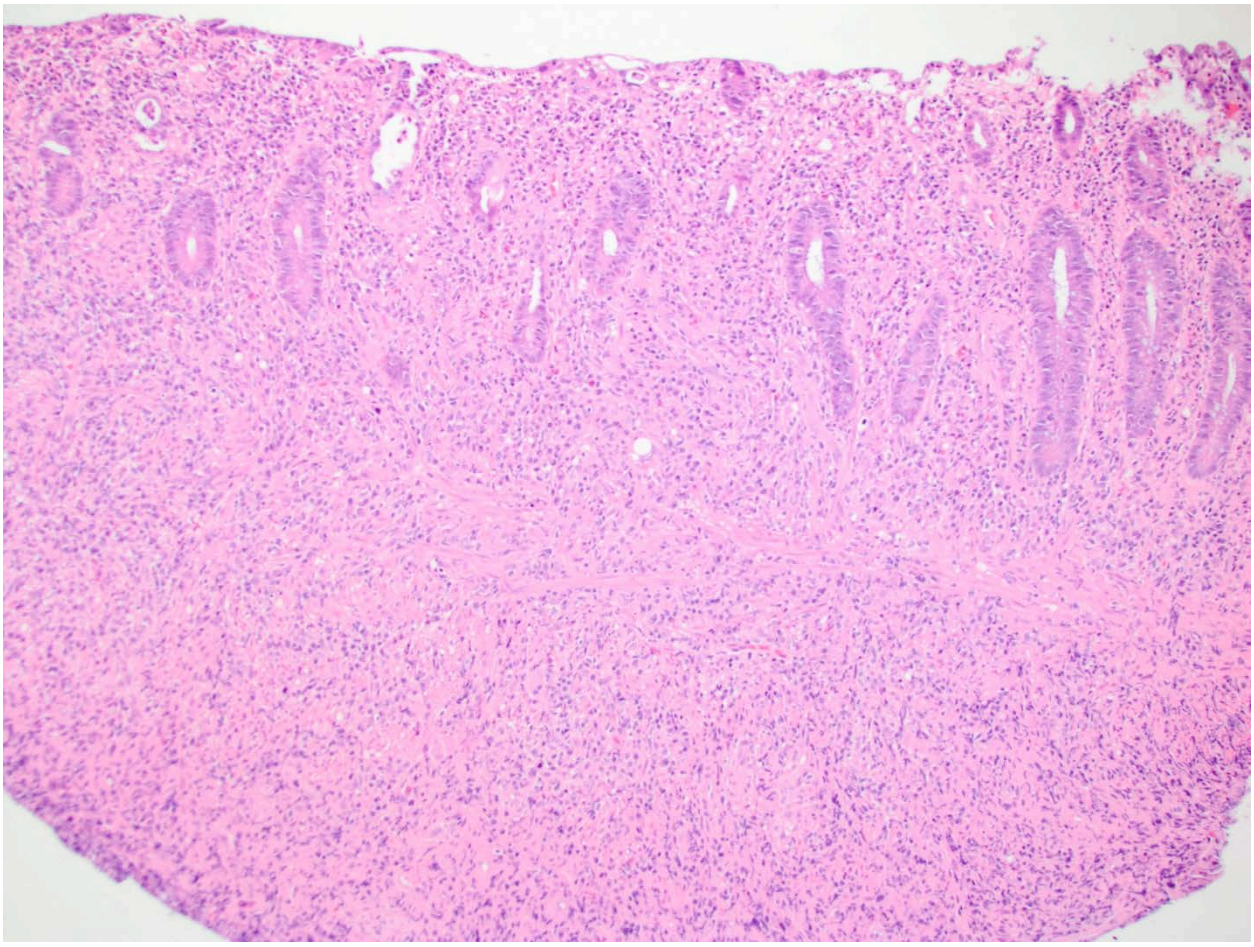
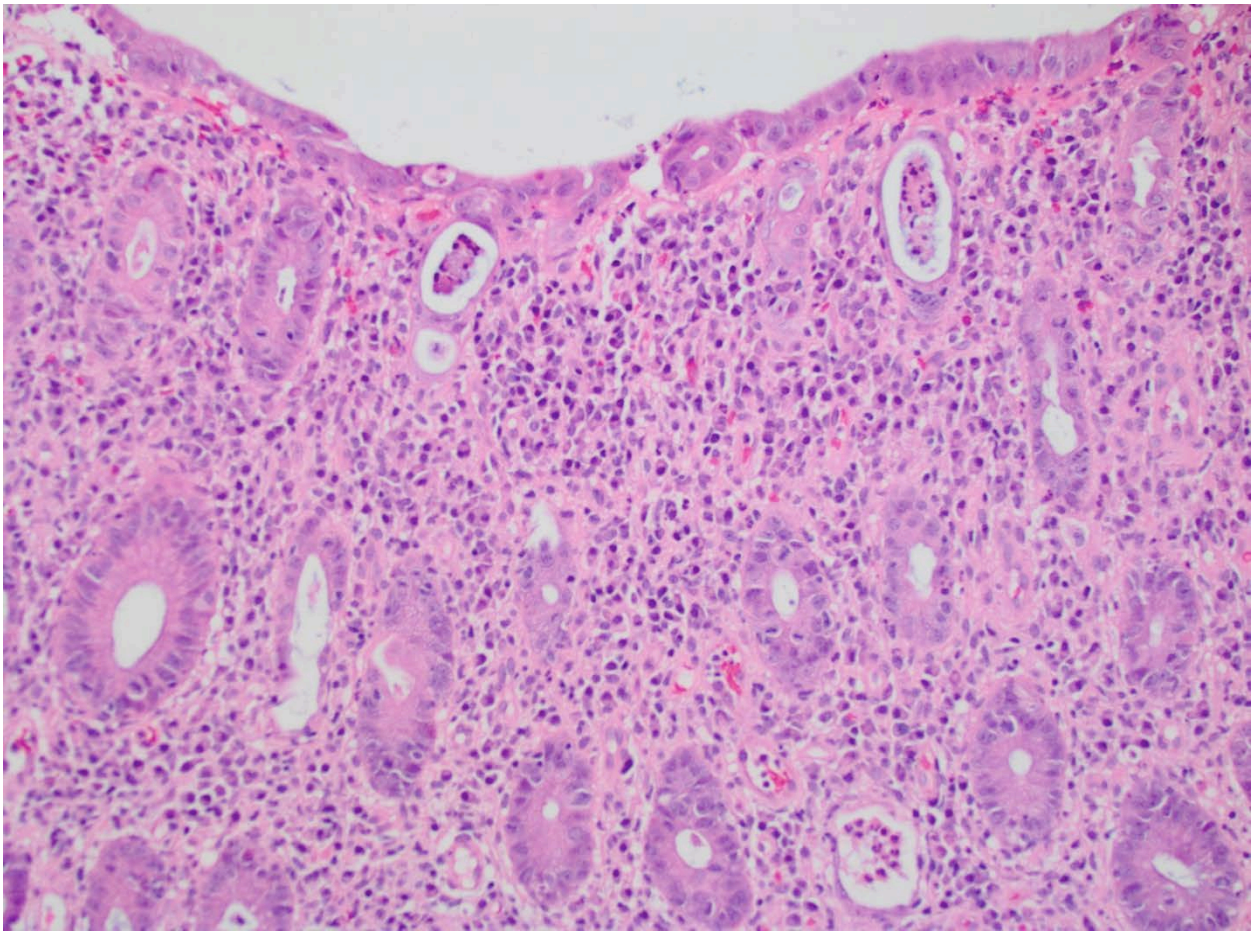
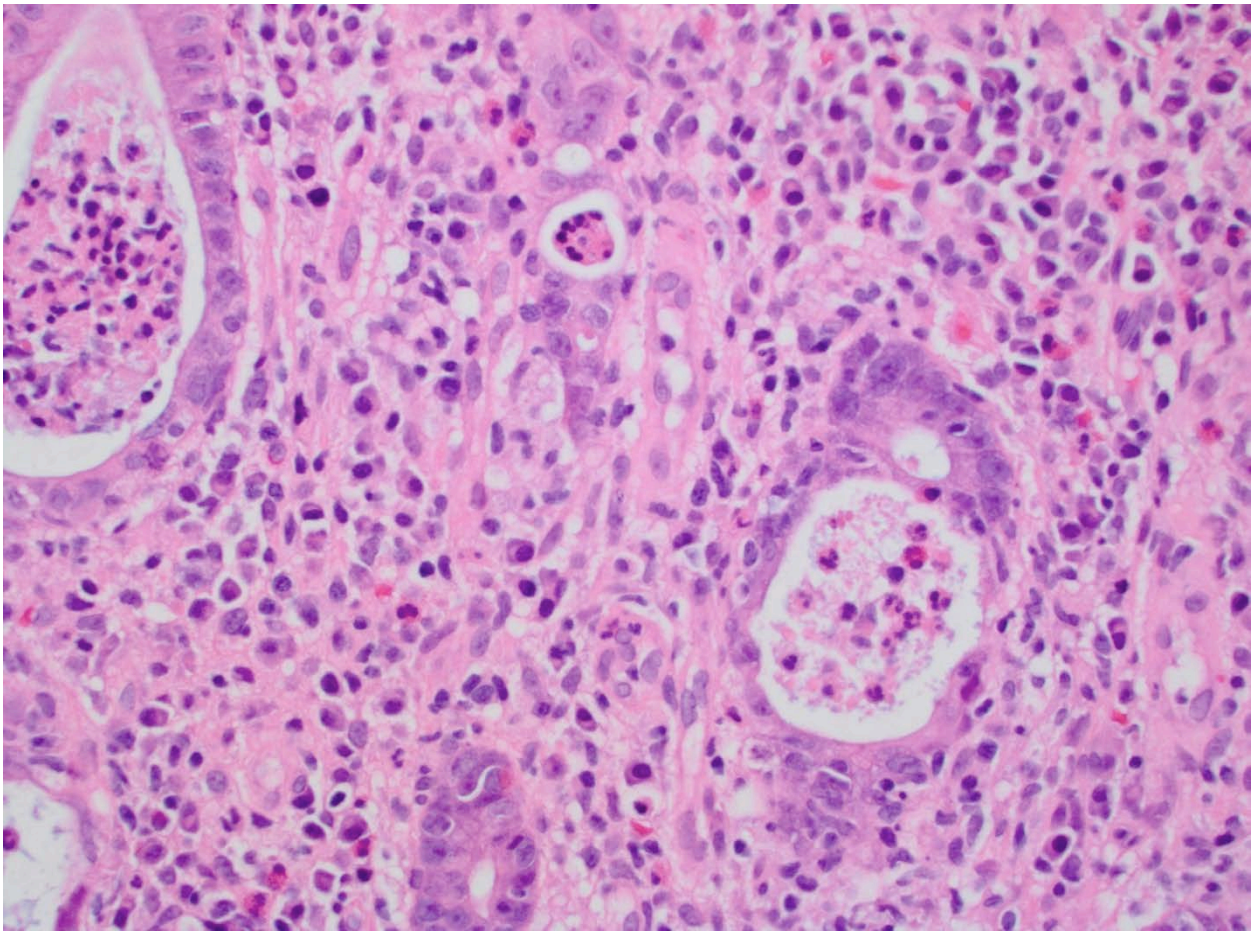
The patient is a 40 year old man with a clinical history of occult blood in the stool. Colonoscopic examination demonstrated a thickened fold in the rectum. The remainder of the colon and terminal ileum were endoscopically normal.







What is your diagnosis?

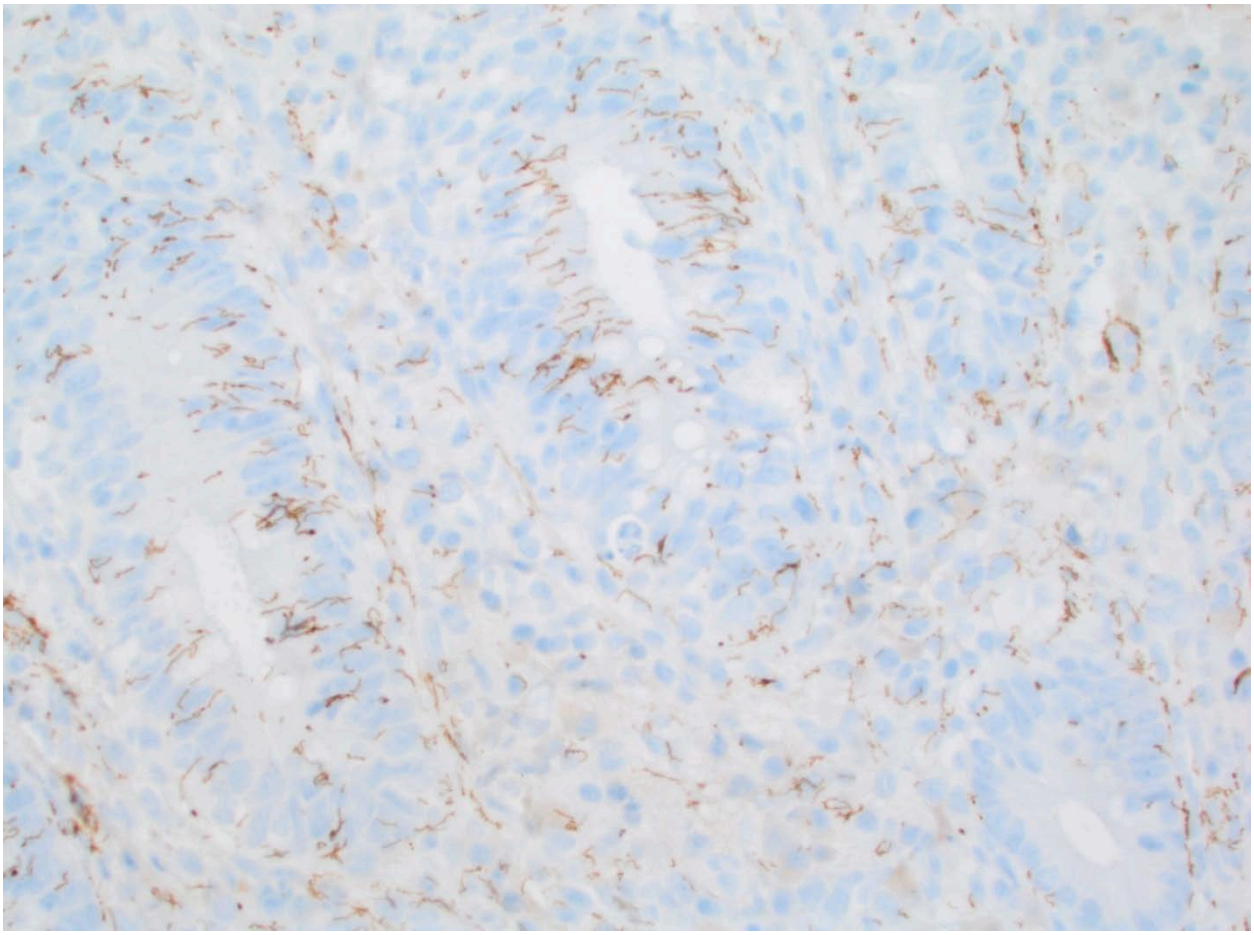
A) Crohn disease
B) Lymphogranuloma venereum
C) Drug/toxic injury
D) Syphilitic proctocolitis
E) Signet ring cell adenocarcinoma

Answer and Discussion:

D. Syphilitic proctocolitis

Comment: The photomicrographs demonstrate rectal mucosa with only minor architectural alterations and an inflammatory infiltrate occupying the lamina propria and extending into the underlying submucosa. This infiltrate is predominantly lymphocytes, plasma cells and histiocytes, although scattered eosinophils are also seen. The crypts appear damaged, and in some areas have a withered

appearance. Neutrophils are present within the crypt epithelium, and scattered crypt abscesses are present. Immunohistochemical staining for *Treponema pallidum* was performed, and showed innumerable spirochetes within the glandular epithelium, lamina propria and submucosa. Subsequent discussion of the findings with the treating clinician revealed that the patient was HIV+.



T. pallidum immunohistochemical stain

A) "Crohn disease" is incorrect. Crohn's disease often enters the differential diagnosis of syphilitic proctocolitis both endoscopically and histologically. Although some features suggestive of IBD are seen (predominantly active inflammation in the form of cryptitis with crypt abscess formation), the absence of chronic injury features makes the diagnosis of Crohn disease unlikely.

B) Lymphogranuloma venereum is incorrect. Lymphogranuloma venereum is caused by a *Chlamydia trachomatis* infection, and may appear nearly identical to syphilitic proctocolitis histologically. Ancillary studies are necessary to exclude this diagnosis. The presence of spirochetes on the T. pallidum immunohistochemical stain establishes the diagnosis of syphilis. It is important to be aware, however, that patients may be infected with both *T. pallidum* and *C.*

trachomatis. There is no existing stain for *C. trachomatis*, and therefore, this diagnosis must be excluded clinically with the use of a *C. trachomatis* nucleic acid probe test or culture from a rectal swab. Clinical symptoms typical of LGV include exquisite rectal pain, inguinal lymphadenopathy and fever.

C) Drug/toxic injury is incorrect. The presence of withered appearing crypts raises the possibility of drug or toxic injury. However, the amount of inflammation seen in this case exceeds that usually encountered in association with toxic injury, and should raise the suspicion of an infectious process.

E) Signet ring cell adenocarcinoma is incorrect. While syphilitic proctocolitis may produce a mass lesion simulating carcinoma, clinically, the histologic features in this case are not supportive of a malignant diagnosis. Immunohistochemical staining for cytokeratin and/or histiocyte markers may be used to exclude the possibility of carcinoma.

D) Syphilitic proctocolitis is the correct answer. The incidence of syphilis is increasing in the United States, particularly among HIV+ males with a history of having sex with men. In a recent study of syphilitic proctocolitis, all affected patients were HIV+ males with an average age of 40.9 years (1). The most common presenting symptom is rectal bleeding, followed by anal pain, tenesmus and discharge. Rectal ulcers are the most common endoscopic finding, and often raise clinical suspicion for inflammatory bowel disease. Syphilitic proctocolitis may also present endoscopically as a mass lesion simulating malignancy (1, 2). Histologically, an intense lymphohistiocytic infiltrate rich in plasma cells is characteristic. There may additionally be active inflammation present, but this is generally only of mild to moderate severity. Basal plasmacytosis and crypt architectural alterations are inconspicuous. Rare granulomas or foci of Paneth cell metaplasia may be present. Ulcers and erosions are common. The diagnosis may be confirmed with immunohistochemical staining for *Treponema pallidum*. Immunohistochemical staining is preferred over use of silver stains which are often difficult to interpret due to their non-specific nature, and lack of sensitivity for detecting the organisms. It is important to note that stains for Treponemal organisms are frequently negative in biopsies from patients with syphilis. Therefore, the diagnosis should be excluded clinically in the setting of a biopsy with typical histologic findings, but negative staining for organisms.

References:

1) Arnold CA, et al. Syphilitic and lymphogranuloma venereum (LGV) proctocolitis: clues to a frequently missed diagnosis. Am J Surg Pathol 2013;37:38-46.
2) Cha JM, et al. Rectal syphilis mimicking rectal cancer. Yonsei Med J 2010;51:276-278.

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