University of Alberta

Changing Intravenous Administration Sets: Is 48 Versus 24 Hours Safe for Neutropenic Cancer Patients?

by

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Dedication:

To my husband Mike for encouraging and supporting me every step of the way, to our daughters Jodie and Michelle for helping me in more ways than they will ever know, and to my Mom and Dad for always believing in me.

Abstract

Recent studies suggest that intravenous (IV) administration sets may safely be changed at intervals up to 120 hours. To date, however, studies investigating the relationship between the frequency with which administration sets are changed and the incidence of infusion-related septicemia have excluded neutropenic patients or have examined them as part of a heterogenic group, thereby diluting neutropenia as a critical variable. In order to evaluate the effects of changing IV administration sets on the incidence of infusion-related septicemia, in neutropenic cancer patients, 50 subjects were randomly assigned to have their IV sets changed every 24 or 48 hours. Ten milliliters (ml) of IV infusate was collected prior to changing administration sets. Colonized IV infusate was detected in 9 of 236 (3.81%) specimens in the 24-hour group and 9 of 177 (5.09%) specimens in the 48-hour group. Group differences related to the rate of infusate colonization were not statistically significant ($p > 0.05$). The mean number of colony forming units (cfu)/ml of infusate was 91.67 ± 147.14 and 239.44 ± 335.13 for IV administration sets changed at 24 and 48 hours, respectively. Eight (32%) subjects in each of the two groups had microorganisms in excess of 15 cfu/ml isolated from their infusate, at some point during this study. None of the subjects with colonized IV infusate developed a subsequent infusion-related septicemia.

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CHAPTER ONE

Introduction

Intravenous (IV) administration sets are routinely changed to reduce the risk of developing an infusion-related septicemia. Researchers have examined various intervals to determine the frequency with which IV administration sets can be changed safely, using rates of infusate colonization as an indicator of the risk of developing an infusion-related septicemia (Band & Maki, 1979; Buxton et al., 1979; Gorbea, Snydman, Delaney, Stockman, & Martin, 1984; Jakobsen et al., 1986; Josephson, Gombert, Sierra, Karanfil, & Tansino, 1985; Maki, Botticelli, LeRoy, & Thielke, 1987; Snydman, Donnelly-Reidy, Perry, & Martin, 1987). Higher rates of infusate colonization are believed to be associated with frequent manipulations of the IV administration sets (Barry & Miller, 1988; Hampton & Sherertz, 1988), the use of central catheters (Maki, 1989, 1992; Moro, Vigano, & Lepri, 1994), the administration of parenteral nutrition (Goldmann & Maki, 1973; Snydman, Murray, Kornfeld, Majka, & Ellis, 1982), frequent blood transfusions (Maki, 1982), the practice of injecting additives either into minibags or directly into injection ports (Maki, 1976a), and withdrawing blood specimens from infusion catheters (Maki, 1989). However, current literature related to these variables remains inconclusive and at times even contradictory.

Despite the findings of recent studies that suggest IV administration sets may safely be changed at intervals up to but not exceeding 120 hours (Gorbea et al., 1984; Jakobsen et al., 1986; Josephson et al., 1985; Maki et al., 1987; Sitges-Serra, Linares, Perez, Jaurrieta, & Lorente, 1984; Snydman et al., 1987), neutropenic cancer patients are likely at greater risk for infection due to their compromised immune status. Neutropenic cancer patients are frequently exposed to many, if not all, of the aforementioned variables associated with higher rates of infusate colonization. Studies have not examined these variables as a collective nor explored the interrelationship(s) among these variables. Furthermore, cancer patients with protracted neutropenia are

susceptible to rates of infection not experienced by other hospitalized populations (Jamulitrat, Meknavin, & Thongpiyapoom, 1994) and tend to be less responsive to therapeutic intervention (Rubio et al., 1994). To date, neutropenic subjects have either been examined as part of a heterogenic population (Jakobsen et al., 1986; Josephson et al., 1985; Snydman et al., 1987) or excluded from study completely (Maki et al., 1987). In order to further knowledge regarding rates of infusate colonization and the risk of developing an infusion-related septicemia, related to frequency with which IV administration sets are changed, additional research with neutropenic cancer patients is warranted.

Purpose of the Study

The purpose of this study was to examine the effects of changing IV administration sets every 48, versus every 24 hours, on the incidence of infusion-related septicemia in neutropenic cancer patients, using rates of infusate colonization as an indicator of risk. Two specific hypotheses were tested: (a) there is no difference in the rate of infusate colonization between neutropenic cancer patients whose IV administration sets are changed every 24 hours and those whose IV administration sets are changed every 48 hours, and (b) there is no difference in the incidence of infusion-related septicemia between neutropenic cancer patients whose IV administration sets are changed every 24 hours and those whose IV administration sets are changed every 48 hours. Relationships among infusate colonization and neutropenia, central catheters, manipulating IV administration sets, blood transfusions, blood specimen collection, parenteral nutrition, comorbidities, antibiotic use, the addition of additives, and the incidence of infusion-related septicemia were also examined.

Because the incidence of infusion-related septicemia is so infrequent, determining the relative importance of each of these variables would require a substantial sample (Freiman, Chalmers, Smith, & Kuebler, 1978). Therefore, the intention was to show a trend of low rates of colonization, by microorganisms unrelated to those found in positive blood cultures, with no associated infusion-related

septicemia.

Significance of the Study

Examination of literature that addressed the relationship between the incidence of infusion-related septicemia and the frequency with which IV administration sets were changed, showed that gaps in knowledge exist. The rate of infusate colonization, an indicator of the risk of septicemia, is believed to be influenced by numerous variables, many of which have been excluded to some degree in previous studies. The administration of parenteral nutrition and blood products are two such variables. Furthermore, findings related to other variables such as the use of central catheters, hematological seeding and retrograde contamination, the use of antibiotics and additives, and/or manipulating IV administration sets, remain inconclusive or even contradictory.

Neutropenic oncology patients are especially vulnerable to infection and are routinely exposed to many, if not all, the aforementioned variables associated with higher rates of infusate colonization. To date, studies have excluded these patients (Maki et al., 1987) or have examined neutropenic subjects as part of a heterogenic population (Jakobsen et al., 1986; Josephson et al., 1985; Snydman et al., 1987), thereby diluting the influence of neutropenia as a critical variable. By comparing rates of infusate colonization in IV administration sets changed at 24 and at 48 hours, in neutropenic oncology patients, this relationship could be investigated. Guidelines could then be developed to improve patient care. Guidelines that reduce the incidence of infusion-related septicemia have the potential to improve the quality of life for these patients by reducing the need for additional therapy and, consequently, the length of hospitalization. Although the incidence of infusion-related septicemia is low, it constitutes a significant problem because of the number of neutropenic individuals receiving IV therapy through CVC and substantial cost in terms of human suffering (Banerjee et al., 1991). The identification and treatment of infusion-related septicemia is insufficient, the ultimate goal must be to prevent sepsis from occurring.

During a time of fiscal responsibility, measures with the potential to positively influence financial savings cannot be ignored. The purchase and storage of reduced numbers of administration sets would result in sizable savings for this institution. Nursing hours may be reallocated to other activities, as less time will be needed for changing IV administration sets. Potential savings may also be accrued from funds previously allocated for treatment of infusion-related septicemias.

CHAPTER TWO

Literature Review

Intravenous therapy, introduced in the early 1900's, has become an essential feature of modern patient care. It has been estimated that approximately one half of all patients currently admitted to acute care facilities will receive intravenous (IV) therapy in some form to restore fluid balance, administer antibiotics, electrolytes and/or parenteral nutrition, or to transfuse blood or blood products (Hampton & Sherertz, 1988; Maki, 1989; Simmons, 1983). Nevertheless, IV therapy carries with it a generally under-appreciated potential for producing nosocomial infection, specifically septicemia (Buxton et al., 1979; Gorbea et al., 1984; Hampton & Sherertz, 1988; Maki & Ringer, 1987; Maki, 1981; Maki & Martin, 1975; Rumsey & Richardson, 1995). Maki (1989) maintains that infusion-related septicemias are, and that even those that occur are frequently attributed to some other source. Two potential sources of infection associated with IV therapy include colonization of the cannulae with bacteria or fungi (Cronin, Germanson, & Donowitz, 1990) and colonization of infusate administered through the cannula (Maki, 1989, 1982). Although neither cannulas nor infusates are routinely cultured, the incidence of septicemia originating from the cannula has been estimated to be as much as ten times more frequent than microbial colonization of infusate (Band & Maki, 1979; Goldmann & Maki, 1973; Johnson & Oppenheim, 1992; Josephson et al., 1985; Maki, 1976b, 1992; Maki et al., 1987). Levels of infusate contamination too low to produce clinical symptoms of septicemia may, however, colonize the fibrin sleeve formed at the distal end of the catheter, thereby contributing to a catheter-related infection (Maki et al., 1976). Because frequent and prolonged periods of hospitalization is associated with infusion-related morbidity, additional research related to the risk of infusion-related septicemia is integral to improving the quality of life for these individuals. The following review will focus on variables associated with colonization of the infusate and the subsequent incidence of septicemia attributable to this source of infection.

Infusion-related Septicemia

Infusion-related septicemias originating from colonized infusate may be intrinsic, with microorganisms present in the fluid prior to use, or more commonly extrinsic, with microorganisms gaining entry into the system during use (Kelly et al., 1986; Maki, 1989; Raad & Bodey, 1992). It is estimated that the incidence of infusion-related septicemia is approximately one in 1,000 (Conly, 1995; Maki, 1982; Snydman et al., 1987). Once introduced into the infusion system, microorganisms can perpetuate despite periodic replacement of intravenous bags or bottles (Maki, 1976b) and rapid infusion rates (Maki, Anderson, & Shulman, 1974). Over time, there appears to be a cumulative effect whereby microorganisms grow to critical numbers, capable of entering the blood stream and producing clinical evidence of a septicemia (Gorbea et al., 1984; Maki, 1976a; Maki et al., 1987, 1991; Sitges-Serra, Puig, Linares, Perez, Farrero, Jaurrieta, & Garau, 1984).

Following a series of outbreaks in the United States during the early 1970's, the Center for Disease Control recommended the daily changing of IV administration sets to reduce the incidence of infusion-related septicemia (Bryan, 1987; Buxton et al., 1979; Maki, 1976b; Maki et al., 1974). Recognizing that the risk of septicemia related to contaminated infusate was rare, Band and Maki (1979) and Buxton et al. (1979) conducted prospective randomized trials to determine rates of infusate colonization in IV administration sets changed at 24 and 48 hour intervals and concluded that 48 hours was both safe and cost effective. More recent findings suggest that changing IV administration sets every 48 hours may also be excessive. Examination of infusate in IV administration sets changed at intervals up to but not exceeding 120 hours revealed no clinically significant increase in the frequency of colonization (Jakobsen et al, 1986; Josephson et al., 1985; Sitges-Serra, Linares, Perez, Jaurrieta, & Lorente, 1984; Snydman et al., 1987). Maki (1992) suggests that the majority of microorganisms introduced as a result of manipulating the system are probably cleared quickly from the infusate, especially if they grow poorly in the IV solution, hence the low rates of

colonization and even lower risk of developing an infusate-related septicemia.

Comparisons between studies examining the incidence of contaminated infusate are limited due to differences in inclusion criteria and the variables studied. For example, Buxton et al. (1979) examined medical, surgical, and intensive care patients with peripheral (butterflies and plastic catheters) and central catheters. Six hundred patients were randomly assigned to have their IV administration sets changed every 24 versus 48 hours. Administration sets used for parenteral nutrition or blood products were excluded. Twelve of the 600 infusions (2%) were culture positive, five in the 24 hour group and seven in the 48 hour group. Group differences were not statistically significant ($p > 0.05$); power analysis was not reported. Seven of the 12 positive specimens grew gram-negative rods or yeast, three in the 24 hour group and four in the 48 hour group. This finding is somewhat inconsistent with other studies that found coagulase-negative staphylococci and other skin commensals to be the predominant organisms isolated from infusate. Nevertheless, none of the twelve contaminated systems were associated with a subsequent septicemia.

Band and Maki (1979) conducted a prospective study to determine whether or not changing IV administration sets at intervals longer than 24 hours could be justified. Of the 790 infusions examined, contaminated infusate was detected in one of the 258 infusions (0.39%) sampled after 1 to 24 hours, three of the 359 infusions (0.84%) sampled after 25 to 48 hours, and one of 173 infusions (0.58%) sampled after 49 to 71 hours. Group differences again were not statistically significant ($p > 0.05$) and no contaminated infusates were associated with septicemia. Concentrations of 2 to 6 colony forming units (cfu) per milliliter (ml) of infusate, predominantly skin commensals, were found in the five contaminated specimens. Indications for catheterization included intravenous therapy, central venous pressure monitoring, total parenteral nutrition, and arterial pressure monitoring.

Gorbea et al. (1984) examined 676 IV systems containing in-line burettes, in intensive care units, believing that stagnant columns of fluid subjected to frequent

manipulations pose an even greater risk of infusion-related septicemia. Subjects were alternatively assigned to have their IV administration sets changed at 24 or 48 hour intervals. Excluded were subjects receiving parenteral nutrition through central catheters. Contamination rates were nine of 452 sets (2.0%) in the 24 hour group and nine of 224 sets (4.0%) in the 48 hour group. Colonization with greater than or equal to 10 cfu/ml of burette fluid occurred in five of the administration sets (1.1%) changed at 24 hours and two of the administration sets (0.9%) changed at 48 hours. *Staphylococci epidermidis* was isolated from 15 of the 18 culture positive infusates. Group differences were not statistically significant ($p > 0.05$) and no contaminated specimens were associated with septicemia.

Sitges-Serra, Linares, Perez, Jaurrieta, and Lorente (1984) examined only surgical patients receiving parenteral nutrition through central catheters to determine the effects of the frequency of tubing changes on hub colonization and catheter sepsis. These researchers differentiated between hub colonization ($< 10^3$ cfu) and infection ($> 10^3$ cfu) rather than infusate colonization as a factor in infusion-related septicemia. They found that of the 52 patients receiving parenteral nutrition, three (5.7%) developed septicemia; one of 20 patients (5%) in the 48 hour group and two of 32 patients (6.25%) in the 120 hour group. Group differences were statistically non-significant ($p > 0.05$); no power analysis was provided.

Josephson et al. (1985) examined only medical patients receiving IV therapy through both peripheral and central catheters and excluded subjects receiving parenteral nutrition and blood products. Of the 219 IV administration sets cultured, 115 were changed at 48 hours, 104 were not changed for the period the catheter was in place; contamination rates were one of 115 sets (0.87%) changed at 48 hours and one of 104 sets (0.96%) unchanged for the duration of the IV therapy. Group differences were not statistically significant ($p > 0.05$). Culture positive infusate in the 48 hour group revealed less than 2 cfu of *S. epidermidis*; in the no change group, less than 2 cfu of alpha-hemolytic streptococci were isolated. Neither of the colonized administration sets

were associated with septicemia. One subject developed a septicemia during the study, however, infusate specimens belonging to this patient were consistently sterile. The possibility of a catheter-related etiology was not discussed.

Jakobsen et al. (1986) examined the incidence of intralumenal contamination and phlebitis among medical and surgical patients with peripheral catheters. Primary IV administration sets used for parenteral nutrition were excluded. Intravenous administration sets were changed at varying intervals from 24 to 120 hours. The theoretical assumption underlying this study was that breaks in the connection between the catheter and the administration set would contribute to increased rates of septicemia. Culture positive IV lumens were as follows: 25 of 96 lumens (26.0%) in the 24 hour group; 21 of 86 lumens (24.4%) in the 48 hour group; 20 of 60 lumens (33.3%) in the 72 hour group; 12 of 43 lumens (27.9%) in the 96 hour group; and, 13 of 40 lumens (32.5%) in the 120 hour group. The rate of contamination was lower for the 48 hour group than the 72 or 96 hour groups ($p < 0.05$), but, there was no statistically significant difference between the 24 and 120 hour groups. Higher contamination rates in this study are probably related to the difference in culture method. The predominant organisms isolated were skin commensals, with no significant differences found between groups. Patients with a preexisting pyrexia showed higher rates of contamination, but again, this was not statistically significantly.

Maki et al. (1987) examined both peripheral and central catheters in medical and surgical patients who were non-neutropenic. Of the 1374 administration sets cultured, the contamination rate was six of 710 sets (0.8%) in the 48 hour group and ten of 664 sets (1.5%) in the 72 hour group. Microorganisms identified were almost exclusively small numbers (1 to 27 cfu/ml of infusate) of coagulase-negative staphylococci. Differences between groups were not statistically significant ($p > 0.05$) and no contaminated infusates were associated with a septicemia. These researchers also found that microorganisms were cultured less frequently from peripheral infusions (0.6%) than from central catheters infusions (1.5%) or the administration of parenteral

nutrition (3.6%). Furthermore, administration sets used in intensive care units were more frequently colonized (2.5%) than those used on medical or surgical wards (0.9%).

Snydman et al. (1987) examined the safety of changing IV administration sets, with in-line burettes, at 72 versus 48 hours in an intensive care setting. Both peripheral and central catheters were examined; IV administration sets used for parenteral nutrition and blood transfusions were excluded. Microorganisms were recovered from 100 of the 2082 burette fluids (4.8%) cultured; 60 of 1181 burettes (5.0%) in the 48 hour group and 40 of 901 burettes (4.4%) in the 72 hour group, respectively. In this study, researchers used ≥ 10 cfu/ml of IV infusate as an indication of significant contamination. Seven of 60 burette (0.6%) cultures in the 48 hour group and three of 40 burettes (0.3%) in the 72 hour group were considered significantly contaminated. Contamination rates did not differ significantly between these two groups ($p > 0.05$) and there were no bacteremias associated with culture positive burette fluid in either group. Microorganisms were also remarkably similar between the two groups with *S. epidermidis* isolated from 55 of the 100 positive burette fluids. Seven patients developed a catheter-related infection, five (4.7%) in the 48 hour group and two (3.1%) in the 72 hour group. None of these patients had colonized burette fluid prior to the onset of the infection.

The most recent study examining the relationship between the frequency with which IV administration sets are changed (24 versus 72 hours) and the incidence of infusion-related septicemia was by Robathan, Woodger and Merante (1995). These researchers prospectively examined the IV administration sets of 279 pediatric patients, receiving parenteral nutrition, through both peripheral and central catheters. Patients whose administration sets were changed every 72 hours experienced fewer infusion-related septicemias, eight of 152 sets (5.3%) versus 17 of 127 sets (13.4%) ($p=0.018$). The higher incidence of septicemia in this study was probably related to the way in which researchers defined infusion-related septicemia. Instances of infusion-

related septicemia were defined as follows: first, organisms isolated from blood cultures, unrelated to infection at another site and, second, physician instituted antibiotic therapy for clinical signs of sepsis in the absence of isolated organisms. A second factor found to influence the incidence of septicemia in this study was the length of time the patient received parenteral nutrition. Furthermore, patients receiving parenteral nutrition for >10 days not only had a higher incidence of septicemia, but, tended to be immunocompromised, thereby confounding the interpretation of study findings. The influence of the aforementioned and other variables on the rate of infusate colonization and the incidence of infusion-related septicemia will be further described in the following pages.

Hematological Seeding and Retrograde Colonization

Theoretically, IV infusate could become colonized by organisms from a preexisting foci of infection through hematological seeding (Maki, 1992; Michel, McMichan, & Bachy, 1979; Press, Ramsey, Larson, Fefer, & Hickman, 1984) and the retrograde spread of microorganisms up into the IV administration set (Maki, Goldmann, & Rhame, 1973; Maki, 1976b; Miller & Grogan, 1973). Hamptom and Sherertz (1988) suggest that most catheter-related fungal infections are the result of hematological dissemination from a distant source. Maki et al. (1973) confirmed higher rates of colonization in the lower portion of the IV administration set compared to rates found in the upper portion, which appears to support this theory. Meticulous aseptic catheter maintenance appears to be even more important in patients with an identified source of infection (Maki, 1976b).

In studies employing in-line filters, colonization was found primarily on the proximal or bag side of the filter membrane with a high correlation between organisms obtained from the infusate and the filter membrane (Miller & Grogan, 1973). In two filter systems, microorganisms were rarely isolated between the filters, thus demonstrating the efficiency of the filter membrane. It is unclear, however, whether microorganisms on the distal or patient side of the lower filter are the result of

retrograde contamination, poor aseptic technique during manipulations, or endogenous organisms from the patient's integument (Maki, 1976b; Maki et al., 1973; Miller & Grogan, 1973). Organisms were found less frequently on the patient side of the distal filter than above it (Maki, 1976b; Maki, 1976), suggesting that the migration of organisms up into the infusion system is rare and unlike that established for urinary drainage systems (Meers, 1976). Though possible, it appears that hematological seeding and the retrograde spread of microorganisms occur infrequently (Press et al., 1984; Maki, 1992; Maki et al., 1973). Rather, it is believed that infusate is more frequently colonized, primarily by small numbers of skin commensals, during compounding procedures and manipulations of IV administration sets (Maki, 1992).

Manipulating the System

Manipulations of IV administration sets clearly facilitates the introduction of microorganisms into the blood stream (Barry & Miller, 1988; Hampton & Sherertz, 1988; Maki, 1992; Sitges-Serra, Puig, Linares, Perez, Farrero, Jaurrieta, & Garau, 1984; Snydman et al., 1982). Microorganisms may gain entry into the infusion system following manipulation of any component of this system (Maki, 1976b; 1987; 1992; Simmons, 1983). Examples of these manipulations include compounding admixtures; administering IV medications or blood products; adding, piggybacking or changing administration sets; utilizing stopcocks, extension tubing, or Y-connectors; or heparin locking unused lumens. In a study by Miller and Grogan (1973), the rate of infusate contamination increased proportionately with the addition of in-line filters (one filter, 23.9%; two filters, 30.8%; three filters, 41.6%). This increase in infusate contamination was attributed to the increased number of manipulations of the IV administration set(s) as a result of adding filters to the system, as well as to manipulations of the administration set(s) to unblock filters. In an effort to reduce the risk associated with necessary manipulations, it has been recommended that connections be cleansed with 70% isopropanol, povidone-iodine, or chlorhexidine prior to the manipulation of administration sets (Elliott, Faroqui, Armstrong, & Hanson,

1994; Goldmann & Maki, 1973; Hampton & Sherertz, 1988).

Although aseptic technique is recommended when manipulating IV administration sets, any connection that is broken and then remade, or any injection into the infusion system could provide an opportunity for the introduction of microorganisms into the IV system. Conly (1995) suggests that the origin of microorganisms colonizing catheter hubs is quite conceivably the hands of hospital personnel manipulating the catheter hub, rather than endogenous cutaneous flora from the patient. Therefore, as a general rule, it is important that both manipulations of IV administration sets and the number of connections in IV systems be kept to a minimum (Conly, 1995; Maki, 1976b).

The relative significance of each manipulation on the incidence of infusion-related septicemia remains unknown and attempting to quantify the specific risk associated with each manipulation would be arduous. However, the effects of manipulating the system over time appear to be cumulative, with the risk of extrinsic colonization increasing proportionately with the duration of the infusion (Buxton et al., 1979; Cleri, Corrado, & Seligman, 1980; Hampton & Sherertz, 1988; Kelly et al., 1986; Maki, 1989; Maki et al., 1974; Moro et al., 1994). It has, therefore, been suggested that IV administration sets be maintained as closed systems as much as possible (Elliott et al., 1994; Maki, 1982; Simmons, 1983; Weightman, Simpson, Speller, Mott, & Oakhill, 1988) and that any advantage derived from changing IV administration sets daily be weighed against the effects of opening this system so often (Buxton et al., 1979; Parras et al., 1994; Weightman et al., 1988).

Neutropenia

Neutropenia associated with bone marrow failure predisposes patients to infections, including septicemias (Berenguer et al., 1990; Blacklock et al., 1980; Carlisle, Gucalp, & Wiernik, 1993; Ehni, Reller, & Ellison, 1991; Hughes et al, 1990; Landoyet al., 1984; Ranson, Oppenheim, Jackson, Kamthan, & Scarffe, 1990; Wickham, Purl, & Welker, 1992), particularly in individuals with hematological

malignancies (Farber et al., 1991; Jamulitrat et al., 1994; Landoy et al., 1984; Lowder, Lazarus, & Herzig, 1982; Rubio et al., 1994). Qi-nan and Zhong-da (1989) concluded that neutropenia was the predominant variable associated with infection. In their study of 257 patients with acute leukemia, hospitalized 346 times, 205 of 232 hospitalizations (88.4%) where neutrophil counts were $< 1{,}000/mm^3$ were associated with an infection compared to 47 of 114 hospitalizations (41.4%) where neutrophil counts were $> 1{,}000/mm^3$ ($p < .0001$). Furthermore, the degree of neutropenia was reflected in mortality rates of 56.4% and 40.0%, respectively ($p < 0.05$).

Lowder et al. (1982) found that patients with leukemia had significantly higher rates of septicemia than patients with solid tumors and lymphomas. Similarly, when researchers compared individuals infected with the Human Immunodeficiency Virus (HIV) to patients with hematological malignancies, they found that T-cell mediated neutropenia did not appear to be associated with the same degree of risk as neutropenia secondary to bone marrow failure (Farber et al., 1991). In addition to being at greater risk of infection, neutropenic cancer patients tend to have a poorer response to therapeutic interventions (Rubio et al., 1994). It was, therefore, proposed that surveillance techniques or protocols used in some areas of the hospital may require modifications to be appropriate for use with neutropenic cancer patients (Carlisle et al., 1993).

Central Venous Catheters

The introduction of central venous catheters (CVC) in the management of oncology patients has revolutionized the delivery of long-term chemotherapy, antibiotics, blood products, and nutritional support (Blacklock et al., 1980; Johnson & Oppenheim, 1992; Kelly et al., 1986; Landoy et al., 1984; Maki, 1982, 1989; Wickham et al, 1992), as well as blood sampling (Johnson & Oppenheim, 1992; Mackinnon et al., 1987). Used to facilitate patient care while minimizing discomfort, CVC are the intravascular device of choice (Maki, 1989) and are ideally inserted early in the treatment of these individuals (Decker & Edwards, 1988). However, CVC may

contribute to the infectious complications experienced by neutropenic cancer patients (Conly, 1995; Lowder et al., 1982) and are more frequently implicated in nosocomial septicemias than peripheral catheters (Maki et al., 1987; Maki, 1989, 1992; Moro et al., 1994; Raad & Bodey, 1992). Furthermore, there appears to be a shift from predominantly gram negative (*Klebsiella pneumoniae*, *Enterobacter* species, and *Escherichia coli*) to gram positive (*Corynebacteria* species, *S. epidermidis*, and *S. aureus*) organisms isolated from patients with central rather than peripheral catheters (Lowder et al., 1982).

The CVC itself has been implicated in the transcutaneous spread of microorganisms into the vascular bed (Armstrong et al., 1990; Cleri, Corrado, & Seligman, 1980; Conly, 1995; Mackinnon et al., 1987; Maki & Ringer, 1987; Pinilla, Ross, Martin, & Crump, 1983), primarily with skin commensals (Blacklock et al., 1980; Kelly et al., 1986; Maki, 1992; Maki, Weise, & Sarafin, 1977). Surgically tunnelled long-term CVC, frequently used for neutropenic cancer patients, possess a subcutaneous dacron cuff with the potential to provide a mechanical barrier resistant to microbial colonization (Press et al., 1984). For this reason, long-term tunnelled catheters are reportedly associated with lower rates of septicemias than short-term noncuffed CVC (Maki, 1992).

The incidence of catheter-related septicemia varies from study to study ranging from four to 60% with variability associated with the immunocompetence of the patient, insertion techniques, the type of catheter and number of lumens, routine maintenance, and the physical condition of the patient (Maki et al., 1991; Raad & Bodey, 1992; Wickham et al., 1995). Highest rates are, however, reported among neutropenic populations (Ranson et al., 1990). Many of the organisms implicated in catheter-related septicemias are of low virulence with levels of contamination insufficient to produce clinical illness in non-neutropenic populations. However, skin commensals may be a predominant cause of septicemia in neutropenic patients (Ehni et al., 1991; Kelly et al., 1986; Landoy et al., 1984; Lowder et al., 1982; Mackinnon et

al., 1987; Press et al., 1984; Ranson et al., 1990; Snydman et al., 1982), possibly because cancer therapy compromises both the integument and the immune response.

It is also possible that the incidence of infusion-related septicemia is influenced by circumstances that warrant the need for central access in the first place (Landoy et al., 1984; Michel et al., 1979; Moro et al., 1994). Hospitalized neutropenic cancer patients are acutely ill, often requiring double and triple lumen CVC to accommodate the multiple IV antibiotics, chemotherapeutic agents, electrolyte boluses, blood transfusions and nutritional support frequently required to manage their disease process. McCarthy, Shives, Robinson, and Broadie (1987) found that multilumen catheters were associated with higher rates of infection than single lumen catheters. One explanation for this finding was that multilumen catheters and associated administration sets are subjected to frequent manipulations to accommodate the prescribed therapies, which further contributes to the incidence of infusion-related septicemia (Gorbea et al., 1984; Press et al., 1987). Consequently, the relationship between the CVC itself and the incidence of infusion-related septicemia is further confounded by variables associated with cancer therapy. Michel et al. (1979) concluded that the severity of the underlying disease was the principle factor in determining the susceptibility of patients to infection and also central catheters to contamination.

In a study examining the incidence of catheter-related infection among 79 cancer patients, Landoy et al. (1984) found that patients with two CVC were at greater risk of infection than those with a single central catheter, 47 versus 10% respectively ($p < 0.05$). Among patients with hematological malignancies, this finding was even more remarkable with rates of infection of 53.3 versus 13.5% for individuals with solid tumors ($p < 0.005$). This finding was attributed to the existence of two exit sites.

Total Parenteral Nutrition

Total parenteral nutrition (TPN), used to achieve an anabolic state in compromised patients, has also been associated with an increased risk of infusion-related septicemia, primarily because it provides microorganisms a source of nutrients not ordinarily available (Goldman & Maki, 1973; Snydman et al., 1982; Raad & Bodey, 1992; Stotter, Ward, Waterfield, Hilton, & Sim, 1987). Although most TPN-related septicemias are believed to be catheter-related (Maki, 1976b; Sitges-Serra, Puig, Linares, Perez, Farrero, Jaurrieta, & Garau, 1984), with the intralipid/dextrose solution creating an environment that is selectively advantageous to fungal growth (Band & Maki, 1979; Baron et al, 1994; Goldmann & Maki, 1973; Maki, 1992; Soloman et al., 1984; Simmons, 1983), the route of ingress remains unclear. Sitges-Serra, Puig, Linares, Perez, Farrero, Jaurrieta, and Garau (1984) believe that connections in the TPN administration set are the predominant portals of entry for microorganisms. A study by Stotter et al. (1987) examining junctional care appears to support this theory. In their study, the adoption of a catheter with an integral hub offered two advantages: first, it reduced the number of connections from two to one and, secondly, it allowed the hub connection to lie away from the patient's skin and its flora. Infection rates dropped from 39% to 8% following this change in protocol.

Snydman et al. (1982) acknowledge a similar relationship between the frequency with which TPN administration sets are manipulated and the incidence of infection. Intravenous administration sets with multiple connections are manipulated more frequently than sets with fewer connections. However, there appears to be a concurrent relationship between the frequency with which IV administration sets are manipulated and the acuity of the patient receiving TPN, with the administration sets of the more acutely ill patients being manipulated more frequently (Moro et al., 1994) and, therefore, susceptible to higher rates of colonization.

The migration of microorganisms, from the infusate towards the catheter, may also facilitate the colonization of the catheter hub and fibrin sleeve, formed at the distal

portion of the CVC (Sitges-Serra, Puig, Linares, Perez, Farrero, Jaurrieta, & Garau, 1984), thereby producing a catheter, rather than infusion-related septicemia (Maki, 1976b). In a study by Maki et al. (1977), semi-quantitative culture of the catheter following an identified case of septicemia related to heavily contaminated infusate revealed only six colonies of the infecting organism. Similarly, Armstrong et al. (1990) found heavier populations of microorganisms on the external, rather than internal, surface of infected CVC. Miller and Grogan (1973) reported high rates of colonized TPN infusate with no clinically recognized septicemia. Maki (1982) also found little evidence to support an association between heavily contaminated TPN infusate and the subsequent development of a septicemia.

Historically, the administration of TPN through a CVC has been thought to be one of the most vulnerable forms of IV therapy (Gorbea et al., 1984; Snydman et al., 1987). Any relationship between TPN and nosocomial infection, in patients with CVC, is confounded by the relationship between CVC and infection (Jamulitrat et al., 1994) described earlier. Host factors such as debilitating illness, long-term use of broad-spectrum antibiotics, and a compromised immune response, further increase susceptibility to infusion-related infections (Goldmann & Maki, 1973; Maki, 1992) and obscure attempts to identify the primary sources of colonization.

Blood Transfusions and Specimen Collection

The need for frequent blood transfusions introduces another variable with the potential to influence the incidence of infusion-related septicemia for neutropenic cancer patients. Though rarely a cause of extrinsic contamination (Maki, 1982), blood products have the potential to buffer acidic solutions while providing organic nutrients capable of supporting a broad spectrum of organisms in IV fluid (Band & Maki, 1979; Maki, 1976a; Maki et al., 1973). Traditionally, administration sets used for transfusion therapy are discarded following use; however, even minute traces of blood remaining at the connection site may potentially support microbial growth.

Given that connections are recognized portals of entry for microorganisms (Stotter et al., 1987), breaking and remaking connections following transfusion therapy may facilitate their ingress. Similarly, it has been demonstrated that the backup of blood into the IV administration set, as a result of a break in the connection or because of changes in pressure (Maki, 1976a), and the aspiration of blood specimens from the CVC (Maki, 1989) encourages fungal colonization of the infusate in a comparable manner (Maki, 1989). Accordingly, the transfusion of blood and blood products, the backup of blood into IV administration sets, and the withdrawal of blood specimens through the CVC are believed to be associated with an increased risk of colonization of the IV infusate. However, it remains questionable whether this colonization could be commensurate with the subsequent development of a septicemia.

Additives and Admixtures

The final variable to be considered addresses the practice of adding medications and/or electrolytes to commercially prepared IV fluid or directly into IV administration sets. Examples of this practice include reconstituting antibiotics on the nursing unit, administering IV push medications, and adding potassium chloride, magnesium sulphate or sodium bicarbonate to prepackaged IV solutions. If additives are inoculated into a stagnant reservoir, such as a minibag or burette, the growth potential of microorganisms poses the greatest risk (Maki, 1992). It has, therefore, been recommended that compounded solutions be refrigerated until needed and used as soon as possible (Maki, 1976b). Idle IV administration sets, disconnected from the CVC for varying periods of time, provide a stagnant reservoir equally susceptible to microbial colonization. Growth of particular microorganisms may, however, be inhibited by antibiotics administered through the IV administration set, thereby selectively favoring the growth of other nonsusceptible organisms (Duma, Warner, & Dalton, 1971).

Maki (1976a) found that IV fluid sampled following compounding and in-use infusate have similar rates of colonization, suggesting that compounding constitutes a significant source of extrinsic contamination. Woodside, Woodside, D'Arcy, and Patel

(1975) found that additives were associated with an increased rate of contaminated infusate, 6.7 versus 3.6%, respectively. In a study by D'Arcy (1976), analysis of 1003 infusions demonstrated a higher incidence of contamination in containers with additives, 19 of 284 (6.7%), than in containers without additives, 26 of 719 (3.6%). However, the highest colony counts were found in containers without additives; ten of 26 containers (22.2%) without additives had >100 cfu/ml of infusate, none of the containers with additives were found to be colonized to this degree. Given the frequency with which additives are utilized, D'Arcy suggests that it is unlikely that this practice represents a significant source of extrinsic contamination. Conversely, Hughes (1973) found higher rates of infusate contamination in containers with rather than without additives, 5.5% versus 3.3% respectively. Jakobsen et al. (1986) found no correlation between contamination and the use of additives in 387 patient administration sets. Outcomes related to this practice are, therefore, arguable and the issue of risk unresolved. It is clear, however, that additives do not constitute the only source, nor the primary source, of extrinsic colonization of infusion fluid.

Microorganisms Implicated in Infusion-related Septicemias

The risk to the patient infused with contaminated infusate depends in part on the microbial characteristics of the organism per se and the numbers present. Most human pathogens require a very specific pH and temperature to survive and are harmful in that they are nutritionally demanding (Baron, Chang, Howard, Miller, & Turner, 1994). Intravenous fluids rarely satisfy these demands, therefore, microorganisms are frequently unable to multiply or perpetuate within the infusate for any significant period of time. The microorganisms recovered most frequently from in-use infusate are skin commensals (Band & Maki, 1979; Cleri et al., 1980; Hamptom & Sherertz, 1988; Maki et al., 1976; Meers, 1976). Contamination was often of low level, <10 cfu/ml (Maki, 1992), by microorganisms believed to be of low virulence, and able to grow poorly, if at all, in parenteral fluids (Ranson et al., 1990). This level of colonization is presumed to be too low to produce clinical illness, even in an immunocompromised

patient (Maki, 1992).

Gram positive, coagulase-negative staphylococci (CNS) are the predominant cause of septicemia in neutropenic cancer patients (Blacklock et al., 1980; Carlisle et al., 1993; Lowder et al., 1982; Press et al., 1984; Snydman et al., 1982), possibly because cancer therapy compromises both the integument and the immune response (Rubio et al., 1994). Colonization with CNS is associated with catheter- rather than infusion-related infections (Banerjee et al., 1991; Blacklock et al., 1980; Decker & Edwards, 1988; Pinilla et al., 1983; Press et al., 1984; Ricard, Martin, & Marcoux, 1985). The intrinsic microbial characteristics of *S. epidermidis* allow this bacterium to adhere to catheter surfaces and protect it from antibiotics, phagocytosis and natural antibodies, thereby allowing it to perpetuate at the catheter site (Baron et al., 1994; Press et al., 1984; Raad & Bodey, 1992). Even in the absence of extrinsic nutrients, this bacterium is able to proliferate on central catheters using the catheter itself as a nutrient source (Sheth et al., 1983).

In contrast, aerobic gram-negative bacilli, known to grow rapidly at room temperature, are the most common organisms associated with septicemias linked to contaminated infusate (Maki et al., 1974, 1976; Maki, 1992; Raad et al., 1992). Examples of these organisms include *Klebsiella*, *Neisseria*, *Enterobacter*, *Pseudomonas*, *Citrobacter*, and *Serratia* species. Since gram-negative bacilli have been demonstrated in high frequency on the hands of hospital personnel and patients (Maki & Martin, 1975; Maki, 1976b) they may be introduced during manipulations of administration sets. Alternatively, some species such as *Klebsiella* tend to colonize the gastrointestinal tract of patients receiving antibiotics and then invade the blood stream when neutrophil counts are low (Jamulitrat et al., 1994). Contamination of the infusate with the gram-negative bacilli carries with it a significant risk of septicemia, septic shock (Maki, 1992) and even death (Qi-nan & Zhong-da, 1989).

A study that evaluated the growth of microorganisms in 5% dextrose in water (D5W), a frequently used IV solution, found that 50 of 51 strains of the tribe

Klebsielleae reached concentrations of >100,000 cfu/ml of infusate within 24 hours (Maki & Martin, 1975). Examples of these organisms include *Klebsiella*, *Enterobacter*, and *Serratia* species. In contrast, staphylococci, *E. coli*, *Pseudomonas* species, and *Candida* organisms showed minimal, if any, growth in the same period of time. Normal saline (NS) appears to support most bacterial growth, with the exception of *Candida* which grows poorly (Maki, 1992). *Candida* species also tend to grow slowly in amino acid/dextrose solutions; but, like most microorganisms, are prolific in 10% lipid emulsion. Findings of a study by Maki (1980, cited in Maki 1992) suggest that 12 of 13 microorganisms and *Candida* were as prolific in a lipid emulsion as in a bacteriologic media. Nevertheless, microbial growth in most parenteral fluids is quite limited.

The identity of the specific organism implicated in a septicemia may be indicative of the etiology of the infection. The isolation of *Enterobacter* species, *Serratia*, *Pseudomonas*, or *Acinetobacter* in blood cultures is suggestive of contaminated infusate (Conly, 1995; Maki, 1989). In contrast, the isolation of staphylococci, *E. coli*, *Proteus* species, or *Candida* suggests that the infection is probably catheter-related or due to some other non-infusion-related source (Maki, 1989, 1992). Microorganisms causing septicemia in neutropenic patients do not differ significantly from those identified in non-neutropenic patients, however, polymicrobial infections are more common in neutropenic populations (Rubio et al., 1994; Weinstein, Reller, Murphy, & Lichtenstein, 1983).

Summary

It is believed there is a relationship between the frequency with which IV administration sets are changed and the incidence of infusion-related septicemia. This relationship, however, is confounded by several variables including: the presence of a CVC; the number of IV administration sets in use, the number of connections within each set, and the frequency with which each set is manipulated; and, the type of the infusate in use including TPN, antibiotics, additives, and blood products. Furthermore,

neutropenic cancer patients are frequently exposed to many of the aforementioned variables, are believed to be at greater risk of infection, and exhibit a poorer response to therapeutic intervention. Morbidity associated with infusion-related infection results in frequent and prolonged periods of hospitalization for these individuals. Therefore, additional research related to the risk of infusion-related septicemia is integral to improving the quality of life for neutropenic cancer patients.

CHAPTER THREE

Method

Design

A randomized clinical trial with repeated measures was used to compare colonization rates in the intravenous (IV) administration sets, of neutropenic cancer patients, changed at 24 versus 48 hours. The independent variable was the frequency with which IV administration sets were changed, either 24 or 48 hours. The dependent variable was the rate of infusate colonization. The rate of infusate colonization was used as an indicator of the risk of developing an infusion-related septicemia; the higher the rate of colonization, the higher the risk of developing an infusion-related septicemia (Maki et al., 1973; Jakobsen & Grabe, 1983 cited in Jakobsen et al., 1986). An intermediate value of $\geq$ 15cfu/ml of infusate was chosen to represent clinically significant colonization, capable of producing an infusion-related septicemia (Band & Maki, 1979; Gorbea et al., 1984; Josephson et al., 1985; Maki et al., 1987; Syndman et al., 1987). Given the prevalence of febrile neutropenia among cancer patients, accruing afebrile subjects to establish a causal relationship between the frequency with which IV administration sets were changed and the incidence of infusion-related septicemia was not possible. Therefore, positive blood cultures and infusate specimens were compared to determine whether or not a relationship existed between types of microorganisms isolated from blood specimens and those found in the IV infusate. The research questions were: (a) Is there a difference in the rate of infusate colonization between neutropenic cancer patients whose IV administration sets are changed every 48 versus 24 hours? Furthermore, is there a relationship between the microorganisms isolated from positive blood cultures and those found in the IV infusate? (b) Is there a difference in the incidence of infusion-related septicemia between neutropenic cancer patients whose IV administration sets are changed every 48 versus 24 hours?

Based on a review of the literature and personal clinical experience, several extraneous variables were identified and attempts were made to control for group

differences with regard to these variables either through sampling or design. Variables controlled through sampling included protracted neutropenia secondary to bone marrow failure (as a result of chemotherapy or specific disease process) and the existence of a surgically tunnelled CVC, routinely used for blood specimen collection. Only those patients with absolute neutrophil counts (ANC) of $\leq 1{,}000/mm^3$ of blood were eligible to be included. Similarly, only patients with double or triple lumen, surgically tunnelled CVC were included in this study. Variables controlled through random assignment of subjects to the treatment or control group included the frequency with which IV administration sets were manipulated (excluding changing the administration sets), the number of IV administration sets in use, the number of connections in situ, the frequency with which blood specimens were collected, the existence and number of comorbidities, the possibility of receiving parenteral nutrition, antibiotics, additives, and/or blood transfusions. Statistical comparisons were made to determine whether or not group differences existed related to these variables.

Definition of Terms

The IV administration set was defined as the intravenous delivery system from the bottle or bag at the upper end of the system, the IV tubing, secondary medication sets, and all Y-connections and/or extensions, up to but not including the CVC lumen. Each IV administration set was sampled and analysed separately.

Neutropenia was defined as an ANC of less than or equal to $1{,}000/mm^3$ of blood (Brown, 1990; Carlisle et al., 1993; Ehni et al., 1991; Farber et al., 1991; Hughes et al., 1990). The ANC was calculated by multiplying the total percent of neutrophils (segmented and band neutrophils) by the WBC, then dividing by 100 (Brown, 1990). Neutrophils, the first line of defence against infection, normally comprise approximately 50-60% or $2{,}500\text{-}7{,}000/mm^3$ of the body's white blood cell (WBC) count (Brown, 1990). A rapid loss of neutrophils and/or protracted neutropenia (greater then 10 days) are believed to be significant risk factors for infection (Hughes et al., 1990).

A febrile episode was signalled by a tympanic temperature of greater than or equal to 38.5° C, in the absence of environmental causes (Hughes et al., 1990) and unrelated to blood transfusion therapy, for a minimum of one hour. Febrile episodes in patients with neutrophil counts below 1,000/mm^3 were considered to be medical emergencies.

Extrinsic colonization was defined as the introduction of microorganisms into the infusion system during the manipulation of the IV administration set (Band & Maki, 1979; Barry & Miller, 1988; Hamptom & Sherertz, 1988; Maki, 1976b; Snydman et al., 1987). Microorganisms may gain access to the infusate through connections in the system (Buxton et al., 1979; Jakobsen et al., 1986; Meers, 1976), from the immediate environment and/or the hands of both patients and health care professionals (Maki & Martin, 1975; Meers, 1976).

Intrinsic colonization was defined as the introduction of microorganisms into infusion fluid during the manufacturing process (Band & Maki, 1979), often precipitating an outbreak (Maki et al., 1987; Simmons, 1983).

Colonization and contamination were used to describe the presence of microorganisms in the infusate. Although used synonymously in the literature, in this study colonization referred to greater than or equal to 15 cfu/ml of aspirate and was associated with an increased risk of developing an infusion-related septicemia (Band & Maki, 1979; Maki et al., 1987; Sitges-Serra, Puig, Linares, Perez, Farrero, Jaurrieta, & Garau, 1984). Contamination referred to the presence of microorganisms in quantities less than 15 cfu/ml of infusate and unlikely to produce a septicemia.

An infusate-related septicemia included clinical features of a blood stream infection, isolation of the same organism from both the infusate and peripheral blood cultures, blood cultures drawn from the CVC negative for the infecting organism, and the absence of an alternative identifiable source of the septicemia (Band & Maki, 1979; Maki et al., 1987 Snydman et al., 1987).

Catheter-related septicemia included clinical features of a blood stream

infection, positive blood cultures drawn from the catheter with isolation of the same organism from blood cultures drawn from a peripheral site (Weightman et al., 1988), cultured infusate negative for the infecting organism, and the absence of an alternative identifiable source of the septicemia (Band & Maki, 1979; Maki et al., 1987; Snydman et al., 1987).

Sample

The population from which subjects were recruited were adult in-patients at the Cross Cancer Institute (CCI), Edmonton, Alberta, with a primary diagnosis of a hematological malignancy, breast or testicular cancer, or the recent recipient of a stem cell transplant. Inclusion criteria for subjects were as follows: (a) 18 years of age and older; (b) receiving ongoing intravenous therapy; (c) possess a surgically tunnelled CVC; (d) have been neutropenic for a minimum of two days; and, (e) able and willing to give consent. The sample population consisted of 25 subjects in each of two groups for a total of 50 subjects. Each subject agreed to have infusate withdrawn from each of their IV administration sets, for a proposed period of five consecutive measurements. Data collection spanned a period of eight months from March, 1995 to November, 1995 .

Data Collection Protocol

Subjects were identified either by the Assistant Unit Manager at the CCI, or the researcher, following a chart review to ensure they met the inclusion criteria. If subjects were identified by the Assistant Unit Manager, the researcher was subsequently notified. The researcher approached subjects to explain the study and obtain informed consent (Appendix A). Demographic data was collected related to the subject's gender, age, primary diagnosis, comorbidities, type of CVC, tympanic temperature, and absolute neutrophil count (ANC) (Appendix B). A table of random numbers was used to assign subjects to one of two groups: Group A with IV administration sets changed every 24 hours, or Group B with IV administration sets changed every 48 hours. Subjects were usually entered into the study at the time of

consent. If consent was obtained later in the day, subjects were entered into the study the following morning. Subjects continued in the study for a maximum of five days (Group A) or 10 days (Group B), until they were no longer neutropenic, or were transferred or discharged from hospital.

Intravenous infusate samples were collected daily for subjects assigned to Group A (24 hours) and every second day for subjects assigned to Group B (48 hours). Immediately prior to changing the IV administration set(s), infusate specimens were collected by the researcher as follows:

1. Using hemostats, the IV administration set (Gemini®) was clamped on the patient side of the distal injection port.
2. The injection port was swabbed with 70% isopropyl alcohol (Webcol®) and allowed to air dry for approximately 30 seconds.
3. Ten ml of infusate was aspirated from the distal port using a 22 gauge, one inch needle (B-D®) and a 10 ml sterile syringe (Slip Tip®).
4. Specimens were refrigerated until transported. Capped infusate specimens were hand delivered to the microbiology laboratory for culturing.

Prior to aspirating infusate specimens, antibiotics were flushed from the IV administration set(s) with normal saline or a similar primary solution. The IV administration set(s) and primary solution were changed at a predetermined time (plus or minus one hour) and each IV administration set was sampled separately. Administration sets used to transfuse blood and blood products are routinely changed every four hours or after two units of packed cells, therefore, these sets were excluded from study. In cases where the protocol for changing administration sets was broken, subjects were excluded from further study. Subjects discharged from hospital were reentered into the study on subsequent admissions providing consent was again obtained. Additional data related to study variables, were collected by either staff nurses or the researcher on a daily basis (Appendix C).

To ensure reliability in the data collection process, staff nurses involved in this

study received an inservice prior to commencing the data collection phase of this study. The purpose of this inservice was to describe the data collection process and provide staff nurses with an opportunity to ask questions to ensure a shared understanding of the purpose of the study and the information required to complete the data collection forms. Daily observations were made by the researcher to promote consistency in data collection and to foster continued interest in this study.

Microbiological Methods

Following transport to the microbiology laboratory, infusate specimens were refrigerated until sampled by laboratory personnel, using the following membrane filtration procedure. Ten ml of aspirated IV infusate was filtered through a sterile 0.20 micropore filter (Acrodisc®). In turn, this filter was transferred aseptically to a glass vial of 5.0 ml brain heart infusion broth. Following mechanical agitation (Vortex®) to uniformly distribute microorganisms throughout the liquid media, a blood agar culture plate was inoculated with .1 ml of this solution, then incubated at 35° C for 48 hours.

Inoculated plates were then examined by laboratory personnel to determine the incidence of colonization; bacterial growth was identified, enumerated, and recorded (Appendix D). A multiple of five was applied to each cfu identified on blood agar plates to calculate the cfu/ml of infusate. Blood agar plates exhibiting three or more organisms were considered colonized, defined as $\geq$15 cfu/ml of infusate. Because the lipids in parenteral nutrition are too large to be filtered, 0.1 ml of the TPN was plated directly; therefore, a multiply of 10 was applied to these specimens to determine the cfu/ml of TPN. The validity of this method rests with the assumption that when culturing a specimen, every microorganism present will develop into a colony. Although some microorganisms fail to multiply and others may adhere together forming a single colony, this method has proven to be invaluable (Smith, 1985).

Cultured organisms were then removed aseptically from the blood agar plates and immersed in vials containing 0.1 ml of double strength skim milk and placed in frozen storage (-20° C) until the conclusion of the study. Speciation was performed on

all infusate specimens belonging to patients found to have positive blood cultures. The remaining 4.9 ml of liquid media (brain heart infusion broth) was also cultured to identify any organisms that may have escaped detection because of low numbers. Organisms identified in liquid media represent microbial contamination equivalent to <5 cfu/ml of infusate. Because these microorganisms could not be quantified precisely, each different organism cultured from liquid media was assigned a value of 1 cfu/ml of infusate, to facilitate analysis.

Blood Cultures

Two sets of aerobic and anaerobic blood cultures were collected from subjects identified as febrile. Resin-containing culture medium (Bactec®) was used to collect blood cultures peripherally (by the physician) and through the CVC (by the nurse), as per CCI policy, prior to commencing antibiotic therapy (Weinstein, Reller, Murphy, & Lichtensin, 1983). For patients already receiving antibiotic therapy, the researcher encouraged the practice of collecting blood cultures just prior to administering the next dose of antibiotic, given that antibiotics would be at trough levels and subsequently yield the best results (Maki, 1992). Additional blood cultures were collected at the discretion of the attending physician. Positive blood cultures and corresponding infusate specimens were compared to investigate the likelihood of an infusate-related etiology and rule out the possibility of a catheter-related septicemia (Appendix E).

Ethical Considerations

Ethical approval was obtained from the Faculty of Nursing, University of Alberta Ethics Review Committee, Clinical Priorities Committee at the CCI, and Alberta Cancer Board Research Ethics Committee. Subject participation in this study was voluntary. The researcher approached subjects to provide information related to the purpose of the study, the manner in which data were to be collected, the intended use of this information, and the expected duration of the study. Subjects were apprized of both the potential risks (a risk of increased infusate colonization) and benefits (a decreased risk of infusate colonization and less frequent manipulations of their IV

administration sets) associated with participation in this study.

A description of the study was provided in language appropriate for the non-professional subject and understanding assessed by inviting subjects to recount in their own words, information related to the study. Subjects were encouraged to ask questions throughout the study. Participants were free to withdraw at any point during this study, with no resulting consequence to their care. An explanation of the potential utility of this study for nursing and for other neutropenic cancer patients was also provided. Subjects were assured of confidentiality; no identifying information is associated with summarized results nor will be associated with the publication of any portion of this study. Disclosure of the results of this study will be made available to all subjects that requested this information by completing the lower portion of the consent form (Appendix A).

CHAPTER FOUR

Findings

The purpose of this study was to examine the effects of changing intravenous (IV) administration sets every 48 hours, versus every 24 hours, on the incidence of infusion-related septicemia in neutropenic cancer patients, using rates of infusate colonization as an indicator of risk. Mean colony counts from IV administration sets were then compared between the two groups, over time. Descriptive statistics were used to describe Group A (24 hours) and Group B (48 hours) with regard to demographic and study variables, rates of infusate contamination and colonization, microorganisms identified, and the incidence of infusion-related septicemia. Analysis of variance (ANOVA) with repeated measures was used to compare colony counts from the IV administration sets between subjects in the 24-hour and 48-hour groups, across the five time frames. The incidence of infusion-related septicemia in the two groups was compared using Chi-square. Subanalysis of study variables was accomplished using Chi-square, ANOVA, and analysis of covariance (ANCOVA). Relationships among study variables were examined using Pearson's r where appropriate. Data were analysed using SPSS® for Windows™ 6.0 and the level of significance was set at ≤ 0.05. Study findings will be presented as follows: first, sample characteristics including demographic and infusion related variables will be described using subjects (N=50) as the unit of analysis; secondly, characteristics of the infusion therapy will be described using the intravenous (IV) administration sets (N=423) as the unit of analysis; thirdly, microbiological findings will be presented as they relate to the sample and infusion therapy; and lastly, findings related to the incidence of infusion-related septicemia will be provided.

Characteristics of the Sample

Demographic Variables

For a period of eight months, data were collected on 50 subjects, 25 in each of two groups, with a total of 423 IV administration sets. Fourteen males and 36 females consented to be in this study (Table 1). In the 24-hour group, eight of 25 subjects (32%) were male and 17 (68%) were female. In the 48-hour group, six of 25 subjects (24%) were male and 19 (76%) were female. Gender differences between groups were not statistically significant (χ^2=.0890, df=1, p=.5287).

Table 1

Gender of Subjects

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	f	%	f	%	f	%
Male	8	32	6	24	14	28
Female	17	68	19	76	36	72

It is believed that as one ages, the body's immune response is less able to respond quickly to microbial challenges (Linn & Jensen, 1983). Subjects in this study ranged in age from 25 to 75 years with a mean, plus or minus one standard deviation (±), of 46.00 ± 10.70 years (Table 2). Subjects in the 24-hour group ranged in age from 27 to 75 years with a mean of 46.24 ± 11.60 years. Subjects in the 48-hour group were slightly younger and ranged in age from 25 to 65 years with a mean of 45.76 ± 9.96 years. Differences between subjects in the 24-hour and 48-hour groups with regard to age (in years) were not statistically significant (F=.02, df=1, p=.876).

Table 2

Age of Subjects

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	**M**	**SD**	**M**	**SD**	**M**	**SD**
Age in Years	46.24	11.60	45.76	9.96	46.00	10.70

To maintain as homogenous a sample as possible, subjects were limited to those previously diagnosed with leukemia (n=26), lymphoma (n=6), breast cancer (n=4), testicular cancer (n=1), or individuals having received a stem cell transplant (n=13) (Table 3). The two groups were not found to be statistically different with regard to subjects' primary diagnosis (χ^2=.2591, df=4, p=.4996).

Table 3

Primary Diagnosis of Subjects

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	**f**	**%**	**f**	**%**	**f**	**%**
Leukemia	13	52	13	52	26	52
Lymphoma	2	8	4	16	6	12
Breast Cancer	1	4	3	12	4	8
Testicular Cancer	1	4	0	0	1	2
Stem Cell Transplant	8	32	5	20	13	26

In addition to a cancer diagnosis, 35 of the 50 subjects (70%) had comorbidities that made them even more vulnerable to infection; 18 of 25 subjects (72%) in the 24-hour group and 17 of 25 subjects (68%) in the 48-hour group (Table 4). Nine of the 50 subjects (18%) had a septicemia (confirmed by positive blood cultures) at the time of entry into the study; three in the 24-hour group and six in the 48-hour group. Group differences with regard to the existence of a septicemia were not significant (χ^2=.1091, df=1, p=.4404). Twenty-four of 50 subjects (48%) were diagnosed with febrile neutropenia, 13 (52%) in the 24-hour group and 11 (44%) in the 48-hour group. Significant group differences related to the incidence of febrile neutropenia were not found (χ^2=.0800, df=1, p=.5713).

Ten of the 50 subjects (20%) had a stomatitis at the time of entry into the study, six (24%) in the 24-hour group and four (16%) in the 48-hour group. Group differences with regard to stomatitis were not statistically significant (χ^2=.1000, df=1, p=.4795). Five of the 50 subjects (10%) had a confirmed central venous catheter (CVC) infection; two subjects (8%) in the 24-hour group and three subjects (12%) in the 48-hour group. There were no statistically significant group differences in the incidence of central catheter infections (χ^2=.0667, df=1, p=.6374).

The final comorbidity examined was pneumonia. Two of 50 subjects (4%) had a preexisting pneumonia; both were in the 24-hour group. Group differences with respect to pneumonia were not significant (χ^2=.2041, df=1, p=.1489). The total number of comorbidities among subjects ranged from 1 to 4, with a mean of 1.22 $\pm$ 1.13. Subjects in the 24-hour group had between 0 and 4 comorbidities with a mean of 1.36 $\pm$ 1.29; whereas, subjects in the 48-hour group had fewer comorbidities with a range of 0 to 3 and a mean of 1.08 $\pm$ .95. Group differences with regard to the total number of comorbidities experienced by subjects were not found to be statistically significant (F=.76, df=1, p=.387).

Table 4

Comorbidities of Subjects

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	**f**	**%**	**f**	**%**	**f**	**%**
Septicemia	3	12	6	24	9	18
Febrile Neutropenia	13	52	11	44	24	48
Stomatitis	6	24	4	16	10	20
Infected Catheter	2	8	3	12	5	10
Pneumonia	2	8	0	0	2	4
No. of Subjects with Comorbidities	18	72	17	68	35	70
Characteristic	**M**	**SD**	**M**	**SD**	**M**	**SD**
Comorbidities	1.36	1.29	1.08	.95	1.22	1.13

All 50 subjects possessed surgically tunnelled, double (n=13) or triple (n=37) lumen CVC (Table 5). In the 24-hour group, five subjects (20%) had double and 20 subjects (80%) had triple lumen CVC. In the 48-hour group, eight subjects (32%) had double and 17 subjects (68%) had triple lumen CVC. Group differences related to the proportion of subjects with double versus triple lumen central catheters were not found to be statistically significant (χ^2=.1368, df=1, p=.3334).

Table 5

Type of Central Venous Catheter

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	**f**	**%**	**f**	**%**	**f**	**%**
Double Lumen	5	20	8	32	13	26
Triple Lumen	20	80	17	68	37	74

At the time subjects entered the study, they were categorized as febrile (≥ 38.5° C) or afebrile (<38.5° C). Twenty-six of the 50 subjects (52%) were febrile at the time they entered the study. In the 24-hour group, 14 of 25 subjects (56%) were febrile, whereas, in the 48-hour group, only 12 of 25 subjects (48%) were febrile. The proportion of febrile subjects was not found to be significantly different between the two groups (χ^2=.0800, df=1, p=.5713).

Table 6

Initial Temperature of Subjects

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	**f**	**%**	**f**	**%**	**f**	**%**
Febrile (≥ 38.5° C)	14	56	12	48	26	52
Afebrile (< 38.5° C)	11	44	13	52	24	48

All 50 subjects were neutropenic, with absolute neutrophil counts (ANC) ranging from 5 to 1000/mm^3 of blood, with a mean of 296.24 ± 242.74 (Table 7). The

ANC for subjects in the 24-hour ranged from 28 to 1000 with a mean of 296.28 ± 253.87/mm^3 of blood. For those in the 48-hour group, the ANC ranged from 5 to 1000 with a mean of 296.20 ± 231.61/mm^3 of blood. Subjects in the two groups were not significantly different with regard to their ANC at the time of entering the study ($F=.00$, $df=1$, $p=.999$). Appendix F contains a summary of the aforementioned demographic variables, by group assignment.

Table 7

Initial Absolute Neutrophil Count (ANC) of Subjects

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	M	SD	M	SD	M	SD
Initial ANC	296.28	253.87	296.20	231.61	296.24	242.74

Throughout this study, additional information was collected related to subjects' daily temperatures, the blood cultures collected, the organisms isolated from blood cultures, tips of CVC cultured, the number of days subjects were febrile, subjects' daily ANC, reasons for discharge from the study, and finally, the number of subjects completing the proposed five measures. The rationale behind collecting this additional information will be discussed along with the pertinent data.

Because microorganisms replicate best within a narrow range of temperatures, information related to subjects' daily tympanic temperatures and subsequent interventions were of importance in examining rates of infusate colonization and the incidence infusion-related septicemia. Thirty-two of the 50 subjects (64%) were febrile (≥ 38.5° C) at some point during the data collection process (Table 8). Fourteen of 25 subjects (56%) in the 24-hour group and 18 of 25 subjects (72%) in the 48-hour group were febrile at least once during the study. Subjects' temperatures in the 24-hour group

ranged from 33.7° C to 40.2° C, with a mean of 37.33 ± 1.08° C. Subjects' temperatures in the 48-hour group ranged from 34.7° C to 40.5° C, with a mean of 37.40 ± .70° C. Group differences with regard to tympanic temperatures throughout the study were statistically non-significant (F=.07, df=1, p=.797). The mean number of days subjects were febrile during this study were 1.44 ± 1.84 and 2.48 ± 2.62 for subjects in the 24-hour and 48-hour groups, respectively. Group differences related to the number of days subjects were febrile were not found to be statistically significant (F=2.63, df=1, p=.111). When the number of days subjects were in the study were controlled, group differences related to the number of days subjects were febrile remained statistically non-significant (F=.00, df=1, p=.972).

Table 8

Daily Temperature of Subjects

	Interval for Changing IV Administration Sets					
	24-hours n=25		**48-hours n=25**		**Total n=50**	
Characteristic	**f**	**%**	**f**	**%**	**f**	**%**
No. Febrile Subjects	14	56	18	72	32	64
Characteristic	**M**	**SD**	**M**	**SD**	**M**	**SD**
No. of Days Febrile	1.44	1.84	2.84	2.62	2.14	2.23
Mean Temperature	37.33	1.07	37.40	.69	37.37	.88

Subjects with tympanic temperatures ≥ 38.5° C, in the absence of environmental causes and unrelated to blood transfusion therapy, were to have two sets of aerobic and anaerobic blood cultures collected, in order to identify possible contributing microorganisms. Normal routine at the Cross Cancer Institute (CCI) is that blood cultures are to be collected once every 48 hours, and at the discretion of the attending physician, on patients with persistent fever. Nine of 25 subjects (36%) in the

24-hour group and 18 of 25 subjects (72%) in the 48-hour group had blood cultures collected. This group difference was found to be statistically significant ($F=7.20$, $df=1$, $p=.010$). Five subjects in the 24-hour group failed to have the blood cultures collected, when febrile. In three cases, cultures were drawn the day prior to entering the study and were, therefore, deferred at the time they became febrile; the remaining two cases were the result of a break in protocol. Six subjects in the 48-hour group failed to have a total of nine cultures collected while febrile. Eight missing blood cultures were the result of breaks in protocol and one collection was deferred because blood cultures had been collected the prior day.

A total of 62 blood cultures were collected during the study, 20 of the 62 cultures (32%) were collected from subjects in the 24-hour group, while 42 of the 62 cultures (68%) were from subjects in the 48-hour group. Again, group differences in the number of blood cultures collected were found to be statistically significant ($F=4.41$, $df=1$, $p=.041$). When the number of days subjects were in the study was controlled for, because subjects in the 48-hour group were followed for twice as long as those in the 24-hour group, differences with regard to the number of blood cultures collected between the two groups became non-significant ($F=.00$, $df=1$, $p=.999$).

Of the blood cultures collected, four of 20 cultures (20%) collected from subjects in the 24-hour group and 18 of 42 cultures (43%) collected from subjects in the 48-hour group yielded positive results. This group difference in the number of positive blood cultures was also found to be statistically significant ($F=4.06$, $df=1$, $p=.050$). The four positive blood culture specimens in the 24-hour group were collected from three different subjects, while the 18 positive specimens in the 48-hour group were collected from 10 different subjects. Group differences related to the number of subjects with positive blood cultures were also found to be statistically significant ($F=4.06$, $df=1$, $p=.050$) (Table 9). The particular microorganisms isolated from these cultures will be described in the microbiological section of this chapter.

Table 9

Blood Cultures

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	**f**	**%**	**f**	**%**	**f**	**%**
No. Subjects Cultured**	9	36	18	72	27	54
No. Subjects Positive*	3	12	10	40	13	26
No. Cultures Collected*	20	32	42	68	62	100
No. Positive Cultures*	4	20	18	43	22	44

*p< 0.05 **p<0.01

The tips of all CVC removed at the CCI are routinely cultured to identify any possible microbial growth. No CVC were removed from subjects in the 24-hour group, however, two subjects in the 48-hour group had their CVC removed; only one yielded positive results. One subject was asymptomatic and the CVC tip was found to be culture negative. The second subject was persistently febrile and the CVC tip was found to be positive for the same organism isolated from blood cultures collected both from a peripheral site and from the CVC, prior to its removal (Table 10). Due to small numbers, group differences were not calculated statistically.

Table 10

Cultured Central Venous Catheter (CVC) Tips

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	**f**	**%**	**f**	**%**	**f**	**%**
No. of Tips Cultured	2	8	0	0	2	4
No. of Positive Tips	1	4	0	0	1	2

Subjects in this study were febrile for a mean of 1.96 ± 2.24 days. Subjects in the 24-hour group were febrile for a mean of 1.44 ± 1.85 days, compared to subjects in the 48-hour who were febrile a mean of 2.48 ± 2.62 days (Table 11). Although subjects in the 48-hour group were followed for twice as long, group differences related to the number of days subjects were febrile were not found to be statistically significant ($F=2.63$, $df=1$, $p=.111$).

Table 11

Number of Days Subjects were Febrile

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	M	SD	M	SD	M	SD
No. of Days Febrile	1.44	1.85	2.48	2.62	1.96	2.24

Neutrophils, the bodies first line of defence against microorganisms, comprise approximately 50-60% or 2,500-7,000/mm^3 of the body's white blood cell count. Neutropenia, defined in this study as an absolute neutrophil count of ≤ 1,000/mm^3 of blood, is a significant risk factor for infection. Subjects included in this study were neutropenic for a minimum of two days prior to their admission and were subsequently excluded if, or when, their ANC exceeded 1,000/mm^3 of blood. The mean daily ANC during this study was 271.42 ± 196.00/mm^3 of blood and 261.13± 136.67/mm^3 of blood for subjects in the 24-hour and 48-hour groups, respectively. Group differences related to subjects' daily ANC were not found to be statistically significant ($F=.05$, $df=1$, $p=.830$) (Table 12).

Table 12

Daily Absolute Neutrophil Counts (ANC)

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	**M**	**SD**	**M**	**SD**	**M**	**SD**
ANC	271.42	196.00	261.13	136.67	266.28	166.34

Data were also collected related to reasons for discharge from this study (Table 13). Four of 25 subjects (16%) in the 24-hour group and three of 25 subjects (12%) in the 48-hour group were discharged from hospital prior to obtaining the proposed five measurements. Two of 25 subjects (8%) in the 24-hour group and three of 25 subjects (12%) in the 48-hour group were excluded from study because of an ANC $> 1{,}000/mm^3$ of blood. One of 25 subjects (4%) in the 48-hour group was transferred to another health care facility. Two of 25 subjects (8%) in the 48-hour group had their CVC removed prior to obtaining the five measurements. A break in study protocol occurred with one of 25 subjects (4%) in the 24-hour group and two of 25 subjects (8%) in the 48-hour group, resulting in their exclusion from further investigation. One of 25 subjects (4%) in the 24-hour group refused to continue treatment for their cancer and was subsequently discharged from hospital. A total of 31 subjects (62%) completed the proposed five measures, 17 of 25 subjects (68%) in the 24-hour group and 14 of 25 subjects (56%) in the 48-hour group ($\chi^2 = .3472$, df=1, p=.5557). Group differences related to reasons for discharge from the study were not found to be statistically significant ($\chi^2 = .3151$, df=6, p=.5481).

Table 13

Reasons for Discharge from the Study

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	**f**	**%**	**f**	**%**	**f**	**%**
Completed Measures	17	68	14	56	31	62
Discharged Home	4	16	3	12	7	14
ANC > 1,000/mm^3	2	8	3	12	5	10
Transferred from Unit	0	0	1	4	1	2
CVC Removed	0	0	2	8	2	4
Break in Protocol	1	4	2	8	3	6
Refused Treatment	1	4	0	0	1	2

Finally, the number of days subjects remained in this study was examined (Table 14). Thirty-two of the 50 subjects (64%) remained in the study for the proposed number of days; 17 of 25 subjects (68%) in the 24-hour group and 15 of 25 subjects (60%) in the 48-hour group (χ^2=.9675, df=1, p=.0000). Subjects in the 48-hour group, however, were measured for twice as long as those in the 24-hour group. Subjects in the 24-hour group were measured for a total of 104 days while those in the 48-hour group were measured for a total of 192 days. Although a maximum of five measures was proposed, subjects remained in the study anywhere from one to ten days depending, in part, on group assignment. Mean number of days subjects were studied were 4.16 $\pm$ 1.34 and 7.68 $\pm$ 3.20 for subjects in the 24-hour and 48-hour groups, respectively. Although group differences with regard to the proportion of subjects completing the five measures were non-significant, the two groups were found to be significantly different with regard to the number of days subjects remained in the study (F=25.74, df=1, p=.000). Appendix G contains a summary of the distribution of

subjects completing each of the measures.

Table 14

Subjects Completing the Proposed Number of Days

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	**f**	**%**	**f**	**%**	**f**	**%**
No. of Subjects	17	68	15	60	32	64
Characteristic	M	SD	M	SD	M	SD
No. of Days Studied**	4.16	1.34	7.68	3.20	5.92	2.27

**$p < 0.01$

Infusate Variables

Intravenous therapy was initiated for a variety of reasons. Indications for IV therapy included the administration of antibiotics which were received by 22 of the 25 subjects (88%) in the 24-hour group and 23 of 25 subjects (92%) in the 48-hour group ($\chi^2 = .0667$, df=1, $p = .6374$) (Table 15). Although a total of 17 different antibiotics were prescribed during the study period, the mean number of IV antibiotics prescribed per subject were 2.48 $\pm$ 1.61 and 2.12 $\pm$ 1.33 for subjects in the 24-hour and 48-hour groups, respectively. Group differences related to the number of different antibiotics received were not statistically significant (F=.74, df=1, $p = .393$).

Ceftazidime and vancomycin were the two most frequently prescribed antibiotics. Fourteen subjects (56%) in each of the two groups received vancomycin while 14 subjects (56%) in the 24-hour group and 16 subjects (64%) in the 48-hour group received ceftazidime. Acyclovir (n=8), ciprofloxacin (n=8) and amphotericin B (n=7) were the next most frequently prescribed antibiotics. Appendix H contains a description of all the IV antibiotics prescribed and the number of subjects receiving

each of the different antibiotic agents.

Table 15

Intravenous Antibiotic Therapy

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	**f**	**%**	**f**	**%**	**f**	**%**
No. of Subjects	22	88	23	92	45	90
Characteristic	**M**	**SD**	**M**	**SD**	**M**	**SD**
No. of Antibiotics	2.48	1.61	2.12	1.33	2.30	1.47

Because of the potential to influence microbial growth, information related to the administration of oral antibiotics was also collected (Baron et al., 1994). Nine of 25 subjects (36%) in the 24-hour group and 14 of 25 subjects (72%) in the 48-hour group received oral antibiotics (Table 16). Differences in the proportion of subjects receiving this form of therapy in each of the two groups were not found to be statistically significant (χ^2=.2006, df=1, p=.1559).

The mean number of oral antibiotics received were 0.52 ± 0.87 and 0.92 ± 1.08 for subjects in the 24-hour and 48-hour groups, respectively. Group differences related to the number of oral antibiotics subjects received were also found to be statistically non-significant (F=2.08, df=1, p=.155). Ciprofloxacin (n=12) and fluconazole (n=10) were the two most frequently prescribed oral antibiotics. Appendix I contains a description of the different oral antibiotics prescribed and the frequency with which subjects received this form of antibiotic therapy.

Table 16

Oral Antibiotic Therapy

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	f	%	f	%	f	%
No. of Subjects	9	36	14	56	23	46
Characteristic	M	SD	M	SD	M	SD
No. of Oral Antibiotics	0.52	0.87	0.92	1.08	.72	.98

Non-antibiotic IV therapy including analgesics, anti-emetics, anti-histamines, steroids, diuretics, and anti-coagulants may also influence infusate colonization. Non-antibiotic therapies were the predominant form of IV therapy, particularly in symptomatic subjects. Given the frequency with which subjects received this form of therapeutic intervention, non-antibiotic therapy contributed significantly to the number of obligate manipulations of IV administration sets. Forty-two of the 50 subjects (84%) in this study received non-antibiotic IV therapy; 20 of 25 subjects (80%) in the 24-hour group and 22 of 25 subjects (88%) in the 48-hour group (Table 17). Group differences related to the proportion of subjects receiving non-antibiotic IV therapy were not found to be statistically significant (χ^2=.1091, df=1, p=.4404).

The mean number of non-antibiotic therapies received were 4.12 ± 3.14 and 4.40 ± 2.84 for subjects in the 24 and 48-hour groups, respectively. Group differences with regard to the number of non-antibiotic therapies received were not statistically significant (F=.11, df=1, p=.742). Appendix J contains a description of all the non-antibiotic IV therapies prescribed and the frequency with which subjects received this form of IV therapy.

Table 17

Intravenous Non-antibiotic Therapy

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	f	%	f	%	f	%
No. of Subjects	20	80	22	88	44	88
Characteristic	M	SD	M	SD	M	SD
No. of Non-antibiotics	4.12	3.14	4.40	2.84	4.26	2.99

Electrolyte imbalances are a common occurrence among this patient population, in part, as the result of drug induced nausea and vomiting or renal failure. Twenty-four of 50 subjects (48%) received IV electrolyte boluses during the course of this study, to correct these imbalances. Intravenous electrolyte therapy included potassium chloride and/or magnesium sulphate boluses, frequently administered in sequential minibags (Table 18). Twelve subjects in each of the two groups received IV electrolyte therapy. Group differences are, therefore, statistically non-significant (χ^2=.000, df=1, p=1.000).

The mean number of IV electrolytes received were 0.60 $\pm$ 0.71 and 0.56 $\pm$ 0.65 for subjects in the 24-hour and 48-hour groups, respectively. Group differences with regard to the administration of IV electrolyte boluses were not found to be statistically significant (F=.04, df=1, p=.836). Appendix K contains a description of the IV electrolytes prescribed and the frequency with which subjects received this from of IV therapy.

Table 18

Intravenous Electrolyte Therapy

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	f	%	f	%	f	%
No. of Subjects	12	48	12	48	24	48
Characteristic	M	SD	M	SD	M	SD
No. of Electrolytes	0.60	0.71	0.56	0.65	0.58	.68

Chemotherapy was the least frequently administered infusate, with only 10 of the 50 subjects (20%) receiving this form of IV therapy. Six of 25 subjects (24%) in the 24-hour group and only four of 25 subjects (16%) in the 48-hour group received chemotherapy during the study period (Table 19). Group differences related to the proportion of subjects receiving chemotherapy were not found to be statistically significant (χ^2=.1000, df=1, p=.4795).

The mean number of chemotherapeutic agents subjects received were 0.40 ± 0.76 for subjects in the 24-hour group and 0.24 ± 0.60 for subjects in the 48-hour group. Group differences related to the number of chemotherapeutic agents subjects received were not found to be statistically significant (F=.68, df=1, p=.413). Cytarabine (n=8) and Idarubicin (n=4) were the two most frequently prescribed chemotherapeutic agents, during the study period. Appendix L contains a summary of the types of chemotherapy prescribed and the number of subjects receiving this form of IV therapy.

Table 19

Intravenous Chemotherapy

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	f	%	f	%	f	%
No. of Subjects	6	24	4	16	10	20
Characteristic	M	SD	M	SD	M	SD
No. of Chemotherapeutic Agents	0.40	0.76	0.24	0.60	0.32	.68

Granulocyte stimulating factor (GCSF) was used to stimulate neutrophil recovery, in an attempt to restore the subject's immune response. A total of 14 subjects (28%) received IV GCSF, eight of 25 subjects (32%) in the 24-hour group and six of 25 subjects (24%) in the 48-hour group (Table 20). Group differences in the proportion of subjects receiving IV GCSF were not found to be statistically significant (χ^2=.0890, df=1, p=.5287).

The mean number of days subjects received GCSF were 3.13 $\pm$ 1.89 for subjects in the 24-hour group and 7.00 $\pm$ 3.29 for subjects in the 48-hour group. Because GCSF is administered on a daily basis, the number of days subjects received this form of therapy is equivalent to the number of doses received. Group differences in the number of days subjects received GCSF were statistically significant (F=7.83, df=1, p=.016). However, when controlling for the number of days subjects were in the study, because subjects in the 48-hour group were measured for twice as long as those subjects in the 24-hour group, group differences became statistically non-significant (F=.24, df=1, p=.631). Appendix M contains a summary of the number of subjects receiving GCSF and the duration in which they received this therapy.

Table 20

Intravenous Granulocyte Stimulating Factor (GCSF)

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	f	%	f	%	f	%
No. of Subjects	8	32	6	24	14	28
Characteristic	M	SD	M	SD	M	SD
No. of Days of GCSF*	3.13	1.89	7.00	3.29	4.79	3.17

*$p < 0.05$

Total parenteral nutrition (TPN) was initiated in 18 of the 50 subjects (36%), 11 of 25 subjects (44%) in the 24-hour group and seven of 25 subjects (28%) in the 48-hour group (Table 21). Group differences related to the proportion of subjects receiving parenteral nutrition in each of the two groups were not found to be statistically significant ($\chi^2 = 1667$, df=1, p=.2386).

The mean number of days subjects received TPN was 3.46 ± 1.57 and 6.00 ± 3.32 for subjects in the 24-hour and 48-hour groups, respectively. Although group differences related to the number of days subjects received TPN are apparent, these differences were not found to be statistically significant (F=3.92, df=1, p=.065). As with the administration of GCSF, when one controls for the number of days subjects were in the study, group differences with regard to the administration of TPN remain statistically non-significant (F=.03, df=1, p=.866). Appendix N contains a summary of the number of subjects receiving TPN and the duration in which they received this form of IV therapy.

Table 21

Total Parenteral Nutrition (TPN)

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	**f**	**%**	**f**	**%**	**f**	**%**
No. of Subjects	11	44	7	28	18	36
Characteristic	**M**	**SD**	**M**	**SD**	**M**	**SD**
No. of Days of TPN	3.46	1.57	6.00	3.32	4.73	2.45

The administration of blood or blood products have been indirectly implicated in the colonization of IV administration sets and were, therefore, included among study variables (Maki, 1992). Included among these products are packed red cells, platelets, plasma, and albumin. A total of 38 subjects (76%) received blood transfusions during the study period. Seventeen of 25 subjects (68%) in the 24-hour group and 21 of 25 subjects (84%) in the 48-hour group received IV blood or blood products (Table 22). Group differences related to the number of subjects receiving blood products were not found to be significant (χ^2=.1873, df=1, p=.1853).

The mean number of blood or blood products received were 6.80 ± 6.80 and 12.08 ± 9.91 for subjects in the 24-hour and 48-hour groups, respectively. Group differences were found to be statistically significant (F=5.31, df=1, p=.026). However, when controlling for the number of days subjects were in the study, group differences with regard to the number of blood products received became statistically non-significant (F=.08, df=1, p=.774). Appendix G contains a summary of the different types of blood products prescribed and the frequency with which subjects received these products.

Table 22

Blood and Blood Product Transfusion Therapy

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	f	%	f	%	f	%
No. of Subjects	17	68	21	84	38	76
Characteristic	M	SD	M	SD	M	SD
No. of Blood Products*	6.80	6.80	12.08	9.19	9.44	8.00

*$p < 0.05$

As with the transfusion of blood products, blood specimen withdrawal from the CVC provide microorganisms at the CVC/administration set junction with nutrients not otherwise available. Blood specimen collection included daily complete cell counts (CBC), aminoglycoside monitoring, blood cultures, and cross matching for blood transfusions. Blood specimens were withdrawn through the CVC on 47 of 50 subjects (94%) during this study. Twenty-three of 25 subjects (92%) in the 24-hour group and 24 of 25 subjects (96%) in the 48-hour group had routine blood specimens collected (Table 23). Group differences related to the number of subjects having blood specimens collected from their CVC were not found to be significant ($\chi^2=2041$, df=1, p=.1489).

The mean number of blood specimens collected from CVC were 6.04 ± 5.09 and 10.20 ± 5.75 for subjects in the 24-hour and 48-hour groups, respectively. Group differences in the number of specimens collected were, however, found to be statistically significant (F=7.35, df=1, p=.009). When controlling for the number of days subjects were in the study, group differences became statistically non-significant (F=.59, df=1, p=.448). Appendix P contains a summary of the indications for, and number of subjects having, blood specimens collected from their CVC.

Table 23

Blood Specimen Collection

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	**f**	**%**	**f**	**%**	**f**	**%**
No. of Subjects	23	92	24	96	47	94
Characteristic	**M**	**SD**	**M**	**SD**	**M**	**SD**
No. of Blood Specimens**	6.04	5.09	10.20	5.75	8.12	5.42

**$p < 0.01$

During the course of this study, data on 423 IV administration sets belonging to 50 subjects were examined. Of the 423 administration sets examined, 241 sets (57%) were changed after 24 hours (plus or minus one hour), while 182 sets (43%) were changed after 48 hours (plus or minus one hour) (Table 24). The total number of IV administration sets per subject ranged from 1 to 27 over the five measures. Subjects in the 24-hour group had anywhere from 1 to 27 IV administration sets per subject, while those in the 48-hour group had somewhat less with 1 to 17 IV sets per subject. The mean number of administration sets per subject was 8.42 ± 5.32. Subjects in the 24-hour group had a mean of 9.64 ± 5.77 IV administration sets, whereas subjects in the 48-hour group had a mean of 7.28 ± 4.63 IV administration sets, respectively. Group differences related to the number of IV administration sets per subject were not found to be statistically significant ($F=2.71$, $df=1$, $p=.106$).

Table 24

Intravenous (IV) Administration Sets

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	**f**	**%**	**f**	**%**	**f**	**%**
No. of Intravenous Sets	241	57	182	43	423	100
Characteristic	**M**	**SD**	**M**	**SD**	**M**	**SD**
No. of IV Sets/Subject	9.64	5.77	7.28	4.63	8.42	5.32

Characteristics of Intravenous Therapy

Although subjects were considered to be the unit of analysis when determining the incidence of infusion-related septicemia, statistical analyses were also performed on several variables using IV administration sets as the denominator, in order to identify trends associated with colonization of IV infusate. Because microorganisms require a very specific pH and source of nutrients (Baron et al., 1994; Maki, 1992), the type of IV solution infused through IV sets may potentially influence microbial survival. The predominant background solution received by subjects in this study was normal saline (NS). Two hundred and sixty-eight of 423 administration sets (64%) had NS as a background solution; 149 of 241 administration sets (62%) in the 24-hour group and 119 of 182 administration sets (65%) in the 48-hour group, respectively.

A combination of dextrose and saline (2/3 1/3) was infused through 17 of 423 IV administration sets (4%). Seven of 241 administration sets (3%) in the 24-hour group and 10 of 182 administration sets (6%) in the 48-hour group had 2/3 1/3 as a drive solution. Five percent dextrose in water (D5W) was infused through 74 of 423 IV sets (18%); 44 of 241 administration sets (18%) in the 24-hour group and 30 of 182

administration sets (17%) in the 48-hour group. Total parenteral nutrition (TPN) was infused through a total of 63 administration sets (15%); 41 of 241 administration sets (17%) in the 24-hour group and 22 of 182 administration sets (12%) in the 48-hour group. Although not used in the 24-hour group, ringer's lactate was the background solution in one of 182 administration sets (0.6%) in the 48-hour group (Table 25). The two groups were not found to be significantly different with regard to the type of background solutions infused (χ^2=.1102, df=4, p=.2735).

Table 25

Intravenous (IV) Solution Infused

	Interval for Changing IV Administration Sets					
	24-hours n=241		**48-hours n=182**		**Total n=423**	
Characteristic	**f**	**%**	**f**	**%**	**f**	**%**
Normal Saline	149	62	119	65	268	63
2/3 1/3	7	3	10	6	17	4
D5W	44	18	30	17	74	18
TPN	41	17	22	12	63	15
Ringer's Lactate	0	0	1	.6	1	.2

In addition to the background solution, information related to the specific IV therapy(s) administered through each administration set was also collected, because of the potential to influence rates of colonization (Table 26). Intravenous antibiotics were administered through a total of 178 (42%) administration sets. Ninety-three of 241 sets (39%) in the 24-hour group and 85 of 182 sets (47%) in the 48-hour group were used to administer IV antibiotics. Group differences related to the proportion of IV sets used to deliver antibiotic therapy were not found to be statistically significant (χ^2=.0814, df=1, p=.0942).

Non-antibiotic IV therapy was delivered through 197 of the 423 IV administration sets (47%); 102 of 241 sets (42%) in the 24-hour group and 95 of 182 sets (52%) in the 48-hour group. Group differences related to the administration of non-antibiotic therapies were found to be statistically significant (χ^2=.0980, df=1, p=.0438). A total of 42 of 423 IV administration sets (10%) were used to infuse IV electrolytes. Nineteen of 241 administration sets (8%) in the 24-hour group and 23 of 182 sets (13%) in the 48-hour group were used to deliver electrolyte boluses. Group differences were not found to be significant with regard to the administration of IV electrolytes (χ^2=.0787, df=1, p=.1055).

A single administration set may have been used to deliver IV antibiotics, non-antibiotic IV therapy, or IV electrolytes either concurrently or sequentially and have, therefore, been included in each of the abovementioned categories. As a result, some of the IV sets have been counted more than once. The total number of IV administration sets included in this section, therefore, exceeds the actual number of sets examined.

Table 26

Infusion Therapy: Antibiotics, Non-antibiotics and Electrolytes

	Interval for Changing IV Administration Sets					
	24-hours n=152		48-hours n=133		Total n=285	
Intravenous Therapy	**f**	**%**	**f**	**%**	**f**	**%**
Antibiotics	93	39	85	47	178	42
Non-antibiotics*	102	42	95	52	197	47
Electrolytes	19	8	23	13	42	10
Total †	214	89	203	112	417	97

*p<0.05

† Antibiotic, non-antibiotic and/or electrolyte IV administration sets may have been used to infuse more than one type of infusate, therefore, the total number of IV administration sets included in this section exceeds the total of 285 or 100%.

Twenty-nine of the 423 IV administration sets (7%) were used to deliver chemotherapy. Twenty-three of 241 administration sets (10%) in the 24-hour group and 6 of 182 sets (3%) in the 48-hour group were used for chemotherapy. Group differences were found to be statistically significant (χ^2=.1224, df=1, p=.0118).

Granulocyte stimulating factor was administered through a total of 46 of 423 administration sets (11%). Twenty-five of 241 administration sets (10%) in the 24-hour group and 22 of 182 administration sets (12%) in the 48-hour group were used to administer GCSF. Group differences in the number of IV administration sets used to deliver GCSF were not found to be statistically significant (χ^2=.0185, df=1, p=.7032).

Total parenteral nutrition was administered through 63 of 423 IV administration sets (15%); 41 of 241 sets (17%) were in the 24-hour group and 22 of 182 sets (12%) were in the 48-hour group (Table 27). Group differences with regard to the number of IV administration sets used to administer TPN were also not found to be statistically significant (χ^2=.0685, df=1, p=.1590).

Table 27

Infusion Therapy: Chemotherapy, Granulocyte Stimulating Factor (GCSF) and Total Parenteral Nutrition (TPN)

	Interval for Changing IV Administration Sets					
	24-hours n=89		48-hours n=49		Total n=138	
Characteristic	f	%	f	%	f	%
Chemotherapy*	23	10	6	3	29	7
GCSF	25	10	21	12	46	11
TPN	41	17	22	12	63	15
Total	89	37	49	27	138	33

*p<0.05

The IV administration sets of patients not requiring continuous infusions are frequently disconnected for varying periods of time, in part to facilitate ambulation. Because idle administration sets provide a stagnant column of infusate, information specific to these administration sets was also collected in order to investigate potential differences between stagnant and continuously infusing IV infusate and rates of colonization (Table 28). A total of 161 of 423 IV administration sets (38%) were idle for some variable period of time. Eighty-nine of 241 administration sets (37%) belonging to subjects in the 24-hour group were idle compared to 72 of 182 administration sets (40%) in the 48-hour group. Group differences related to the number of IV sets idle during the study period were not found to be statistically significant (χ^2=.0301, df=1, p=.5408).

Sixteen IV sets (7%) in the 24-hour group and three sets (2%) in the 48-hour group were disconnected between one and 12 hours. Seventy-three IV administration sets (30%) in the 24-hour group and 15 sets (8%) in the 48-hour group were disconnected between 12.5 and 24 hours. Six IV administration sets (3%) in the 48-hour group were disconnected between 24.5 and 36 hours, while 48 administration sets (26%) in the 48-hour group were disconnected between 36.5 and 48 hours. The mean number of hours IV administration sets were idle were 19.38 $\pm$ 5.91 and 36.79 $\pm$ 11.74 hours for subjects in the 24-hour and 48-hour groups, respectively. Group differences in the number of hours IV administration sets were idle were found to be statistically significant (F=149.25, df=1, p=.000).

Table 28

Idle Intravenous Administration Sets

	Interval for Changing IV Administration Sets					
	24-hours n=241		48-hours n=182		Total n=423	
Characteristic	**f**	**%**	**f**	**%**	**f**	**%**
No. of Idle Sets	89	37	72	40	161	38
1 to 12 hours	16	7	3	2	19	5
12.5 to 24 hours	73	30	15	8	88	21
24.5 to 36 hours	--	--	6	3	6	1
36.5 to 48 hours	--	--	48	26	48	11
	M	**SD**	**M**	**SD**	**M**	**SD**
No. of Hours Idle**	19.38	5.90	36.79	11.74	28.09	8.82

**$p < 0.01$

Any connection(s) within the IV administration set is a potential portal of entry for microorganisms. Connections, for the purpose of this study were defined as any "joint" within the IV system, for example: between the IV solution bag and the spike on the proximal end of the administration set; the injection ports use to attach secondary medication administration sets; the Y-connector site, used to join two administration sets together; the point at which extension tubing is added to the distal end of the administration set; or the point at which the CVC lumen has been joined to the luer end of the IV administration set. The number of connections in the IV administration sets in this study ranged from 2 to 5 per set. The mean number of connections per IV administration set was 3.25 ± 0.90 and 3.37 ± 0.84 for subjects in the 24-hour and 48-hour groups, respectively (Table 29). Group differences related to the number of connections within the IV administration sets were not found to be

statistically significant (F=1.92, df=1, p=.167).

Table 29

Connections within Intravenous Administration Sets

	Interval for Changing IV Administration Sets					
	24-hours n=241		48-hours n=182		Total n=423	
Characteristic	**M**	**SD**	**M**	**SD**	**M**	**SD**
No. of Connections	3.25	.90	3.37	.84	3.31	.87

It has also been reported that there is a relationship between the number of entries into an IV administration set, to prime the line, deliver IV therapy, to disconnect an infusion, or to change the IV solution or administration set, and the subsequent microbial colonization of the administration set (Barry & Miller, 1988; Hampton & Sherertz, 1988; Maki, 1992; Sitges-Serra, Puig, Linares, Perez, Farrero, Jaurrieta, & Garau, 1984; Snydman et al., 1982). Increased numbers of manipulations are believed to be commensurate with increased rates of colonization and, consequently, an increased incidence of infusion-related septicemia.

The number of entries into an IV administration set, during this study, ranged from 1 to 60 during a single measurement period. Entries into the administration sets of subjects in the 24-hour group ranged from 2 to 31 and from 2 to 60 for subjects in the 48-hour group. The mean number of entries into an IV administration set was 7.22 $\pm$ 5.50 and 14.15 $\pm$ 11.70 for subjects in the 24-hour and 48-hour groups, respectively. Group differences related to the number of entries into IV administration sets to deliver treatment were found to be statistically significant (F=65.43, df=1, p=.000) (Table 30).

Table 30
Entries into Intravenous Administration Sets

	Interval for Changing IV Administration Sets					
	24-hours n=241		48-hours n=182		Total n=423	
Characteristic	**M**	**SD**	**M**	**SD**	**M**	**SD**
No. of Entries**	7.22	5.50	14.15	11.70	10.20	9.37

**$p < 0.01$

Microbiological Findings

Microbiological Findings Related to the Sample

Of the 50 subjects that agreed to participate in this study, 36 (72%) had microorganisms isolated from IV infusate, at least once during the study period. Nineteen of these subjects had their IV administration sets changed every 24 hours, while 17 subjects had their IV administration sets changed every 48 hours. The number of microorganisms isolated from IV infusate per subject, over the five measures, ranged from 1 to 1,001 cfu/ml of infusate. The mean number of microorganisms per subject was 36.40 ± 95.40 for subjects in the 24-hour group and 89.40 ± 226.57 for subjects in the 48-hour group. Group differences related to the number of microorganisms to which subjects were exposed, via their IV administration sets over the five measures, were not found to be statistically significant ($F=1.16$, $df=1$, $p=.286$) (Table 30). Appendix Q contains a summary of all microorganisms isolated from IV infusate by subject, over time.

Table 31

Subjects with Contaminated Intravenous Administration Sets

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Characteristic	**f**	**%**	**f**	**%**	**f**	**%**
No. of Subjects	19	76	17	68	36	72
	M	**SD**	**M**	**SD**	**M**	**SD**
No. of Microorganisms	36.40	95.40	89.40	226.57	62.90	174.12

For the purpose of this study, microbial counts ≥15 cfu/ml of infusate were considered to be of clinical significance, because of the potential relationship between this degree of colonization and the risk of developing an infusion-related septicemia. In order to differentiate colonized IV administration sets from those sets where microorganisms were isolated in lesser quantities, infusate harbouring <15 cfu/ml were considered to be contaminated, rather than colonized. Sixteen of 50 subjects (32%) were found to have at least one IV administration set considered colonized, with ≥15 cfu/ml of infusate. Subjects with colonized administration sets were equally distributed between the two groups; eight subjects in each of the two groups had one colonized administration set, while one subject in each group had two colonized sets. Changing IV administration sets at 48 hours did not result in colonization rates significantly different than the rate of colonization occurring in IV administration sets changed every 24 hours ($F=1.17$, $df=1$, $p=.285$). Within-subject variability or differences in colonization rates between the five measures were not found to be statistically significant ($F=.73$, $df=4$, $p=.571$). Finally, tests for an interaction effect, between group assignment and time, were also not found to be statistically significant

in this study (F=1.10, df=4, p=.369) (Table 32).

Table 32

Colonization of Intravenous Administration Sets

Source of Variation	SS	DF	MS	F	Significance
Between-Subjects	290512.80	1	6052.35	1.17	.285
Within-Subjects	19798.40	4	4949.60	.73	.571
Interaction		4		1.10	.369

Correlations between demographic variables and contamination or colonization were also determined (Table 33a, 33b). Statistically significant, positive correlations were found between rates of colonization and contamination (r=.2188, p=.000). As the number of cfu/ml of infusate increased, there was a corresponding increase in the number of different organisms isolated. Similarly, there was a significant, positive correlation between rates of contamination and the subject's initial ANC (r=.1291, p=.009). As the number of different organisms isolated from IV infusate increased, there was an associated increase in subjects' ANC.

Correlations between infusate contamination and demographic variables were also determined. These correlations were as follows: subjects' age in years (r=-.0076, p=.878); number of comorbidities (r=-.0379, p=.442); gender (r=.0148, p=.761); type of CVC (r=.0073, p=.882); and, primary diagnosis (r=-.0021, p=.966). Correlations between infusate colonization and demographic variables were as follows: subjects' age in years (r=-.0901, p=.067); number of comorbidities (r=.0700, p=.156); gender (r=-.0411, p=.405); type of CVC (r=.0105, p=.832); and, primary diagnosis (r=-.0086, p=.861). The aforementioned correlations were not found to be statistically significant.

Table 33a

Correlations Between Infusate Contamination, Colonization, Initial Absolute Neutrophil Count (ANC), Age, and Number of Comorbidities

Variable	< 15 cfu/ml	≥ 15 cfu/ml	ANC	Age in Years	No. of Comorbidities
< 15 cfu/ml	--	.2188**	.1291**	- .0076	- .0379
≥ 15 cfu/ml		--	.0206	- .0901	.0700
ANC			--	N/A	N/A
Age in Years				--	N/A
No. of Comorbidities					--

**$p < 0.01$

Table 33b

Correlations Between Infusate Contamination, Colonization, Gender, Type of Central Venous Catheter (CVC), and Diagnosis

Variable	< 15 cfu/ml	≥ 15 cfu/ml	Gender	Type of CVC	Diagnosis
< 15 cfu/ml	--	.2188**	- .0148	- .0021	- .0073
≥ 15 cfu/ml		--	- .0411	- .0086	.0105
Gender			--	N/A	N/A
Type of CVC				--	N/A
Diagnosis					--

**$p < 0.01$

Microbiological Findings Related to the Infusion Therapy

Data were collected on a total of 423 IV administration sets. Ten of these sets (2.4%) were inadvertently discarded at some point prior to collecting the infusate specimen and were, therefore, excluded from further analysis. Microorganisms were isolated from 41 of 241 IV administration sets (17.38%) in the 24-hour group and 37 of 182 IV administration sets (20.90%) in the 48-hour group, respectively. The mean number of cfu/ml of infusate was 22.195 ± 75.69 for sets changed every 24 hours ($n=41$) and 60.405 ± 188.55 for sets changed every 48 hours ($n=37$), respectively. Group differences related to the number of microorganisms isolated from IV infusate

were not found to be statistically significant ($F=1.43$, $df=1$, $p=.235$).

Nine of 241 IV administration sets (3.81%) in the 24-hour group were considered to be colonized. Similarly, 9 of 182 sets (5.09%) in the 48-hour group harboured microorganisms in quantities ≥ 15 cfu/ml of infusate and were, therefore, considered to be colonized. The number of cfu isolated from these IV administration sets ranged from 15 to 1000/ml of infusate. The mean number of cfu/ml of infusate in IV sets considered to be colonized were 91.67 ± 147.14 for IV sets changed every 24 hours ($n=9$) and 239.44 ± 335.13 for sets changed every 48 hours ($n=9$), respectively. The two groups were not statistically different with regard to the number of microorganisms isolated from the IV infusate ($F=1.47$, $df=1$, $p=.234$) (Table 34).

Table 34

Contaminated and/or Colonized Intravenous Administration Sets

	Interval for Changing IV Administration Sets					
	24-hours n=236		48-hours n=177		Total n=413	
Characteristic	f	%	f	%	f	%
Contaminated Sets	41	17.37	37	20.90	78	18.89
Colonized Sets	9	3.81	9	5.09	18	4.36
	24-hours n=41		**48-hours n=37**		**Total n=78**	
Contaminated Sets	**M**	**SD**	**M**	**SD**	**M**	**SD**
Microorganisms	22.20	75.69	60.41	188.55	41.31	132.12
	24-hours n=9		**48-hours n=9**		**Total n=18**	
Colonized Sets	**M**	**SD**	**M**	**SD**	**M**	**SD**
Microorganisms	91.67	147.14	239.44	335.13	165.56	262.34

Colonization of IV administration sets appeared to be independent of the nature of the infusate, with colonization occurring to some extent in administration sets used for any of the prescribed therapies (Table 35). Four of 92 IV sets (4.35%) in the 24-hour group and three of 84 sets (3.6%) in the 48-hour group, used to administer antibiotics, were found to be colonized. One IV set in each of the two had been inadvertently discarded prior to culturing. Colonization of IV administration sets used to deliver non-antibiotic therapy occurred in four of 101 sets (3.96%) in the 24-hour group and three of 94 sets (3.2%) in the 48-hour group. As above, one administration set in each of these two had been discarded prior to being cultured. One of 19 sets (5.3%) used to deliver IV electrolyte therapy in the 24-hour group and two of 23 sets (8.7%) in the 48-hour group, were also significantly colonized. No IV sets used to deliver electrolyte therapy had been discarded prior to culturing.

One of 23 administration sets (4.4%) used to administer chemotherapy and one of 24 sets (4.2%) used to deliver GCSF, in the 24-hour group, were found to be colonized. No corresponding colonized sets were found in the 48-hour group. None of the IV administration sets used for chemotherapy were discarded prior to culturing, however, one IV administration set used for GCSF in the 24-hour group and two sets in the 48-hour group were discarded and, therefore, excluded from analysis. One of 39 sets (2.6%) used to administer TPN in the 24-hour group and four of 21 sets (19.1%) in the 48-hour group were also colonized. Group differences related to colonization by prescribed therapy were not found to be statistically significant ($\chi^2=.4714$, $df=1$, $p=.5494$); however, it must be noted that 12 of 12 cells in this analysis contain less than five cases. Although group differences related to colonization by prescribed therapy were not found to be statistically significant, differences with regard to colonization and the administration of TPN warrants further consideration.

Table 35

Colonization by Prescribed Infusion Therapy

	Interval for Changing IV Administration Sets					
	24-hours n=236 5 discarded			48-hours n=177 5 discarded		
Characteristic	**f**	**%**	**n**	**f**	**%**	**n**
Antibiotic Therapy	4	4.4	92	3	3.6	84
Non-Antibiotic Therapy	4	4.0	101	3	3.2	94
Electrolyte Therapy	1	5.3	19	2	8.7	23
Chemotherapy	1	4.4	23	0	0.0	6
GCSF Therapy	1	4.2	24	0	0.0	22
Total Parenteral Nutrition	1	2.6	39	4	19.1	21
Total †	12	--	298	12	--	250

† Antibiotic, non-antibiotic and/or electrolyte IV administration sets may have been used to infuse more than one type of infusate, therefore, the total number of IV administration sets included in this section exceeds 423 or 100%.

Correlations between the aforementioned variables and the incidence of contamination or colonization were also determined (Table 36a, 36b). As was expected, a positive correlation between contaminated and colonized IV administration sets was found ($r=.2188$, $p=.000$). There was also a significant, positive correlation between the incidence of colonization and the administration of TPN ($r=.1196$, $p=.015$). Correlations between other types of IV therapy and contamination or colonization were not found to be statistically significant.

Table 36a

Correlations Between Infusate Contamination, Colonization, Antibiotic, Non-antibiotic and Electrolyte Therapy

Variable	< 15 cfu/ml	≥ 15 cfu/ml	Antibiotics	Non-Antibiotics	Electrolytes
< 15 cfu/ml	--	.2188**	- .0594	- .0067	- .1117
≥ 15 cfu/ml		--	- .0353	- .0490	.0683
Antibiotics			--	N/A	N/A
Non-Antibiotics				--	N/A
Electrolytes					--

**p < 0.01

Table 36b

Correlations Between Infusate Contamination, Colonization, Granulocyte Stimulating Factor (GCSF), Total Parenteral Nutrition (TPN) and Chemotherapy

Variable	< 15 cfu/ml	≥ 15 cfu/ml	GCSF	TPN	Chemotherapy
< 15 cfu/ml	--	.2188**	.0895	- .0733	.0699
≥ 15 cfu/ml		--	- .0371	.1196*	- .0284
GCSF			--	N/A	N/A
TPN				--	N/A
Chemotherapy					--

*p < 0.05 **p < 0.01

Of the 241 IV administration sets in the 24-hour group, four of 147 sets (2.72%) in continuous use and five of 89 sets (5.62%) idle for some portion of the 24-hour period were found to be colonized. Conversely, in the 48-hour group, six of 105 administration sets (5.71%) in continuous use and three of 72 sets (4.17%) idle for some portion of the 48-hour period were found to be colonized. Group differences related to the proportion of colonized, idle IV sets were not found to be statistically significant ($\chi^2 = .2236$, df=1, p=.3428) (Table 37).

Table 37

Colonization by Hours in Use

	Interval for Changing IV Administration Sets					
	24-hours n=236			48-hours n=177		
Characteristic	f	%	n	f	%	n
No. of Sets in Continuous Use	4	2.72	147	6	5.71	105
No. of Idle Administration Sets	5	5.62	89	3	4.17	72

Correlations between the incidence of contamination or colonization and variables related to the IV administration sets were also investigated (Table 38). A statistically significant, positive relationship was found between contamination ($r=.0952$, $p=.053$) and colonization ($r=.1004$, $p=.041$) and the length of time IV sets were idle. As the number of hours IV sets were idle increased, the number of cfu isolated from the infusate escalated and the number of different microorganisms identified grew. There was also a statistically significant, negative relationship between the number of connections in IV administration sets and the number of hours IV sets were idle ($r= -.3128$, $p=.000$). As the number of connections within IV sets increased, the number of hours sets were idle decreased. A similar relationship existed between the number of entries into IV administrations sets and the number of hours IV sets were idle ($r= -.2934$, $p=.000$). As the number of entries into IV sets increased, the number of hours sets were idle decreased.

A statistically significant, positive correlation was also found between the number of connections within IV administration sets and the number of times the sets were entered to deliver treatment ($r=.4455$, $p=.000$). As the number of connections within IV sets increased, the number of manipulations increased accordingly. The final correlation found to be statistically significant was between the number of connections within IV sets and the incidence of contamination. As the number of connections within

IV administration sets increased, the incidence of colonization decreased (r= -.1058, p=.032). Surprisingly, negative relationships were also found between the number of entries into the IV system and the rate of colonization and/or contamination (r=-.0144, p=.770; r=- .0057, p=.908). As the number of entries into the IV set increased, the number of cfu isolated from IV infusate and the number of different organisms identified decreased. These latter two correlations were not, however, statistically significant.

Table 38

Correlations Between Infusate Contamination, Colonization and Intravenous Administration Set Variables

Variable	<15 cfu/ml	≥15 cfu/ml	Connections	Entries	Hours Idle
<15 cfu/ml	--	.2188**	- .0332	- .0057	.0952*
≥15 cfu/ml		--	- .1058*	- .0144	.1004*
Connections			--	.4455**	- .3128**
Entries				--	- .2934**
Hours Idle					--

*p<0.05 **p<0.01

Microorganisms Isolated from Intravenous Infusate

Several different microorganisms were isolated from IV infusate collected from the 50 subjects. Included among these microorganisms were: coliforms, including *Escherichia coli*; diphtheroids, most likely *Corynebacterium* species; *Staphylococcus aureus* and coagulase-negative staphylococci (CNS); non-pathogenic *Neisseria* species (NPN); streptococci including viridans group (VGS), beta-haemolytic (BHS), non-haemolytic (NHS), and enterococci; *Acinetobacter* species; aerobic spore bearing bacilli; *Micrococcus* species; and, fungi including *Candida* species and *Rhodotorula pilmonae*. Group differences with regard to the particular organisms isolated from infusate specimens were not calculated statistically, as 28 of 30 cells would contain expected values of less than five. Appendix Q contains a summary of the

microbiological findings from IV infusate specimens per subject.

Multiple strains of CNS, all common inhabitants of the integument, were isolated from IV infusate. Of particular importance was determining whether or not these staphylococci are *S. aureus*, then determining their antibiotic susceptibilities. Extensive colonization of IV administration sets, with various strains of CNS was found. Streptococci, NPN, micrococci, and coliforms are also colonizers of the skin, gastrointestinal tract and/or oral mucosa. As with CNS, these microorganisms gain access to IV administration sets following breaks in the IV system, to deliver therapy. Diphtheroids, including *Corynebacterium* species, are frequently found in the upper airways of patients and are capable of surviving for extended periods of time on fomites including bedrails and stethoscopes. Although generally considered to be non-pathogenic, any of the aforementioned microorganisms are capable of producing a septicemia when found within the individual's bloodstream. Additionally, many of these microorganisms colonize patients after their admission to hospital and, therefore, carry with them an antibiotic resistance attributable to the antibiotic utilization within the particular admitting institution (Baron et al, 1994).

Acinetobacter species, *C. parapsilosis*, and *R. pilmonae* are considered to be environmental pathogens. Colonization with these organisms is frequently associated with external contamination and breaks in aseptic technique. As workloads become heavier and patient acuity increases, it is conceivable that colonization with these kinds of microorganisms may also increase.

Coagulase-negative staphylococci were the predominant organisms isolated from IV infusate specimens with 58 of 78 positive infusates (74.36%) harbouring between one and three different strains of CNS. Thirty-two of 50 subjects (64%) had CNS isolated from the infusate of at least one IV administration set. This microorganism was found in 30 of 41 administration sets (73.17%) in the 24-hour group and 28 of 37 sets (75.68%) in the 48-hour group and, was the only organism to have multiple strains isolated from a single infusate specimen. Aerobic and anaerobic blood cultures

collected from the CVC of one subject was found to be positive for CNS, on two separate occasions. Nevertheless, IV infusate specimens collected from this subject, over the five measures, were never positive for this microorganism. Group differences with regard to CNS contamination or colonization of infusate were not found to be statistically significant ($F=.18$, $df=1$, $p=.673$).

Viridans group streptococci were the second most frequently isolated organisms. Microorganisms in this group were found in 8 of 78 infusate specimens (10.26%) during this study. Six of these specimens (14.63%) were from IV sets changed every 24 hours and two specimens (5.41%) from sets changed every 48 hours. No subject was found to have more than a single IV administration set positive for this organism. Five subjects had blood cultures positive for VGS prior to admission into this study. One of these subjects had VGS isolated from an infusate specimen on day 4 of the study. Further speciation of these specimens, however, revealed two different species: *S. sanguis* from the IV infusate specimen and *S. mitis* from both central and peripheral blood cultures. Viridans group streptococci were found in the blood cultures of four subjects in the 48-hour group during the study, nevertheless, this organism was never isolated from IV administration sets belonging to these subjects.

Enterococci were isolated from the infusate of 5 of 78 administration sets (6.41%); 2 of 41 (4.88%) in the 24-hour group and 3 of 37 (8.11%) in the 48-hour group. None of the subjects with enterococci isolated from IV infusate specimens had corresponding serum cultures positive for the same organism. Similarly, the two subjects with blood cultures positive for *Enterococcus* failed to have this organism isolated from their IV infusate, at any time during the study.

Non-pathogenic *Neisseria* species, *Acinetobacter* species, coliforms, BHS, NHS, and aerobic spore bearing bacilli were each isolated once (2.44%) from infusate specimens in the 24-hour group. Two IV administration sets (4.88%) in the 24-hour group were positive for *S. aureus* and diphtheroids while three sets (7.32%) were culture positive for micrococci. Subjects had no corresponding blood cultures positive

for any of these organisms.

Microorganisms isolated from infusate specimens collected from administration sets changed every 48 hours were similar to those in the 24-hour group. Non-pathogenic *Neisseria* species, *E. coli*, and aerobic spore bearing bacilli were isolated once (2.70%) from these sets. Non-haemolytic streptococci were isolated from three of the 37 infusate specimens (8.11%) in this group. As with the 24-hour group, there were no subjects in the 48-hour group with blood cultures positive for any of these organisms.

Although not isolated from infusate specimens of subjects in the 24 hour group, fungi were identified in four of 37 infusate specimens (10.81%) collected from IV sets changed every 48 hours, as well as the blood cultures of three subjects. *C. albicans* was isolated from the liquid media culture of an IV administration set used to administer GCSF. Two days later, this subject had a peripheral blood culture positive for the same organism. The single colony of *Candida* present in the infusate was of insufficient quantity (<15 cfu/ml) to be of clinical significance in this study.

Two infusate specimens from a single subject were found to be culture positive for *C. parapsilosis*. One specimen with $>1,000$ cfu/ml was cultured from an IV administration set used to deliver parenteral nutrition. *C. parapsilosis* was also isolated from a second IV administration set piggy-backed to the TPN set, in order to administer antibiotics. Blood cultures were also positive for this organism. The subsequent removal of this subject's CVC, and culture of the CVC tip, confirmed a diagnosis of catheter-related infection.

A fourth infusate specimen positive for fungi, was isolated from an administration set used to deliver ceftazidime and vancomycin. Blood cultures collected from the subject at the time the infusate was positive, were negative for fungi. A third subject with positive fungal blood cultures had no corresponding IV infusate specimens positive for fungi. Table 39 provides a summary of the types of microorganisms isolated from both IV infusate and blood culture specimens collected from subjects over

the course of this study.

Table 39

Microorganisms Isolated from Intravenous Infusate and/or Blood Cultures

	Interval for Changing IV Administration Sets							
	24-hours				48-hours			
	IV Infusate n =41		Blood Cultures n=4		IV Infusate n = 37		Blood Cultures n=18	
Microorganism	f	%	f	%	f	%	f	%
Coagulase-negative staphylococcus	30	73	2	50	28	76	0	0
Staphylococci aureus	2	5	0	0	0	0	0	0
Micrococcus species	3	7	0	0	0	0	0	0
Viridans group streptococcus	6	15	0	0	2	5	4	22
Beta-haemolytic streptococcus	1	2	0	0	0	0	0	0
Non-haemolytic streptococcus	1	2	0	0	0	0	0	0
Enterococcus species	2	5	0	0	3	8	2	11
Diphtheroids	2	5	0	0	0	0	5	27
Aerobic spore bearing bacillus	1	2	0	0	1	3	0	0
Burkholderia species	0	0	0	0	0	0	1	6
Stenotrophomonas maltophila	0	0	0	0	0	0	2	11
Coliforms	1	2	0	0	0	0	0	0
Escherichia coli	0	0	1	25	1	3	0	0
Klebsiella pneumoniae	0	0	1	25	0	0	0	0
Acinetobacter species	1	2	0	0	0	0	0	0
Non-pathogenic *Neisseria* species	1	2	0	0	1	3	1	6
Candida species	0	0	0	0	3	8	3	17
Rhodotorula pilmonae	0	0	0	0	1	3	0	0
Sum †	51	132	4	100	40	109	18	100

† Sum is greater than 78 positive infusate specimens or 100% because multiple organisms were isolated from some of the IV administration sets.

Study variables associated with colonized administration sets were remarkably similar between the 24-hour and 48-hour groups (Table 40). The 18 colonized IV administration sets were equally divided between the two groups. Group differences with regard to the type of infusate delivered through the administration set were non-significant, with the exception of TPN. The mean number of connections within colonized administration sets were also similar between the two groups with 3.00 ±

1.00 and 3.33 ± .71 connections for the 24-hour and 48-hour groups, respectively. These group differences were not found to be statistically significant (F=.67, df=1, p=.426). There were, however, group differences related to the number of times IV administration sets were entered to provide treatment. Colonized administration sets changed every 24 hours were entered 6.56 ± 3.97 times, whereas sets changed every 48 hours were entered 16.78 ± 12.50 times. Differences between the 24 and 48-hour groups with regard to the number of entries into the system were found to be statistically significant (F=5.47, df=1, p=.033). The mean number of microorganisms found in colonized administration sets was 91.67 ± 147.14 for subjects in the 24-hour group and 239.44 ± 335.13 for subjects in the 48-hour group. Although the numbers of microorganisms isolated vary considerably, group differences related to the number of microorganisms isolated within IV infusate were not found to be statistically significant (F=1.47, df=1, p=.243).

Table 40

Characteristics of Colonized Intravenous Administration Sets

	Interval for Changing IV Administration Sets					
	24-hours n = 9		48-hours n = 9		Total n=18	
Characteristic	**M**	**SD**	**M**	**SD**	**M**	**SD**
No. of Connections	3.00	1.00	3.33	.71	3.17	.86
No. of Entries*	6.56	3.97	16.78	12.50	2.11	12.67
No. of Microorganisms	91.67	147.14	239.44	335.13	165.56	262.34

*p<0.05

Seven different organisms were isolated from IV infusate, in quantities ≥15 cfu/ml of infusate (Table 41). Coagulase-negative staphylococci were again the predominant organisms identified from the infusate of five administration sets (56%) in the 24-hour group and six sets (67%) in the 48-hour group. Semi-quantitative culture analysis of these infusate specimens revealed CNS in quantities ranging from 15 to 440

cfu/ml of infusate. Group differences related to the number of colonies isolated were not found to be statistically significant ($F=.05$, $df=1$, $p=.827$).

The remaining IV infusate specimens in the 24-hour group were found to be colonized by multiple organisms. Micrococci and CNS were isolated from the infusate of two administration sets (22%) changed at 24 hours. Micrococci (75 cfu/ml) and CNS (150 cfu/ml) were isolated from the first set. Micrococci and CNS, each in quantities of 25 cfu/ml, were isolated from the infusate of the second set. Coagulase-negative staphylococci (5 cfu/ml) and *S. aureus* (15 cfu/ml) were isolated from a third IV set. The final colonized set in the 24-hour group was positive for NPN (10 cfu/ml) and VGS (5 cfu/ml).

Non-pathogenic *Neisseria* species (80 cfu/ml) and VGS (75 cfu/ml) were isolated from a single infusate specimen in the 48-hour group. The remaining two colonized IV administration sets in the 48-hour group were culture positive for fungus; *C. parapsilosis* was isolated from one set in quantities of 1,000 cfu/ml of infusate while *R. pilmonae* (500 cfu/ml) was isolated from the infusate of a second set.

Table 41

Microorganisms in Quantities >15 cfu/ml

	Interval for Changing IV Administration Sets					
	24-hours n = 9		48-hours n = 9		Total n=18	
Microorganism	**f**	**%**	**f**	**%**	**f**	**%**
Coagulase-negative staphylococcus	5	56	6	67	11	61
Coagulase-negative staphylococcus & *Micrococcus* species	2	22	0	0	2	11
Coagulase-negative staphylococcus & *Staphylococcus aureus*	1	11	0	0	1	6
Non-pathogenic *Niesseria* species & viridans group streptococcus	1	11	1	11	2	11
Candida parapsilosis	0	0	1	11	1	6
Rhodotorula pilmonae	0	0	1	11	1	6

Note: Unable to calculate group differences statistically due to small numbers.

Infusion-related Septicemia

For the purpose of this study, an infusion-related septicemia included the following attributes: clinical features of a blood stream infection; isolation of the same organism from both the infusate and peripheral blood cultures; blood cultures drawn from the CVC negative for the infecting organism; and the absence of an alternative identifiable source of the septicemia (Band & Maki, 1979; Maki et al., 1987; Snydman et al., 1987). Although considered to be a rare event, infusion-related septicemias are not only possible, but probable, given the frequency with which IV therapy is indicated and IV administration sets are manipulated, especially among this patient population.

Monetary costs associated with treating these individuals are outweighed only by the human costs in terms of quality of life. Febrile neutropenia was the most frequently cited comorbidity among study subjects and, infection the predominant indication for hospitalization. However, despite the fact that infusate specimens from 18 of 423 IV administration sets were found to harbour microorganisms in quantities ≥ 15 cfu/ml, there were no corresponding blood cultures positive for the same organism(s). Five of the 16 subjects (31%) were febrile at the time they were found to have positive infusate specimens. Eleven of 16 subjects (69%) were asymptomatic, however, all but two subjects were receiving between one and five different antibiotics. Therefore, despite the fact that 16 subjects had 18 IV administration sets with microorganisms in excess of 15 cfu/ml of infusate, no subject developed an infusion-related septicemia throughout this study period. Chi-square analysis for group differences related to the incidence of infusion-related septicemia was not found to be statistically significant ($\chi^2 = .000$, df=1, p=1.000).

CHAPTER FIVE

Discussion of Findings

The purpose of this study was to examine the following questions: (a) Is there a difference in the rate of infusate colonization between neutropenic cancer patients whose intravenous (IV) administration sets are changed every 48 versus 24 hours? And, (b) Is there a difference in the incidence of infusion-related septicemia between neutropenic cancer patients whose IV administration sets are changed every 48 versus 24 hours? Recognizing that the incidence of infusion-related septicemia is a rare event, the rate of colonization of IV administration sets was proposed as an indicator of the risk. Fifty subjects, 25 in each of two groups, agreed to participate in this randomized clinical trial.

Factors Affecting Infusate Colonization

Demographic Variables of Subjects

Prior to comparing findings related to rates of colonization, it was important to compare subjects in the 24-hour and 48-hour groups, on variables reported to influence IV infusate colonization. Demographic variables believed to influence infusate colonization include: gender, age, primary diagnosis, comorbidities, type of central venous catheter (CVC), body temperature, and absolute neutrophil count (ANC). The groups were not found to differ significantly on any of these variables.

The 24-hour group had slightly more males than the 48-hour group, 8 versus 6 males, respectively. Because staff nurses have questioned whether males may be more susceptible to infection than females, it was important to determine whether, or not, the two groups were similar on this variable. Group differences related to the proportion of males to females were not found to be statistically significant. Gender differences were, therefore, not believed to differentially influence IV colonization rates. The higher prevalence of females to males in this study was anticipated, given the diagnoses selected for inclusion. Generally, women with breast cancer outnumber men with testicular cancer in the hospital setting and the majority of the transplant recipients had

previously been treated for cancer of the breast.

Similarly, it has been suggested that as one ages, the body's immune response is less capable of mounting an effective response (Gransden, 1991; Linn & Jensen, 1983). Subjects in the 24-hour group were slightly older than their 48-hour counterparts. The mean difference in age between the two groups was approximately six months; again, this difference was not statistically significant and not believed to differentially advantage the 48-hour group over the 24-hour group.

Minor group differences were also noted with regard to subjects' primary diagnosis and the nature of comorbidities. Thirteen of the 25 subjects in each of the two groups had a primary diagnosis of leukemia. Two subjects in the 24-hour group and four subjects in the 48-hour group were diagnosed with lymphoma. Two subjects in the 24-hour group were diagnosed with solid tumor malignancies, one subject with breast cancer and one subject with testicular cancer. Three subjects in the 48-hour group had a breast cancer diagnosis and there were no subjects in this group with cancer of the testicle(s). Eight subjects in the 24-hour group and five subjects in the 48-hour group had received a stem cell transplant. Although hematological malignancies are generally associated with higher rates of infection than are solid tumors (Farber et al., 1991; Jamulitrart et al., 1994; Rubio et al., 1994), group differences identified above were not statistically significance and, therefore, unlikely to influence rates of infusion-related septicemia.

Comorbidities, for the purpose of this study, were limited to complications with an infectious etiology including: septicemia, febrile neutropenia, stomatitis, CVC infection, and pneumonia. Thirty-five of the 50 subjects (70%) had at least one infectious complication at the time of entering this study. Eighteen subjects in the 24-hour group and 17 subjects in the 48-hour group had one or more of the aforementioned complications. The predominant comorbidity identified was febrile neutropenia with 13 subjects in the 24-hour group and 11 subjects in the 48-hour group sharing this diagnosis. Six subjects in the 24-hour group and four subjects in the 48-

hour group had a coexisting stomatitis. Septicemia was confirmed in three subjects in the 24-hour group and six subjects in the 48-hour group. Two subjects in the 24-hour group had a pneumonia and two had an infected CVC. In the 48-hour group, there were no subjects with pneumonia and three with infected CVC. The rationale behind identifying comorbidities was to ensure that compromised subjects were similarly distributed between the two groups. Minor group differences related to comorbidities were not found to be statistically significant and, therefore, unlikely to influence infusate colonization to any meaningful extent.

There is an extensive body of literature addressing the infectious complications associated with CVC (Conly, 1995; Lowder et al., 1982; Maki, 1989, 1992; Moro et al., 1994; Raad & Bodey, 1992). Included among this literature is an ongoing debate related to infection rates associated with double versus triple lumen central catheters (Conly, 1995; McCarthy et al., 1987; Raad & Bodey, 1992; Wickham et al, 1992). While the most convincing evidence suggests that triple lumen CVC are associated with higher rates of infection than are double lumen catheters, this relationship is confounded by the possibility that triple lumen catheters may be manipulated more frequently than their double lumen counterparts (Conly, 1995). Subjects in the 24-hour group had five double and 20 triple lumen CVC compared to subjects in the 48-hour group with eight double and 17 triple lumen CVC. These group differences in the number of subjects with double versus triple lumen CVC were not statistically significant. If, however, the increased number of triple lumen catheters in the 24-hour group (20 versus 17) were to contribute differentially to the rate of infusate colonization, it would be this group that would be unequally disadvantaged. The higher proportion of triple to double lumen catheters was expected given the frequency with which multiple infusates are delivered simultaneously. Double lumen CVC are often placed when the individual's anatomy prohibits the insertion of a larger intravascular device.

Because of the possibility of retrograde travel of microorganisms from preexisting sites of infection, subjects were categorized as febrile ($\geq$ 38.5° C) or afebrile ($<$38.5° C). Fourteen subjects (56%) in the 24-hour group and 12 (48%) in the 48-hour group were febrile at the time they were entered into the study. Group differences in the proportion of febrile/afebrile subjects in these two groups were not statistically significant and not believed to differentially influence subsequent study findings.

Data related to the ANC were collected prior to admitting subjects into the study. The rationale behind collecting this information was to secure answers to questions related to the body's ability to mount an immunological response, following exposure to microorganisms introduced during the delivery of IV therapy. For example, are subjects with lower ANC at greater risk of developing infusion-related infections? Group differences related to ANC were statistically non-significant, therefore, the relationship between subjects' ANC and the incidence of infusion-related septicemia could be investigated.

Additional information related to subjects' daily temperatures, number of days febrile, interventions for temperatures $\geq$ 38.5° C, daily ANC, number of measures taken, and reason for discharge was also collected throughout this study. Because many of the normal signs and symptoms of infection, such as redness or purulence, are absent among neutropenic patients, regular measures of body temperature provides a means of identifying possible infection(s). Group differences related to mean daily temperatures were not statistically significant. The mean number of days subjects were febrile were 1.44 $\pm$ 1.84 and 2.84 $\pm$ 2.62 for subjects in the 24-hour and 48-hour groups, respectively. Though not statistically significant, group differences related to the number of days subjects were febrile were apparent. However, subjects in the 48-hour group were measured for approximately twice as many days as those in the 24-hour group, therefore, when the number of days subjects were studied was controlled,

group differences became statistically non-significant.

Blood cultures were collected once every 48 hours on subjects with temperatures ≥ 38.5° C. Nine subjects in the 24-hour group and 18 subjects in the 48-hour group had blood cultures collected. Group differences related to the number of subjects cultured were statistically significant ($p=.010$). Three subjects in the 24-hour group had blood cultures collected the day prior to entering the study. Although these three subjects were febrile while in the study, blood cultures were not recollected at that time. Two subjects in the 24-hour group failed to have the appropriate blood cultures collected due to a break in protocol. Similarly, five subjects in the 48-hour group failed to have a total of eight blood cultures collected due to a break in protocol; and, one subject had blood cultures collected the day prior to entering the study. Breaks in protocol included the following explanations: six subjects had been febrile for extended periods of time and were receiving broad spectrum antimicrobial/antifungal coverage, therefore, collecting blood culture specimens was deemed inappropriate; in one case, the on call physician failed to collect the required specimens; and, in three cases, nursing staff were unfamiliar with the study protocol.

A total of 62 blood cultures were collected during the study, 20 from subjects in the 24-hour group and 42 from subjects in the 48-hour group. Fifty-four percent of subjects were cultured and 26% of subjects had positive results. Group differences related to the number of blood cultures collected were statistically significant ($p=.041$), however, when the number of days subjects were studied was again controlled for, group differences were not found to be significant. Because subjects in the 48-hour group had twice as many blood cultures collected, it would be reasonable to expect more positive blood cultures in this group as well. Of the 62 blood cultures collected, 36% were positive; 20% of blood cultures in the 24-hour group and 43% in the 48-hour group, respectively. Group differences related to the number of positive results were also statistically significant ($p=.050$).

Findings related to the number of positive blood cultures are inconsistent with

findings reported in the literature. Weinstein, Reller, Murphy, and Lichtenstein (1983) found rates of positivity ranging from 91.5% from the first blood culture to 99.3% by the first two sets of cultures. Aronson and Bor (1987) and Washington and Ilstrup (1986) agree that a single blood culture is seldom sufficient to detect a septicemia or fungemia and that greater than three blood cultures is unnecessary, but, report positive findings in excess of 90%. This inconsistency is, in part, related to the rapidity with which broad spectrum antimicrobial therapy is instituted among this patient population. Because a temperature of 38.5° C or greater is considered to be a medical emergency among the patients in this study, antibiotics are commenced immediately following the initial blood cultures and certainly prior to collecting a second set. Rather than having the benefit of choosing therapy on the basis of positive cultures, the patient's response to the prescribed broad spectrum antibiotic(s) is frequently used to guide subsequent interventions. The 36% positivity rate found in this study is consistent with the norm for this institution.

A significant risk factor for infection, including septicemia, is a low neutrophil count (Berenguer et al., 1990; Blacklock et al., 1980; Carlisle et al., 1993; Ehni et al., 1991; Ranson et al., 1990; Wickham et al., 1992). Subjects in this study had mean ANC of 271.42 ± 196.00 and 261.13 ± 136.67 in the 24-hour and 48-hour groups, respectively. It was this variable, neutropenia, that initially prompted interest in this study. Although it has been reported that IV administration sets can safely be changed at intervals up to every 120 hours, the degree of infusate colonization is believed to increase proportionately as the length of time IV sets are utilized increases (Band & Maki, 1979; Buxton et al., 1979; Maki et al., 1987). What was not reported in the literature is the degree of infusate colonization that would ultimately overwhelm the immune response. Group differences related to the degree of neutropenia among study participants were not found to be statistically significant.

The final subject variable examined was related to the reason for discharge from the study. Seventeen subjects (68%) in the 24-hour group completed the proposed five

measures with the mean number of 4.16 ± 1.34 days in the study. Fifteen subjects (60%) in the 48-hour group completed the five measures with the mean number of 7.68 ± 3.20 days in the study. Although more subjects in the 24-hour group completed the proposed five measures than subjects in the 48-hour group, group differences related to the proportion of subjects completing the five measures were not statistically significant. Subjects in the 24-hour and 48-hour groups were just as likely to be excluded, at any point in time, from further study. Significant group differences exist, however, with regard to the total number of days subjects were measured ($p=.000$).

Subjects in the 48-hour group remained in the study for approximately twice as long as subjects in the 24-hour group, but, were measured with similar frequency. Given the trend towards shorter hospital stays, it was thought that following subjects in the 48-hour group for 10 days would be difficult. This concern did not, however, prove to be problematic. Group differences related to the various reasons for discharge were not found to be statistically significant. Therefore, the only significant group differences found were related to the number of days subjects were febrile (prior to controlling for the number of days studied), the number of blood cultures collected, the number of positive blood cultures, and the number of days subjects remained in the study.

Infusate Variables

Intravenous therapy was initiated for a variety of reasons including: to hydrate subjects; to deliver antibiotics, non-antibiotics, electrolytes, or chemotherapy; to administer IV granulocyte stimulating factor (GCSF) or total parenteral nutrition (TPN); and/or to transfuse blood or blood products. Because microorganisms require a supportive environment to replicate, it was believed that the nature of the infusate itself may play a limiting or facilitating role in the microbial colonization of IV administration sets (Baron et al., 1994).

A total of 17 different antibiotics were administered to 45 subjects (90%) throughout the course of this study. Intravenous antibiotics generally consisted of broad

spectrum cephalosporins such as ceftazidime (60% of subjects), glycopeptides such as vancomycin (56% of subjects), antifungal agents such as amphoteric n B (14% of subjects), and antianaerobic agents such as metronidazole (10% of subjects). Information related to antibiotic therapy was important in that the presence of an antimicrobial agent should in theory limit the growth of susceptible microorganisms (Baron et al., 1994). Intravenous antibiotics were administered to 22 subjects (88%) in the 24-hour group and 23 subjects (92%) in the 48-hour group. These minor group differences in the number of subjects receiving antibiotic therapy were not found to be statistically significant. Furthermore, the mean number of antibiotics subjects received were remarkably similar; 2.48 $\pm$ 1.61 in the 24-hour group and 2.12 $\pm$ 1.33 in the 48-hour group, respectively.

Information related to oral antibiotics was collected for similar reasons; therapeutic blood levels of a particular antibiotic should inhibit the growth of susceptible organisms (Baron et al., 1994). A total of 46% of subjects received oral antibiotics; nine subjects (36%) in the 24-hour and 14 subjects (56%) in the 48-hour groups. Group differences were not, however, statistically significant. Not only did more subjects in the 48-hour group receive oral antibiotics, these subjects also received more medications per subject. The mean number of oral antibiotics per subject was .52 $\pm$ .87 for subjects in the 24-hour group and .92 $\pm$ 1.08 for subjects in the 48-hour group. Group differences related to the number of oral antibiotics subjects received were also not statistically significant.

Non-antibiotic therapy was received by 88% of subjects; 20 subjects in the 24-hour group and 22 subjects in the 48-hour group. Non-antibiotic therapy included primarily analgesics, anti-emetics, and antihistamines and accounted for the vast majority of entries into IV administration sets. Non-antibiotic therapy was examined separately because analgesics, anti-emetics, and antihistamines, lack the antimicrobial properties of the antibiotics previously described. Group differences were not found to be statistically significant. The two groups were also similar with regard to type of

non-antibiotics received as well as the mean number of non-antibiotics infused; 4.12 ± 3.14 and 4.40 ± 2.84 medications for subjects in the 24-hour and 48-hour groups, respectively. Group differences related to the number of non-antibiotic therapies received were not found to be statistically significant.

Data related to the administration of potassium chloride and magnesium sulfate were collected for reasons similar to that described for non-antibiotic therapy, IV electrolytes lack the antimicrobial characteristics of antibiotic therapy. Additionally, electrolytes may acidify IV infusate and thereby negatively influence bacterial colonization. A total of 24 subjects, 12 in each of the two groups received IV electrolyte replacement. The mean number of electrolyte boluses received were .60 ± .71 for subjects in the 24-hour group and .56 ± .65 for subjects in the 48-hour group, respectively. These group differences were not found to be statistically significant.

Chemotherapy was the least frequently administered infusion therapy for two reasons: (a) newly diagnosed cancer patients generally have normal or elevated white cell counts and would, therefore, not meet the inclusion criteria for this study, and (b) consolidation chemotherapy is generally indicated when cell counts have recovered to the point that subjects are no longer neutropenic. Because a large percentage of subjects had a preexisting febrile neutropenia, it was expected that very few subjects would be receiving chemotherapy. Six subjects (24%) in the 24-hour group and only four subjects (16%) in the 48-hour group received chemotherapy during the study period. This group difference, again, was not found to be statistically significant. Furthermore, these two groups were not significantly different with regard to the mean number of chemotherapeutic agents administered.

Granulocyte stimulating factor (GCSF) was prescribed to stimulate neutrophil recovery among patients with cancer, following their chemotherapy. Until recently, GCSF was delivered through an IV administration set, primed with a dextrose and saline solution, subsequently discarded after a single infusion. About six months into this study, the protocol was changed to allow other IV therapy to be delivered through

these IV sets, if needed, following the administration of GCSF. For the duration of this study, however, the initial GCSF protocol was maintained. Intravenous administration sets for the eight subjects in the 24-hour group were protected with a sterile syringe and sampled 24 hours later. Intravenous administration sets used for the six subjects in the 48-hour group were reconnected and reused on the second day. Subjects in the 48-hour group received GCSF for approximately twice as many days, again, because they were measured for twice as long. When controlling for patients days, group differences related to the number of doses of GCSF were found to be statistically non-significant.

The administration of total parenteral nutrition (TPN) through a CVC is believed to be one of the most vulnerable forms of IV therapy (Gorbea et al., 1984; Snydman et al., 1987). It has been reported that the lipid emulsion component of TPN can support microbial growth as well as bacteriologic culture medium (Maki, 1992). For this reason, IV sets used to administer parenteral nutrition were examined separately. Eighteen subjects (36%) received parenteral nutrition during the study; 11 subjects (44%) in the 24-hour group and seven subjects (28%) in the 48-hour group. Group differences related to the proportion of subjects receiving TPN were not found to be statistically significant. However, because of the potential for infection, even minor group differences were considered to be of clinical importance. The mean number of days subjects received TPN were 3.46 $\pm$ 1.57 and 6.00 $\pm$ 3.32 for subjects in the 24 and 48-hour groups, respectively. When controlling for the number of days subjects were studied, group differences related to the number of days subjects received TPN were not found to be statistically significant.

The transfusion of blood products, like TPN, provides microorganisms a source of nutrients not normally available (Maki, 1992). Seventeen subjects in the 24-hour group and 21 subjects in the 48-hour group received blood or blood product transfusions. Although the administration sets used to deliver blood products were not sampled, per se, it was the presence of residual blood at the connection site, following the transfusion, that was believed to influence infusate colonization. Minor group

differences between the 24-hour and 48-hour groups, related to the number of subjects receiving transfusions, were not found to be statistically significant. Group differences related to the number of transfusion subjects received, however, were statistically significant ($p=.026$). Nevertheless, when controlling for the number of days subjects were in the study, group differences related to the number of blood products transfused became statistically non-significant.

Blood specimen withdrawal, through the CVC, has the potential to influence infusate colonization in a way comparable to that of administering blood products. Blood withdrawal provides microorganisms a source of nutrients not ordinarily available. Twenty-three subjects (92%) in the 24-hour group and 24 subjects (96%) in the 48-hour group had daily blood specimens collected from their CVC. Group differences related to the proportion of subjects having blood withdrawn from their CVC were not found to be statistically significant. Group differences related to the mean number of specimens collected were, however, found to be significant ($p=.009$). When controlling for the number of days subjects were measured, group differences became statistically non-significant.

Data on 423 IV administration sets from 50 subjects were collected during the course of this study. Subjects had anywhere from 1 to 27 IV sets with a mean of 9.64 $\pm$ 5.77 sets for subjects in the 24-hour group and 7.28 $\pm$ 4.60 sets for subjects in the 48-hour group. Although there were slightly more IV sets per subject in the 24-hour group, group differences were not found to be statistically significant. In summary, group differences on many of the variables believed to influence IV infusate colonization were not found to be statistically significant in this study.

Intravenous Therapy Variables

Five different background solutions were infused through 423 IV administration sets during this study including normal saline (NS), dextrose and saline (2/3 1/3), dextrose and water (D5W), TPN, and ringer's lactate. Normal saline was by far the most common solution infused through 268 sets (63%); 149 sets (62%) in the 24-hour

group and 119 sets (65%) in the 48-hour group; the other four solutions made up the remaining 37%. Group differences related to the frequency with which the various background solutions were utilized were not found to be statistically significant.

Antibiotics were infused through a total of 178 IV administration sets (42%); 93 (39%) in the 24-hour group and 85 (47%) in the 48-hour group. Group differences related to the administration of antibiotics were not statistically significant. Non-antibiotic therapy, the most frequently administered IV therapy, was infused through 197 (47%) administration sets; 102 sets (42%) in the 24-hour group and 95 sets (52%) in the 48-hour group. Statistically significant group differences were found with regard to the number of IV sets used to deliver non-antibiotic therapy ($p=.0438$). The administration of non-antibiotic therapy may, therefore, have differentially affected subjects in the 48-hour group. Ten percent of IV sets (42) were used to deliver IV electrolyte boluses; 19 sets (8%) in the 24-hour group and 23 sets (13%) in the 48-hour group. Although minor group differences existed related to IV electrolyte therapy, this difference was not found to be statistically significant. It is important to note also that a single IV set may have been used to administer antibiotics, non-antibiotics, and/or electrolyte therapy. Therefore, the total number of IV sets in this section actually exceeds the total number examined. Because of the small numbers involved, determining precisely the nature of the therapy delivered through each IV set would not be meaningful.

Twenty-nine administration sets (7%) were used to administer chemotherapy; 23 sets (10%) in the 24-hour group and 6 sets (3%) in the 48-hour group. Statistically significant group differences were found with regard to the administration of chemotherapy ($p=.0118$). Granulocyte stimulating factor was delivered through 46 sets (11%); 25 sets (10%) in the 24-hour group and 22 sets (12%) in the 48-hour group. Group differences were not found to be statistically significant. Lastly, parenteral nutrition was infused through 41 sets (17%) in the 24-hour group and 22 sets (12%) in the 48-hour group. Again, group differences were not found to be statistically

significant.

The IV sets of patients not requiring continuous infusion therapy were frequently disconnected, and the tip capped, for varying periods of time. Because little is known about colonization of idle administration sets, information related to the period of time IV sets were disconnected was also collected. One hundred and sixty-one IV sets (38%) were disconnected for some period of time. Eighty-nine sets (37%) in the 24-hour group and 72 sets (40%) in the 48-hour group were stagnant for varying periods of time. Group differences were not found to be statistically significance. Of significance, however, were the number of hours IV administration sets were idle ($p=.000$). Administration sets in the 24-hour group were idle on average for 19.38 $\pm$ 5.91 hours, whereas, IV sets in the 48-hour group were idle for 36.79 $\pm$ 11.74 hours.

Because of the reported influence of manipulations on the colonization of IV administration sets (Barry & Miller, 1988; Hampton & Sherertz, 1988; Maki, 1992; Sitges-Serra, Puig, Linares, Perez, Farrero, Jayrrieta, & Garau, 1984; Snydman et al., 1982), information related to the number of connections within IV sets and the number of entries into these sets was collected. The mean number of connections within IV administration sets were 3.25 $\pm$ .90 and 3.37 $\pm$ .84 for IV sets in the 24 and 48-hour groups, respectively. Group differences related to the number of connections were not statistically significant. The mean number of entries into IV administration sets were 7.22 $\pm$ 5.50 and 14.15 $\pm$ 11.70 for IV sets in the 24-hour and 48-hour groups, respectively. Group differences related to the number of entries into IV sets were found to be statistically significant ($p=.000$). Because IV administration sets in the 48-hour group remained in use for an extended period of time, it was reasonable to expect that the number of entries into these sets would be greater than those into IV sets belonging to subjects in the 24-hour group. When the number of days IV sets were used was controlled for, group differences related to the number of entries became statistically non-significant.

In summary, minor group differences were noted with regard to the number of IV administration sets used to deliver the different IV therapies. However, the only group differences that were statistically significant were related to the number of sets used to administer non-antibiotics and chemotherapeutic agents. Furthermore, group differences in the number of hours IV administration sets were idle and the number of entries into IV sets to deliver therapy were found to be statistically significant. These findings are directly related to the fact that IV administration sets in the 48-hour group were examined for twice as long. When the length of time IV administration sets were in use was controlled for, group differences became statistically non-significant.

Infusate Contamination and Colonization

Sample Variables

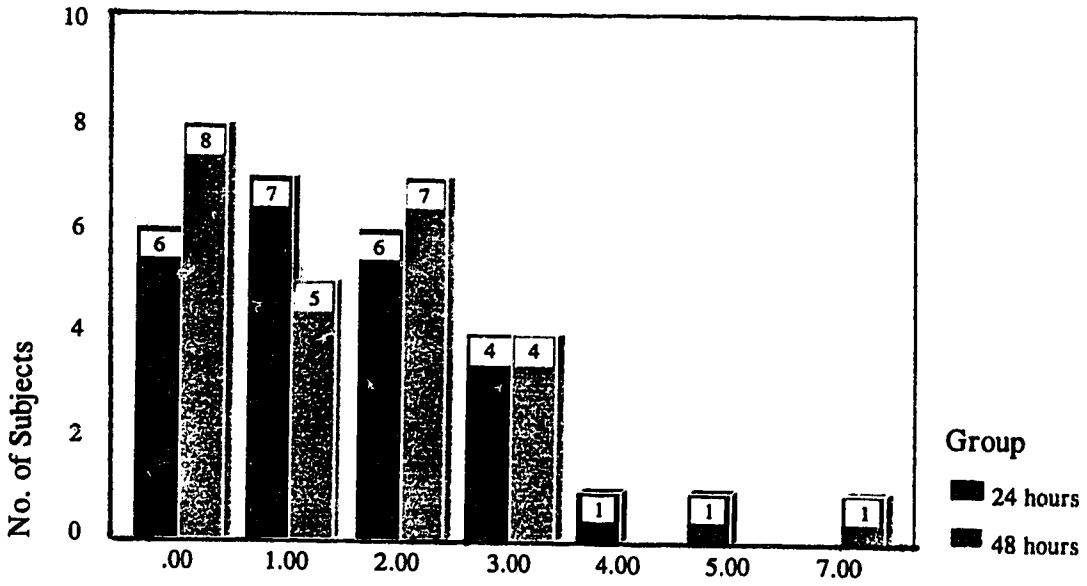
There exists an assumption among nurses that IV infusate is predictably sterile (Potter & Perry, 1985). This belief was not supported by the findings of this study. Of the 50 subjects that agreed to participate in this study, 36 (72%) had microorganisms cultured from their IV infusate at some time during the proposed five measures. Nineteen (76%) of these subjects had their IV sets changed on a daily basis while 17 (68%) of these subjects had their IV sets changed every 48 hours. Group differences related to the proportion of subjects with bacteria and/or fungus in their IV infusate were not found to be statistically significant (Figure 1). This finding is consistent with the literature that reports no significant difference in the rate of infusate colonization between administration sets changed every 24 versus 48 hours (Band & Maki, 1979; Buxton et al., 1979; Gorbea et al., 1984; Jakobsen et al., 1885).

Twelve of the 50 subjects (24%) were readmitted into the study on a subsequent admission to hospital. Subjects were again randomly assigned to one of the two groups. Two of these subjects, one in each group, had colonized IV administration sets on both admissions. The subject in the 24-hour group had the same organism isolated from IV infusate on both admissions. Unfortunately, speciation was not performed to determine whether or not these organisms were of the same strain. The subject in the 48-hour

group had multiple organisms isolated from the IV infusate on the first admission and a single organism isolated on the second admission. None of the isolates identified were of the same species. Given that the individual is frequently the source of organisms isolated from IV infusate, it was hypothesized that the particular microorganism(s) identified in IV infusate, initially, may colonize IV administration sets on subsequent admissions.

Figure 1

Contamination by Group Assignment



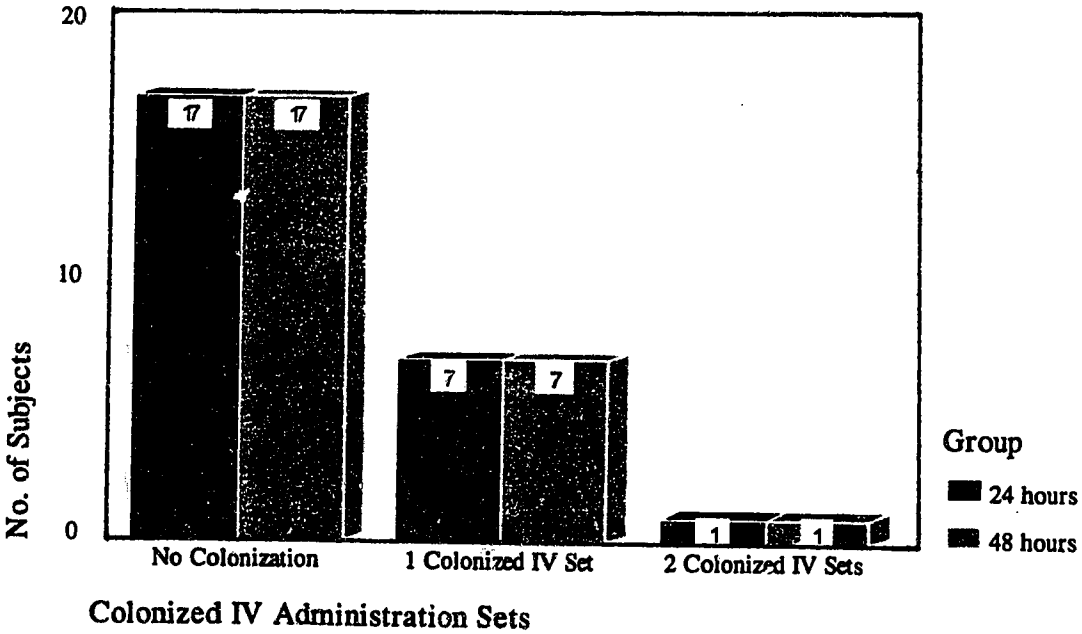
Contaminated and/or Colonized IV Administration Sets

Subjects in the 24-hour group had a mean of 36.40 ± 95.40 colony forming units (cfu)/ml isolated from their IV infusate. Subjects in the 48-hour group had a mean of 89.40 ± 226.57 cfu/ml isolated from their infusate. The number of cfu/ml isolated from the infusate of subjects whose IV sets were changed every 48 hours is more than twice that of subjects whose IV sets were changed after 24 hours. Nevertheless, group differences related to the number of cfu/ml were not statistically significant. Increased numbers of microorganisms in the 48 hour versus 24 hour change group is also consistent with findings reported in the literature (Maki et al., 1987).

For the purpose of this study, colonization was defined as ≥15 cfu/ml of infusate. Sixteen subjects (32%) were found to have microorganisms in excess of 15 cfu/ml of infusate, at some time during the proposed five measures. Subjects with colonized IV administration sets were equally distributed between the two groups; seven subjects in each group had a single colonized IV administration set and one subject in each group had two colonized administration sets (Figure 2). No statistically significant group differences were found related to the number of colonized IV administration sets. When groups were compared over time, no statistically significant group differences were found between subjects whose IV sets were changed at 24 hours and subjects whose IV sets were changed at 48 hours. Differences in colonization rates over the five measures were also found to be statistically non-significant, as were tests for an interaction effect between group and time. In conclusion, there was no statistically significant difference in the rate of infusate colonization between subjects whose IV administration sets were changed every 48 versus 24 hours.

Figure 2

Colonization by Group Assignment



Correlations between demographic variables, rates of contamination, and colonization were also examined. As expected, there was a statistically significant correlation between the rate of contamination and colonization ($r=.2188$, $p=.000$) whereby, as the number of different microorganisms in the IV infusate increased, so too did the number of cfu/ml of infusate. There was also a statistically significant, positive correlation between subjects' initial ANC and infusate contamination ($r=.1291$, $p=.009$). As the subject's ANC increased, the number of different microorganisms in the infusate also increased. Given that subject's ANC is a reflection of their immune response, an inverse relationship between the ANC and the number of microorganisms in the infusate was anticipated. The possibility of a confounding variable such as attention to aseptic technique while making and breaking connections or entering the IV system is a possible explanation for this unexpected finding.

No meaningful correlations were found between infusate contamination and the subject's age ($r=-.0076$); number of comorbidities ($r=-.0379$); gender ($r=-.0148$); type of CVC ($r=-.0021$); and, primary diagnosis ($r=-.0073$). Similarly, non-significant correlations were found between infusate colonization and demographic variables including the subject's initial ANC ($r=.0206$); age ($r=-.0901$); number of comorbidities ($r=.0700$); gender ($r=-.0411$); type of CVC ($r=-.0086$); and, primary diagnosis ($r=.0105$). Given the small sample size and the weak correlations found between demographic variables and rates of contamination or colonization, attempting to interpret these findings and determine the relative importance of each of these variables was believed to be of limited benefit.

Infusate Variables

Data were collected on a total of 423 IV administration sets, 10 of which were inadvertently discarded prior to being cultured. Information related to these 10 IV sets was, therefore, excluded from further analysis. Of the remaining 413 sets, microorganisms were isolated from the infusate of 78 sets (19.14%); 41 sets (17.38%) in the 24-hour group and 37 sets (20.90%) in the 48-hour group. The mean number of

cfu/ml of infusate was 22.20 ± 75.69 for IV sets changed every 24 hours and 66.41 ± 188.55 for IV sets changed every 48 hours. Group differences related to the number of microorganisms isolated from the infusate were not found to be statistically significant.

Comparisons between the findings of this study and that of previous studies is limited due to differences in inclusion criteria, methodology (amount of infusate collected), definitions (contamination and colonization frequently used synonymously), and the variables examined. During the late 1970's, rates of infusate contamination were reported to be approximately 2% (Buxton et al., 1979) and 0.5% (Band & Maki, 1979). Both studies reported low level contamination (≤6 cfu/ml of infusate) in IV administration sets used for a variety of different therapies, infused through both peripheral and central catheters. Gorbea et al. (1984) found contamination rates lower than that found in this study, approximately 2% in IV sets changed at 24 hours and 4% in sets changed every 48 hours. Josephson et al. (1985) also found lower rates of contamination than was found in this study, 0.87% in IV sets changed at 48 hours and 0.96% in administration sets unchanged for the duration of the therapy. These researchers excluded from examination all subjects receiving TPN and/or blood products. Josephson et al. also isolated smaller numbers of microorganisms with <2 cfu/ml of infusate found in contaminated administration sets.

Jakobsen et al. (1986) reported contamination rates of between 26.0% and 33.3% in peripheral administration sets. Higher rates of contamination, however, were believed to be associated with the different culture method (swabbing the lumen of the IV set rather than aspirating an aliquot of fluid). Maki et al. (1987) examined both peripheral and central catheters in non-neutropenic subjects. Rates of contamination were 0.8% in administration sets changes every 48 hours and 1.5% in sets changed every 72 hours. The degree of colonization was very low ranging from 1 to 27 cfu/ml of infusate. Syndman et al. (1987) examined in-line burettes to determine the rate of colonization in stagnant infusion fluids and found microorganisms in 5.0% of the sets changed every 48 hours and 4.4% in the sets changed every 72 hours. Only 2 ml of

infusate was examined and levels of contamination were not reported.

The higher incidence of microbial contamination found in this study (19%), compared to previous studies, is believed to be related in part to variables associated with cancer therapy. Arguably, neutropenic cancer patients are among the most compromised patients to receive IV therapy. In addition to receiving infusion therapy through CVC, subjects in this study were recipients of some of the most vulnerable forms of therapy including TPN and blood products and had blood specimens collected at least daily, from their CVC. Intravenous therapy used to counter the adverse effects of cancer therapy contributes to a rate of manipulation that exceeds that of most patients receiving IV therapy. Non-antibiotic therapy accounted for the largest proportion of manipulations, followed closely by IV antibiotic therapy. Although only 50 subjects were followed in this study, these subjects represented >96% of the hospitalized population to meet the inclusion criteria, during an eight month period.

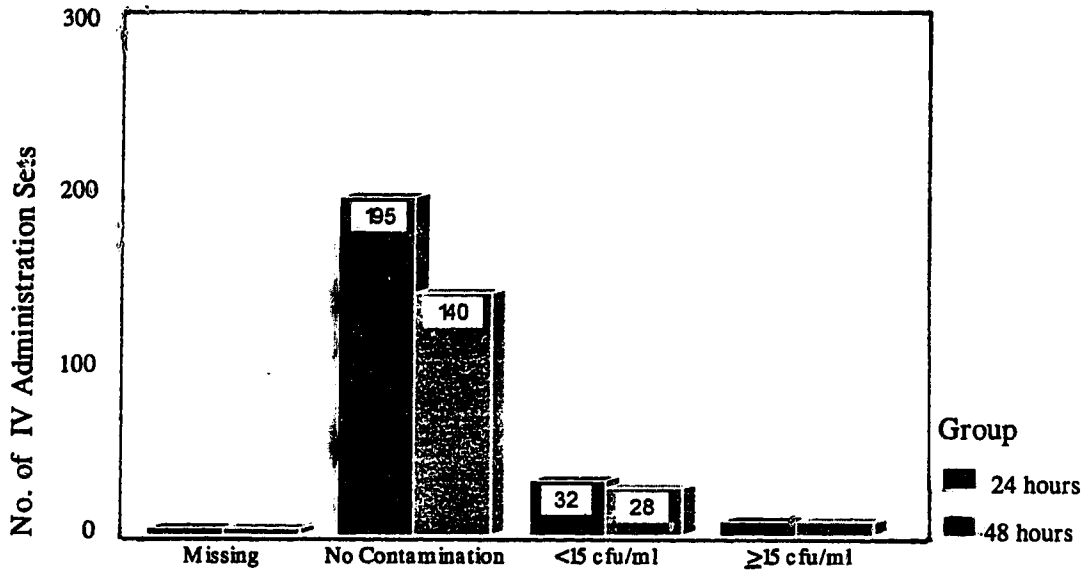
Another factor believed to contribute to the higher contamination rate in this study is related to the methodology. Ten ml of infusate was aspirated from IV administration sets because this volume represented the total volume of fluid within the IV tubing. This fluid was then filtered through a micropore filter, prior to inoculating blood agar plates or liquid media, in order to concentrate the aspirate. It is believed that the larger volume of infusate collected increased the likelihood of isolating microorganisms.

In this study, 18 IV administration sets (4.45%) contained microorganisms in quantities ≥ 15/ml of infusate. Nine sets (3.81%) had been changed at 24 hours, and the remaining nine sets (5.09%) had been changed at 48 hours. Again, this finding is high compared to that reported by Gorbea et al. (1984), but, is consistent with the findings of Snydman et al. (1987). The mean number of cfu/ml of infusate in this study was 91.67 ± 147.14 for IV sets changed every 24 hours and 239.44 ± 335.13 for IV sets changed every 48 hours, respectively. Group differences related to the number of microorganisms isolated from colonized infusate were not found to be statistically

significant. Although the overall degree of colonization (cfu/ml) is high in this study, the increased number of cfu/ml found in sets changed at 48 versus those changed at 24 hours is consistent with findings reported by Maki et al. (1987). These findings affirm conclusions reported in the literature that there is no difference in the prevalence of colonization between IV administration sets changed at 48 versus 24 hours (Figure 3).

Figure 3

Contamination and /or Colonization of Infusate by Group



Microorganisms Isolated from IV Infusate

Colonization was found to be independent of the type of infusate administered though the IV set, with colonization occurring in IV sets used for any of the prescribed therapies. One hundred and seventy-six IV sets used to administer antibiotics were cultured, seven sets (3.98%) were found to be colonized; three sets (4.35%) in the group changed at 24 hours and three sets (3.6%) in the group changed at 48 hours. One hundred and ninety-five IV sets used to administer non-antibiotic therapies were cultured, seven sets (3.59%) were found to be colonized; four sets (3.96%) in the group changed at 24 hours and three sets (3.2%) in the group changed at 48 hours. Intravenous electrolyte therapy was delivered through 42 sets, three sets (7.0%) were

found to be colonized; one set (5.3%) in the 24 hour change group and two sets (8.7%) in the group changed every 48 hours. Twenty-nine IV sets were used to administer chemotherapy, of these, one set (2.2%) was colonized. This IV set was changed at 24 hours; the colonization rate for IV chemotherapy sets in the 24 hour group was 4.4%. Similarly, of the 46 IV sets used to infuse GCSF, one set (2.1%) was colonized. This single set was again in the 24 hour change group; colonization rate for GCSF sets in this group was 4.2%. Sixty IV sets used to administer TPN were cultured, five sets (10.9%) were found to be colonized; one set (2.6%) in the group changed at 24 hours and four sets (19.1%) in the group changed at 48 hours.

Group differences in the number of colonized IV administration sets, by prescribed therapy, were not statistically significant. However, when only TPN administration sets were considered, statistically significant group differences were found related to the rate of colonization (χ^2=.2845, p=.0276). When TPN administration sets were changed every 48 hours, there was an associated 19.1% colonization rate. This is compared to a 2.6% colonization rate in TPN administration sets changed every 24 hours.

The overall colonization rate for the different IV therapies administered in this study is relatively consistent at approximately 3 to 5%. Two exceptions are IV sets in the 48 hour group used to deliver electrolytes (8.7%) and, as previously described, IV sets used to administer TPN (19.1%). The addition of potassium and magnesium, or any other additive, on the nursing unit has been identified in the literature as a contributing factor in the colonization of IV infusate (Woodside et al., 1975). Possible explanations for higher colonization rates associated with the addition of medications on the unit include working without the benefit of a laminar flow hood and poor aseptic technique. Lower rates of colonization related to IV electrolyte therapy were anticipated, given the acidity of electrolytes and the potentially adverse effect on the survival of microorganisms.

Although findings in the literature report that IV administration sets used for TPN can safely be changed at between 72 (Maki et al., 1987; Robathan et al., 1995) and 120 hours (Sitges, Linares, Perez, Jaurrieta, & Lorente, 1984), this finding was not supported in this study. Once introduced into the IV infusate, microorganisms appear to thrive in this medium. Several factors may contribute to the colonization of these sets: (a) TPN sets are Y-connected to allow the simultaneous administration of lipids and amino acids. Additional joints in the IV set are reportedly associated with higher rates of colonization. (b) Subjects are occasionally disconnected from their TPN lines for showers, tests, or other unanticipated interruptions. Given the physical consistency of this infusate, making and breaking connections without losing small amounts of this solution at the luer site is difficult. Microorganisms at connection sites not only are guaranteed a rich nutrient source, but, also access to the lumen of the administration set. (c) Swabbing connections prior to making or breaking them does not appear to be a mandatory step in the delivery of IV therapy at this institution. Stotter et al. (1987) demonstrated a significant reduction in colonization of TPN sets following the introduction of a protocol that reduced the number of connections in the delivery system and maintained asepsis at the connect site. (d) The TPN medium, in particular the lipid emulsion, provides a viable nutrient source for a wide variety of microorganisms gaining access to the IV administration set.

Correlations between the different kinds of infusate and rates of contamination and colonization were performed. Non-significant correlations were found between infusate contamination and antibiotic therapy (r=- .0594); non-antibiotic therapy (r=- .0067); electrolyte therapy (r=- .1117); GCSF therapy (r=.0895); the administration of TPN (r=.0733); and, chemotherapy (r= .0699). Similarly, non-significant correlations were found between infusate colonization and antibiotic therapy (r=- .0353); non-antibiotic therapy (r=- .0490); electrolyte therapy (r=- .0683); GCSF therapy (r=- .0371); and, chemotherapy (r=- .0284). A statistically significant relationship was found, however, between the administration of TPN and infusate

colonization (r=.1196, p=.015). Although there was no significant relationship between the number of different organisms isolated from TPN, there was a significant relationship between the degree of colonization and the administration of TPN. However, given the small sample size, caution must be exercised when interpreting these findings.

In summary, overall group differences related to rates of infusate colonization (and contamination) were not associated with the frequency with which IV administration sets are changed. However, the degree of colonization increased proportionately as one moves from changing IV administration sets every 24 hours to 48 every hours. Additionally, the nature of the infusate was not correlated with the rate of colonization when IV sets are changed at 24 hour intervals. However, there was a trend toward increased colonization of IV sets in the 48 hour group used to administer TPN (19.1%) and to a lesser extent electrolytes (8.7%).

Administration Set Variables

. In the 24-hour group, four sets (2.72%) in continuous use and five sets (5.62%) disconnected for a period of time were found to be colonized. Conversely, in the 48-hour group, six sets (5.71%) in continuous use and three sets (4.17%) idle for some period of time were found to be colonized. Determining statistically whether or not group differences exist related to the rate of colonization among IV sets in continuous use versus those idle for a period of time was difficult due to small sample size. However, IV administration sets in continuous use were less frequently colonized than IV sets idle for a period of time.

Idle IV sets were more frequently colonized than IV sets in continuous use and weak, but statistically significant, positive correlations were found between the number of hours IV administration sets were idle and the incidence of both infusate contamination (r=.0952, p=.053) and colonization (r=.1004, p=.041). The longer IV sets were idle, the greater the number of different organisms isolated from the infusate and the greater the number of cfu/ml of infusate. Research examining the question of

risk associated with stagnant infusion fluids has not been investigated thus far. Gorbea et al. (1984) had questioned whether an increased risk of sepsis might be associated with stagnant infusion fluid, nevertheless, this hypothesis was not supported in their study of 676 IV systems containing in-line burettes.

There was also a statistically significant relationship found between the number of connections in the IV administration sets and the number of hours sets were idle ($r = -.3128$, $p = .000$). As the number of hours sets were idle increased, there was an associated decrease in the number of connections within the IV set. This finding seems logical given that connections are generally added to accommodate increasing numbers of prescribed therapies or simultaneous infusions. If IV sets are idle for increasing periods of time, IV therapy is probably intermittent or delivered on an as needed basis. Similarly, study findings revealed a statistically significant, positive correlation between the number of connections within an IV administration set and the number of entries into the system ($r = .4455$, $p = .000$). Using the same logic as above, as the need to deliver increasing numbers of IV medications occurs, connections are added to IV systems to accommodate additional therapies.

What was not anticipated was a negative correlation between the number of entries into the IV set and the incidence of both infusate contamination ($r = -.0057$, $p = .908$) and colonization ($r = -.0144$, $p = .770$). These correlations were not, however, statistically significant. Explanations for this finding may include the lack of standardization associated with entries into IV sets. For example, most nurses swabbed injection ports with alcohol prior to inserting the needle, but, very few waited the recommended 30 to 60 seconds for the alcohol to dry and, therefore, afford the bacterial static action sought. Additionally, swabbing connections with a bacterial static preparation prior to breaking them was not a standard practice. Literature hailing the cost-effectiveness of IV teams, in managing infection, identified consistency related to aseptic techniques to be the cornerstone for reducing infusion-related infections (Baron et al., 1994; Johnson & Oppenheim, 1992; Mackinnon et al., 1987; Maki, 1992).

A statistically significant, negative correlation was also found between the number of connections in the IV set and the number of cfu/ml of infusate ($r = -.1058$, $p = .032$). One possible explanation could be that the relationship between the number of connections within the IV set and the incidence of colonization is confounded by the type of infusate administered through these IV sets. Intravenous administration sets used to administer antibiotics frequently have four connections, whereas, sets used to administer TPN generally have three connections. As indicated previously, the overall rate of colonization associated with IV sets used to administer antibiotic therapy was 3.5%, whereas, colonization associated with administration sets used to deliver TPN was approximately 10.9%.

Microorganisms Isolated from Intravenous Infusate

Coagulase-negative staphylococci were the most frequently isolated microorganisms in IV infusate. This finding is consistent with much of the research to date investigating colonization of IV infusate (Band & Maki, 1979; Jakobsen et al., 1985; Maki et al., 1987; Sitges-Serra, Linares, Perez, Jaurrieta, & Lorente, 1984; Sitges-Serra, Puig, Linares, Perez, Farrero, Jaurrieta, & Garau, 1984; Snydman et al., 1987). The extent to which CNS colonized IV sets was, however, more prominent in this study than in the previous work in this area. Seventy-eight percent of contaminated IV sets harboured from one and three strains of CNS. Possible explanations for these findings include: (a) Colonization of IV infusate by CNS appears to be associated with the use of CVC rather than peripheral IV sets (Lowder et al., 1982). Because previous studies investigating the incidence of infusate colonization have included both peripheral and central catheters, the influence of CNS may have been diluted. (b)The intrinsic microbial characteristics of CNS allow this bacterium to adhere to the catheter surface and protect it from antibiotics, phagocytosis, and antibodies; this organism is even capable of using the catheter itself as a source of nutrients. Neutropenic cancer patients are particularly vulnerable to invasion by CNS because cancer therapy compromises the individual's integument, but also their immune response. (c)

Retrograde travel of microorganisms up into administration sets may not be as rare as suggested in the literature (Press et al., 1984; Maki, 1992; Maki et al., 1973). (d) CNS is endogenous to the hands of the health care providers manipulating the IV administration sets. Conly (1995) suggests that health care professionals may be the primary source of CNS infection of catheter hubs.

Other gram positive cocci isolated from the IV infusate include: *Micrococci* species, *Staphylococci aureus*, viridans group streptococci (VGS), non-hemolytic streptococci (NHS), beta-hemolytic streptococci (BHS), and *Enterococci* species. These endogenous flora were isolated from 20 of the IV administration sets cultured. Potential sources of these organisms include subjects themselves and, to a lesser extent, health care professionals, support staff, and visitors. Organisms are transferred from person to person through touch (hence the emphasis on hand washing), sneezing/coughing, and sharing objects such as drinking glasses. Given the proximity of connections and injection ports to subject's integument, as well as the lack of standardization associated with cleansing joints prior to making and breaking connections, the route of ingress of many of these organisms seems clear. Additionally, staff entering these lines immediately after washing their hands (ungloved) set in flight those microorganisms released from the crevasses of their own hands.

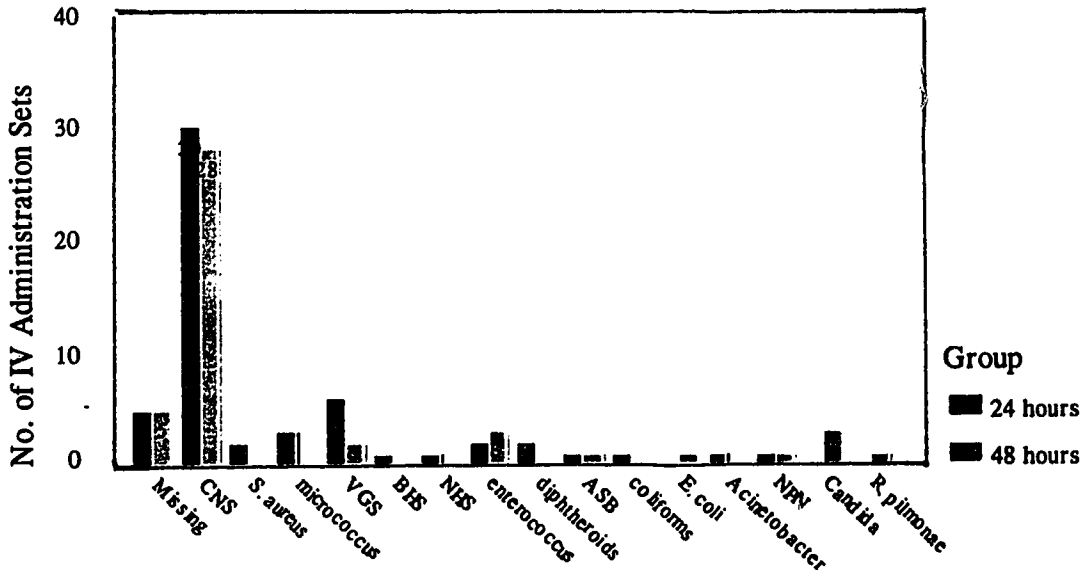
Diphtheroids, isolated from two IV sets, are gram positive bacilli, endogenous to the upper respiratory and urinary tracts of human beings. These organisms were isolated from approximately two percent of the IV administration sets cultured. Diphtheroids are often multiple antibiotic resistant and have a propensity for surviving on fomites for extended periods of time. Gram negative bacilli and cocci, isolated from four infusate specimens include: non-pathogenic *Neisseria* species (NPN), coliforms, and *Escherichia coli*. Like the aforementioned organisms, these organisms are also endogenous to the human body and are transmitted from person to person as described above. *Candida albicans*, isolated from one infusate specimen, is also native to the human body. Occupying primarily the mucous membranes of the mouth, vagina, and

gastrointestinal tract, this fungi responds readily to the antibiotic supression of other normal flora. Passage into the IV infusate is, in part, related to poor aseptic technique while breaking connections and/or injecting into infusion ports.

Acinetobacter species, however, is an opportunistic pathogen. This bacterium, isolated from one set, survives on hospital equipment, for example, nasal cannulae or humidifiers for oxygen therapy. Colonization by this organism is often associated with poor aspectic techique during procedures and environmental conditions within the institution. Other environmental pathogens isolated from IV infusate were *C. parapsilosis* and *Rhodotorula pilmonae*. Transmission of these microorganisms may occur via the institution's water supply, on fruits and salads, diagnostic and/or therapeutic equipment, and other environment amenities. Access to IV infusate occurs as the result of breaks in protocol and/or aseptic technique (Figure 4).

Figure 4

Microorganisms Isolated from Intravenous Infusate



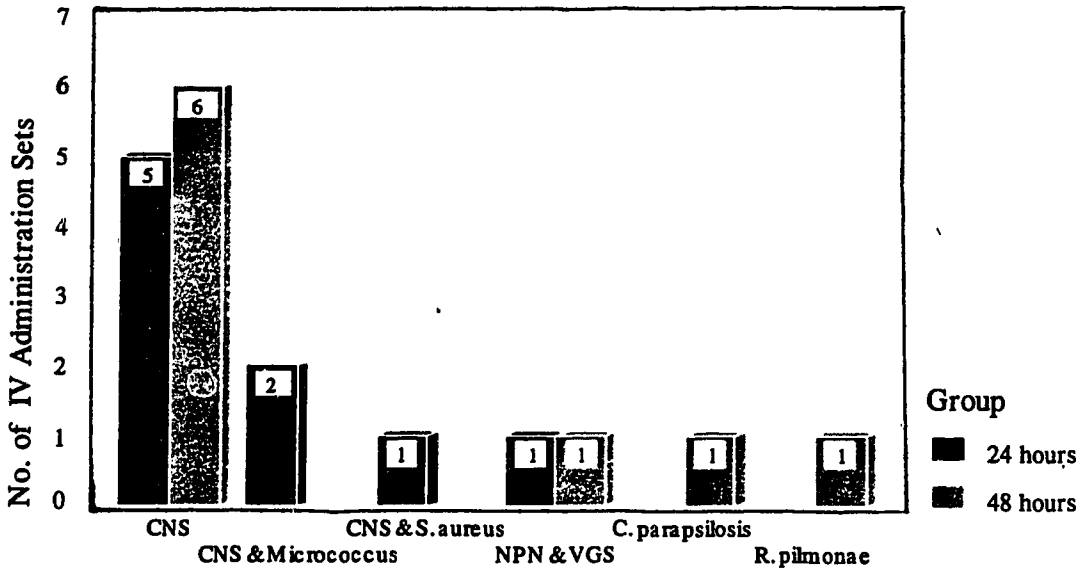
Microorganisms Isolated from IV Administration Sets

Microorganisms isolated in quantities ≥15 cfu/ml of infusate included: CNS, *Micrococcus* species, *S. aureus*, NPN, VGS, *C. parapsilosis*, and *R. pilmonae*.

Coagulase-negative staphylococci were again the most prominent isolate. Fourteen of the 18 colonized IV sets (78%) harboured between one and three strains of CNS. Five IV sets had polymicrobial colonization; three sets contained CNS and a second organism while two sets were colonized with *Neisseria* species and VGS (Figure 5).

Figure 5

Microorganisms Isolated from Colonized Intravenous Administration Sets



Microorganisms Colonizing IV Administration Sets

Colonized IV administration sets had a mean of 165.56 ± 262.34 cfu/ml of infusate. Although group differences related the mean number of cfu/ml of infusate were not statistically significant, colonization of IV administration sets changed after 48 hours harboured increased numbers of microorganisms; 91.67 ± 147.14 cfu/ml in the 24-hour group compared to 239.44 ± 335.13 cfu/ml in the 48-hour group, respectively. Comparisons with existing research is difficult given that the degree of colonization was rarely reported in literature. Maki et al. (1987) reported higher numbers of cfu/ml in their 72 versus 48-hour change group, however, the number of organisms isolated ranged from 1 to 27 cfu/ml of infusate. Josephson et al. (1985) isolated only two cfu/ml in each of the two colonized administration sets. Snydman et

al. (1987) found from 4 to 7 cfu/ml, however, these researchers examined only four and two ml of IV infusate, respectively. Had they sampled 10 ml of IV infusate, as was done in this study, it would be interesting to see if the number of organisms isolated would have been higher. Given the complexity of patient care within this study, comparisons with existing research may be not only difficult but meaningless.

In summary, the overall contamination rate (<15 cfu/ml) for IV administration sets in this study was approximately 19%, however, only four percent of IV administration sets were considered to be significantly colonized (≥ 15 cfu/ml). Many of the variables believed to influence the rate of infusate colonization behaved in predictable ways. Correlations between these variables and the rate of contamination and colonization were, however, weak and often not statistically significant. Nevertheless, the rate of infusate colonization did not differ significantly between subjects whose IV administration sets were changed every 24 hours and those whose administration sets were changed every 48 hours. Group differences related to the number of cfu/ml were also statistically non-significant. As well, tests for interaction effects between group assignment and time were not found to be statistically significant. Without obvious benefit from changing IV administration sets more frequently, the cost of this practice in terms of patient comfort, nursing hours, and physical resources, warrants reconsideration.

Infusion-related Septicemia

Although extrinsic colonization of IV infusate is believed to be a rare cause of septicemia, risk of an infusion-related septicemia continues to be the motivating force behind changing IV administration sets every 24 hours, in high risk populations. In order to test this theory, comparisons were made between microorganisms isolated from IV infusate specimens and those isolated from blood cultures collected from febrile subjects. Twenty-two positive blood cultures were collected, three of which appeared to correspond with positive IV infusate cultures collected from the same subjects. Two days prior to entering the study, a subject in the 48-hour group had

viridans group streptococci isolated from both peripheral and central blood cultures and was subsequently started on appropriate antibiotic therapy. On day four of the study, viridans group streptococci was isolated from an IV infusate specimen. Speciation of these organisms confirmed they were two different species; *S. mitis* was isolated from blood cultures and *S. sanguis* from IV infusate.

A second subject in the 48-hour group had *C. albicans* isolated from a peripheral blood culture on day nine of the study. On day eight, this subject had a single cfu of *C. albicans* isolated from one of two infusate specimens collected that day. Because infusate colonization was defined as ≥ 15 cfu/ml of infusate, this finding did not meet the criteria of an infusion-related septicemia.

A third subject in the 48-hour group had blood cultures positive for *C. parapsilosis* prior to and on day one of this study. On day two of the study, IV infusate was positive for *C. parapsilosis* in quantities > 1000 cfu/ml. Given the gravity of this subject's condition, removal of the CVC was undertaken. The tip of this catheter was also positive for *C. parapsilosis*, thus confirming a catheter rather than infusion-related etiology for this septicemia.

Although similar organisms were isolated from blood cultures and administration sets, no other subjects with positive blood cultures had the same organism isolated from their IV infusate, in quantities ≥ 15 cfu/ml, at any time during the course of the study. Five of the 16 subjects (31%) with positive IV infusate, were receiving between one and five different antibiotics which would have limited any attempt to culture infecting organisms. Nevertheless, there were no subjects in this study with an infusion-related septicemia.

Limitations of This Study

There were several limitations in this study, the most predominant being the size of the sample. Attempting to answer questions designed to determine the risk associated with infusion therapy is multi-faceted. In addition to subject variables

including gender, age, neutrophil count, diagnosis and comorbidities, there were variables associated with IV therapy, per se. Variables including the type of solutions infused, the number of connections within the delivery set, and the frequency with which administration sets were manipulated to administer IV therapy influence rates of colonization and ultimately, the incidence of infusion-related septicemia. Attempting to identify the contribution of these variables to infusate colonization was limited by the complexity of the relationship(s) between variables and the small sample. Given the vulnerability of neutropenic cancer patients to infection, it was important to examine the question of susceptibility in relation to all the confounding variables previously described. Amassing a sample large enough to evaluate the contribution of each of the confounding variables and guard against type II error was clearly impossible. The intention, therefore, was to design a study to identify a trend, of low rates of infusate colonization and no related infusion-related septicemias.

A second limitation was in determining the kinds of differences that would be considered meaningful or important, in the absence of statistical evidence. For example, are group differences related to the colonization of IV sets used to administer TPN clinically important? Literature addressing the negative sequelae associated with parenteral nutrition is vague and even contradictory. Many of the studies examining the risk of colonization of IV administration sets deliberately excluded IV sets used to deliver TPN from investigation. Consequently, some of the conclusions drawn in this study were based, in part, on clinical experience and are, therefore, open to deliberation. Findings, nevertheless, are representative of >96% of the population at the CCI, meeting the inclusion criteria, over a period of eight months.

A third limitation in this study is related to the proposed microbiological investigations. Given the expense associated with speciating microorganisms, especially coagulase-negative staphylococci, speciation was limited to like organisms isolated from the blood cultures and IV infusate of a particular subject. This strategy proved effective for determining the likelihood of an infusion-related septicemia, however, it

limited insight into the origin of infecting microbes, especially endogenous flora. To illustrate, when diphtheroids were isolated from IV infusate, did they originate with the subject, the subject's visitor, or the health care professional? Literature speculating on the origin of infecting organisms is also conflicting in this regard.

A fourth limitation of this study was in differentiating between contamination and colonization of IV infusate. Based on a review of the literature, infusate colonization ≥ 15 cfu/ml of infusate was believed to be an appropriate indicator of the risk of developing an infusion-related septicemia. In hindsight, any degree of contamination is clinically meaningful in that it represents a violation to the integrity of the IV system. If protocols related to IV therapy are such that a single organism can gain access to the infusate, others may gain entry in a similar manner. Additionally, once microorganisms have gained entry, the growth potential is limited only by the nature of the IV solution and the immune response of the subject.

Implications of This Study

Many nurses, this author included, assume that IV infusate is invariably sterile and that colonization of IV administration sets is a rare occurrence. Findings from this study suggest that colonization of IV infusate is more common than initially thought. Thirty-six of 50 subjects (72%) had microorganisms isolated from their IV administration. The frequency with which contamination occurred appeared to be independent of the frequency with which IV administration sets were changed with 19 subjects (76%) in the 24-hour group and 17 subjects (68%) in the 48-hour group having microorganisms isolated from IV infusate at least once during the study. Microorganisms grew to numbers ≥ 15 cfu/ml of infusate in 18 administration sets belonging to 16 different subjects. Implications for nursing are numerous.

Group differences related to the frequency with which IV administration sets are changed were not found to be statistically significant, therefore, changing IV administration sets every 48 hours, rather than every 24 hours as is the current policy,

is recommended. Exceptions to this recommendation would be the IV administration sets used to administer blood products and/or TPN. Although the degree of infusate colonization found in this study was higher than in other studies examining rates of infusate colonization related to the frequency with which IV administration sets are changed, this finding is believed to be related, in part, to the methodology chosen and the population studied.

Higher rates of colonization found in this study are also believed to be associated with the practice of breaking, without first disinfecting, connections within IV sets. Attention to aseptic technique while manipulating IV administration sets may be even more important in limiting infusate colonization than the frequency with which IV sets are changed. A judicious approach to IV therapy, particularly in this patient population is, therefore, advisable. Although a negative correlation between the number of entries into the IV administration set and the rate of infusate colonization was found, this correlation was weak, non-significant, and inconsistent with findings reported in the literature. This finding may well be confounded by the divergent approaches to making and breaking connections within IV administration sets, within this institution. Strategies that may reduce the incidence of infusate colonization include those that attend to the chain of infection. Given the frequency with which endogenous flora were isolated from IV infusate, it seems reasonable to conclude that strategies need to include cleansing connections with an anti-bacterial solution prior to breaking them (Sitges-Serra, Linares, Perez, Jaurrieta, & Lorente, 1984).

Because higher contamination rates are associated with more complicated and heavily manipulated IV systems (Maki et al., 1987), reducing the number of entries into IV sets is another strategy with the potential to reduce colonization. Four examples specific to this institution come to mind: (a) Cytarabine is delivered to the unit in two 250 ml bags and is infused over a 24 hour period. This chemotherapeutic agent, prepared in pharmacy, could be delivered to the unit in a single 500 ml bag. Not only would this practice reduce the number of times IV sets were interrupted, but, potential

exposure to this agent by patients and staff would also be lessened. (b) Potassium chloride boluses are frequently administered in sequential minibags. If the equivalent amount of KCL were added to a 500 ml bag, the IV system would be interrupted less frequently. (c) For patients receiving frequent analgesics (one subject received 20 individual doses of morphine over a 24 hour period), a continuous infusion or infusion device, for example, a patient controlled analgesia pump or Edmonton injector, would limit the number of interruptions into the system and may, therefore, be more appropriate. (d) When administering compatible solutions, for example, many antibiotics are compatible with potassium chloride, using a single minibag to administer both products simultaneously would limit the number of entries into the IV administration set to deliver treatment as well as limit the amount of fluid delivered parenterally.

Because conclusions in this study are based in part on clinical judgement, rather than statistically sound cause and effect relationships, it is imperative that trends be monitored to ensure rates of colonization do not increase following a protocol change to 48 hours. If an increase in rates of infusate colonization is suspected, it would be reasonable to reinstitute the original policy until reasons for this increase were identified and corrected. As with any proposed change, a new policy and an educational program are required to support the proposed change. Should this institution's protocol for changing IV administration sets be changed to 48 hours, staff education may include a description of the proposed change, the rationale for implementing this change, and specified period of time in which this change would occur. Some monitoring may be required to ensure that this change is accepted and that changing IV administration sets every 48 hours becomes the norm.

Future research related to the frequency with which IV administration sets are changed should include further investigations into the relationship(s) between parenteral nutrition and IV infusate colonization. Investigating the effects of changing IV administration sets every 72 hours on infusate colonization and subsequently the

incidence of infusion-related septicemia could be considered, but, only after instituting measures to reduce colonization associated with manipulating administration sets.

Conclusion

Despite the findings of recent studies that suggest IV administration sets may safely be changed at intervals up to but not exceeding 120 hours, it was believed that neutropenic cancer patients are somewhat unique and that protocols used for general medical, surgical, or even intensive care populations may not be appropriate for this population. The purpose of this study, therefore, was to examine the effects of changing IV administration sets every 48 rather than 24 hours, on the incidence of infusion-related septicemia in neutropenic cancer patients. Because infusion-related septicemia is believed to be rare, rates of infusate colonization were used as an indicator of the degree of risk.

Two hypotheses were tested: (a) there is no difference in the rate of infusate colonization between neutropenic cancer patients whose IV administration sets are changed every 24 hours and those whose IV administration sets are changed every 48 hours; and (b) there is no difference in the incidence of infusion-related septicemia between neutropenic cancer patients whose IV administration sets are changed every 24 hours and those whose IV administration sets are changed every 48 hours. Both hypotheses were supported in this study.

Relationships among confounding variables including neutropenia, central catheters, age, gender, manipulating IV administration sets, blood transfusions, blood specimen collection, parenteral nutrition, comorbidities, antibiotic, non-antibiotic, and electrolyte therapy, the addition of additives, and the rate of infusate colonization were also examined. Attempting to identify the contribution of each of these variables was limited by the complexity of the relationship(s) between variables and the small sample. Nevertheless, many of these variables appeared to influence infusate colonization in predictable ways.

The intention of this study was to identify a trend of low rates of colonization with no associated infusion-related septicemias. Approximately four percent of IV administration sets were found to be colonized. Group differences related to the rate of colonization of IV administration sets changed at 48 versus 24 hours were not found to be statistically significant. The number of organisms isolated from IV infusate ranged from 15 to 1000, with a mean of 165.56 $\pm$ 262.34 cfu/ml of infusate. Group differences related to the number of cfu/ml of infusate were not statistically significant. Despite higher levels of colonization than expected, no subjects developed an infusion-related septicemia.

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Appendix A

Consent Form

Protocol Title: Changing Intravenous (IV) Administration Sets: Is 48 Versus 24 Hours Safe for Neutropenic Cancer Patients?

(A Study Comparing the Rate of Infection in Patients with IV Tubing Changes Every 24 Versus Every 48 Hours)

This consent form, a copy of which has been given to you, is only a part of the process of informed consent. It should give you the basic idea of what the research project is about and what your participation will involve. If you would like more detail about something mentioned here, or information not included here, you should feel free to ask. Please take the time to read this carefully and to understand any accompanying information.

Purpose: The purpose of this study is to examine the safety of changing IV (into a vein) tubing every 48 hours in patients with cancer and low white blood cell counts. At the present time, IV tubing is changed every 24 hours at the Cross Cancer Institute. It is believed that opening and closing your IV tubing less often may reduce your risk of infection. Changing IV tubing every 48 hours has been shown to be safe in patients with normal white blood cell counts.

Description of the study: If you agree to be in this study you will be randomly assigned to one of two groups. This means that each patient will be assigned to one of the two treatment groups according to a computer generated code. The chance of being assigned to Group A or Group B are almost equal. Patients in Group A will have their intravenous tubing changed every 24 hours. Patients in Group B will have their intravenous tubing changed every 48 hours.

If you agree to be in this study, a small amount of fluid will be collected from the rubber stopper near the end of your IV tubing. Fluid samples will be collected from your IV tubing daily if you are in Group A and every other day if you are in Group B. These samples will be collected just before your IV tubing is changed. A total of five specimens will be collected from each patient. This fluid will be examined in the laboratory to look for bacteria. Information such as your temperature and white blood cell count will also be collected by your nurse or the researcher daily.

Date _____ Initials _____

Time requirement: Collecting the IV fluid samples from your IV tubing will take less than two minutes, each of the five days. Other blood tests will remain the same as the normal practice, as ordered by your doctor. If you decide to be in this study, no extra time in hospital will be needed.

Risks and benefits: If you are in the 48 hour group, it is possible you may have an increased risk of infection because your IV tubing is used for a longer time. It is believed, however, that you may be at less risk of infection because your IV tubing is opened and closed less frequently. Opening and closing your IV tubing less often reduces the chance of bacteria entering your IV tubing. It is believed that being in this study poses minimal to no risk to you. If you were to develop an infection, medical attention will be provided. Due to the experimental nature of this study, there is the potential for unknown side effects. Participation in this study may be of no personal benefit to you. However, based on the results of this study it is hoped that, in the long-term, patient care can be improved.

Right to refuse: Your doctor has given permission for you to be approached to be in this study. However, the decision to participate is yours to make. If you decide to be in this study, you may change your mind at any time by telling your nurse or the researcher. No questions will be asked and the choices you make will not affect the care you receive while in hospital.

Confidentiality: Your name will appear on blood samples but your identity will remain confidential. You will be given a code number for all other information collected. Only persons involved in this study will have access to this information. All material and data obtained from this study will be stored and may be used for future analysis without obtaining further consent from you. However, each study arising as a result of information obtained in this study will be submitted for ethical approval.

Understanding of the subject: My signature on this form indicates that I have understood to my satisfaction the information regarding my participation in the research project, and agree to participate as a subject. In no way does this waive my legal rights nor release the investigators, sponsors, or involved institutions from their legal and professional responsibilities.

I am free to withdraw from the study at any time without jeopardizing my health care. My continued participation will be as informed as my initial consent, so I am free to ask for clarification or new information throughout my participation.

Date _____ Initials _____

I understand that Donna deMoissac (403) 462-5096 or her supervisor Louise Jensen (403) 492-6795 will answer any questions I have about the research project.

If at any time during the course of this study I feel that I have been inadequately informed of the risks, benefits, or alternatives, or that I have been encouraged to continue in this study beyond my wish to do so, I can contact the Patient Advocate at (403) 492-8585.

A copy of this consent form will be given to me to keep for my records and future reference.

Name of Patient	Signature of Patient
Name of Witness	Signature of Witness
Name of Investigator	Signature of Investigator
Date	

If you would like to know the results of this study, please provide your complete name and address:

Name: _____

Address: _____

_____

Appendix B

Demographic Data Record

ID # _____

1. Gender (male or female) _____

2. Age _____ (years)

3. Primary Diagnosis _____

4. Comorbidities _____

   _____

   _____

5. CVC (double/triple) _____ lumen

6. Tympanic temperature _____°C

7. Absolute neutrophil count _____/mm^3

Appendix C

Daily Data Collection Record

ID #_____ From _____ /95 to _____ /95 Measure #____ Date:_____/95

1. IV administration set(s) changed at _____ hrs Specimen: # 1 2 3 4 5

2. Tympanic temperature (Q 4 hours)

0800 _____; 1200 _____; 1600 _____; 2000 _____; 2400 _____; 0400 _____

3. If ≥ 38.5° C, blood cultures were drawn both: Peripherally _____, CVC_____

4. WBC _____ Neutrophils _____ Bands _____ ANC _____/mm^3

5. Administration set (circle the appropriate number)

#1 _____ (lumen) # of connections 1 2 3 4 5 6 other____

#2 _____ (lumen) # of connections 1 2 3 4 5 6 other____

#3 _____ (lumen) # of connections 1 2 3 4 5 6 other____

#4 _____ (lumen) # of connections 1 2 3 4 5 6 other____

6. Idle administration set(s) # ____, _____ hrs; # ____, _____ hrs

7. IV Antibiotics

Name: _____ Q _____ hrs

Name: _____ Q _____ hrs

Name: _____ Q _____ hrs

8. Chemotherapy

Name: _____ Q _____ hrs

Name: _____ Q _____ hrs

Name: _____ Q _____ hrs

9. Non-antibiotic IV Therapy (regular and/or prn)

Name: _____ Q _____ hrs; if prn, # of doses _____

Name: _____ Q _____ hrs; if prn, # of doses _____

Name: _____ Q _____ hrs; if prn, # of doses _____

Name: _____ Q _____ hrs; if prn, # of doses _____

10. Additives: Yes / No K^+_____ Mg^{++}_____ CA^{++}_____ Other_____

11. TPN in use: Yes / No Set # _____

12. Blood Products: Yes / No PCs x #_____ Plts x #_____ Other_____

Premeds: 1_____, 2_____, 3_____, repeat x ____

13. Blood specimens (including pre/post levels) collected from CVC: Yes / No # _____

14. CVC tip cultured: Yes / No Results _____ N/A_____

Appendix D

Microbiological Data Record

ID No.	Day #1	Day #2	Day #3	Day #4	Day #5
1.01	Red_____ Wh/Yel_____ Blue_____	Red_____ Wh/Yel_____ Blue_____	Red_____ Wh/Yel_____ Blue_____	Red_____ Wh/Yel_____ Blue_____	Red_____ Wh/Yel_____ Blue_____
1.02	Red_____ Wh/Yel_____ Blue_____	Red_____ Wh/Yel_____ Blue_____	Red_____ Wh/Yel_____ Blue_____	Red_____ Wh/Yel_____ Blue_____	Red_____ Wh/Yel_____ Blue_____
1.03	Red_____ Wh/Yel_____ Blue_____	Red_____ Wh/Yel_____ Blue_____	Red_____ Wh/Yel_____ Blue_____	Red_____ Wh/Yel_____ Blue_____	Red_____ Wh/Yel_____ Blue_____

Appendix E

Blood Culture Data Record

ID No.	Day #1	Day #2	Day #3	Day #4	Day #5
1.01	Positive BC __ _____ _____ _____ _____ Positive IV Infusate _____ _____ _____ _____ _____	Positive BC _ _____ _____ _____ _____ Positive IV Infusate _____ _____ _____ _____ _____	Positive BC __ _____ _____ _____ _____ Positive IV Infusate _____ _____ _____ _____ _____	Positive BC __ _____ _____ _____ _____ Positive IV Infusate _____ _____ _____ _____ _____	Positive BC __ _____ _____ _____ _____ Positive IV Infusate _____ _____ _____ _____ _____
1.02	Positive BC __ _____ _____ _____ _____ Positive IV Infusate _____ _____ _____ _____ _____	Positive BC _ _____ _____ _____ _____ Positive IV Infusate _____ _____ _____ _____ _____	Positive BC __ _____ _____ _____ _____ Positive IV Infusate _____ _____ _____ _____ _____	Positive BC __ _____ _____ _____ _____ Positive IV Infusate _____ _____ _____ _____ _____	Positive BC __ _____ _____ _____ _____ Positive IV Infusate _____ _____ _____ _____ _____
1.03	Positive BC __ _____ _____ _____ _____ Positive IV Infusate _____ _____ _____ _____ _____	Positive BC _ _____ _____ _____ _____ Positive IV Infusate _____ _____ _____ _____ _____	Positive BC __ _____ _____ _____ _____ Positive IV Infusate _____ _____ _____ _____ _____	Positive BC __ _____ _____ _____ _____ Positive IV Infusate _____ _____ _____ _____ _____	Positive BC __ _____ _____ _____ _____ Positive IV Infusate _____ _____ _____ _____ _____

Appendix F

Demographic Characteristics of Sample

24-hour Group

Case	Gender	Age	Diagnosis	Comorbidities	CVC	Temperature	ANC
1.01	Female	64	Leukemia	Stomatitis Infected CVC Pneumonia	Double	Afebrile	198
1.02	Female	46	Leukemia	none	Triple	Afebrile	28
1.03	Female	43	CA Breast	none	Triple	Afebrile	1000
1.04	Female	57	Leukemia	none	Double	Afebrile	75
1.05	Male	60	Leukemia	Feb. Neutropenia Stomatitis	Triple	Febrile	400
1.06	Female	40	Transplant	none	Triple	Afebrile	200
1.07	Female	32	Transplant	none	Triple	Afebrile	300
1.08	Male	39	Transplant	Stomatitis	Triple	Afebrile	100
1.09	Female	57	Leukemia	none	Double	Febrile	200
1.10	Female	47	Leukemia	none	Triple	Afebrile	689
1.11	Male	45	CA Testes	Feb. Neutropenia Infected CVC	Triple	Febrile	100
1.12	Female	47	Transplant	none	Triple	Febrile	588
1.13	Female	29	Transplant	none	Triple	Febrile	200
1.14	Female	40	Lymphoma	none	Triple	Afebrile	84
1.15	Female	29	Transplant	Feb. Neutropenia	Triple	Febrile	300
1.16	Female	48	Leukemia	Septicemia	Triple	Febrile	200
1.17	Male	54	Lymphoma	Feb. Neutropenia	Double	Febrile	910
1.18	Female	27	Leukemia	Feb. Neutropenia	Triple	Febrile	300
1.19	Female	75	Leukemia	Septicemia Stomatitis Pneumonia	Triple	Febrile	90

Case	Gender	Age	Diagnosis	Comorbidities	CVC	Temperature	ANC
1.20	Male	52	Leukemia	Feb. Neutropenia	Triple	Febrile	200
1.21	Female	47	Leukemia	Feb. Neutropenia Stomatitis	Triple	Febrile	200
1.22	Female	40	Transplant	Stomatitis	Triple	Afebrile	300
1.23	Male	52	Leukemia	none	Triple	Febrile	45
1.24	Male	34	Transplant	none	Double	Afebrile	400
1.25	Male	52	Leukemia	Septicemia	Triple	Febrile	300

48-hour Group

Case	Gender	Age	Diagnosis	Comorbidities	CVC	Temperature	ANC
2.01	Female	32	Transplant	Feb. Neutropenia	Triple	Febrile	100
2.02	Female	46	CA Breast	Septicemia	Double	Afebrile	100
2.03	Male	56	Leukemia	Septicemia	Triple	Febrile	200
2.04	Male	25	Leukemia	Feb. Neutropenia	Double	Febrile	300
2.05	Female	46	Leukemia	Stomatitis	Triple	Afebrile	400
2.06	Male	56	Leukemia	none	Double	Afebrile	200
2.07	Female	57	Leukemia	Feb. Neutropenia Stomatitis	Double	Febrile	500
2.08	Female	48	CA Breast	Septicemia	Triple	Febrile	100
2.09	Female	46	CA Breast	none	Double	Afebrile	99
2.10	Female	47	Leukemia	Infected CVC	Triple	Afebrile	987
2.11	Female	43	Transplant	none	Triple	Afebrile	400
2.12	Female	46	Transplant	Feb. Neutropenia	Double	Febrile	100
2.13	Female	47	Leukemia	none	Double	Afebrile	646
2.14	Female	47	Leukemia	Septicemia	Triple	Febrile	100
2.15	Female	40	Lymphoma	Stomatitis	Triple	Febrile	300
2.16	Male	45	Lymphoma	none	Double	Afebrile	100

Case	Gender	Age	Diagnosis	Comorbidities	CVC	Temperature	ANC
2.17	Female	40	Lymphoma	Stomatitis Infected CVC	Triple	Afebrile	385
2.18	Male	65	Leukemia	none	Triple	Afebrile	660
2.19	Female	40	Transplant	none	Triple	Afebrile	140
2.20	Female	47	Leukemia	none	Triple	Afebrile	532
2.21	Female	40	Lymphoma	Feb. Neutropenia	Triple	Febrile	251
2.22	Male	65	Leukemia	Feb. Neutropenia	Triple	Febrile	5
2.23	Female	27	Leukemia	Septicemia Infected CVC	Triple	Febrile	400
2.24	Female	37	Leukemia	Septicemia	Triple	Febrile	200
2.25	Female	56	Transplant	none	Triple	Afebrile	200

Appendix G

Patient Days

Patient Days

	Interval for Changing IV Administration Sets					
	24-hours n = 25		48-hours n = 25		Total n=50	
Patient days	**f**	**%**	**f**	**%**	**f**	**%**
One	2	8	0	0	2	4
Two	1	4	4	16	5	10
Three	5	20	0	0	5	10
Four	0	0	2	8	2	4
Five	17	68	0	0	17	34
Six	--	--	3	12	3	6
Seven	--	--	0	0	0	0
Eight	--	--	1	4	1	2
Nine	--	--	0	0	0	0
Ten	--	--	15	60	15	30
No. of Patient Days	104	35	192	65	296	100

Appendix H

Intravenous Antibiotic Administration

Intravenous Antibiotics

	Interval for Changing IV Administration Sets					
	24-hours n = 25		48-hours n = 25		Total n=50	
Medication	**f**	**%**	**f**	**%**	**f**	**%**
Acyclovir	6	24	2	8	8	16
Amphotericin B	4	16	3	12	7	14
Ampicillin	0	0	1	4	1	2
Cefazolin	0	0	3	12	3	6
Ceftazidime	14	56	16	64	30	60
Ceftriaxone	1	4	0	0	1	2
Ciprofloxacin	7	28	1	4	8	16
Clindamycin	3	12	1	4	4	8
Cloxacillin	3	12	0	0	3	6
Erythromycin	1	4	1	4	2	4
Fluconazole	1	4	3	12	4	8
Imipenim	2	8	2	8	4	8
Metronidazole	1	4	4	16	5	10
Penicillin G	1	4	0	0	1	2
Tobramycin	3	12	2	8	5	10
Vancomycin	14	56	14	56	28	56

Appendix I

Oral Antibiotic Administration

Oral Antibiotics

	Interval for Changing IV Administration Sets					
	24-hours n = 25		48-hours n = 25		Total n=50	
Medication	**f**	**%**	**f**	**%**	**f**	**%**
Acyclovir	1	4	5	20	6	12
Ciprofloxacin	7	28	5	20	12	24
Co-trimoxazole	0	0	3	12	3	6
Fluconazole	3	12	7	28	10	20
Metronidazole	1	4	3	12	4	8
Penicillin	1	4	0	0	1	2

Appendix J

Intravenous Non-antibiotic Administration

Intravenous Non-antibiotics

	Interval for Changing IV Administration Sets					
	24-hours n = 25		48-hours n = 25		Total n=50	
Medication	**f**	**%**	**f**	**%**	**f**	**%**
Dexamethazone	0	0	2	8	2	4
Dilaudid	2	8	2	8	4	8
Dimenhydrinate	9	36	12	48	21	42
Diphenhydramine	16	64	21	84	37	74
Furosemide	10	40	7	28	17	34
Heparin	0	0	2	8	2	4
Hydrocortisone	10	40	11	44	21	42
Novolin Toronto Insulin	1	4	0	0	1	2
Meperidine	7	28	12	48	19	38
Methylprednisolone	1	4	2	8	3	6
Metoclopramide	4	16	7	28	11	22
Morphine	5	20	6	24	11	22
Ondansetron	6	24	6	24	12	24
Prochlorperazine	2	8	1	4	3	6
Ranitidine	10	40	7	28	17	34

Appendix K

Intravenous Electrolyte Administration

Intravenous Electrolytes

	Interval for Changing IV Administration Sets					
	24-hours n = 25		48-hours n = 25		Total n=50	
Medication	f	%	f	%	f	%
Potassium Chloride	11	44	11	44	22	44
Magnesium Sulphate	4	16	3	12	7	14

Appendix L

Intravenous Chemotherapy Administration

Intravenous Chemotherapy

	Interval for Changing IV Administration Sets					
	24-hours n = 25		48-hours n = 25		Total n=50	
Medication	f	%	f	%	f	%
Amasacrine	0	0	1	4	1	2
Bleomycin	1	4	0	0	1	2
Cytarabine	5	20	3	12	8	16
Etoposide	0	0	1	4	1	2
Idarubicin	3	12	1	4	4	8
Vincristine	1	4	0	0	1	2

Appendix M

Intravenous Granulocyte Stimulating Factor (GCSF)

GCSF Administration

	Interval for Changing IV Administration Sets					
	24-hours n = 8		48-hours n = 6		Total n=14	
No. of Days	f	%	f	%	f	%
1 Day	3	38	--	0	3	21
2 Days	--	0	1	17	1	7
3 Days	1	13	--	0	1	7
4 Days	1	13	1	0	2	14
5 Days	3	38	--	0	3	21
6 Days	--	0	--	0	--	0
7 Days	--	0	--	0	--	0
8 Days	--	0	2	34	2	14
9 Days	--	0	--	0	--	0
10 Days	--	0	2	34	2	14
Total No. of Subjects	8	57	6	43	14	100

Appendix N

Total Parenteral Nutrition (TPN)

TPN Administration

	Interval for Changing IV Administration Sets					
	24-hours n = 11		48-hours n = 7		Total n=18	
No. of Days	f	%	f	%	f	%
1 Day	1	9	--	0	1	6
2 Days	3	27	1	14	4	22
3 Days	2	18	1	14	3	17
4 Days	--	0	1	14	1	6
5 Days	5	46	1	14	6	33
6 Days	--	0	--	0	--	0
7 Days	--	0	--	0	--	0
8 Days	--	0	1	14	1	6
9 Days	--	0	--	0	--	0
10 Days	--	0	2	28	2	11
No. of Subjects	11	61	7	39	18	100
No. of Days	38	48	42	52	80	100

Appendix O

Blood Product Administration

Blood Products

	Interval for Changing IV Administration Sets					
	24-hours n = 25		48-hours n = 25		Total n=50	
Product	**f**	**%**	**f**	**%**	**f**	**%**
Red Blood Cells	12	48	18	72	30	60
Random Donor Platelets	14	56	15	60	29	58
Single Donor Platelets	3	12	8	32	11	22
Albumin	0	0	2	8	2	4
Fresh Frozen Plasma	1	4	1	4	2	4

Appendix P

Blood Specimen Withdrawal

Blood Specimens

	Interval for Changing IV Administration Sets					
	24-hours n=25		48-hours n=25		Total n=50	
Specimens	f	%	f	%	f	%
AM blood work	23	92	24	96	47	94
Pre/Post Levels	8	32	10	40	18	36
CVC blood cultures	6	24	13	52	19	38
Cross Match	9	36	13	52	22	44
Glucose Monitoring	1	4	0	0	1	2

Appendix Q

Microorganisms Isolated from Intravenous Infusate

Case	Measure 1	Measure 2	Measure 3	Measure 4	Measure 5
1.01	1. No growth 2. No growth	1. No growth 2. No growth	1. No growth 2. No growth		
1.02	1. No growth 2. Discarded	1. No growth 2. Discarded	1. No growth		
1.03	1. No growth	1. No growth	1. 15 cfu CNS	1. No growth	1. 10 cfu NPN 5 cfu VGS
1.04	1. 1 cfu VGS 1 cfu NHS 2. No growth	1. 1 cfu CNS 2. 1 cfu BHS	1. No growth 2. No growth	1. No growth 2. No growth	1. No growth 2. No growth
1.05	1. 10 cfu VGS				
1.06	1. No growth 2. No growth	1. No growth 2. No growth	1. No growth 2. 25 cfu CNS 25 Micrococcus	1. No growth 2. No growth 3. No growth	1. No growth 2. No growth 3. No growth
1.07	1. No growth 2. Discarded	1. No growth 2. 2 cfu CNS	1. No growth 2. No growth 3. No growth	1. No growth 2. No growth 3. No growth	1. 5 cfu CNS 2. No growth 3. No growth
1.08	1. No growth 2. No growth 3. No growth	1. No growth 2. No growth 3. No growth	1. No growth 2. No growth		
1.09	1. No growth	1. No growth	1. No growth 2. No growth	1. No growth 2. No growth	1. No growth 2. No growth 3. 5 cfu CNS
1.10	1. No growth 2. 1 coliforms 3. 5 Enterococci 1 Diphtheroids 5 cfu CNS	1. No growth 2. No growth 3. No growth	2. No growth 3. 5 cfu CNS		
1.11	1. No growth 2. No growth	1. No growth 2. No growth	1. No growth 2. No growth	1. No growth 2. No growth	1. 80 cfu CNS 260 cfu CNS 100 cfu CNS 2. No growth
1.12	1. No growth 2. No growth 3. 150 cfu CNS 75 Micrococcus	1. 1 Enterococcus 2. No growth	1. No growth 2. No growth	1. No growth 2. No growth	1. No growth 2. No growth 3. 1 Acinetbacter

Case	Measure 1	Measure 2	Measure 3	Measure 4	Measure 5
1.13	1. No growth 2. No growth	1. No growth 2. No growth 3. 1 cfu CNS	1. 1 cfu CNS 2. No growth 3. 1 cfu CNS 4. 25 cfu CNS 1 cfu CNS	1. No growth 2. No growth 3. No growth 4. No growth	1. No growth 2. No growth 3. 1 cfu CNS 4. No growth 5. No growth
1.14	1. No growth 2. No growth 3. Discarded	1. No growth 3. No growth	1. 1 cfu CNS 3. No growth	1. No growth 3. No growth	1. No growth 3. No growth
1.15	1. No growth 2. No growth 3. 15 cfu CNS	1. No growth 3. 1 cfu CNS	1. No growth 3. No growth	1. No growth 3. No growth	1. No growth 3. No growth
1.16	1. No growth 2. No growth 3. No growth 4. No growth 5. No growth 6. No growth	1. No growth 3. No growth 4. No growth 5. No growth 6. 15 S.aureus 5 cfu CNS 1 cfu CNS	1. No growth 2. No growth 3. No growth 4. No growth 5. No growth 6. No growth	1. No growth 3. No growth 4. No growth 5. No growth 6. 5 cfu CNS 1 S.aureus	1. No growth 3. No growth 4. No growth 5. No growth 6. No growth
1.17	1. 1 cfu CNS 2. No growth				
1.18	1. No growth 2. No growth 3. 1 cfu CNS 1 cfu CNS	1. No growth 2. No growth	1. 1 cfu VGS 2. No growth 3. No growth 4. No growth 5. No growth	1. 1 cfu ASB 2. No growth 3. No growth 4. No growth 5. No growth	1. No growth 2. No growth 3. No growth 4. No growth
1.19	1. 1 cfu VGS 1 cfu CNS 2. No growth	1. 1 cfu CNS 2. No growth 3. 1Diphtheroids	1. No growth 2. No growth 3. No growth	1. No growth 2. No growth 3. No growth	1. No growth 2. No growth 3. 1 cfu CNS
1.20	1. Discarded 2. No growth	1. 1 cfu CNS 2. 20 cfu CNS	1. No growth	1. No growth	1. No growth
1.21	1. No growth	1. No growth	1. No growth	1. No growth	1. No growth
1.22	1.1 Micrococcus 2. No growth	1. 1 cfu CNS 2. No growth	1. No growth 2. No growth	1. No growth 2. No growth	1. No growth 2. No growth
1.23	1. No growth	1. No growth			
1.24	1. No growth 2. 1 cfu CNS 1 cfu VGS	1. No growth 2. 10 cfu CNS 1 cfu CNS	1. No growth 2. No growth		
1.25	1. No growth	1. No growth 2. No growth	1. No growth 2. No growth	1. No growth 2. No growth	1. No growth 2. No growth

Case	Measure 1	Measure 2	Measure 3	Measure 4	Measure 5
2.01	2. No growth 3. No growth	1. No growth 2. No growth 3. No growth	1. No growth 2. No growth 3. No growth 4. No growth	1. 5 cfu CNS 2. No growth 3. No growth 4. 25 cfu CNS	1. No growth 2. No growth 3. No growth 4. No growth
2.02	1. No growth	1. No growth	1. No growth 2. No growth	1. No growth 2. No growth	1. No growth 2. No growth
2.03	1. No growth	1. 80 cfu NPN 75 cfu VGS	1. No growth	1. No growth 2. No growth	1. No growth 2. No growth
2.04	1. No growth	1. 500 cfu R. pilmonae	1. No growth	1. 5 cfu CNS	1. No growth
2.05	1. No growth				
2.06	1. No growth 2. No growth	1. No growth 2. No growth	1. 30 cfu CNS 2. No growth	1. No growth 2. No growth	1. No growth 2. No growth
2.07	1. No growth	1. No growth	1. No growth 2. No growth		
2.08	1. No growth	1. No growth	1. No growth	1. No growth	
2.09	1. No growth	1. Discarded			
2.10	1. Nc growth				
2.11	1. No growth	1. No growth 2. No growth 3. Discarded	1. No growth 2. 15 cfu CNS	1. 1 cfu Candida 2. No growth	1. Discarded 2. No growth
2.12	1. No growth 2. No growth	1. 1 cfu ASB 1 cfu CNS			
2.13	1. No growth 2. No growth 3. 5 cfu CNS	1. No growth 2. 1 cfu CNS 3. No growth	1. No growth 2. No growth	1. No growth	1. Discarded
2.14	1. No growth 2. No growth	1. No growth 2. 1 cfu CNS	1. 5 cfu CNS 2. 5 cfu CNS		
2.15	1. No growth 2. No growth 3. No growth 4. 1 cfu CNS	1. 1 cfu CNS 1 cfu CNS 2. 5 cfu CNS 3. 10 cfu CNS	1. No growth 2. No growth 3. 30 cfu CNS	1. 5 cfu CNS 2. No growth 3. 30 cfu CNS	1. 1 cfu CNS 2. No growth 3. No growth
2.16	1. No growth 2. No growth 3. No growth	1. No growth 2. No growth 3. No growth	1. 1 cfu CNS 2. No growth 3. No growth	1. No growth 2. No growth 3. 10 cfu CNS	1. No growth 2. No growth 3. 1 Enterococci
2.17	1. No growth 2. No growth 3. No growth	1. No growth 3. No growth	1. No growth 3. No growth		

Case	Measure 1	Measure 2	Measure 3	Measure 4	Measure 5
2.18	1. No growth	1. No growth	1. No growth 2. No growth	1. No growth	1. No growth
2.19	1. No growth 2. No growth	1. 5 cfu VGS 2. No growth	1. No growth 2.1 enterococci	1. 340 cfu CNS 30 cfu CNS 2. No growth	2. No growth
2.20	1. 1 cfu CNS 2. No growth				
2.21	1. 1 cfu CNS	1. No growth	1. No growth	1. No growth	1. 1 cfu CNS
2.22	1. No growth	1. No growth	1. 1 cfu CNS	1. No growth 2. No growth	1. 1 cfu CNS 2. No growth
2.23	1. No growth 2. 1 cfu Candida 3. 1000 cfu Candida 4. No growth				
2.24	1. No growth 2. No growth 3. 1 cfu E.coli 1 Enterococcus	1. No growth 2. No growth 3. No growth	1. No growth 2. No growth 3. Discarded	1. No growth 2. No growth 3. No growth	1. No growth 2. No growth 3. No growth
2.25	1. 1 cfu CNS	1. No growth	1. No growth 2. No growth	1. No growth 2. No growth	1. No growth 2. No growth

Note: See text for abbreviations.