Ulcerative colitis is a chronic inflammatory bowel disease, usually diagnosed in early adulthood. The hallmark symptoms include bloody diarrhea, rectal urgency and pain, cramping, and feeling unable to completely empty the bowel, even after defecation. Ulcerative colitis is defined based on disease location: proctitis (limited to the rectum), left-sided disease (limited to descending colon and rectum), and extensive disease (entire colon). Most patients with ulcerative colitis have proctitis or left-sided disease. Only about 10% to 30% of patients have extensive disease. Most patients with ulcerative colitis are classified as having mild to moderate disease. Up to one in four patients with ulcerative colitis require hospitalization for acute severe ulcerative colitis. The chart below answers common questions about the management of acute severe ulcerative colitis in adults.

### Abbreviations: CMV = cytomegalovirus; CRP = c-reactive protein; ESR = erythrocyte sedimentation rate; IV = intravenous; NSAID = nonsteroidal anti-inflammatory drug.

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| **What is acute severe ulcerative colitis?** | • Acute severe ulcerative colitis is defined as six or more bloody stools per day PLUS at least one of the following:1,5,6,12  
  o Fever (>100° F [37.8° C])  
  o Tachycardia (>90 beats per minute)  
  o Anemia (hemoglobin <10.5 g/dL)  
  o Elevated CRP (>30 mg/L)  
  o Elevated ESR (>30 mm/hour)  
  • Triggers for acute ulcerative colitis flares may include:1,7  
  o Recent smoking cessation  
  o NSAID use  
  o *Clostridium difficile* infection  
  o Nonadherence to maintenance therapy |
| **What general care should be provided to patients who experience an acute severe ulcerative colitis flare?** | • The following labs and tests should be completed on admission:5,12  
  o Labs will include a complete blood count (CBC), urea, electrolytes, creatinine, CRP, ESR, liver function tests, lipid profile, and CMV IgG and IgM.  
  o Abdominal x-ray (to assess for toxic megacolon).  
  o Stool cultures, including testing for *Clostridium difficile*.  
  o Flexible sigmoidoscopy (within 48 hours of admission) with biopsies to assess disease severity and for CMV (CMV is associated with poor outcomes and increased need for colectomy). |
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| **General care, continued** | - Full colonoscopies should be avoided, as this can increase risk of perforation.  
- In anticipation of the possible need for biologic therapy, testing for hepatitis B, tuberculosis, and human immunodeficiency virus (HIV) can be done on admission.  
- Most patients will need IV fluids with correction of abnormal electrolytes (e.g., hypokalemia).  
- Patients should receive a nutritional assessment. Most patients should start a regular diet. However, patients who have toxic megacolon should not receive anything by mouth (i.e., made NPO).  
- Bowel rest and parenteral nutrition are NOT necessary. Use enteral nutrition for patients unable to tolerate a regular diet. Enteral nutrition is associated with fewer complications than parenteral nutrition.  
- Patients should receive pharmacologic prophylaxis (e.g., heparin, low-molecular-weight heparin [LMWH]) to prevent venous thromboembolism (VTE).  
- Daily monitoring should include vital signs, physical exam (e.g., abdominal distension, tenderness), and frequency of bowel movements, including assessment for blood in stool. |
| **How should maintenance meds be addressed during acute severe ulcerative colitis?** | - Review meds and, if possible, avoid the following during acute severe ulcerative colitis:  
  - Medications that can slow gut motility, which may increase the risk of toxic megacolon:  
    - Antidiarrheal medications (e.g., loperamide)  
    - Anticholinergics (e.g., cyclobenzaprine, diphenhydramine, dicyclomine, tricyclic antidepressants)  
    - Opioids (if necessary, use sparingly and at low doses)  
  - NSAIDs and oral iron which aggravate mucosal inflammation.  
  - Recently initiated mesalamine or other aminosalicylates, as these can sometimes trigger colitis. |
| **What is the role for steroids in patients with acute severe ulcerative colitis?** | - IV corticosteroids are the cornerstone of acute severe ulcerative colitis management.  
  - Two of the commonly used IV steroids (and doses) include:  
    - Methylprednisolone 60 mg/day  
    - Hydrocortisone 300 to 400 mg/day  
  - Higher doses do NOT appear to provide additional benefit [Evidence Level B-2].  
  - There is no difference in steroid efficacy when given as a single dose, in divided doses, or as continuous infusion.  
  - Rectal steroids (e.g., foams, enemas) can be added for additional relief, especially in patients who have proctitis.  
  - Monitor patients closely for a lack of response. Non-responders require rescue therapy or surgery (e.g., colectomy).  
  - Transition patients showing improvement (e.g., reduced pain, CRP, or fever) from IV to oral steroids on about day three.  
    - Convert IV steroids to oral prednisone. Prednisone 5 mg is considered equivalent to IV hydrocortisone 20 mg or methylprednisolone 4 mg.  
  - Avoid continuing IV steroids for more than seven days to ten days. There is unlikely to be additional benefit and longer therapy may increase risk of complications (e.g., fluid retention, electrolyte abnormalities, arrhythmias). |
### Topic/Question

**What is the role for rescue therapy in patients with acute severe ulcerative colitis refractory to IV steroids?**

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<td>• About one-third of patients do NOT respond to IV steroids and require rescue therapy.¹</td>
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<td>• Add infliximab (e.g., <em>Remicade</em>, <em>Inflectra</em>, <em>Renflexis</em>) or IV cyclosporine (e.g., <em>Sandimmune</em>) as rescue therapy after about three days of IV steroids if not improving, to try to avoid a colectomy.¹,⁵</td>
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<td>• The choice between infliximab and cyclosporine should be based on prescriber experience with each medication, patient specific factors, and risk for complications.¹,⁶ Infliximab is often the most commonly used salvage therapy given its similar efficacy, fewer adverse effects (compared to cyclosporine), and use as maintenance therapy.¹² Infliximab may be preferred over cyclosporine for patients:¹,⁴</td>
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<td>o Who failed outpatient immunomodulators (e.g., azathioprine)</td>
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<td>o With low albumin levels (e.g., &lt;2.3 g/dL)</td>
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<td>o With low cholesterol or magnesium levels (these can increase the risk of neurotoxicity with cyclosporine).</td>
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<td>• Can consider tacrolimus as rescue therapy (target trough levels of 10 to 15 ng/mL) if infliximab and cyclosporine are not options (e.g., not available, contraindicated). However, there are limited long-term data using tacrolimus as rescue therapy in acute severe ulcerative colitis.¹</td>
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<td>• There are no data to support the use of other biologics as rescue therapy (e.g., adalimumab [<em>Humira</em>], tofacitinib [<em>Xeljanz</em>], vedolizumab [<em>Entyvio</em>]).¹</td>
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<td>• There are not good data to use a second rescue medication if initial rescue meds (cyclosporin, infliximab) fail.¹ Using multiple courses of rescue therapy for a single acute severe ulcerative colitis flare is associated with significant adverse outcomes (e.g., death from sepsis, herpetic esophagitis, acute pancreatitis with bacteremia). If patients fail either cyclosporine or infliximab, colectomy is recommended.¹,⁹</td>
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### What is important to know about using infliximab rescue therapy?

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<td>• If not already completed on admission (as results can take a few days), additional tests or screening are needed prior to starting infliximab. Screen patients for:³,⁵,¹⁶</td>
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<td>o Tuberculosis (TB; with interferon gamma release assay and chest x-ray)</td>
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<td>o Hepatitis B (with hepatitis B surface antigen, surface antibody, and core antibody)</td>
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<td>o Human immunodeficiency virus (HIV; with HIV antibody)</td>
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<td>• Follow hospital protocols for premedication (e.g., methylprednisolone, cetirizine, acetaminophen, diphenhydramine) to reduce infusion-related reactions (e.g., chills, fever, flushing, headache, rash).⁴,¹⁷</td>
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<td>• An initial dose of infliximab 5 mg/kg is given (considered day one of infliximab therapy).² Infusions require a dedicated IV line, a filter (1.2 micron or less), and should be given over at least two hours within three hours of reconstitution.⁴ If well tolerated, the same dose is repeated at two and six weeks.</td>
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<td>o Limited data suggest an accelerated course of infliximab (e.g., &gt;5 mg/kg given at shorter intervals) may be an option for patients with acute severe ulcerative colitis.³ However, randomized trials are needed to compare these dosing schedules.³</td>
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| What is important to know about using cyclosporine rescue therapy?           | • Avoid cyclosporine rescue therapy in patients who have been intolerant of or not responded to thiopurines (e.g., azathioprine, 6-mercaptopurine) as this is what patients are transitioned to for maintenance therapy.13  
  • Cyclosporine has a rapid onset of action, but use may also be limited by side effects (e.g., paresthesias, increased blood pressures, headache, nephrotoxicity, seizures).4,6  
  • Cyclosporine 2 mg/kg/day is usually preferred over higher doses (4 mg/kg/day). Cyclosporine dosed at 2 mg/kg/day provides similar efficacy with a lower risk of cyclosporine-induced encephalopathy compared to doses of 4 mg/kg/day [Evidence Level B-1].1,6  
    o Doses are adjusted to maintain target trough concentrations of about 200 to 250 ng/mL.2,13  
  • Cyclosporine is prepared in glass containers, not polyvinyl chloride (PVC) bags, to prevent diethylhexylphthalate (DEHP) leaching from the PVC into the solution.4  
  • Cyclosporine should be infused slowly (over a minimum of two to six hours) to reduce the risk of adverse effects (e.g., acute nephrotoxicity, flushing, nausea). Cyclosporine is usually given as a continuous infusion, as the IV solution remains stable for up to 24 hours.4,13  
  • For patients who respond to IV cyclosporine, transition to oral cyclosporine (usually double the IV dose, divided twice daily) after about a week.1,2,5,6,13 There are not data to support the use of oral cyclosporine as maintenance therapy. Patients who respond to cyclosporine are transitioned to thiopurines (e.g., azathioprine, 6-mercaptopurine) for maintenance therapy.13 However, oral cyclosporine may be used as a bridge for a few months while the thiopurine kicks in. |
| What is the role of antibiotics in acute severe ulcerative colitis?          | • Antibiotics are associated with an increased risk of *Clostridium difficile* infections in patients with ulcerative colitis.1  
  • Avoid routine use of empiric antibiotics in the management of acute severe ulcerative colitis.1,5,10 Antibiotics (e.g., ciprofloxacin, metronidazole, tobramycin, rifaximin, vancomycin) do not seem to impact response to medical therapy or the need for surgery in acute severe ulcerative colitis.5  
  • Can consider broad-spectrum antibiotics for patients who have:1,5,10,12,13  
    o Worsening symptoms despite maximal medication therapy (e.g., signs of sepsis)  
    o Toxic megacolon (due to risk for microperforation)  
  • In patients with concurrent acute pouchitis (complication of total proctocolectomy), ciprofloxacin 1,000 mg/day (divided twice daily) may be considered.10,11 |
| How should patients be transitioned to maintenance therapy?                 | **Steroids**  
  • If possible, avoid long-term use of *systemic steroids* as maintenance therapy for ulcerative colitis.1  
  • At discharge, provide instructions for patients to slowly taper off prednisone, usually over two to three months.1 One commonly used protocol uses prednisone 40 mg/day for two to four weeks, then tapers the dose by:13  
    o 5 mg per week to a daily dose of 20 mg.  
    o Then further tapers the dose by 2.5 to 5 mg per week, until prednisone is discontinued. |

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<td>Maintenance therapy, continued</td>
<td><strong>Infliximab</strong>&lt;br&gt;• Patients who respond well to infliximab rescue therapy usually receive two additional doses at two and six weeks after the initial dose.²⁴ Infliximab can then be used to maintain remission at a dose of 5 mg/kg every eight weeks.⁴&lt;br&gt;• At discharge, work with the outpatient specialists to schedule follow-up infliximab doses.</td>
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<td><strong>Cyclosporine</strong>&lt;br&gt;• Patients who respond well to cyclosporine rescue therapy are switched to oral cyclosporine (usually double the IV dose, divided twice daily) after about a week.¹²⁵⁶¹³&lt;br&gt;  ○ Doses are adjusted to maintain target trough concentrations of about 200 to 250 ng/mL.²¹³&lt;br&gt;• Overlap oral cyclosporine with a thiopurine (e.g., azathioprine, 6-mercaptopurine) for about two to three months, while tapering off steroids and allowing the thiopurine to kick in.⁶¹³</td>
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Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.
Levels of Evidence
In accordance with our goal of providing Evidence-Based information, we are citing the LEVEL OF EVIDENCE for the clinical recommendations we publish.

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<tr>
<th>Level</th>
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| A     | Good-quality patient-oriented evidence.* | 1. High-quality RCT  
2. SR/Meta-analysis of RCTs with consistent findings  
3. All-or-none study |
| B     | Inconsistent or limited-quality patient-oriented evidence.* | 1. Lower-quality RCT  
2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings  
3. Cohort study  
4. Case control study |
| C     | Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening. |

*Outcomes that matter to patients (e.g., morbidity, mortality, symptom improvement, quality of life).

RCT = randomized controlled trial; SR = systematic review


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References

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