

# Clinical Pathways

## Fever in Patients with Intestinal Failure and Central Venous Catheter (CVC)

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# What is a Clinical Pathway?

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An evidence-based guideline that decreases unnecessary variation and helps promote safe, effective, and consistent patient care.

# Objectives of the Pathway

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- Ensure effective and efficient treatment for febrile intestinal failure patients with indwelling catheters
- Provide standard of care practices among these patients upon presentation to the Emergency Department
- Decrease time to administration of antibiotics
- Identify potential areas of process improvement

# Why is the Pathway Necessary?

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Patients with Intestinal Failure (IF) often require central venous catheter (CVCs) for extended periods of time used for administration of parenteral nutrition (PN), which is required to maintain adequate growth and hydration.

This puts them at a risk of recurrent central-line associated bloodstream infections (CLABSIs), with rates being higher than other pediatric patients with central lines.

# Background

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**Bacterial translocation** in patients with short bowel syndrome (SBS) is thought to contribute to the risk for recurrent CVC infection.

Septic complications, related to catheter-related bacteremia and liver failure, are the leading causes of morbidity and mortality in these PN-dependent patients.

# Background: Frequency



In 2018, Szydłowski *et. al*/performed a five-year retrospective study<sup>a</sup> which showed **69% positivity**, with 60% being **enteral organisms**.

- *Other pediatric populations with CLIs mostly have gram+ organisms.*
- *More than double of Heme-Onc patients with BSIs (20-30%).*

Drews *et. al*'s two-year retrospective study<sup>b</sup> in 2009 showed **62% positivity**.

| Central blood culture pathogens (N = 501)                  | N  | %    |
|--|----|------|
| *denotes Enteric organisms                                 |    |      |
| * <i>Klebsiella</i> species                                | 99 | 19.8 |
| Coagulase-negative <i>Staphylococcus</i>                   | 89 | 17.8 |
| * <i>Escherichia coli</i>                                  | 51 | 10.2 |
| * <i>Enterococcus faecalis</i>                             | 46 | 9.2  |
| <i>Candida</i> species                                     | 41 | 8.2  |
| Methicillin-sensitive <i>Staphylococcus aureus</i>         | 37 | 7.4  |
| * <i>Enterobacter</i> species                              | 35 | 7.0  |
| Methicillin-resistant <i>Staphylococcus aureus</i>         | 12 | 2.4  |
| *Vancomycin-resistant <i>Enterococci</i>                   | 11 | 2.2  |
| Alpha-hemolytic <i>Streptococcus</i>                       | 10 | 2.0  |
| * <i>Bacillus</i> species non-anthraxis                    | 10 | 2.0  |
| * <i>Lactobacillus</i> species                             | 9  | 1.8  |
| * <i>Citrobacter</i> species                               | 9  | 1.8  |
| * <i>Serratia marcescens</i>                               | 8  | 1.6  |
| * <i>Acinetobacter</i> species                             | 8  | 1.6  |
| * <i>Proteus mirabilis</i>                                 | 6  | 1.2  |
| <i>Streptococcus pneumoniae</i>                            | 4  | 0.8  |
| <i>Streptococcus</i> , Non-hemolytic                       | 3  | 0.6  |
| * <i>Leuconostoc</i> species                               | 3  | 0.6  |
| * <i>Pseudomonas</i>                                       | 2  | 0.6  |
| Group B <i>Streptococcus</i>                               | 2  | 0.6  |
| * <i>Aeromonas hydrophila</i>                              | 1  | 0.2  |
| *Diphtheroids  | 1  | 0.2  |
| * <i>Kluyvera ascorbata</i>                                | 1  | 0.2  |
| <i>Neisseria</i> species not <i>Neisseria meningitidis</i> | 1  | 0.2  |
| * <i>Pantoea (Enterobacter) agglomerans</i>                | 1  | 0.2  |
| <i>Stenotrophomonas (Xanthomonas) maltophilia</i>          | 1  | 0.2  |

a Children's Hospital of Pittsburgh  
 b Children's Medical Center of Dallas

# National Recommendations

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## Blood Cultures

- Obtain culture from catheter tip
- Obtain both peripheral and central cultures

## Treatment

- **Vancomycin** is recommended for institutions with high MRSA rate
- Empirical coverage for **gram-negative bacilli** based on local resistance pattern

# Management: Timely Intervention

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There is a research-proven association between time to antibiotics (TTA) to survival in patients with sepsis or septic shock.

- A study<sup>d</sup> published by Gaieski *et al.* in 2010 showed improved survival among patients who had TTA <1hr
- In 2006, Kumar *et al.* also showed that each hour's delay to TTA was associated with about 7.6% increase in mortality



# Management: Timely Intervention

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Therefore, there are many efforts across different institutions to reduce the time to antibiotics (TTA) for these patients.

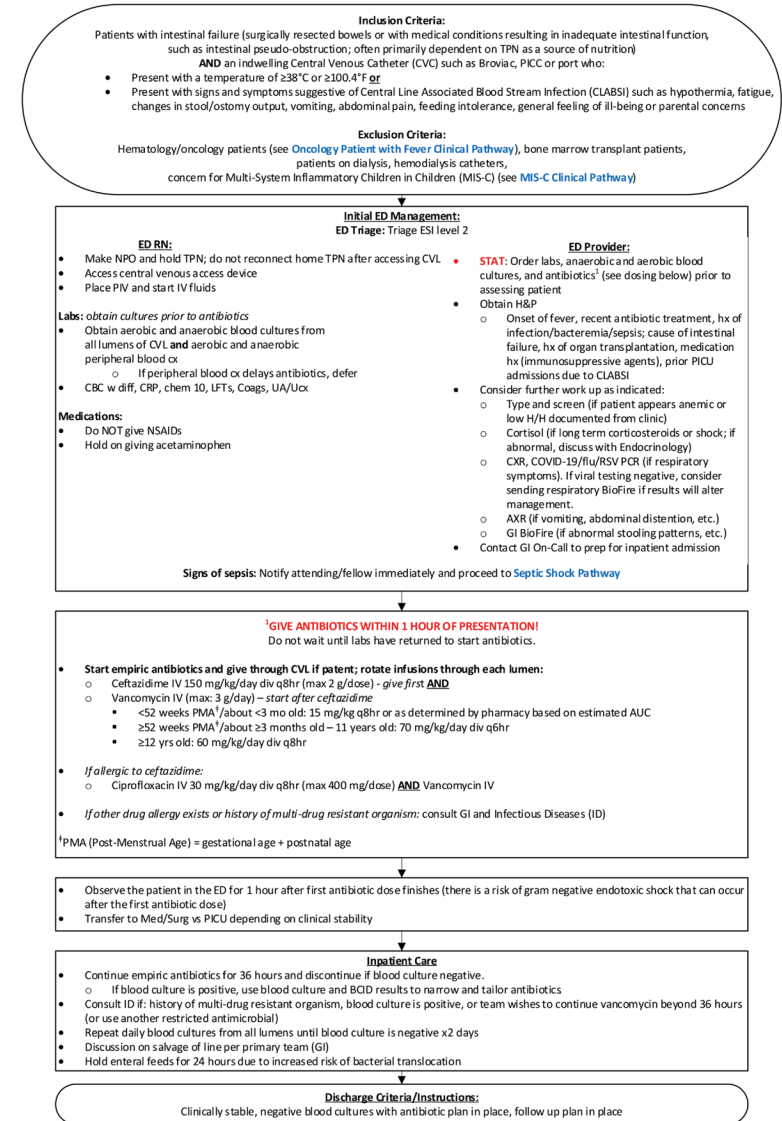
- Hudgins *et al.* (2017) study<sup>c</sup> found a reduction to TTA with the initiation of a QI project for increased education and order set initiation
  - Mean TTA decreased from 112 to 39 minutes
  - ED LOS decreased from 286 to 247 minutes

This is the Intestinal Failure with Fever Clinical Pathway.

We will be reviewing each component in the following slides.

**CLINICAL PATHWAY:**  
Fever in a Patient with Intestinal Failure and Central Venous Catheter (CVC)

THIS PATHWAY  
SERVES AS A GUIDE  
AND DOES NOT  
REPLACE CLINICAL  
JUDGMENT.



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## Inclusion Criteria:

This pathway is specifically for patients with intestinal failure who also have an indwelling CVC (Broviac, PICC, or port) and presents with:

- fever, **or**
- signs suggestive of a CLABSI (Central Line Associated Blood Stream Infection).

## Exclusion Criteria:

This pathway should exclude any oncology patient (who should instead follow the Oncology Patient with Fever Clinical Pathway), bone marrow transplant patients, patients on dialysis or have hemodialysis catheters. These patients require separate work up and management plans.

### CLINICAL PATHWAY:

## Fever in a Patient with Intestinal Failure and Central Venous Catheter (CVC)

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.

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Patients with intestinal failure (surgically resected bowels or with medical conditions resulting in inadequate intestinal function, such as intestinal pseudo-obstruction; often primarily dependent on TPN as a source of nutrition)

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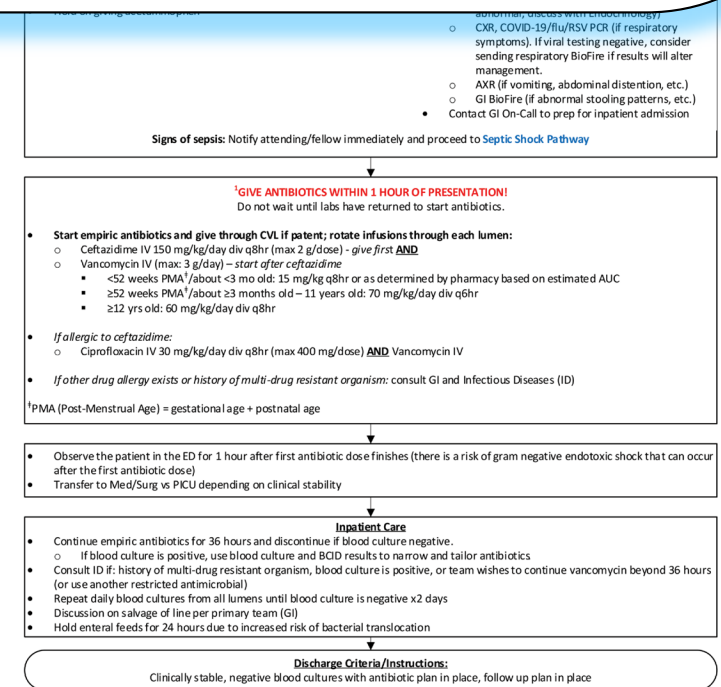
Patients with intestinal failure (surgically resected bowels or with medical conditions resulting in inadequate intestinal function, such as intestinal pseudo-obstruction; often primarily dependent on TPN as a source of nutrition)

**AND** an indwelling Central Venous Catheter (CVC) such as Broviac, PICC or port who:

- Present with a temperature of  $\geq 38^{\circ}\text{C}$  or  $\geq 100.4^{\circ}\text{F}$  **or**
- Present with signs and symptoms suggestive of Central Line Associated Blood Stream Infection (CLABSI) such as hypothermia, fatigue, changes in stool/ostomy output, vomiting, abdominal pain, feeding intolerance, general feeling of ill-being or parental concerns

### **Exclusion Criteria:**

Hematology/oncology patients (see [Oncology Patient with Fever Clinical Pathway](#)), bone marrow transplant patients, patients on dialysis, hemodialysis catheters, concern for Multi-System Inflammatory Children in Children (MIS-C) (see [MIS-C Clinical Pathway](#))



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**If the patient meets the inclusion criteria:**

- They will first be triaged and cared by the nursing team.
- The MD/Provider will initiate the pathway's order set, which will include orders for labs and antibiotics.
- There will then be simultaneous assessments done by the provider, and lab collection/antibiotics preparation and administration by the RN.
- The patient will then be treated and observed.

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**AND** an indwelling Central Venous Catheter (CVC) such as Broviac, PICC or port who:

**Initial ED Management:**  
**ED Triage:** Triage ESI level 2

**ED RN:**

- Make NPO and hold TPN; do not reconnect home TPN after accessing CVL
- Access central venous access device
- Place PIV and start IV fluids

**Labs:** *obtain cultures prior to antibiotics*

- Obtain aerobic and anaerobic blood cultures from all lumens of CVL **and** aerobic and anaerobic peripheral blood cx
  - If peripheral blood cx delays antibiotics, defer
- CBC w diff, CRP, chem 10, LFTs, Coags, UA/Ucx

**Medications:**

- Do NOT give NSAIDs
- Hold on giving acetaminophen

**ED Provider:**

- **STAT:** Order labs, anaerobic and aerobic blood cultures, and antibiotics<sup>1</sup> (see dosing below) prior to assessing patient
- Obtain H&P
  - Onset of fever, recent antibiotic treatment, hx of infection/bacteremia/sepsis; cause of intestinal failure, hx of organ transplantation, medication hx (immunosuppressive agents), prior PICU admissions due to CLABSI
- Consider further work up as indicated:
  - Type and screen (if patient appears anemic or low H/H documented from clinic)
  - Cortisol (if long term corticosteroids or shock; if abnormal, discuss with Endocrinology)
  - CXR, COVID-19/flu/RSV PCR (if respiratory symptoms). If viral testing negative, consider sending respiratory BioFire if results will alter management.
  - AXR (if vomiting, abdominal distention, etc.)
  - GI BioFire (if abnormal stooling patterns, etc.)
- Contact GI On-Call to prep for inpatient admission

**Signs of sepsis:** Notify attending/fellow immediately and proceed to [Septic Shock Pathway](#)

**Inpatient Care**

- Continue empiric antibiotics for 36 hours and discontinue if blood culture negative.
  - If blood culture is positive, use blood culture and BCID results to narrow and tailor antibiotics
- Consult ID if: history of multi-drug resistant organism, blood culture is positive, or team wishes to continue vancomycin beyond 36 hours (or use another restricted antimicrobial)
- Repeat daily blood cultures from all lumens until blood culture is negative x2 days
- Discussion on salvage of line per primary team (GI)
- Hold enteral feeds for 24 hours due to increased risk of bacterial translocation

**Discharge Criteria/Instructions:**

Clinically stable, negative blood cultures with antibiotic plan in place, follow up plan in place

**CLINICAL PATHWAY:**  
Fever in a Patient with Intestinal Failure and Central Venous Catheter (CVC)

# Triage and Nursing

- Triage the patient and place in an exam room *as soon as possible*
- Obtain vitals
- Notify the ED provider immediately if the patient:
  - Has abnormal vitals (e.g., fever, tachycardia, widened pulse pressure, hypotension)
  - Appears ill
  - Has altered mental status or is lethargic
  - Or, if the patient's parent has significant concerns
- Make NPO and hold TPN; be sure not to reconnect the home TPN after accessing the CVL

**Labs:**

- Before giving antibiotics, obtain cultures (both aerobic and anaerobic cultures) and labs. Label the specimens accordingly.
- LFTs: gram negative sepsis is a risk factor for cholestasis

**Medications:**

- HOLD on giving acetaminophen until labs obtained and do *not* give NSAIDS

**Inclusion Criteria:**  
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**ED RN:**

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  - Place PIV and start IV fluids
- ★ **Labs:** *obtain cultures prior to antibiotics*
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    - If peripheral blood cx delays antibiotics, defer
  - CBC w diff, CRP, chem 10, LFTs, Coags, UA/Ucx
- Medications:**
  - Do NOT give NSAIDs
  - Hold on giving acetaminophen

**ED Provider:**

- **STAT:** Order labs, anaerobic and aerobic blood cultures, and antibiotics<sup>1</sup> (see dosing below) prior to assessing patient
- Obtain H&P
  - Onset of fever, recent antibiotic treatment, hx of infection/bacteremia/sepsis; cause of intestinal failure, hx of organ transplantation, medication hx (immunosuppressive agents), prior PICU admissions due to CLABSI
- Consider further work up as indicated:
  - Type and screen (if patient appears anemic or low H/H documented from clinic)
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- Consult ID if: history of multi-drug resistant organism, blood culture is positive, or team wishes to continue vancomycin beyond 36 hours (or use another restricted antimicrobial)
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**Discharge Criteria/Instructions:**  
Clinically stable, negative blood cultures with antibiotic plan in place, follow up plan in place



## Provider Role:

- The provider will order cultures, labs, and antibiotics *prior to* assessing the patient.
- The provider will then assess the patient. If the patient is in septic shock, the provider should proceed to the Septic Shock Clinical Pathway.
- The H&P should include specific questions listed here
- Additional tests can be considered, as necessary
- The provider will then call the on-call GI attending and prepare for inpatient admission

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## Antibiotics:

- The goal is to give antibiotics *within 1 hour* of initial presentation.
- Give antibiotics through CVL if patent, rotating through each lumen.
- Empiric antibiotics include:
  - Ceftazidime (give first), AND
  - Vancomycin (give second)
- If there is an allergy to ceftazidime:
  - Use ciprofloxacin (in place of ceftazidime) AND vancomycin
- If there are additional/other drug allergies, consult GI and Infectious Diseases for further management

### CLINICAL PATHWAY:

### Fever in a Patient with Intestinal Failure and Central Venous Catheter (CVC)

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### **<sup>1</sup>GIVE ANTIBIOTICS WITHIN 1 HOUR OF PRESENTATION!**

Do not wait until labs have returned to start antibiotics.

- **Start empiric antibiotics and give through CVL if patent; rotate infusions through each lumen:**
  - Ceftazidime IV 150 mg/kg/day div q8hr (max 2 g/dose) - **give first AND**
  - Vancomycin IV (max: 3 g/day) – **start after ceftazidime**
    - <52 weeks PMA<sup>†</sup>/about <3 mo old: 15 mg/kg q8hr or as determined by pharmacy based on estimated AUC
    - $\geq 52$  weeks PMA<sup>†</sup>/about  $\geq 3$  months old – 11 years old: 70 mg/kg/day div q6hr
    - $\geq 12$  yrs old: 60 mg/kg/day div q8hr
- **If allergic to ceftazidime:**
  - Ciprofloxacin IV 30 mg/kg/day div q8hr (max 400 mg/dose) **AND** Vancomycin IV
- **If other drug allergy exists or history of multi-drug resistant organism:** consult GI and Infectious Diseases (ID)

<sup>†</sup>PMA (Post-Menstrual Age) = gestational age + postnatal age

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- Observe the patient in the ED for 1 hour after first antibiotic dose finishes (there is a risk of gram negative endotoxemic shock that can occur after the first antibiotic dose)
- Transfer to Med/Surg vs PICU depending on clinical stability

#### Inpatient Care

- Continue empiric antibiotics for 36 hours and discontinue if blood culture negative.
  - If blood culture is positive, use blood culture and BCID results to narrow and tailor antibiotics
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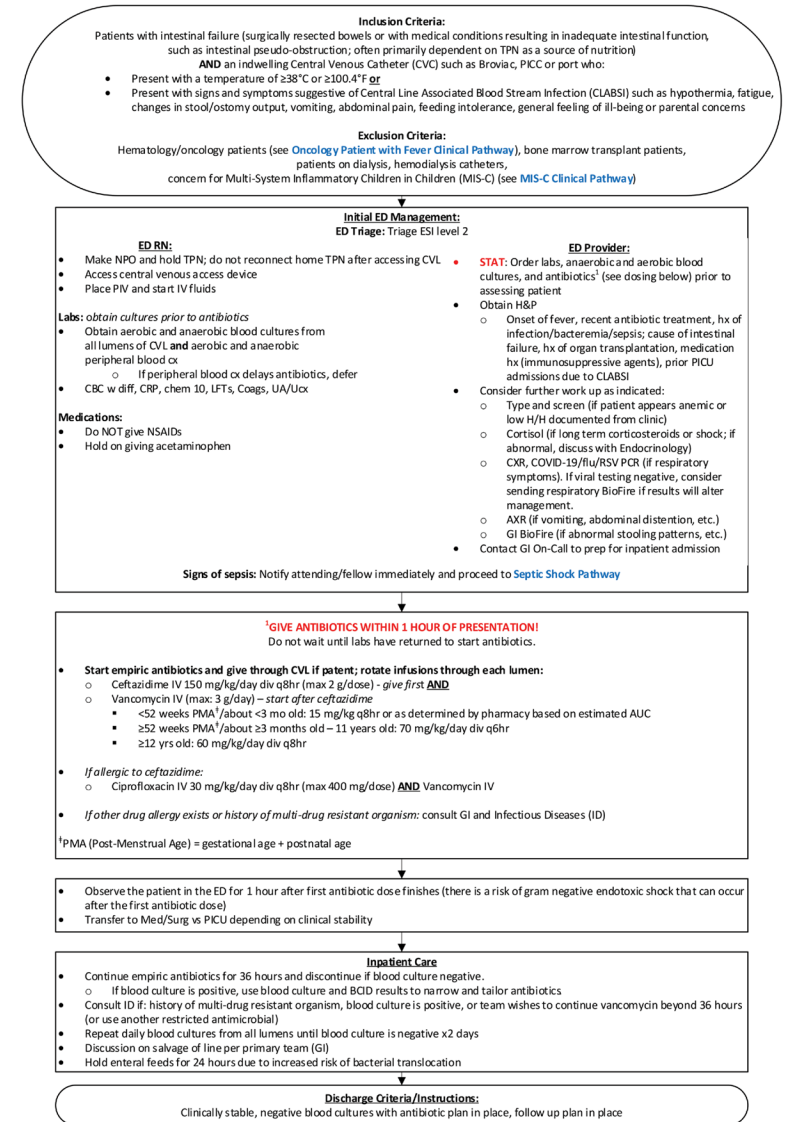
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## Additional Interventions:

- Acetaminophen:
  - If there is evidence of liver dysfunction, consult with the on-call GI provider prior to administering
  - Acetaminophen can be given for temperatures above 38°C (101°F) or pain if:
    - the patient has no evidence of liver dysfunction (or cleared by GI to give)
    - has not yet received acetaminophen, or
    - it has been 6 hours since the last dose
  - Dose: give 15 mg/kg PO. Do not administer it PR.

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## Observation and Transfer of Care:

### Observation:

- Observe the patient in the ED for 1 hour after the first antibiotic dose *finishes*
  - Patients with intestinal failure and CVCs are at risk of gram negative endotoxic shock, which usually occurs *after* the first antibiotic dose

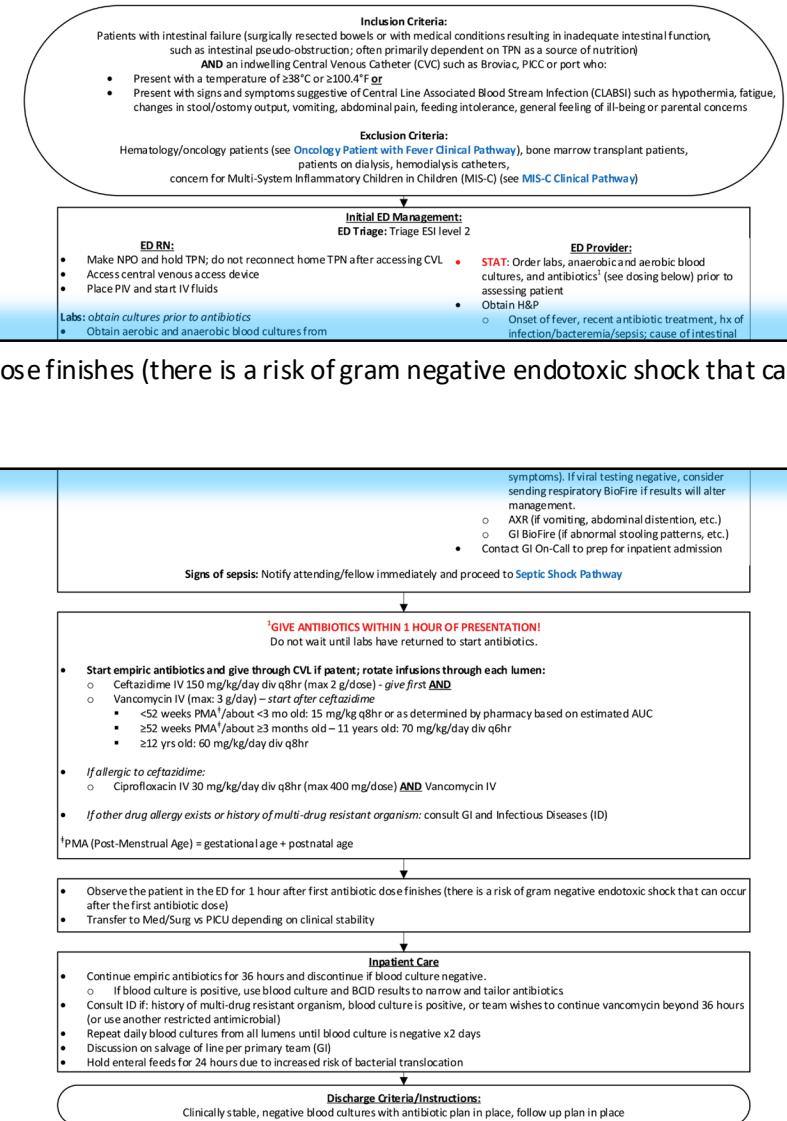
### Transfer:

- Transfer the patient to the med/surg floors or the PICU after clinical assessment and consultations with GI and/or PICU teams

- Observe the patient in the ED for 1 hour after first antibiotic dose finishes (there is a risk of gram negative endotoxic shock that can occur after the first antibiotic dose)
- Transfer to Med/Surg vs PICU depending on clinical stability

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**CLINICAL PATHWAY:**  
**Fever in a Patient with Intestinal Failure and Central Venous Catheter (CVC)**

**Inpatient Care**

- Note that enteral feeds should be HELD for 24 hours!
- Empiric antibiotics should continue until cultures from all lumens are negative for 36 hours.
- If the blood culture is positive, utilize sensitivities and BCID results to tailor antibiotics.
- Blood cultures should be repeated until cultures are negative for 2 days.
- Considerations for consulting ID are listed here.
- Discussions on salvaging the line is per the primary team.



**Inpatient Care**

- Continue empiric antibiotics for 36 hours and discontinue if blood culture negative.
  - If blood culture is positive, use blood culture and BCID results to narrow and tailor antibiotics.
- Consult ID if: history of multi-drug resistant organism, blood culture is positive, or team wishes to continue vancomycin beyond 36 hours (or use another restricted antimicrobial)
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**Initial ED Management:**  
 ED Triage: Triage ESI Level 2

**ED RN:**  
 • Make NPO and hold TPN; do not reconnect home TPN after accessing CVL  
 • Access central venous access device

**ED Provider:**  
 • STAT: Order labs, anaerobic and aerobic blood cultures, and catheter tip cultures (if indicated)

**Signs of sepsis:** Notify attending/fellow immediately and proceed to [Septic Shock Pathway](#)

• Contact GI On-Call to prep for inpatient admission

**<sup>1</sup>GIVE ANTIBIOTICS WITHIN 1 HOUR OF PRESENTATION!**  
 Do not wait until labs have returned to start antibiotics.

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    - $\geq 12$  yrs old: 60 mg/kg/day div q8hr
- **If allergic to ceftazidime:**
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<sup>1</sup>PMA (Post-Menstrual Age) = gestational age + postnatal age

- Observe the patient in the ED for 1 hour after first antibiotic dose finishes (there is a risk of gram negative endotoxin shock that can occur after the first antibiotic dose)
- Transfer to Med/Surg vs PICU depending on clinical stability

**Inpatient Care**

- Continue empiric antibiotics for 36 hours and discontinue if blood culture negative.
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**Discharge Criteria/Instructions:**  
 Clinically stable, negative blood cultures with antibiotic plan in place, follow up plan in place



**CLINICAL PATHWAY:**  
**Fever in a Patient with Intestinal Failure and Central Venous Catheter (CVC)**

**Discharge Criteria:**

- Discharge criteria includes clinical stability, negative blood cultures with an antibiotic plan in place, and adequate follow up in place after discharge.

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- Present with signs and symptoms suggestive of Central Line Associated Blood Stream Infection (CLABSI) such as hypothermia, fatigue, changes in stool/ostomy output, vomiting, abdominal pain, feeding intolerance, general feeling of ill-being or parental concerns

**Exclusion Criteria:**  
Hematology/oncology patients (see [Oncology Patient with Fever Clinical Pathway](#)), bone marrow transplant patients, patients on dialysis, hemodialysis catheters, concern for Multi-System Inflammatory Children in Children (MIS-C) (see [MIS-C Clinical Pathway](#))

**Initial ED Management:**  
ED Triage: Triage ESI Level 2

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|--|--|
| <p><b>ED RN:</b></p> <ul style="list-style-type: none"> <li>Make NPO and hold TPN; do not reconnect home TPN after accessing CVL</li> <li>Access central venous access device</li> <li>Place PN and start IV fluids</li> </ul> <p><b>Labs:</b> obtain cultures prior to antibiotics</p> <ul style="list-style-type: none"> <li>Obtain aerobic and anaerobic blood cultures from all lumens of CVL and aerobic and anaerobic peripheral blood cx                             <ul style="list-style-type: none"> <li>If peripheral blood cx delays antibiotics, defer</li> </ul> </li> </ul> | <p><b>ED Provider:</b></p> <p><b>STAT:</b> Order labs, anaerobic and aerobic blood cultures, and antibiotics<sup>1</sup> (see dosing below) prior to assessing patient</p> <ul style="list-style-type: none"> <li>Obtain H&amp;P                             <ul style="list-style-type: none"> <li>Onset of fever, recent antibiotic treatment, hx of infection/bacteremia/sepsis, cause of intestinal failure, hx of organ transplantation, medication hx (immunosuppressive agents), prior PICU admissions due to CLABSI</li> </ul> </li> </ul> |
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**Discharge Criteria/Instructions:**  
Clinically stable, negative blood cultures with antibiotic plan in place, follow up plan in place

**Signs of sepsis:** Notify attending/fellow immediately and proceed to [Septic Shock Pathway](#)

- symptoms), if vital testing negative, consider sending respiratory BioFire if results will alter management.
- AXR (if vomiting, abdominal distention, etc.)
- GI BioFire (if abnormal stooling patterns, etc.)
- Contact GI On-Call to prep for inpatient admission

**<sup>1</sup>GIVE ANTIBIOTICS WITHIN 1 HOUR OF PRESENTATION!**  
Do not wait until labs have returned to start antibiotics.

- Start empiric antibiotics and give through CVL if patent; rotate infusions through each lumen:**
  - Ceftazidime IV 150 mg/kg/day div q8hr (max 2 g/dose) - give first **AND**
  - Vancomycin IV (max: 3 g/day) - start after ceftazidime
    - <52 weeks PMA<sup>1</sup>/about <3 mo old: 15 mg/kg q8hr or as determined by pharmacy based on estimated AUC
    - $\geq 52$  weeks PMA<sup>1</sup>/about  $\geq 3$  months old - 11 years old: 70 mg/kg/day div q6hr
    - $\geq 12$  yrs old: 60 mg/kg/day div q8hr
- If allergic to ceftazidime:
  - Ciprofloxacin IV 30 mg/kg/day div q8hr (max 400 mg/dose) **AND** Vancomycin IV
- If other drug allergy exists or history of multi-drug resistant organism: consult GI and Infectious Diseases (ID)

<sup>1</sup>PMA (Post-Menstrual Age) = gestational age + postnatal age

- Observe the patient in the ED for 1 hour after first antibiotic dose finishes (there is a risk of gram negative endotoxin shock that can occur after the first antibiotic dose)
- Transfer to Med/Surg vs PICU depending on clinical stability

**Inpatient Care**

- Continue empiric antibiotics for 36 hours and discontinue if blood culture negative.
  - If blood culture is positive, use blood culture and BCID results to narrow and tailor antibiotics
- Consult ID if: history of multi-drug resistant organism, blood culture is positive, or team wishes to continue vancomycin beyond 36 hours (or use another restricted antimicrobial)
- Repeat daily blood cultures from all lumens until blood culture is negative x2 days
- Discussion on salvage of line per primary team (GI)
- Hold enteral feeds for 24 hours due to increased risk of bacterial translocation

**Discharge Criteria/Instructions:**  
Clinically stable, negative blood cultures with antibiotic plan in place, follow up plan in place



# Quality Metrics

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- % patients with pathway order set usage
- Time from ED arrival to antibiotic order
- Time from antibiotic order to administration
- Time from ED arrival to antibiotic administration
- ALOS (ED, minutes)
- ALOS (IP/OBS days)

# Pathway Contacts

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# Thank You!



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## About Connecticut Children's Pathways Program

Clinical pathways guide the management of patients to optimize consistent use of evidence-based practice. Clinical pathways have been shown to improve guideline adherence and quality outcomes, while decreasing length of stay and cost. Here at Connecticut Children's, our Clinical Pathways Program aims to deliver evidence-based, high value care to the greatest number of children in a diversity of patient settings.

These pathways serve as a guide for providers and do not replace clinical judgment.