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## In brief

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Crohn's disease (CD) is a chronic idiopathic disease of the gastrointestinal (GI) tract that can manifest as 3 separate phenotypes including inflammatory, stricturing, and penetrating. Penetrating, or fistulizing, CD can occur at any location along the GI tract, and is notoriously difficult to treat, requiring a multidisciplinary approach including gastroenterologists, surgeons, radiologists, pathologists, and nutritionists for optimal management.

Perianal fistulizing CD is one of the most common forms of fistulizing CD and may be present even without concomitant intestinal disease. Patients will present with a perianal abscess or drainage, occasionally with incontinence, pain, and tenesmus. Unfortunately, despite the number of medical therapies available with antibiotics, corticosteroids, immunomodulators, and biologics, no particular medical therapy works well for longstanding perianal remission. Antibiotics achieve good symptom control, and combination immunomodulator and biologic may help

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achieve resolution, but most patients require surgical intervention. Unfortunately, even surgical intervention is often met with recurrent disease due to uncontrolled proctitis or scarring from prior operations, and multiple fistula branches. Mesenchymal stem cell therapy is a promising novel alternative that is being increasingly studied in clinical trials, and is now a commercially available product in Europe.

Similarly, the presence of a rectovaginal fistula is an extremely morbid condition with foul-smelling air, stool, or pus discharge from the vagina. Rectovaginal fistulas in CD are complex and notoriously difficult to treat, with various studies reporting recurrence in 25% to 80% of patients following treatment. There is currently no consensus regarding the optimal medical treatment for CD-related rectovaginal fistulas and surgery remains the mainstay of treatment as up to 83% of patients fail medical treatment. There are few prospective studies and no randomized studies specifically addressing this population. Rectal and vaginal advancement flaps are simple repairs with good healing rates and may be attempted repeatedly following treatment failure. Surgical techniques with transposition of tissue to the rectovaginal space such as a Martius or gracilis flap provide the highest healing rates. Fecal diversion, unfortunately, does not improve healing rates. The application of mesenchymal stem cells is also being studied in Crohn's rectovaginal fistulas.

Ileal pouch fistulas most often are related to pelvic sepsis or anastomotic leak from the ileal pouch anal anastomosis, but, on occasion, patients can also develop CD of the pouch with peripouch fistulas. These are incredibly difficult to treat medically despite the number of biologics available. Often patients will at least be intestinally diverted to control the perianal sepsis. Most patients are not candidates for a reconstructive pouch given the CD, so most patients will end up undergoing a pouch excision and permanent end ileostomy.

Enterocutaneous fistula, or fistula from the bowel to the skin, can be a challenging problem to manage from a wound care perspective, enteral feeding, and ongoing fluid losses. Once the effluent is controlled and nutritional parameters have improved, medical and surgical therapy can be considered for fistula closure. Surgical intervention can sometimes result in worsening of the overall clinical picture, with new enterocutaneous fistulas forming. Thus, non-operative treatment strategies until a patient is optimized for a surgical intervention is critically important.

Enteroenteric fistulas are quite common. Typically, one segment of bowel is quite inflamed and diseased and this fistulizes to another segment of bowel that is the "innocent bystander" without inflammation. Interloop fistulas can often be treated with biologic therapy and inflammatory control. It is important to control the inflammation to minimize the amount of bowel excised at the time of surgical intervention. In the setting of an ileal-sigmoid fistula, closure of the sigmoid side depends on the level of involvement with the sigmoid, size, and location of the fistula tract.

Enterovesical fistula (EVF) is a rare complication of CD, occurring in approximately 2% to 8% of all patients. CD is the main cause for EVF, while diverticulitis is the most frequent cause for colovesical fistulas, followed by cancer and CD. There is an increased interest in the medical management of EVFs, which used to be an absolute surgical indication. The majority of data comes from studies of infliximab. Despite potential healing with biologics, more than 80% require a surgical intervention with postoperative drainage of the bladder.

Fistulizing CD can involve any segment of the GI tract and truly requires a combination of medical therapy and surgical intervention. Although immunosuppressive therapy generally does not close the fistula tract, it does improve the local inflammation which allows for a more optimal surgical environment for closure and may reduce the amount of bowel resected. In the setting of perianal disease, it allows for mucosal healing which can open the door for surgical options. Surgical intervention is unfortunately not curative and should therefore focus on minimizing the amount of bowel excised and utilizing minimally invasive techniques when able to optimize any future surgical intervention. Care of these patients is lifelong and is best managed with a team approach, all focused on improving the quality of life for these patients.