



## **Characterization of Post-Hospital Infections in Adults Requiring Home Parenteral Nutrition**

Vivian M. Zhao, *Emory University*  
Daniel P. Griffith, *Emory University*  
[Henry Michael Blumberg](#), *Emory University*  
Nisha J. Dave, *Emory University*  
Cynthia H. Battey, *Emory University*  
Therese A. McNally, *Emory University*  
[Kirk Easley](#), *Emory University*  
[John R Galloway](#), *Emory University*  
[Thomas R. Ziegler](#), *Emory University*

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## Characterization of Post-Hospital Infections in Adults Requiring Home Parenteral Nutrition

Vivian M. Zhao, Pharm.D.<sup>1,2</sup>, Daniel P. Griffith, R.Ph.<sup>1,2</sup>, Henry M. Blumberg, M.D.<sup>5</sup>, Nisha J. Dave, Pharm.D.<sup>1,2</sup>, Cynthia H. Battey, R.N.<sup>1,3</sup>, Therese A. McNally, R.N.<sup>1,3</sup>, Kirk A. Easley, M.S.<sup>7</sup>, John R. Galloway, M.D.<sup>1,6,8</sup>, and Thomas R. Ziegler, M.D.<sup>1,4,8</sup>

<sup>1</sup>Nutrition and Metabolic Support Service, Emory University Hospital

<sup>2</sup>Pharmaceutical Services, Emory University Hospital

<sup>3</sup>Nursing Services, Emory University Hospital

<sup>4</sup>Division of Endocrinology, Metabolism and Lipids, Emory University School of Medicine

<sup>5</sup>Division of Infectious Diseases, Department of Medicine, Emory University School of Medicine

<sup>6</sup>Department of Surgery, Emory University School of Medicine

<sup>7</sup>Department of Biostatistics and Bioinformatics, Emory University Rollins School of Public Health

<sup>8</sup>Center for Clinical and Molecular Nutrition, Emory University, Atlanta, GA 30322

### Abstract

**Background**—Limited data are available on the incidence and risk factors for infection among patients requiring home parenteral nutrition (HPN).

**Methods**—Retrospective study of 101 consecutive adults (63 female, 38 male) discharged on HPN from Emory University Hospital, Atlanta, GA. New bloodstream infections (BSI) requiring re-hospitalization and other infections were evaluated.

**Results**—Most infections (75%) developed during the initial 6 months after hospital discharge; rates of BSI were particularly high during the first four months. A total of 56 patients (55.4%) developed a total of 102 BSIs (11.5 BSI/1000 catheter-days). Most BSIs were attributed to Gram positive organisms (46%) including coagulase-negative *staphylococcus*, *staphylococcus aureus*, *enterococcus* species, and others, followed by *Candida* species (20%) and Gram negative organisms (13%). Twenty-one percent of BSIs were polymicrobial. The BSI incidence rate ratio (IRR) was significantly increased for patients with mean pre-hospital discharge blood glucose (BG) concentrations in the highest quartile versus the lowest quartile; IRR 2.4; P = 0.017). Patients with a peripherally inserted central catheter (PICC) versus non-PICC central venous catheters had significantly higher rates of BSI (p = 0.018). Thirty-nine (38.6%) patients developed 81 non-BSI infections, including pneumonia, urinary tract infections, and surgical site infections.

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Correspondence: Thomas R. Ziegler, M.D., Suite GG-23, Atlanta Clinical and Translational Science Institute, Emory University Hospital, 1364 Clifton Road, Atlanta, GA 30322 Telephone: 404-727-7351; fax 404-727-5563; (tzieg01@emory.edu). Alternate correspondence: Vivian M. Zhao, Pharm.D., Department of Pharmaceutical Services, Emory University Hospital, 1364 Clifton Road, Atlanta, GA 30322 Telephone: 404-712-7800; fax 404-712-7795; (vivian.zhao@emoryhealthcare.org).

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Post-discharge PN dextrose, lipid, and total calorie doses were unrelated to BSI but variably related to the rate of non-BSI.

**Conclusions**—Adult HPN patients exhibit a very high incidence of post-hospital infections. Higher mean BG levels during pre-discharge hospitalization and use of PICCs at discharge are associated with an increased risk of BSI in the post-discharge home setting.

### Keywords

Bloodstream infection; post-hospital infection; parenteral nutrition; risk factors

Administration of parenteral nutrition (PN) is routine for patients with intestinal failure unable to maintain adequate nutritional status with enteral and/or oral intake alone. Home PN (HPN) was first implemented in the late 1960s [1], with a yearly prevalence of use of approximately 120 patients per million population in the United States [2]. PN is associated with serious metabolic, mechanical, and infectious complications; infections, particularly catheter-associated bloodstream infections (BSI), are the most serious PN complication and contribute significantly to the cost of care in HPN patients [3–7]. Infections in patients receiving PN may not simply be due to the presence of a central venous catheter and specific macronutrients (calories, dextrose, fat) infused; these patients are typically immunocompromised by virtue of their underlying illnesses and are otherwise at higher risk for infection due to chronic wounds, fistulae, prolonged hospitalization, prior use of broad-spectrum antibiotics and other factors [3–7]. Unfortunately, there are limited data characterizing the BSI and non-BSI infection burden and potential risk factors for infection in the post-hospital setting in patients receiving HPN [8–13].

In recent years, we noted an apparent increase in the rate of BSI and other infections acquired after hospital discharge in complex and high-risk adult HPN patients. Therefore this retrospective study was designed to comprehensively evaluate the incidence of post-hospital infection, putative infection sites, associated microorganisms, and potential risk factors for infection in adults requiring HPN after discharge from Emory University Hospital (EUH), Atlanta, GA.

## METHODS

### Study design, clinical setting, and participants

This retrospective study was conducted using medical records of HPN patients discharged from EUH, a 587-bed tertiary care academic medical center. All patients requiring HPN and discharged during a pre-defined 3-year period (July 2004 through June 2007) were screened for eligibility. Eligible patients were ≥18 years of age who were anticipated to receive HPN for ≥30 days prescribed by the EUH Nutrition and Metabolic Support Service, which is responsible for the home nutritional management and follow-up of all such HPN patients using conventional methods for home-based nutritional support monitoring and care. All catheters for HPN were placed in the Radiology Department of EUH by staff dedicated to central line placement using conventional sterile technique and protocols. Ethanol or antibiotic catheter locks and antibiotic or chlorhexidine-coated dressings were not used during the study period in any patient. The study was approved by the Emory University Institutional Review Board and ethical guidelines were followed throughout the study.

### Data collection

Patient medical records were reviewed for demographic characteristics, primary indication for HPN, days of HPN therapy, number and types of infectious complications, results of blood and other cultures performed, and type of venous access device at hospital discharge.

In addition, the following variables were also recorded: history of diabetes mellitus (Type 1 or 2), type of central venous catheter (CVC), total number of catheters used, number of catheter lumens, total catheter days, time to initial post-hospital infection, mean hospital BG levels prior to initial hospital discharge, and macronutrient content of the HPN administered. Infections diagnosed  $\geq$  48 hours after hospital discharge were included in the analyses to minimize counting infections already developing at hospital discharge.

### Study definitions

Patients were considered to have a BSI based on the U.S. Centers for Disease Control and Prevention (CDC) criteria [14]: (1) a pathogen was isolated from  $\geq$  1 blood culture and pathogen not related to infection at another site; (2) documented fever ( $>38^{\circ}\text{C}$ ), chills or hypotension in association with common skin flora (e.g., *Bacillus* sp., *Propionibacterium* sp., coagulase-negative staphylococci) isolated from  $\geq$  2 blood cultures drawn on separate occasions and unrelated to infection at another site (unless in association with evidence of local infection at the access site of intravascular devices); and (3) common skin contaminant isolated from  $\geq$  2 blood cultures from patient with intravascular access device AND physician institutes appropriate antimicrobial therapy [14]. All non-BSI infections (e.g. pneumonia, urinary tract infection, surgical site infection) that developed after discharge on HPN were also diagnosed according to CDC criteria [14].

Infections were considered polymicrobial if more than one pathogen was isolated from cultures of the same site obtained within 48 hours after initial evaluation, irrespective of whether the isolates came from the same or different cultures. The majority of microbial culture results were obtained from samples analyzed in the Microbiology Laboratory of EUH. In these cases, the investigators reviewed the final microbiological reports and the medical records documenting the clinical data and antimicrobial agents ordered by the primary physicians for the putative infection. A small percentage of cultures [4 BSIs (3.9% of total) and 3 non-BSIs (3.7% of total)] were performed from outside hospital microbiology laboratories during admission to those institutions for infection and the data confirmed after review of available medical records and/or discussion with the attending physicians or home health care company nursing staff.

### Statistical Analyses

Infection rates per 1000 catheter-days of follow-up were estimated and compared using exact methods based on the Poisson distribution [15]. These estimates were calculated for BSIs, non-BSIs, and total infections (BSI + non-BSI). Statistical modeling was limited to data collected in the first six months of follow-up in individual patients because most of the BSIs were identified during the initial 6 months after hospital discharge. The median follow-up was approximately 2 months and the number of patients under follow-up between 6 and 12 months post-hospital discharge was less than 20% of the study patients. However, the incidence of infections was also determined for the entire period of observation in all subjects. Baseline covariates included gender, age, body mass index (BMI;  $\text{kg}/\text{m}^2$ ), history of diabetes mellitus, initial catheter type, and mean pre-discharge hospital BG level. The mean of all BG levels (point of care glucose meter and laboratory values) obtained during each patient's initial hospital stay was calculated, and this single value was assigned to each patient, regardless of the number of separate levels obtained. We also calculated the mean home BG value during the home period of observation for each subject for analysis. Mean daily HPN total calorie (kcal), dextrose, and lipid emulsion dose per kg body weight administered during the period of observation for each subject was determined from medical records and analyzed for effects on infection risk.

Monthly incidence rates of infection were estimated by performing a generalized estimating equations (GEE) Poisson regression analysis of the monthly counts, implemented using SAS Proc Genmod [16], using an exchangeable correlation structure for the repeated monthly counts within subject. The incidence rate ratio (IRR) is the ratio of the incidence density in one group to that of another group. Results by each baseline covariate are presented as the IRR and the 95% confidence interval (CI). Baseline covariates that were significant at  $P < 0.05$  in the univariable analyses of BSI were included in multivariable analyses. The IRR and its 95% confidence interval were calculated for each factor in the presence of others in the final model.

## RESULTS

### Demographic data and nutrition support

During the 3-year observation period, 101 patients (63 female, 38 male) with a mean age of  $51 \pm 13$  years (range 28 to 87 years) met eligibility criteria and were included in the analyses (Table 1). The median follow-up time for study subjects discharged on HPN was 65 days (range 2 to 1045 days) and the median days of HPN administration during the study period were 47 days (range 2 to 921 days), with a frequency of 3 to 7 days of HPN infusion weekly in individual subjects. The indications for HPN included intestinal fistulae, post-operation bowel dysfunction and other forms of intestinal failure, which precluded adequate nutritional delivery via oral food or tube feedings. Given varying degrees of intestinal failure, patients received a relatively wide range of average total HPN calories, dextrose, and lipid doses (expressed as mean daily HPN dose during the observation period for each subject; Table 1). Lipid emulsion was given as a standard soybean-oil based product (Intralipid® Baxter, Deerfield, IL). Most patients were able to consume some oral food during the study despite various types and severity of intestinal failure, but these intakes were not recorded. During the study period, 6 cases of death occurred during hospital readmission in our 101-subject cohort, however, the details of death in these subjects were not recorded and in any event may not be entirely clear. There were 3 patients with terminal illness transferred to hospice care. No other reasons for drop-out were evident.

### Catheter types used for HPN

During the 3-year study period, HPN was infused via a total of 196 CVCs for a total of 12,877 catheter-days; HPN was infused during 6655 days of this total. A total of 69 (68.3%) subjects were initially discharged home with a peripherally inserted central venous catheter (PICC), 26 (25.7%) received a tunneled Hickman® or Groshong® catheter, and 6 (5.9%) received a subcutaneous port. Table 1 shows central vein catheter type for the total number of 196 CVCs placed during the observation period, showing a similar distribution. HPN was not given through peripheral vein catheters in any subject.

### Post-hospital discharge infections

A total of sixty-two (61.4%) of the 101 study patients developed a total of 245 infectious episodes (140 BSIs and 105 non-BSIs) during the observation period. Fifty-nine (58.4%) of 101 study patients experienced at least one BSI (twenty-five subjects had 1, thirteen subjects had 2, eleven subjects had 3, and ten subjects had 4 BSIs, respectively, during the study period). All BSIs required re-hospitalization for treatment. The median time after discharge for the first BSI was 38 days (mean 60 days; range: 2–932 days). Thirty-seven (36.6%) of the subjects had at least one non-BSI (fourteen subjects had 1, six subjects had 2, six subjects had 3, and eleven subjects had 4 non-BSI, respectively). The median time of the first post-hospital discharge non-BSI infection was 40 days (mean: 96 days; range: 3–934 days). Of the non-BSIs, 57% were urinary tract infections (UTI), 28% were wound infections, 11% were pneumonias, and 4% were antibiotic-associated colitis caused by

*Clostridium difficile*. Thus, the overall burden of infection during the early post-hospital course was very high in these individuals with complex disorders requiring HPN.

### Time course for development of infection after hospital discharge

During the initial 6 months of post-hospital follow-up in individual subjects, 183 total infections were identified in 59 patients (58.4% of the 101 subjects studied), with an overall incidence rate of 20.4 infections per 1000 catheter-days (Table 2A). The monthly rate of total infections (combined BSI + non-BSI) was similar during the first 6 months of follow-up ( $P = 0.59$ ).

Of the 59 patients with a diagnosed infection during the initial 6 months post-hospital discharge, 56 experienced 102 BSIs, for a BSI infection rate of 11.5 per 1000 catheter-days. A range of 11.6 to 13.2 BSI per 1000 catheter-days was observed during the first 4 months of observation and then the incidence significantly declined during months 5 and 6 ( $P = 0.05$ , Table 2B). The overall BSI incidence was 13.0 infections per 1000 catheter days of follow-up (95% CI: 10.4 to 16.3) when using days of actual HPN infusion as the time scale.

Eighty-one non-BSIs occurred during the initial 6 months post-hospital discharge in 33 patients, giving an overall incidence rate of 8.8 infections per 1000 catheter-days (Table 2C). The incidence of non-BSI infections did not significantly change over the 6 months of follow-up ( $P = 0.44$ ).

### Microbiology of pathogens recovered from cultures

Causal microorganisms for all infections during the entire observation period are shown in Table 3. Of the BSI, Gram positive microorganisms accounted for 46%, *Candida* species for 20%, Gram negative microorganisms for 13%, and 21% were polymicrobial, respectively. The 105 non-BSI were caused by a variety of Gram positive, Gram negative and fungal organisms (Table 3).

### Incidence rate ratios for risk of infection

Table 4 shows the influence of initial hospital discharge catheter type on infections in HPN patients. Statistical modeling was limited to data collected in the first six months of follow-up when most infections occurred, as noted above. The incidence of BSI was significantly higher for patients initially discharged with a PICC line compared to those patients discharged with other catheter types, which were all centrally inserted and tunneled or featured subcutaneous ports (IRR for BSI = 1.7, 95% CI: 1.10 to 2.86,  $p = 0.018$ ). There was no statistically significant difference in non-BSI or total infection due to catheter type, but study subjects who were initially discharged with PICC lines were associated with a near significant ( $p = 0.054$ ) increase in total post-discharge infection rates compared to subjects discharged with non-PICC lines.

Table 5 shows the association of pre-discharge hospital blood glucose (BG) levels with infection in HPN patients. Higher pre-discharge mean hospital BG concentrations were associated with a significantly higher total infection rate at home [IRR 2.09, upper versus lowest quartile, 95% confidence interval (CI) 1.03–4.26]. Furthermore, the post-discharge BSI IRR for patients with mean hospital BG  $\geq 128$  mg/dL (upper quartile) relative to those patients with mean hospital BG  $< 112$  mg/dL (lowest quartile) was significantly increased by approximately 2.4-fold (95% CI: 1.17 to 4.83,  $p = 0.017$ ). Hospital BG levels did not influence the post-discharge non-BSI infection rates.

The patients' mean hospital BG levels were further subdivided into those obtained in the intensive care unit (ICU) and those obtained on the general hospital ward (Table 5). The

post-discharge BSI and total infection IRR were each significantly increased in patients in the upper versus lowest quartile of mean hospital ward BG values (IRR = 2.28,  $p = 0.012$  and 2.2;  $p = 0.019$ , respectively). Mean BG in the ICU setting did not influence post-discharge infection rates (Table 5). Prior medical history of diabetes mellitus did not influence the risk of infection after hospital discharge in the study cohort (data not shown). We also calculated the mean home BG value during the home period of observation for each subject. Results show that the upper two quartiles of BG were significantly associated with a higher risk of BSI compared to subjects within the lowest quartile of mean home BG. Mean pre-discharge BG was highly correlated with mean home BG (Spearman  $\rho = 0.48$ ,  $P < .001$ ). Further, the upper two quartiles of home BG were significantly associated with a higher risk of BSI compared to subjects within the lowest quartile of mean home BG ( $< 90$  mg/dL) by univariate analysis. The upper quartile of home BG ( $> 108$  mg/dL) was associated with a BSI IRR of 2.41 ( $P=0.01$ ) and the next highest BG quartile (99–107 mg/dL) was associated with a BSI IRR of 1.96 ( $P=0.03$ ) versus the lowest home BG quartile, respectively. Table 6 shows the influence of PN macronutrient dose on infection in HPN patients. The mean daily dose of HPN dextrose, lipids and calories were not associated with BSI. However, when compared to the lowest quartile, the higher quartiles of mean daily HPN dextrose doses were associated with a significantly higher IRR for non-BSI and total infections. The highest quartile of HPN lipid dose was associated with a significantly higher IRR for non-BSI infections, while the higher quartiles of total caloric dose were associated with a significantly higher risk of non-BSI infections. Neither patient age nor BMI correlated with home infection risk (data not shown).

### Multivariable Analysis for BSI

In univariate analysis, three covariates with a potential effect on the BSI incidence density rate were included in the multivariable analysis (time post-discharge, initial discharge catheter type and pre-discharge overall mean BG). These analyses suggest that BSI rates may remain higher over the first 4 months after hospital discharge, and both higher mean blood glucose levels during hospitalization and an initial PICC catheter may independently increase the rate of post-hospital BSI (Table 7). Since higher mean BG levels tended to suggest a higher BSI rate, the multivariable model was refit with mean BG dichotomized at the median ( $> 117$  mg/dl). Table 8 provides the IRR and 95% confidence interval for each factor in the presence of the others in the final model. Independent predictors of an increased rate of BSI after hospital discharge include higher mean BG levels during hospitalization and use of PICCs at discharge. Although the IRR for BSI was 1.85 for patients with an early infection compared to patients with a late infection, this suggested relationship was not statistically significant as reflected by the  $P$  value and the wide width of the 95% confidence interval suggests more data may be needed to improve the precision of estimation of the BSI IRR.

## DISCUSSION

This study adds new information to the limited literature on post-hospital infection rates in HPN patients. Although retrospective, the data are comprehensive in outlining the very high rate of BSI and non-BSI, the temporal nature of these infections, and potential predisposing factors (type of catheter, pre-discharge mean BG levels, and macronutrient intake in HPN) in this subgroup of complex patients after hospital discharge. Another novel feature of this study is the assessment of the frequency, type and causative organisms for non-BSIs (and thus total infectious morbidity), which has not been previously studied in HPN patients.

The high rate of BSIs per 1000 catheter days (11.5/1000 catheter days during the first six months after discharge) is similar to the data of Marra et al from a retrospective epidemiologic study of 47 patients receiving long-term HPN over a 24-year period (mean

duration of follow-up 4.5 years) [9]. In that trial, 38 patients (81%) developed a total of 248 BSIs while they received chronic HPN for similar intestinal failure indications, as did this study cohort [9]. In the Marra et al study, greater than one BSI occurred in 79% of the study patients, and 24% of BSIs were polymicrobial (similar to the current study in which 21% of documented BSI were polymicrobial) [9]. A recent retrospective study of post-hospital HPN infections over time in infants and children with primarily short bowel syndrome from Egleston Children's Hospital in Atlanta found a total of 59 BSI occurred in 19 of 29 children (66%), predominately during the first few months after discharge [13]. In a recent retrospective study of predominately oncologic patients (84% of 296 patients), the rate of catheter-related BSI was 2/1000 catheter days, significantly lower than the BSI/1000 catheter day rate in this study [10]. Compared to other published reports, this study primarily focused on the short-term (6-month) period after discharge from the hospital and a large majority of female patients compared to some other series [12]. The indications for HPN in this cohort are similar to Marra et al [9], but differ from some of the other studies of infection in HPN patients. In cross-sectional data from a Canadian HPN registry of 150 patients (66% of whom had short bowel syndrome and 15% intestinal pseudo-obstruction), 29% had at least one episode of catheter-related sepsis in the previous year (range 1 to 6 episodes) [3]. In this study, HPN patients had a variety of complex gastrointestinal complications, but only 10% had short bowel syndrome alone and < 5% were cancer patients. This contrasts with some series in which cancer [10–11] and other diseases were predominant [8, 12]. Thus, these high rates of post-discharge infections may reflect the types of complicated gastrointestinal tract operations many of HPN patients had undergone which resulted in long pre-discharge hospital stays, use of broad-spectrum antibiotics in hospital and other factors, including immune dysfunction and altered catheter biofilm characteristics that may be specific to HPN patients but require further study.

This study showed that the frequency of BSI decreased with time after discharge, especially after the fourth month, a pattern reported in other studies [9, 13]. Although speculative, this time course may reflect, in part, the risk of post-hospital infections due microorganisms acquired during hospitalization, which diminishes over time as the patient's are re-colonized with flora in the home environment. This study also identified use of PICCs, higher BG control in the immediate hospitalization prior to discharge and larger doses of dextrose, lipids and calories administered in PN as variables that may increase the home infection risk.

In this study, Gram positive organisms were the most common pathogens associated with infection, accounting for approximately 69% of the BSIs, consistent with current available data [9–10]. Similar to prior studies, coagulase-negative *Staphylococcus* was the most common causative organism for BSI overall [9], while *Klebsiella pneumoniae* was the most prevalent Gram negative isolate (Table 1). However, this study differs from other reports in that it showed a high rate of fungemia (42 of 140 total episodes of BSI, or 30% of total diagnosed BSI). *Candida* species were the second most-common cause of BSIs, higher than the rate reported in most studies [7–9]. In a recent pilot study, a similarly high rate of fungemias was identified in HPN patients [17]. In the current study, *Candida albicans* was the most common causative pathogen for fungemia, whereas in the most comparable study by Marra et al, *Candida parapsilosis* was most prevalent in HPN patients [9]. Findings from subgroup analysis of patients who had PICC are consistent with the recently published Infectious Diseases Society of America and U.S. CDC guidelines that the most common microorganisms in catheter-related infections in general are coagulase-negative *staphylococcus*, *S. aureus*, and *Candida* species [18–19].

The occurrence of BSIs after hospital discharge was significantly increased in those HPN patients with mean total hospital BG = 128 mg/dL (highest quartile) relative to those with mean hospital BG < 112 mg/dL (lowest quartile). Hyperglycemia has previously been

shown to be associated with an increased incidence of BSI in patients receiving PN [20–21]. Although the upper limit for optimal BG control in the ICU and hospital setting remains controversial [22–24], there are no previous data exploring the risk of hospital BG levels and post-hospital infections in patients requiring HPN. We also analyzed all available home BG measurements during the period of observation in all patients. Results show that the upper two quartiles of BG were significantly associated with a higher risk of BSI compared to subjects within the lowest quartile of mean home BG. Additional studies are needed to confirm the effect of hospital and home BG control on post-hospital infections in HPN patients and to prospectively assess the impact of different degrees of BG control on such infections. Specific information on hemoglobin A1C responses, BG variability and insulin requirements/dosage would also be of interest in future prospective comparative effectiveness trials.

The non-BSI infection rate ratio for patients who received a mean daily HPN dextrose dose of 3.83 gm/kg (highest quartile) relative to those patients who received a mean daily dextrose dose of < 2.17 gm/kg (lowest quartile) was 4.52 (95% CI: 1.49 to 13.8,  $p = 0.0078$ ). This study also found that non-BSI infections (but not BSI) were significantly and positively related to higher mean HPN caloric and lipid doses (Table 6). A recent study has shown that PN containing lipid emulsion was not significantly associated with increased risk of bacterial infection and BSI when compared to lipid-free PN [25]. The underlying reasons for these results regarding PN content are unclear but the increase in non-BSI infections suggests a possible deleterious effect of the higher doses of PN macronutrients on systemic immune function, a hypothesis that requires rigorous prospective analysis.

In a systemic review of 200 published prospective studies of infections association with various types of central venous access devices in unselected patients, Maki and colleagues suggested that tunneled noncuffed central venous catheters reduced the risk of BSI by 33% versus untunneled PICC [26]. Similarly, this study found that the HPN patients initially discharged home with an untunneled PICC catheter had an approximately 2-fold increase in risk for BSI, compared to patients with other catheters (tunneled Hickman<sup>®</sup>, Groshong<sup>®</sup> or port-type catheters).

In recent years, several approaches have been adopted in an attempt to prevent catheter-related BSIs [7, 26–32]. These strategies include the use of appropriate hand hygiene and aseptic technique with catheter insertion and manipulation, avoidance of femoral vein catheters, minimizing the number of lumens in inserted catheters, exchanging the catheter using a subcutaneous fibrous sheath [33], and use of various types of catheters impregnated with antimicrobial agents, chlorhexidine, etc. [32]. Other interventions associated with decreased BSI (but also not conclusively proven) are various catheter site dressing antibiotic/antiseptic ointments, catheter locks containing heparin, vancomycin, ethylenediaminetetraacetic acid (EDTA), citrate, taurolidine, or ethanol [27–32]. A very recent meta-analysis strongly suggests that ethanol locks prevent catheter-related bloodstream infections in patients requiring parenteral nutrition [34]. Given the very high rate of post-discharge hospital infections in the HPN patients reported here, rigorous trials in patients similar to this cohort to define the potential comparative efficacy of these approaches (especially in the immediate post-discharge period) to decrease infections in the acute post-hospital phase are indicated. Such studies are particularly pertinent in light of the need to decrease the relatively high rate of rehospitalizations for BSI among patients in the Medicare program [35].

Limitations of this study include its retrospective nature in a single academic medical center, the fact that several HPN patients with infections were occasionally managed at outside centers by non-Emory University physicians, and the relatively small number of HPN

patients studied. We also do not have information on probiotic use by our cohort or data on hemoglobin A1C levels, insulin requirements/dosage or BG variability indexes.

## CONCLUSIONS

HPN remains lifesaving treatment for patients with intestinal failure unable to maintain adequate hydration and nutrition via the gastrointestinal tract. Patients with primarily gastrointestinal surgical disorders requiring HPN reveals a very high rate of both BSI and non-BSI in the home setting, particularly during the early months after hospital discharge. A wide spectrum of causal Gram positive, Gram negative and fungal microorganisms were identified, and a significant proportion (21%) of the documented BSI were polymicrobial. Higher mean BG levels during hospitalization prior to discharge and an initial PICC (versus a tunneled CVC) independently increased the rate of post-hospital BSI. Additionally, higher mean daily home intake of PN dextrose, calories, and lipid per kg in the home setting were each associated with higher rates of non-BSI. New strategies to decrease this significant infection burden should be rigorously investigated in adults requiring HPN.

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### SUMMARY

Retrospective data from 101 adults with intestinal failure discharged on home parenteral nutrition (HPN) revealed a high rate of both bloodstream and non-bloodstream infections, particularly during the first few months after discharge. A wide spectrum of causal microorganisms was identified.

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**Table 1**

Patient demographics, indication for HPN, catheter type and HPN macronutrient intake

<b>Demographics</b>	
Number of patients	101
Female	63 (62.4%)
Age at starting HPN (years)	50 (range 28–87)
BMI (kg/m <sup>2</sup> )	22.6 (range 12.7–43.9)
Days of observation (days)	65 (range 2–1045)
Number of HPN infusion days (days)	47 (range 2–921)
<b>Primary indication for HPN; number and (% of total group)</b>	
Intestinal fistula	29 (28.7%)
Post-operation bowel dysfunction	15 (14.9%)
Pancreatitis	14 (13.9%)
Short bowel syndrome	10 (9.9%)
Bowel obstruction	10 (9.9%)
Cancer	5 (4.9%)
Malnutrition/malabsorption	4 (3.9%)
Other intestinal failure indications <sup>a</sup>	14 (13.9%)
<b>Catheter type; number and (% of total 196 catheters)</b>	
PICC	123 (62.8%)
Hickman <sup>®</sup> catheter	51 (26.0%)
Subcutaneous port	12 (6.1%)
Other catheter types <sup>b</sup>	10 (5.1%)
<b>Total calories, dextrose and lipid administered in HPN</b>	
Total calories (kcal/kg BW/day)	24 (range: 10 to 41)
Dextrose (g/kg BW/day)	3.04 (range: 0.99 to 6.55)
Lipids (g/kg BW/day)	0.79 (range: 0.07 to 1.82)

Data presented as median and % of total study group, range or total number as indicated during the period of observation for each subject.

BW, body weight; BMI, body mass index; HPN, home parenteral nutrition; PICC, peripherally-inserted central venous catheter

<sup>a</sup> Crohn's disease (n=2); chronic nausea and vomiting (n=2); failure to thrive (n=2); radiation enteritis (n=1); gastroparesis (n=2); high ileostomy output (n=1); cholangitis (n=1); gastro-esophageal junction perforation (n=1); severe dysphagia (n=1); Gardner's syndrome (n=1).

<sup>b</sup> Groshong<sup>®</sup> catheter (n=5); tunneled central venous catheter (n=4); vascath (n=1).

**Table 2A**

Total infections in home parenteral nutrition patients

Time post-discharge	# Infections	# patients affected/month	Rate/1000 catheter-days	95% confidence interval
1 <sup>st</sup> month	50	28	16.9	11.5 to 24.9
2 <sup>nd</sup> month	52	34	24.1	17.6 to 33.1
3 <sup>rd</sup> month	33	25	24.3	17.6 to 33.4
4 <sup>th</sup> month	24	14	22.7	14.6 to 35.4
5 <sup>th</sup> month	15	8	19.2	10.0 to 37.1
6 <sup>th</sup> month	9	4	15.2	6.5 to 33.3
	<b>Total = 183</b>		20.4	16.4 to 25.4

**Table 2B**

## Bloodstream infections

Time post-discharge	# Infections	# patients affected/month	Rate/1000 catheter-days	95% confidence interval
1 <sup>st</sup> month	34	26	11.6	7.9 to 17.1
2 <sup>nd</sup> month	28	26	13.2	9.3 to 18.6
3 <sup>rd</sup> month	17	17	12.4	8.5 to 18.1
4 <sup>th</sup> month	14	13	13.0	8.3 to 20.3
5 <sup>th</sup> month	7	5	8.8	3.7 to 20.6
6 <sup>th</sup> month	2	2	3.3	1.0 to 11.0
Overall	Total = 102		11.5	9.3 to 14.2

**Table 2C**

## Non-bloodstream infections

Time post-discharge	# Infections	# patients affected/month	Rate/1000 catheter-days	95% confidence interval
1 <sup>st</sup> month	16	12	5.4	3.0 to 9.6
2 <sup>nd</sup> month	24	16	11.1	6.8 to 18.2
3 <sup>rd</sup> month	16	11	11.6	6.7 to 20.2
4 <sup>th</sup> month	10	7	9.3	4.4 to 19.9
5 <sup>th</sup> month	8	5	10.0	4.1 to 24.5
6 <sup>th</sup> month	7	4	11.2	4.7 to 26.3
	<b>Total = 81</b>		8.8	6.4 to 12.1

HPN = Home parenteral nutrition

Table 3

Causal microorganisms for infections in patients requiring HPN

Organisms	BSI (n = 140 episodes)		Non-BSI (n = 105 episodes)	
	# cultured	%	# cultured	%
<b>Gram-positive</b>	<b>97</b>		<b>61</b>	
Coagulase-negative <i>staphylococcus</i>	51	52.6	8	13.1
Methacillin-sensitive <i>staphylococcus aureus</i> (MSSA)	14	14.4	5	8.2
Methacillin-resistant <i>staphylococcus aureus</i> (MRSA)	12	12.4	14	23.0
<i>Enterococcus</i> species	14	14.4	28	45.9
Alpha hemolytic <i>streptococcus</i>	2	2.1	1	1.6
Alpha <i>streptococcus</i> species not <i>pneumococcus</i>	1	1.0	-	-
<i>Streptococcus salivarius</i>	1	1.0	-	-
Others	2 <sup>a</sup>	2.1	5 <sup>b</sup>	8.2
<b>Gram-negative</b>	<b>41</b>		<b>59</b>	
<i>Klebsiella pneumoniae</i>	12	29.3	11	18.6
<i>Enterobacter</i> species	7	17.1	6	10.2
<i>Escherichia coli</i>	5	12.3	19	32.2
<i>Acinetobacter baumannii</i>	3	7.3	1	1.7
<i>Serratia marcescens</i>	2	4.9	-	-
<i>Proteus</i> species	2	4.9	2	3.4
<i>Pseudomonas aeruginosa</i>	1	2.4	10	16.9
<i>Citrobacter amalonaticus</i>	1	2.4	-	-
<i>Flavimonas oryzihabitans</i>	1	2.4	-	-
<i>Strenotrophomonas maltophilia</i>	2	4.9	5	8.5
<i>Pseudomonas fluorescens-putida</i>	1	2.4	-	-
<i>Sphingomonas paucimobilis</i>	1	2.4	-	-
<i>Rhizobium radiobacter</i>	1	2.4	-	-
<i>Klebsiella oxytoca</i>	-	-	2	3.4
<i>Providencia rettgeri</i>	-	-	1	1.7
Gram variable or negative rod not speciated	2	4.9	2	3.4
<b>Fungus</b>	<b>41</b>		<b>16</b>	
<i>Candida (C.) albicans</i>	16	39.0	8	50.0
<i>C. glabrata</i>	13	31.7	2	12.5
<i>C. parapsilosis</i>	8	19.5	2	12.5
<i>C. tropicalis</i>	2	4.9	0	0
Yeast, not <i>Cryptococcus</i> species	-	-	4	25.0

Organisms	BSI (n = 140 episodes)		Non-BSI (n = 105 episodes)	
	# cultured	%	# cultured	%
<i>Rhodotorula</i> species	2	4.9	0	0
<b>Others</b>	<b>1</b>		<b>1</b>	
<i>Mycobacterium chelonae</i> /abscessus	1	100	1	100

Note: # = number of organisms; BSI = bloodstream infection; HPN = home parenteral Nutrition

<sup>a</sup> *Bacillus* specie;

<sup>b</sup> *Clostridium difficile* (4); *Clostridium perfringens* (1);

**Table 4**

Influence of initial hospital discharge catheter type on infection in HPN patients

Catheter Type	BSI		Non-BSI		Total Infections	
	IRR	95% CI	IRR	95% CI	IRR	95% CI
PICC	1.78	1.10–2.86	1.58	0.74–3.34	1.67	0.99–2.80
Non-PICC	1.00	--	1.00	--	1.00	--

CI, Confidence interval; HPN, home parenteral nutrition; IRR, Incidence rate ratios; PICC, peripheral inserted central catheter; non-PICC are tunneled Hickman<sup>®</sup>, Groshong<sup>®</sup>, or port-type catheters. Infections are those that occurred during period of observation within the first 6 months after hospital discharge.

**Table 5**

Influence of pre-discharge hospital blood glucose levels on infection in HPN patients

Factor	BSI		Non-BSI		Total Infections				
	IRR	95% CI	IRR	95% CI	IRR	95% CI			
<b>Overall BG (mg/dL)</b>									
128	2.38	1.17-4.83	0.017	1.75	0.63-4.89	0.29	2.09	1.03-4.26	0.041
118-127	1.93	1.03-3.64	0.041	1.56	0.58-4.20	0.38	1.72	0.87-3.42	0.12
112-117	1.42	0.71-2.84	0.33	0.73	0.23-2.31	0.59	1.03	0.48-2.22	0.94
< 112	1.00	--	--	1.00	--	--	1.00	--	--
<b>General ward BG (mg/dL)</b>									
126	2.28	1.20-4.32	0.012	1.97	0.73-5.37	0.18	2.20	1.14-4.26	0.019
118-125	1.77	0.93-3.36	0.08	1.74	0.60-5.05	0.31	1.78	0.88-3.58	0.11
111-117	1.24	0.64-2.37	0.53	0.85	0.29-2.47	0.77	1.04	0.51-2.11	0.91
< 111	1.00	--	--	1.00	--	--	1.00	--	--
<b>ICU BG (mg/dL) (n=35)</b>									
140	1.38	0.68-2.79	0.37	0.81	0.22-2.94	0.75	1.09	0.51-2.31	0.84
126-139	1.29	0.69-2.90	0.35	1.30	0.41-4.09	0.66	1.35	0.65-2.79	0.42
115-125	0.49	0.15-1.63	0.25	0.86	0.22-3.42	0.83	0.47	0.12-1.76	0.26
< 115	1.00	--	--	1.00	--	--	1.00	--	--

BG, blood glucose; CI, Confidence interval; HPN, home parenteral nutrition; ICU, intensive care unit. Infections are those that occurred during period of observation within the first 6 months after hospital discharge.

**Table 6**

Influence of PN macronutrient dose on infection in HPN patients

Factor	BSI			Non-BSI			Total Infections		
	IRR	95% CI	P Value	IRR	95% CI	P Value	IRR	95% CI	P Value
<b>Dextrose (gm/kg BW)</b>									
3.83	1.47	0.81–2.65	0.20	4.52	1.49–3.80	0.0078	2.10	1.11–4.00	0.023
2.79–3.82	1.35	0.72–2.53	0.36	3.48	1.24–9.75	0.018	1.82	0.94–3.53	0.08
2.17–2.78	1.90	0.98–3.66	0.06	5.95	2.15–16.46	0.0006	2.85	1.51–5.37	0.0012
< 2.17	1.00	--	--	1.00	--	--	1.00	--	--
<b>Lipids (gm/kg BW)</b>									
0.99	0.89	0.52–1.53	0.68	2.99	1.19–7.53	0.02	1.47	0.83–2.60	0.19
0.76–0.98	0.99	0.50–1.96	0.97	0.99	0.33–2.97	0.98	1.01	0.52–1.97	0.97
0.54–0.75	0.81	0.47–1.38	0.43	1.94	0.71–5.29	0.20	1.13	0.63–2.04	0.68
< 0.54	1.00	--	--	1.00	--	--	1.00	--	--
<b>Calories (kcal/kg BW)</b>									
29.1	0.85	0.48–1.52	0.58	3.51	1.44–8.55	0.0058	1.42	0.26–2.65	0.28
23.0–29.0	0.96	0.56–1.66	0.89	1.72	0.65–4.59	0.28	1.14	0.63–2.06	0.66
17.8–22.9	1.06	0.56–2.01	0.86	3.54	1.43–8.75	0.006	1.66	0.90–3.06	0.10
< 17.8	1.00	--	--	1.00	--	--	1.00	--	--

BW, body weight; CI, Confidence interval; HPN, home parenteral nutrition; ICU, intensive care unit. Infections are those that occurred during period of observation within the first 6 months after hospital discharge. Doses of parenteral dextrose, lipid emulsion, and total calories, respectively, are the average macronutrient dose/day during the period of observation within the first 6 months after hospital discharge.

**Table 7**

Multivariable Analysis of Factors Associated with BSI in Adults Requiring Home Parenteral Nutrition

	<b>Incidence Rate Ratio, IRR (95% CI)</b>	<b>P value</b>
<b>Effect</b>		
<b>Pre-Discharge Overall Mean BG (mg/dL), Quartile Groups</b>		
128	1.66 (0.75, 3.65)	0.21
118–127	1.78 (0.97, 3.29)	0.07
112–117	1.17 (0.65, 2.28)	0.65
< 112	Reference	
<b>Initial Discharge Catheter Type</b>		0.12
PICC	1.49 (0.90, 2.46)	
Non-PICC	Reference	
<b>Time Post –Discharge (months)</b>		0.18
Early (1 <sup>st</sup> 4 months)	1.82 (0.75, 4.40)	
Late (months 5–6)	Reference	
<b>Home BG (mg/dL)</b>		
	1.64 (0.78, 3.47)	0.19
	1.72 (0.96, 3.06)	0.07
	1.39 (0.72, 4.51)	0.33
	Reference	

**Table 8**

Multivariable Analysis of Factors Associated with BSI in Adults Requiring Home Parenteral Nutrition

	<b>Incidence Rate Ratio, IRR (95% CI)</b>	<b>P value</b>
<b>Effect</b>		
<b>Pre-Discharge Overall Mean BG (mg/dL)</b>		0.04
Above Median ( ≥ 117)	1.53 (1.02, 2.28)	
Below Median (< 117)	Reference	
<b>Initial Discharge Catheter Type</b>		0.04
PICC	1.61 (1.01,2.51)	
Non-PICC	Reference	
<b>Time Post –Discharge (months)</b>		0.18
Early (1 <sup>st</sup> 4 months)	1.82 (0.75, 4.42)	
Late (months 5–6)	Reference	
<b>Home BG (mg/dL)</b>		0.11
Above Median ( ≥ 99)	1.37 (0.93, 2.03)	
Below Median (< 99)	Reference	