Published in final edited form as:

Pediatr Emerg Care. 2017 December ; 33(12): e140–e145. doi:10.1097/PEC.0000000000000812.

Bloodstream Infections in Patients with Intestinal Failure Presenting to a Pediatric Emergency Department with Fever and a Central Line

Ellen G. Szydlowski, MD¹, Jeffrey A. Rudolph, MD², Melissa A. Vitale, MD³, and Noel S. Zuckerbraun, MD, MPH³

¹Division of Pediatric Emergency Medicine, The Children's Hospital of Philadelphia, Philadelphia, PA

²Division of Pediatric Gastroenterology, Children's Hospital of Pittsburgh, Pittsburgh, PA

³Division of Pediatric Emergency Medicine, Children's Hospital of Pittsburgh, Pittsburgh, PA

Abstract

Objective—Previous small studies have found a high occurrence of bloodstream infections (BSIs) in patients with Intestinal Failure, and these rates are higher than reported rates in other pediatric populations with central lines. The primary study objective was to describe the occurrence of BSIs in patients with Intestinal Failure who present to the Pediatric Emergency Department (ED) with fever.

Methods—This 5 year retrospective chart review included febrile patients with Intestinal Failure and central lines who presented to the Children's Hospital of Pittsburgh ED between 2006 and 2011. Each febrile episode was analyzed at the visit level.

Results—During the study, 72 patients with 519 febrile episodes were identified. Central blood cultures were obtained in 93% of episodes (480/519) and 69% were positive (330/480). Of all BSIs, 38% (124/330) were polymicrobial, 32% (105/330) were a single gram-positive organism, 25% (84/330) were a single gram-negative organism and 5% (17/330) were a single fungal organism. Of the bacterial pathogens, 48% were gram-negative (223/460). Overall, 60% were enteric organisms.

Conclusions—Pediatric patients with Intestinal Failure and central lines have a high occurrence of BSIs with 69% of cultures positive in this study of ED febrile episodes. In contrast to reports in other populations with central lines, BSI occurrence in patients with Intestinal Failure and fever is higher and larger proportions are gram-negative and enteric organisms. For these patients, we

Corresponding author: Ellen Szydlowski, 3501 Civic Center Boulevard, Division of Emergency Medicine, Philadelphia, PA 19104, Fax: (215) 590-4454, Phone: 215-590-4410, szydlowske@email.chop.edu.

Contributor's Statement:

Ellen G. Szydlowski: Dr. Szydlowski conceptualized and designed the study, designed data collection instruments, collected data, carried out the initial analyses, drafted the initial manuscript, and approved the final manuscript as submitted.

Jeffrey A. Rudolph, Melissa A. Vitale: Drs. Rudolph and Vitale assisted in the study design, critically reviewed the manuscript, and approved the final manuscript as submitted.

Noel S. Zuckerbraun: Dr. Zuckerbraun assisted in the study design and data analysis, reviewed and revised the manuscript, and approved the final manuscript as submitted.

recommend central and peripheral blood cultures, empiric broad spectrum antibiotics targeting gram-negative and enteric organisms and hospital admission.

Introduction

Intestinal Failure is defined as a condition whereby either an extensive surgical bowel resection or a medical condition results in inadequate intestinal function to maintain fluid, electrolytes or the nutrition needed for growth.^{1, 2} The classic form of Intestinal Failure is “short gut” syndrome, in which the intestine is too short as a consequence of surgical resection.^{3, 4} The incidence of short gut syndrome is estimated to be 5 to 25/100,000 births per year and up to 700 per 100,000 in very low birth weight infants (<1500 grams).⁴⁻⁷ However, the overall incidence of Intestinal Failure is unknown.

Patients with Intestinal Failure require total parenteral nutrition administered via a central line. Unique to patients with indwelling central lines, patients with Intestinal Failure are believed to be at particularly high risk for bloodstream infections (BSIs). This is thought to be due to several reasons including possible bacterial colonization of the total parenteral nutrition, contamination of the central line from high stool output, and the theoretical risk of bacterial translocation at the level of the gut which has been described in multiple animal models.^{8, 9}

Whereas the rate of bacteremia has been shown to be approximately 20% in febrile pediatric oncology patients, data on the occurrence of bacteremia among pediatric patients with Intestinal Failure who present with fever are limited.¹⁰⁻¹² In addition to potentially higher rates of bacteremia, the pathogens for BSIs in Intestinal Failure patients seem to differ from other populations with central lines. Whereas gram-positive infections predominate in other populations, a few small studies of patients with Intestinal Failure have described BSIs with gram-negative and enteric pathogens at rates of 35-44% and 59%, respectively.¹²⁻¹⁵

Given the potential higher risk for BSIs and limited small previous studies, we sought to further investigate the occurrence of bacteremia in pediatric patients with Intestinal Failure and fever presenting to the Emergency Department (ED). The primary objective of this study was to describe the occurrence of BSIs in pediatric Intestinal Failure patients with a central line who present to the ED with fever. The secondary objectives were to describe the pathogens and clinical aspects of BSIs in this population.

Methods

Study Population and Design

A retrospective chart review of febrile patients with Intestinal Failure who presented to the ED at Children's Hospital of Pittsburgh was conducted between July 1, 2006 and June 30, 2011. We identified subjects using a database of patients with Intestinal Failure from the Division of Gastroenterology at our institution. As many of these patients are potential candidates for bowel transplantation, we also cross-referenced the Intestinal Failure database against a list of pre- and post-bowel transplantation patients from the Department of Transplant Surgery. Medical records of patients with Intestinal Failure were reviewed to

identify all eligible ED visits for febrile episodes. ED febrile episodes were included if patients were less than 20 years of age, had a central line, and a fever of 38.0° C or greater either at home, in the ED or at a transferring facility. If a patient underwent organ transplantation during the study, subsequent ED visits for fever post-transplantation were excluded.

A single investigator (E.S.) reviewed all medical records that included transfer, ED and inpatient records. A standardized form developed for this study was used to record all data which included demographics, vital signs, blood culture results, antibiotics administered and disposition. Disposition from the ED was categorized as discharged home from the ED, admitted to the general inpatient unit, admitted directly to the Pediatric Intensive Care Unit (PICU) or initially admitted to the general inpatient unit and transferred to the PICU within 24 hours.

All blood cultures drawn in our institution's ED were included. The protocol at our institution is to obtain central and peripheral blood cultures for patients with Intestinal Failure and central lines who present to the ED with fever greater than or equal to 38.0° C. Blood cultures from transferring institutions were included if there was documentation of the results in the medical records. As is standard in the care of patients with Intestinal Failure, central blood cultures were defined as BSIs when any organism was cultured from blood obtained from a central line during a febrile illness.¹² Urine cultures, if obtained, were recorded and were defined as positive if there were greater than 50,000 colony forming units of a single organism.

Statistical Analysis

Each febrile episode was analyzed independently at the visit level. We chose to analyze at the visit level instead of reporting a subanalysis at the patient level as we felt data describing febrile episodes instead of individual patients would be more practical and valuable for the clinician evaluating patients with Intestinal Failure and fever in the ED. Descriptive statistics were used for demographics and clinical characteristics. The χ^2 test was used for the evaluation of categorical variables. Mann-Whitney U was used for comparison of non-parametric data. Statistical significance was defined as a *P* value <.05. Study data were collected and managed using REDCap electronic data capture tools hosted at the University of Pittsburgh.¹⁶ Statistical analyses were conducted using Statistical Program for the Social Sciences, version 19.1.1 (SPSS). This study was approved by the University of Pittsburgh Institutional Review Board.

Results

Subject Characteristics

There were 422 patients identified from the combined Gastroenterology and Transplant Surgery registries. Of these 422 patients, 72 patients met study criteria and had a total of 519 febrile ED episodes during the 5-year study period (Figure 1). The mean number of febrile ED episodes for the 72 study patients included was 7.2 (SD 6.8, range 1-33).

The median age for patients presenting with febrile episodes was 21 months (interquartile range [IQR] 13 to 38 months) and 52% of patients were male. The most common underlying etiologies of Intestinal Failure at both the patient level and the visit level were necrotizing enterocolitis and gastroschisis (Table 1). The small number of patients with each underlying diagnosis, however, limits the ability to determine if any one etiology confers an increased risk for BSI. Most episodes (97%) involved patients with tunneled central lines and 3% of episodes were in patients with peripherally inserted central catheters. Home use of ethanol locks prior to the ED visit were reported in 18 of the 519 episodes and home antibiotic locks were not recorded. Of note, 8% of patients (42/519) in this study were initially evaluated at other institutions and were transferred to our pediatric ED for further evaluation and 37/42 had blood cultures drawn prior to transfer.

Occurrence of BSI

Central blood cultures were obtained in 93% (480/519) of febrile ED episodes and 69% (330/480) were positive for a BSI. Of all BSIs, 38% (124/330) were polymicrobial, 32% (105/330) were a single gram-positive organism, 25% (84/330) were a single gram-negative organism and 5% (17/330) were a single fungal organism. In total, 501 pathogens were isolated from the 330 positive central cultures. Pathogen types are listed in Table 2. Of the bacterial pathogens, 52% (237/460) were gram-positive and 48% (223/460) were gram-negative. Overall, 60% of pathogens were enteric organisms. All fungal organisms were *Candida* species and accounted in total for 8% of all isolates (41/501).

In order to determine if there is line colonization without spread to the periphery, our institution recommends obtaining both central and peripheral blood cultures when possible, as part of the initial evaluation of patients with Intestinal Failure and fever. Central cultures were obtained in 93% of febrile episodes (480/519), peripheral cultures were obtained in 64% (330/519) and both central and peripheral cultures were obtained in 58% (330/519, Table 3). When both a central and peripheral culture were obtained (303 febrile episodes), the peripheral culture was negative in 26% of episodes (80/303). When both a central and peripheral culture were obtained and were both positive, at least one of the same organism was isolated in 97% of episodes (129/133). Of note in these cases, coagulase-negative *Staphylococcus* was isolated in 38 central cultures and of these, 33 had peripheral cultures that also isolated coagulase-negative *Staphylococcus*.

There were 3 febrile episodes in which the peripheral culture was positive and the central culture was negative, and in all cases the patients were admitted and treated with intravenous antibiotics. In these cases, the peripheral cultures were positive for diphtheroids, coagulase-negative *Staphylococcus* and *Bacillus non-anthraxis*, respectively, and were considered contaminants by the clinicians.

The rate of bacteremia was similar between the patients with a tunneled catheter (321/465, 69%) and peripherally inserted central catheter (9/15, 60%); $P=0.57$. Febrile episodes with BSIs compared to febrile episodes without BSIs showed no statistical significance in regards to age, sex or underlying diagnosis. The median number of days from central line insertion to BSI was 78 (IQR 36 to 180 days). The central line was removed in 34% (111/330) of febrile episodes with a concomitant BSI.

Urinary Tract Infections

Urine cultures were performed in 37% (194/519) of febrile episodes and 9% (18/194) were positive. The mean age of patients with urinary tract infections was 23.8 months (SD 19.6) and 22% were male. The most common urinary organism cultured was *Escherichia coli* (11/18). A concurrent central blood culture with the same organisms consistent with urosepsis was found in 44% (8/18) of episodes (2 *Klebsiella pneumonia*, 2 *Escherichia coli*, 2 *Enterococcus faecalis*, 1 *Proteus* species, and 1 methicillin-sensitive *Staphylococcus aureus*). Both central and peripheral cultures were positive for the same urinary organism in 28% (5/18) of urinary tract infections.

Antibiotics

Antibiotics were administered in the ED in 94% (489/519) of febrile episodes. Excluding those transferred from outlying facilities, the median time from triage to administration of the first dose of antibiotics was 2.3 hours (IQR 1.7 to 3.1 hours). There was no significant difference between median time to antibiotics and ED disposition. The most common antibiotics administered were vancomycin (382/489, 78%) and piperacillin/tazobactam (378/489, 77%). The combination of vancomycin and piperacillin/tazobactam was given in 61% (296/489) of febrile episodes. Antifungal agents were administered in the ED in 5% of febrile episodes (26/489).

BSI Occurrence and ED Disposition

The majority of patients were admitted to the hospital: 85% (443/519) were admitted to the general inpatient unit, 9% (44/519) were admitted directly to the PICU, 2% (12/519) were admitted to inpatient unit and transferred to the PICU within 24 hours due to septic shock and 4% (20/519) were discharged home from the ED. Of the patients discharged home from the ED, 6/20 (30%) returned to the ED within 48 hours and were admitted to the inpatient unit; two returned after report of positive blood cultures, two returned with persistent fevers, one had persistent fatigue and one had a new cellulitis. Of the 519 febrile episodes included in this analysis, there were no patient deaths during the associated hospital admission.

Discussion

In this study, we found 69% of central blood cultures were positive for a BSI in patients with Intestinal Failure and central lines presenting to a single pediatric ED with fever. To our knowledge, these data represent the largest study of BSIs in febrile pediatric Intestinal Failure patients presenting to an ED. The results support prior smaller studies indicating the occurrence of bacteremia in febrile patients with Intestinal Failure and central lines is higher than in other populations with fever and central lines, who have reported occurrences of 6-23%.^{4, 8, 10, 17-24} Although it is possible some of the central blood culture results were contaminants, the extremely high degree of overlap in isolates when both a central and peripheral culture were obtained during a febrile illness suggests these are real pathogens. Our data support that all patients with fever and central lines should not be treated the same given the propensity for positive cultures in the pediatric Intestinal Failure population. Whereas other populations with central line and fever evaluated in the ED setting, such as oncology patients, may be risk stratified into high vs. low risk for infection and possible

candidates for outpatient management, our pediatric Intestinal Failure population patients should be admitted to the hospital and treated with antibiotics pending culture results.^{25, 26}

In addition to the high occurrence of BSIs, we also found that organisms differ from other populations with central lines with a high rate of gram-negative and enteric organisms, consistent with smaller studies.¹²⁻¹⁴ Previous research in pediatric patients with cancer has shown that 20-30% of BSIs are due to gram-negative organisms versus our study population in which 48% of the pathogens were gram-negative.^{23, 27} Interestingly, we found that 60% of BSIs were due to enteric organisms. This may support the theory of gut translocation or may represent the organisms that colonize the skin of these patients. Furthermore, it suggests that typical empiric antibiotic approaches for BSIs in patients with central lines, such as vancomycin and a third or fourth generation cephalosporin may not be appropriate for patients with Intestinal Failure. We recommend initiating antibiotics that cover gram-positive, gram-negative and enteric organisms, such as vancomycin and piperacillin/tazobactam in patients with Intestinal Failure and fever.

Peripheral blood cultures are used by our institution to guide treatment options. A negative peripheral culture with a positive central culture suggests that additional methods of eradication, such as antibiotic locks, may be useful. Our data support the recommendation to obtain peripheral cultures in these patients as we found the combination of a positive central culture with a negative peripheral culture in 26% (80/303) of BSIs in which both a peripheral and central blood culture was obtained. Due to the difficulty of replacing central lines in children, current guidelines recommend the combination of antibiotic lock therapy and systemic antibiotics for catheter salvage when possible.¹⁵

We found the prevalence of urinary tract infection to be 9% in our population with an extremely high rate of concomitant bacteremia (44%, 8/18). This is in contrast to healthy infants and children presenting to the ED with fever, in which the rate of urinary tract infection is 3-5% and the prevalence of bacteremia in those with a urinary tract infection is 4-9%.²⁸⁻³¹ This is also in contrast to a recent study of febrile pediatric patients with cancer and neutropenia who had a similar rate of urinary tract infections (8.6%), yet none of these patients had concurrent bacteremia.³² Of note, the median age of the febrile oncology patients in this study was 8 years which is much higher than the median age in our study population (21 months). As urine cultures were obtained in less than half of febrile episodes in our study, further investigation is warranted to confirm this high risk of urosepsis in febrile pediatric patients with Intestinal Failure.

There have been several studies linking early initiation of antibiotic therapy with decreased mortality in patients with severe sepsis or septic shock.³³⁻³⁵ We used PICU admission or transfer to the PICU within 24 hours as a proxy for severity of illness. Unexpectedly, our study did not find an association between documented time to antibiotics and admission to the PICU or transfer to PICU. Although we do not advocate for delayed antibiotic administration, our data would suggest that timing within 2 to 3 hours did not alter outcomes for our patients in this study.

Limitations

This was a retrospective chart review at a single center and thus, includes limitations inherent to the study design. Although inter-rater reliability was not performed for chart review, a single reviewer and a standardized data collection form designed for this study were utilized to limit recording errors. Febrile episodes that were directly admitted to the inpatient unit or PICU (and bypassed the ED) were excluded which could affect the occurrence of BSIs. However, this is uncommon at our institution and thus, unlikely to alter the BSI rate significantly. We were unable to report a central line associated blood stream infection rate per 1000 catheter days, recurrence rate or prevalence of bacteremia as our study population was limited to those patients evaluated in the ED and not the entire Intestinal Failure population, some of whom may never have had a BSI and others who were evaluated solely at other institutions. However, given our study's large number of ED visits in pediatric patients with Intestinal Failure and fever, we believe the data are representative of the occurrence of BSIs during acute febrile illness and generalizable to this population. Finally, this study was limited to the ED setting and therefore, did not include infants in the neonatal intensive care unit with Intestinal Failure who have a much higher reported rate of mortality.²⁴

Conclusion

In summary, pediatric patients with Intestinal Failure and central lines are a vulnerable population at high risk of BSIs with 69% of cultures positive in this study of ED febrile episodes. Contrary to reports in other populations with central lines, BSI occurrence in patients with Intestinal Failure and fever is higher and larger proportions are gram-negative and enteric organisms. For pediatric Intestinal Failure patients with central lines and fever evaluated in the ED, we recommend central and peripheral blood cultures, empiric broad spectrum antibiotics targeting gram-negative and enteric organisms, and hospital admission.

Acknowledgments

Funding Source: The project described was supported by the National Institutes of Health through Grant Number UL1TR000005

References

1. Goulet O, Ruemmele F, Lacaille F, Colomb V. Irreversible intestinal failure. Journal of pediatric gastroenterology and nutrition. 2004; 38(3):250–269. [PubMed: 15076623]
2. Kocoshis SA. Medical management of pediatric intestinal failure. Seminars in pediatric surgery. 2010; 19(1):20–26. [PubMed: 20123270]
3. Goulet O, Ruemmele F. Causes and management of intestinal failure in children. Gastroenterology. 2006; 130(2 Suppl 1):S16–28. [PubMed: 16473066]
4. Cole CR, Hansen NI, Higgins RD, Ziegler TR, Stoll BJ. Very Low Birth Weight Preterm Infants With Surgical Short Bowel Syndrome: Incidence, Morbidity and Mortality, and Growth Outcomes at 18 to 22 Months. Pediatrics. 2008; 122(3):e573–e582. [PubMed: 18762491]
5. Wallander J, Ewald U, Lackgren G, Tufveson G, Wahlberg J, Meurling S. Extreme short bowel syndrome in neonates: an indication for small bowel transplantation? Transplant Proc. 1992; 24(3): 1230–1235. [PubMed: 1604598]

6. Wales PW, de Silva N, Kim J, Lecce L, To T, Moore A. Neonatal short bowel syndrome: population-based estimates of incidence and mortality rates. *J Pediatr Surg.* 2004; 39(5):690–695. [PubMed: 15137001]
7. Rudolph JA, Squires R. Current concepts in the medical management of pediatric intestinal failure. *Curr Opin Organ Transplant.* 2010; 15(3):324–329. [PubMed: 20489629]
8. Kurkchubasche AG, Smith SD, Rowe MI. Catheter sepsis in short-bowel syndrome. *Arch Surg.* 1992; 127(1):21–24. discussion 24–25. [PubMed: 1734846]
9. Wells C, Maddaus M, Simmons R. Proposed mechanisms for the translocation of intestinal bacteria. *Reviews of Infectious Diseases.* 1988; 10(5):958–979. [PubMed: 3055194]
10. Klastersky J, Ameye L, Maertens J, Georgala A, Muanza F, Aoun M, et al. Bacteraemia in febrile neutropenic cancer patients. *Int J Antimicrob Agents.* 2007; 30(Suppl 1):S51–59. [PubMed: 17689933]
11. Shachor-Meyouhas Y, Sprecher H, Moscoviz D, Zaidman I, Haimi M, Kassis I. Molecular-based diagnosis of bacteremia in the setting of fever with or without neutropenia in pediatric hematology-oncology patients. *Journal of pediatric hematology/oncology.* 2013; 35(7):500–503. [PubMed: 24064965]
12. Cole CR, Frem JC, Schmotzer B, Gewirtz AT, Meddings JB, Gold BD, et al. The rate of bloodstream infection is high in infants with short bowel syndrome: relationship with small bowel bacterial overgrowth, enteral feeding, and inflammatory and immune responses. *J Pediatr.* 2010; 156(6):941–947. 947 e941. [PubMed: 20171649]
13. Piedra PA, Dryja DM, LaScolea LJ Jr. Incidence of catheter-associated gram-negative bacteremia in children with short bowel syndrome. *Journal of clinical microbiology.* 1989; 27(6):1317–1319. [PubMed: 2666441]
14. Piper HG, de Silva NT, Amaral JG, Avitzur Y, Wales PW. Peripherally inserted central catheters for long-term parenteral nutrition in infants with intestinal failure. *Journal of pediatric gastroenterology and nutrition.* 2013; 56(5):578–581. [PubMed: 23221995]
15. Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. *Clin Infect Dis.* 2009; 49(1):1–45. [PubMed: 19489710]
16. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of biomedical informatics.* 2009; 42(2):377–381. [PubMed: 18929686]
17. Diamanti A, Basso MS, Castro M, Calce A, Pietrobattista A, Gambarara M. Prevalence of life-threatening complications in pediatric patients affected by intestinal failure. *Transplant Proc.* 2007; 39(5):1632–1633. [PubMed: 17580205]
18. Edwards JR, Peterson KD, Mu Y, Banerjee S, Allen-Bridson K, Morrell G, et al. National Healthcare Safety Network (NHSN) report: data summary for 2006 through 2008, issued December 2009. *Am J Infect Control.* 2009; 37(10):783–805. [PubMed: 20004811]
19. Moukarzel AA, Haddad I, Ament ME, Buchman AL, Reyen L, Maggioni A, et al. 230 patient years of experience with home long-term parenteral nutrition in childhood: natural history and life of central venous catheters. *J Pediatr Surg.* 1994; 29(10):1323–1327. [PubMed: 7807317]
20. Mouw E, Chessman K, Leshner A, Tagge E. Use of an ethanol lock to prevent catheter-related infections in children with short bowel syndrome. *J Pediatr Surg.* 2008; 43(6):1025–1029. [PubMed: 18558177]
21. Wolf J, Shenep JL, Clifford V, Curtis N, Flynn PM. Ethanol lock therapy in pediatric hematology and oncology. *Pediatr Blood Cancer.* 2013; 60(1):18–25. [PubMed: 22911535]
22. Hakim H, Flynn PM, Knapp KM, Srivastava DK, Gaur AH. Etiology and clinical course of febrile neutropenia in children with cancer. *Journal of pediatric hematology/oncology.* 2009; 31(9):623–629. [PubMed: 19644403]
23. Kelly MJ, Vivier PM, Panken TM, Schwartz CL. Bacteremia in febrile nonneutropenic pediatric oncology patients. *Pediatr Blood Cancer.* 2010; 54(1):83–87. [PubMed: 19774640]

24. Cole CR, Hansen NI, Higgins RD, Bell EF, Shankaran S, Laptook AR, et al. Bloodstream Infections in Very Low Birth Weight Infants with Intestinal Failure. *Journal of Pediatrics*. 2012; 160(1):54–59. [PubMed: 21840538]
25. Freifeld AG, Bow EJ, Sepkowitz KA, Boeckh MJ, Ito JI, Mullen CA, et al. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the infectious diseases society of america. *Clin Infect Dis*. 2011; 52(4):e56–93. [PubMed: 21258094]
26. Lehrnbecher T, Phillips R, Alexander S, Alvaro F, Carlesse F, Fisher B, et al. Guideline for the management of fever and neutropenia in children with cancer and/or undergoing hematopoietic stem-cell transplantation. *J Clin Oncol*. 2012; 30(35):4427–4438. [PubMed: 22987086]
27. Lehrnbecher T, Varwig D, Kaiser J, Reinhardt D, Klingebiel T, Creutzig U. Infectious complications in pediatric acute myeloid leukemia: analysis of the prospective multi-institutional clinical trial AML-BFM 93. *Leukemia*. 2004; 18(1):72–77. [PubMed: 14586478]
28. Bachur R, Caputo GL. Bacteremia and meningitis among infants with urinary tract infections. *Pediatr Emerg Care*. 1995; 11(5):280–284. [PubMed: 8570449]
29. Schnadower D, Kuppermann N, Macias CG, Freedman SB, Baskin MN, Ishimine P, et al. Febrile infants with urinary tract infections at very low risk for adverse events and bacteremia. *Pediatrics*. 2010; 126(6):1074–1083. [PubMed: 21098155]
30. Hoberman A, Chao HP, Keller DM, Hickey R, Davis HW, Ellis D. Prevalence of urinary tract infection in febrile infants. *J Pediatr*. 1993; 123(1):17–23. [PubMed: 8320616]
31. Shaw KN, Gorelick M, McGowan KL, Yakscoe NM, Schwartz JS. Prevalence of urinary tract infection in febrile young children in the emergency department. *Pediatrics*. 1998; 102(2):e16. [PubMed: 9685461]
32. Sandoval C, Sinaki B, Weiss R, Munoz J, Ozkaynak MF, Tugal O, et al. Urinary tract infections in pediatric oncology patients with fever and neutropenia. *Pediatr Hematol Oncol*. 2012; 29(1):68–72. [PubMed: 22304012]
33. Gaieski DF, Mikkelsen ME, Band RA, Pines JM, Massone R, Furia FF, et al. Impact of time to antibiotics on survival in patients with severe sepsis or septic shock in whom early goal-directed therapy was initiated in the emergency department. *Crit Care Med*. 2010; 38(4):1045–1053. [PubMed: 20048677]
34. Kumar A, Roberts D, Wood KE, Light B, Parrillo JE, Sharma S, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Crit Care Med*. 2006; 34(6):1589–1596. [PubMed: 16625125]
35. Dellinger RP, Carlet JM, Masur H, Gerlach H, Calandra T, Cohen J, et al. Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock. *Crit Care Med*. 2004; 32(3):858–873. [PubMed: 15090974]

Figure 1. Flow Diagram of the Study Population. ED – Emergency Department

Table 1
Underlying Etiology of Intestinal Failure by Patient and Febrile ED Episode

Intestinal Failure Etiology	Patients (N = 72)	Febrile ED Episodes (N = 519)
Necrotizing enterocolitis	17 (23.6%)	135 (26%)
Gastroschisis	20 (27.8%)	122 (23.5%)
Volvulus	11 (15.3%)	67 (12.9%)
Intestinal atresia	7 (9.7%)	57 (11%)
Tufting enteropathy	3 (4.2%)	25 (4.8%)
Hirschsprung's Disease	2 (2.8%)	18 (3.5%)
Mitochondrial disorder	1 (1.4%)	18 (3.5%)
Familial Adenomatous Polyposis	2 (2.8%)	16 (3.1%)
Microvillus inclusion disease	1 (1.4%)	16 (3.1%)
Abdominal compartment syndrome	1 (1.4%)	14 (2.7%)
Cystic lymphangioma	1 (1.4%)	9 (1.7%)
Autoimmune enteropathy	1 (1.4%)	8 (1.5%)
Intestinal pseudo-obstruction	1 (1.4%)	6 (1.2%)
Evisceration	1 (1.4%)	4 (0.8%)
Gardner Syndrome	1 (1.4%)	2 (0.4%)
Bladder extrophy and cloaca	1 (1.4%)	1 (0.2%)
Megacystic microcolon intestinal hypoperistalsis syndrome	1 (1.4%)	1 (0.2%)

Table 2
List of Pathogens from Central Blood Cultures

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

Table 3
Central and Peripheral Blood Culture Results

	Central Positive	Central Negative	Central not obtained	Total
Peripheral Positive	133	3	11	147
Peripheral Negative	80	87	16	183
Peripheral not obtained	117	60	12	189
Total	330	150	39	519