



Figure 27-2. (A) Typical transsphincteric fistulas prior to treatment. (B) Without seton placement prior to anti-TNF therapy, one gets premature closure of cutaneous openings and abscess formation. (C) Seton placement prior to initiation of medical treatment prevents abscess formation by allowing the fistula to drain until inflammation is absent.

In ACCENT II (A Crohn's Disease Clinical Trial Evaluating Infliximab in a New Long-Term Treatment Regimen), the infliximab fistula maintenance trial, infliximab was used to maintain fistula closure over the course of 1 year.⁵ In this trial, the 195 patients who were considered responders ($\geq 50\%$ reduction in draining fistulas) at week 14 to the initial induction sequence of 5 mg/kg of infliximab at 0, 2, and 6 weeks were randomized to receive either 5 mg/kg or placebo every 8 weeks. At week 54, 36% of patients who were on maintenance infliximab had complete cessation of drainage of all of their fistulas, compared with only 19% of patients in the placebo cohort ($P = .009$).⁵

Fistula healing was studied as a secondary endpoint in the adalimumab maintenance trial, CHARM (Crohn's Trial of the Fully Human Antibody Adalimumab for Remission Maintenance).⁶ Complete fistula closure at week 56 was seen in 33% of the treated group (combined 40-mg-weekly and every-other-week adalimumab dosing arms), compared with 13% in the placebo arm ($P = .016$). The response was durable. In the patients who demonstrated fistula closure at week 26, all maintained fistula closure at week 56.⁶

Finally, a randomized clinical trial assessed certolizumab pegol's effect on fistula closure.⁷ Participants with draining fistulas received an induction dose of certolizumab pegol at 0, 2, and 4 weeks. Responders at week 6 were randomized to receive additional maintenance therapy with certolizumab pegol or to receive placebo. At week 26, the certolizumab pegol arm showed a 36% response with 100% fistula closure, compared with a 17% response in the placebo arm ($P = 0.038$). The results of these studies suggest that infliximab, adalimumab, and certolizumab pegol have similar benefit in perianal Crohn's disease (36% infliximab versus 19% placebo, 33% adalimumab versus 13% placebo, and 36% certolizumab pegol versus 17% placebo), although the certolizumab pegol study was half as long as the other 2 studies.

Another common approach, especially in those with simple fistulas, is to use antibiotics (ciprofloxacin or metronidazole) as a bridge to immunomodulator treatment in patients with CD perianal fistulas.⁸ A prospective open-label trial of 52 patients with CD perianal fistulas compared those patients treated only with ciprofloxacin or metronidazole for 8 weeks to those patients who transitioned or were already on AZA at a dose of 2.0 to 2.5 mg/kg per day. Although the results