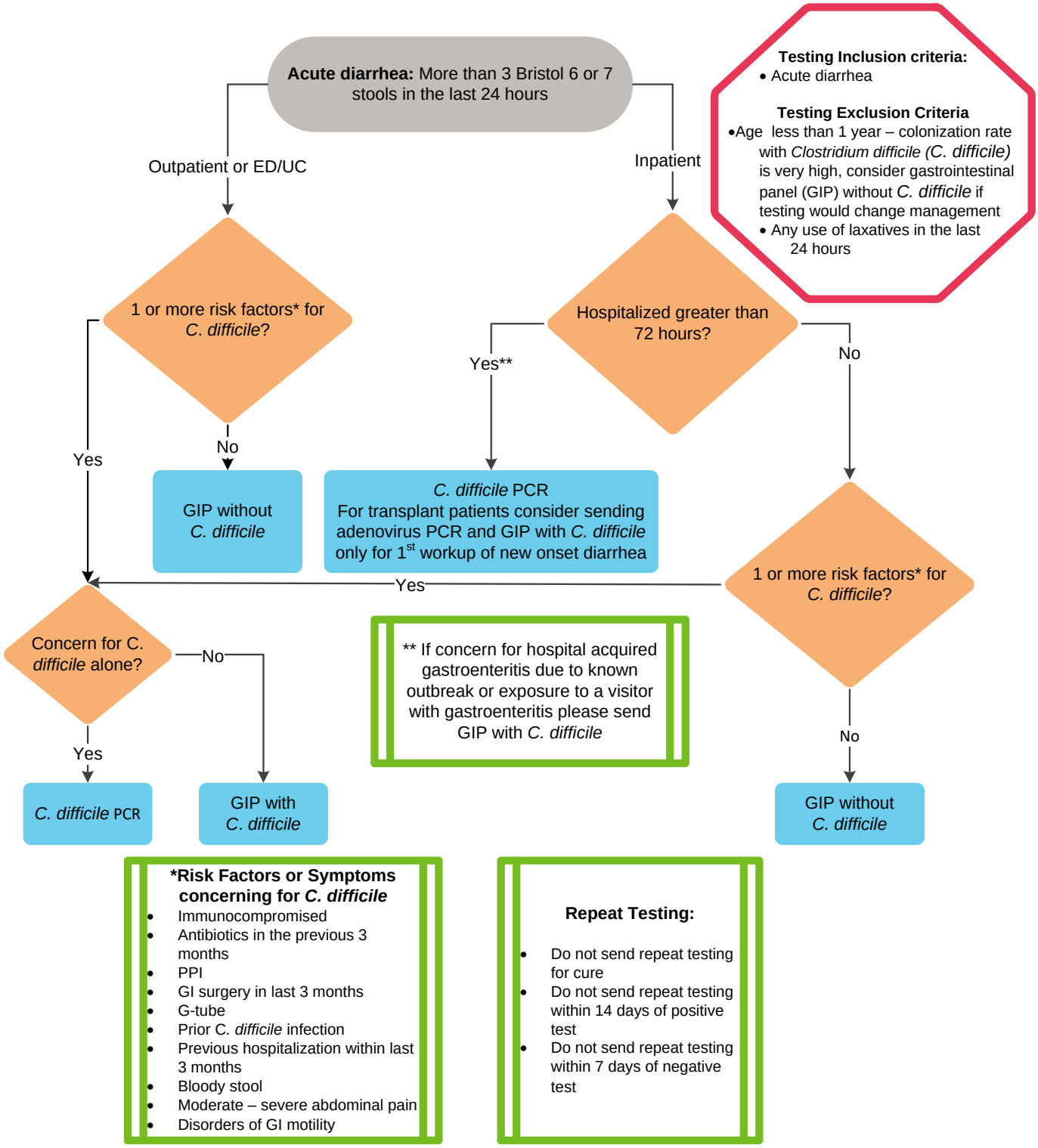
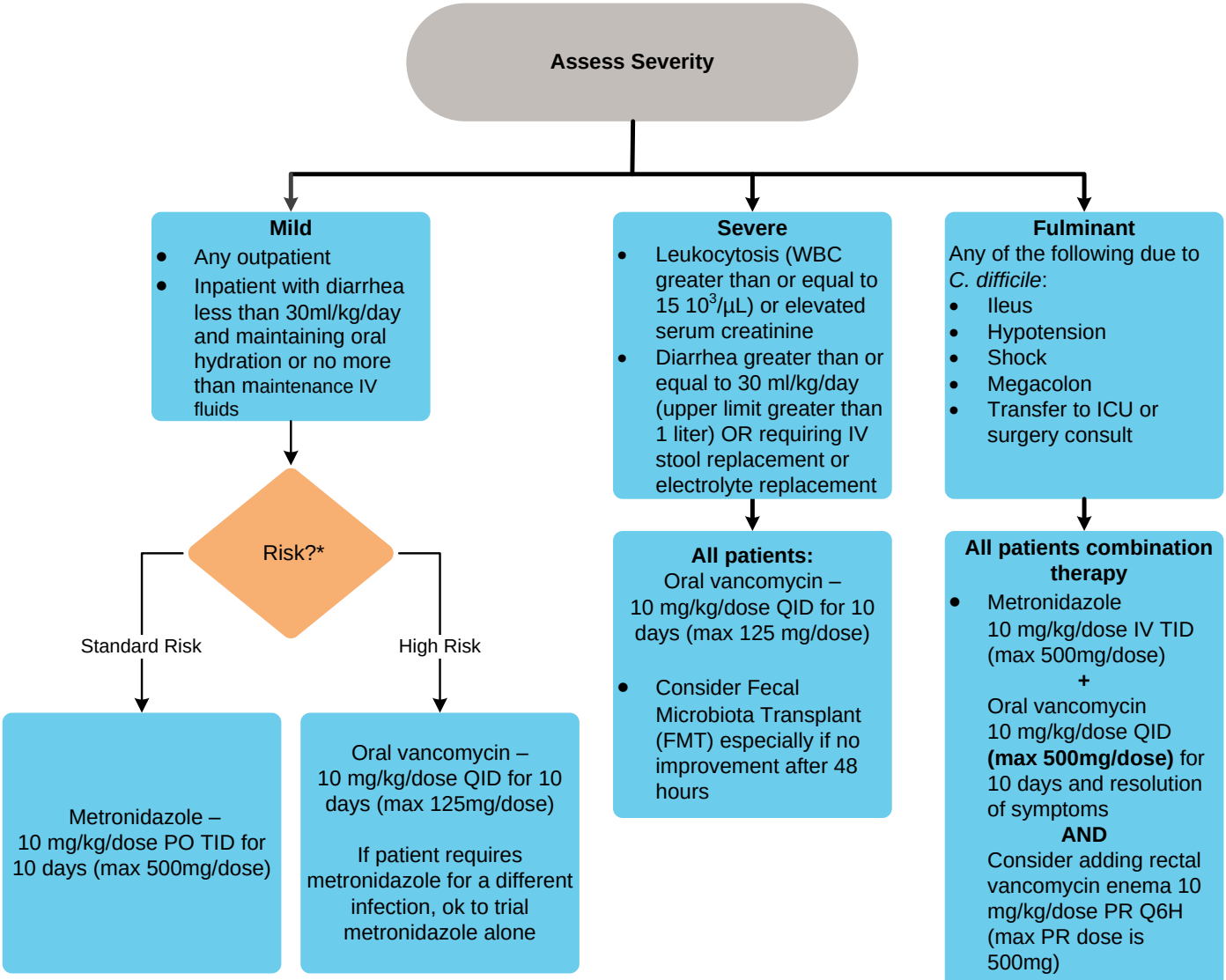
Clostridium Difficile

Testing and Treatment

ALGORITHM 1: TESTING



ALGORITHM 2: TREATMENT OF INITIAL INFECTION



***Risk level definitions**
High Risk Patients:
- Patients with Inflammatory Bowel Disease
- All immunocompromised patients:
  - Chemotherapy (until 3 months after completion), biological therapies and those on chronic steroids (1mg/kg/day for a 2 week period)
  - Bone marrow transplant patients prior to T&B cell reconstitution
  - HIV patients - CD4 less than 15% or less than 200 cells/mm^3
  - All solid organ transplant patients

Standard Risk:
- Any patient not meeting the above criteria for high risk

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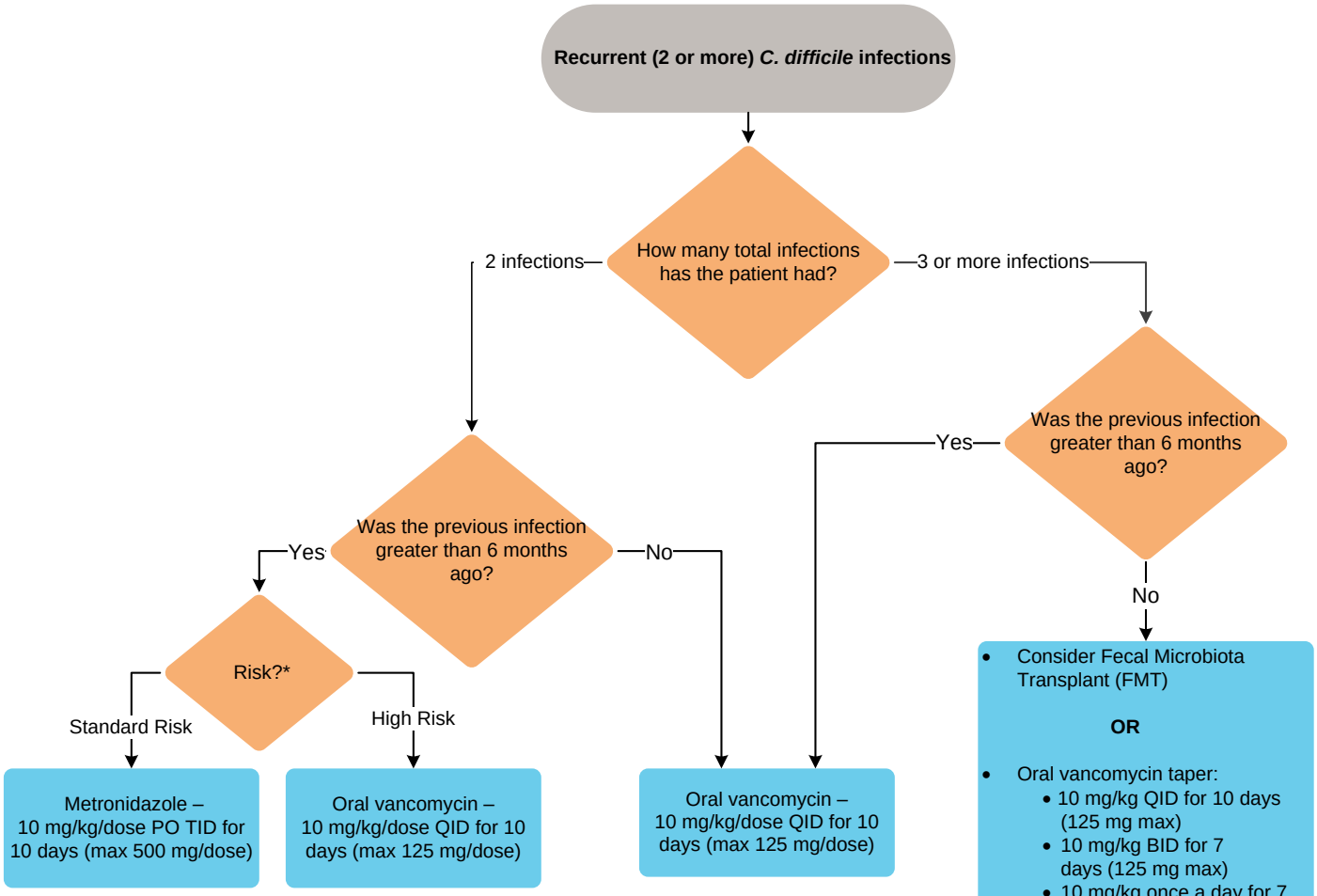
For oral vancomycin recommend liquid formulation vs capsules due to cost. If appropriate have patient fill prescription before discharge.

ALGORITHM 3: TREATMENT OF RECURRENT INFECTION



***Risk Level Definition**
High Risk Patients:

- Patients with Inflammatory Bowel Disease
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Standard Risk:

- Any patient not meeting the above criteria for high risk

!
Fecal Microbiota Transplants (FMT) should be done with caution during periods of neutropenia

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TARGET POPULATION

Inclusion Criteria

- Children over the age of 1 year with acute diarrhea
- Acute diarrhea- more than three Bristol 6 or 7 stools in the last 24 hours (link to Bristol Stool Scale)

Exclusion Criteria

- Age less than 1 year – colonization rate with *Clostridium difficile (C. difficile)* is very high, consider GIP without *C. difficile* if testing would change management
- Any use of laxatives in the last 24 hours

BACKGROUND | DEFINITIONS

- *Clostridium difficile* is an anaerobic, Gram-positive, spore forming, toxin-producing bacillus. The spores are resistant to killing through heat and acid making it difficult to eradicate from hospital environments.
- Symptoms of acute infection are caused by toxin production in the colon.
- Many children are asymptomatic carriers of *C. difficile* making the diagnosis of acute infection challenging.
- Acute infection in children under 1 year is exceedingly rare, but colonization is very common.
- It is the most common cause of hospital acquired diarrhea and is associated with increased mortality, morbidity and hospital length of stay.
- The incidence of acute infection has increased over the past decade.

ABREVIATIONS TABLE

- C. *Difficile*: *Clostridium Difficile*
- GIP: gastrointestinal pathogen panel
- PCR: polymerase chain reaction
- CCBD: Center for Cancer and Blood Disorders
- QID: four times a day
- TID: three times a day
- PO: by mouth
- FMT: fecal microbiota transplant
- PPI: proton pump inhibitor
- CDI: *Clostridium difficile* infection

PREVENTION

- Initiate Contact Precautions at onset of diarrhea.
- For questions regarding duration of isolation, please see the link to the following policies:
  - Discontinuing isolation precautions for non CCBD patients
  - Discontinuing Isolation precautions for CCBD patients
- Good handwashing with soap and water is superior to alcohol based hand sanitizer for removal of *C. difficile* spores from hands.
- Universal gloving is required for all CCBD patient care.
- Bleach wipes should be used in place of standard purple top wipes for all room cleaning.
- All rooms should be terminally cleaned and treated with UV light following discharge or moving rooms.

INITIAL EVALUATION

- Obtain history and perform physical exam
- Evaluate hydration status
- Assess risk factors for *C. difficile* (see below)

History

- Obtain past medical history including previous history of *C. difficile* infection (CDI) and medication use (particular attention to acid suppression, laxatives, antibiotics)
- Obtain pertinent patient symptoms, including typical stooling frequency, stool consistency (see Bristol Stool Scale), duration of change in stool, stool color, presence of blood or mucus in stool, abdominal pain, fever, change in diet, nausea and/or vomiting

Physical exam

- Assess signs of dehydration
- Assess for acute abdomen

Risk factors or Symptoms Concerning for CDI

- Immunocompromised status:

  - Patients on chemotherapies or those within 3 months of completion of chemotherapy
  - Use of biologic therapies
  - Use of chronic steroids (1mg/kg/day for 2 weeks or greater)
  - Bone marrow transplant patients prior to T&B cell reconstitution
  - HIV patients with CD4 less than 15% or less than 200 cells/µL
  - All solid organ transplant patients
- Antibiotic use within the previous 3 months
- PPI use
- GI surgery within the previous 3 months
- Gastrostomy tube
- Prior *C. difficile* infection (CDI)
- Previous hospitalization with in the last 3 months
- Bloody stool
- Moderate-severe abdominal pain

Differential diagnosis

- Medications (laxatives, chemotherapeutics, antibiotics, magnesium)
- Viral gastroenteritis
- Bacterial colitis
- Toddler's diarrhea from excessive juice intake

STOOL TESTING

- Stool diagnostic testing should only be sent if the results will impact your clinical management
- The Gastrointestinal Pathogen Panel (GIP) with *C. difficile* and the *C. difficile* PCR tests will both detect *C. difficile* with similar sensitivity and specificity.
- The C. difficile PCR test is significantly less expensive.
- If suspicion for *C. difficile* is low, send the GIP without *C. difficile* to avoid detecting *C. difficile* carriers who have another cause for their acute diarrhea.
- In outpatients with 1 or more risk factors for *C. difficile* infection, send the *C. difficile* PCR or GIP with C. difficile if there are concerns for other treatable causes of acute diarrhea.
- Inpatients who have been hospitalized for more than 72 hours and have new onset of acute diarrhea should not be tested for organisms other than *C. difficile* unless they have epidemiology risk factors for other pathogens.
- Newly hospitalized patients with one or more risk factors for *C. difficile,* order *C. difficile* PCR or GIP with *C. difficile.*
- Newly hospitalized patients without risk factors for *C. difficile* should have the GIP without *C. difficile* sent.
- Testing for cure should not be sent. Cure should be assessed clinically.
- No repeat testing should be sent within 14 days of a positive test.
- No repeat testing should be sent within 7 days of a negative test.

ANCILLARY LABORATORY STUDIES | IMAGING

Laboratory Testing

- In children with evidence of dehydration a complete blood count and renal function panel or basic metabolic panel should be sent to assess illness severity.

Imaging

- Consider 3-view abdominal X-ray to assess for megacolon in patients with signs/symptoms of fulminant illness or acute abdomen.

CLINICAL MANAGEMENT:

Severity Assessment

Mild Illness

- Any outpatient
- Inpatients with diarrhea less than 30 mL/kg/day AND maintaining oral hydration or requiring no more than maintenance IV fluids.

Severe Illness

- Leukocytosis (WBC ≥ 15 10^3/µL) or elevated serum creatinine for age
- Diarrhea 30 mL/kg/day or greater (upper limit greater than 1 liter) or requiring IV stool or electrolyte replacement

Fulminant Illness

- Any of the following due to *C. difficile:*
  - Ileus
  - Hypotension
  - Shock
  - Megacolon
  - Transfer to ICU or surgery consult

THERAPEUTICS

Treatment of Initial Infection

High Risk Patients - Definition

- Patients with Inflammatory Bowel Disease
- All Immunocompromised patients:
  - Patients on chemotherapies or those within 3 months of completion of chemotherapy
  - Patients on biologic therapies
  - Use of chronic steroids (1 mg/kg/day for 2 weeks or greater)
  - Bone marrow transplant patients prior to T&B cell reconstitution
  - HIV patients with CD4 less than 15% or less than 200 cells/µL
  - All solid organ transplant patients

Mild Disease

- Standard risk patients – metronidazole – 10 mg/kg/dose PO TID for 10 days (max 500 mg/dose)

- High risk patients – oral vancomycin – 10 mg/kg/dose QID for 10 days (max 125 mg/dose)
  - If patient requires metronidazole for a different infection can trial metronidazole alone

Severe Disease

- Oral vancomycin – 10 mg/kg/dose QID for 10 days (max 125 mg/dose)
- Consider Fecal Microbiota Transplant (FMT), especially if no improvement after 48 hours

Fulminant Disease

- All patients – metronidazole 10 mg/kg/dose IV TID (max dose 500 mg/dose) + oral Vancomycin 10 mg/kg/dose (max dose 500 mg/dose) for 10 days
- Consider addition of rectal vancomycin enema 10 mg/kg Q6H (max dose 500 mg/dose)
- Consider consulting GI or ID
- Consider Fecal Microbiota Transplant (FMT), especially if no improvement after 48 hours
- Consult Surgery for consideration of bowel resection or diversion

Treatment of Recurrent Infection

Two Total Infections

Previous Infection was more than 6 months ago

- Standard risk patients - repeat treatment with metronidazole (10 mg/kg/dose PO TID (max 500 mg/dose) for 10 days)
- High risk patients – oral vancomycin (10 mg/kg/dose QID (max 125 mg/dose) for 10 days)

Previous Infection was less than 6 months ago

- Considered failure of initial therapy, all patients should be treated with oral vancomycin (10 mg/kg/dose QID (max 125 mg/dose) for 10 days)

Three or More Total Infections

Most Recent Infection was More than 6 Months ago:

- Oral vancomycin (10 mg/kg/dose QID (max 125 mg/dose) for 10 days)

Most Recent Infection was Less than 6 Months ago:

- Consider Fecal Microbiota Transplant

OR

- Vancomycin treatment plus taper
  - 10 mg/kg/dose PO QID (max dose 125 mg) for 10 days
  - 10 mg/kg/dose PO BID (max dose 125 mg) for 7 days
  - 10 mg/kg/dose PO daily (max dose 125 mg) for 7 days
  - 10 mg/kg/dose PO every 2-3 days (max dose 125 mg) for 2-8 weeks

AND

- Strongly consider consultation with Gastroenterology or Infectious Disease if not already involved

Fecal Microbiota Transplantation

Fecal Microbiota Transplant (FMT) is an infusion of washed fecal material from healthy donors into the GI tract of a patient with recurrent *C. difficile* infection. This infusion can be administered via frozen capsules, nasogastric or transpyloric tube, colonoscopy or rectal enema. At Children's Hospital Colorado, we utilize nasogastric tubes most frequently for administration. The stool bank OpenBiome is the source of our fecal material. Donors undergo extensive screening and samples are tested for a number of infections prior to preparation into donor samples. Preliminary data for the use of FMT in immunocompromised adults suggests that FMT is safe and efficacious. The data in immunocompromised children is emerging. Caution should be used with the use of FMT in neutropenic patients.

FMT should be done with caution during periods of neutropenia

DISPOSITION

Discharge Home

- Well hydrated
- Tolerating oral medications
- For oral vancomycin recommend liquid formulation vs capsules due to cost. Have patient fill prescription before discharge.

Admit to Inpatient

- Requiring IV fluid supplementation or electrolyte repletion

Consider ICU Admission

- For fulminant disease including patients with acute abdomen or megacolon
- Consult surgery for patients with fulminant disease

PARENT | CAREGIVER EDUCATION | FOLLOW UP

- Stools should improve within 1 week of initiation of antibiotics
- Families should return for signs of dehydration
- Patients should remain on contact precautions until antibiotic course is complete AND diarrhea has resolved – families should notify providers of need for precautions at follow up appointments
- No need to follow up with PCP if symptoms resolve

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Clinical Pathways and Measures Committee – November 13, 2018
Pharmacy & Therapeutics Committee – February 7, 2019

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LAST DATE OF REVIEW OR REVISION	February 7, 2019
APPROVED BY	 Lalit Bajaj, MD, MPH Medical Director, Clinical Effectiveness

REVIEW | REVISION SCHEDULE

Scheduled for full review on date here February 7, 2023

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