Central Venous Catheterization for Parenteral Nutrition

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To define the risks associated with central venous catheterization for total parenteral nutrition (TPN) 3291 patient days of this therapy, delivered by an established nutrition support team, were evaluated. One hundred and seventy-five catheters placed in 104 patients were reviewed over an 18 month period. Positive cultures were reported on 11 cannulae for a 6.4% incidence of colonization; five catheters (2.8%) were considered septic. Pleural or mediastinal complications of subclavian or internal jugular venipuncture occurred in eight patients (4.8%). Misdirection of the catheter tip occurred in 11.5% of insertions. Five patients (4.8%) had clinically apparent thrombosis in the superior vena cava, innominate and/or subclavian veins during hospitalization; four others had evidence of thrombosis at autopsy examination, giving an incidence of 8.7% in the entire series. No death directly resulted from the use of this therapy. Compliance with a rigid protocol by an experienced team can allow safe and effective use of central venous catheters and parenteral nutrition therapy.

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SINCE DUDRICK'S LANDMARK PUBLICATION over a decade ago,[1] total parenteral nutrition (TPN) has gained wide acceptance as a valuable adjunct in the care of critically ill patients. A multitude of serious metabolic complications can arise from TPN; these are related to the composition of solutions intended to be nutritionally complete, and range from hyperglycemic coma to vitamin or mineral deficiencies.[2] Central venous access is a necessity due to the high osmolarity of the TPN solutions, which present problems related to the establishment and maintenance of central venous catheters.

Ryan et al. presented a concise review of infectious and mechanical complications associated with venous catheterization for TPN.[3] In that series catheter-related sepsis occurred in 7.0% of the catheters and was correlated with more frequent violations of a standard protocol for line care; eight of 25 cultures were positive for fungal organisms. Colonization was not described per se, but it can be inferred that it occurred in 8.4% of the patients. Pleural and mediastinal complications occurred in 2.5% of their patients, with one death directly attributed to catheterization. Deitel[4] noticed a 24% incidence of catheter tip misplacement following subclavian venipuncture, but did not localize this to one side or the other.

The reported incidence of fungal infections has fallen during the past several years. Maki[5] has recently characterized the incidence and theoretical basis of intravenous infections; the predominant agents normally are inhabitants of the skin. The implication is that these should be well controlled by close monitoring and fastidious skin care at the insertion site.

Occult venous thrombosis was noticed by Ryan et al.[3] at an incidence of 4%; clinical subclavian or vena caval thrombosis was not observed in their series.

Materials and Methods

Methodology

The hospital records and radiographs of 104 consecutive patients who received TPN over an 18 month period were reviewed by a physician. Particular investigation was directed to determining a catheter's type, its site of insertion, the length of time it remained *in situ*, the mechanical and infectious complications of its placement, and the presence of venous thrombosis. Similar data were recorded for all central venous catheters inserted concomitantly for other purposes in the study population. All unsuccessful attempts at percutaneous central placement were noticed. Serial chest radiographs were

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reviewed over the entire period of each patient's cannulation, providing a unique documentation of each catheter's history. Profiles of the patients' diagnoses and courses were recorded, but no attempts were made to describe the metabolic aspects of their nutritional support.

Protocol

A standard protocol was followed with each placement. All catheters inserted specifically for delivery of TPN were placed, electively, at the bedside by members of the nutrition support service. A senior fellow or staff physician was present at each insertion and either supervised or accomplished each catheter placement. After free flow of blood was demonstrated, isotonic fluids were infused slowly, and a chest radiograph obtained. Upon verification of proper placement, appropriate solution orders were written by the Nutrition Support Service.

Infraclavicular subclavian vein cannulation is preferred for nutritional catheters at the New England Deaconess Hospital. The internal jugular vein serves as a reasonable secondary site. Severe coagulation defects are considered a contraindication to percutaneous venipuncture in these areas; central venous access is achieved by cut-down, percutaneous antecubital cannulation, or by infraclavicular catherization following replacement of the necessary procoagulants (*i.e.*, fresh frozen plasma, or platelets).

Dressing Procedure

The patients were closely monitored throughout their courses, including daily physician visits. The "hyperalimentation nurses" replaced occlusive dressings on Monday, Wednesday, and Friday. The skin was cleansed mechanically using acetone, and povidone-iodine ointment was applied. The catheters involved in this study were respected throughout the hospital and were not used for other purposes without clearance from the Nutrition Support Service; however, certain extraordinary situations necessitating exceptions in this policy were permitted.

On a few occasions, a previously placed catheter was taken over as a TPN line and thereafter was strictly preserved for nutrition. In addition, two therapeutic procedures could be considered theoretic violations of this protocol, but both were carried out by the nutrition support team according to defined guidelines. Intravenous fat emulsions were run "piggyback" onto the TPN line; and, on occasion, fluids were delivered only during a portion of each day (cyclic hyperalimentation).[6] With cyclic TPN, glucose administration was limited to a fraction of a 24 hour period and a heparin lock placed for the remainder of the period.

TABLE 1. *Population (104 Patients Treated over 18 Months)*

	Number Patients	Per Cent
Diabetes mellitus	58	56
Septic during hospitalization	55	53
Malignant disease	44	42
Known to have died	42	40
Congestive failure	33	32

Infection and Thrombosis

On occurrence of unexplained fever, a blood culture would be obtained through the catheter; and if the patient's temperature remained both elevated and unexplained the following day, the cannula would be removed. In cases where recatherization could be particularly hazardous, a guide-wire was used to change the catheter and culture its tip.

Catheter-related infectious complications were identified as colonization if a catheter tip culture was positive; or, in the absence of a tip culture, if a blood culture obtained through the catheter was positive, and concomitant peripheral blood cultures were either negative or unavailable. Catheter-related sepsis was then defined as a colonized catheter associated with a systemic bacteremia (documented by peripheral blood culture with the same organism). A decrease in the patient's temperature concomitant with removal of a catheter was useful in confirming suspected catheter sepsis, but was not considered diagnostic. A positive culture of the skin at the insertion site was not accepted as documentation of catheter colonization.

A diagnosis of major venous thrombosis was accepted on the basis of contrast venograms or clearly evident physical findings. Although failure to advance a catheter into proper position may suggest this problem, it was not considered valid as a diagnostic criterion.

Results

Population (Table 1)

The patient population at the NEDH is that of a tertiary care center and is served by the general staff, Lahey Clinic, Overholt Thoracic Clinic, and Joslin Diabetes Clinic. Fifty-five of the patients requiring central venous nutritional support had sepsis, or had demonstrated bacteremia during their period of hospitalization. Forty-two of the 104 patients are known to have died; of those who died while in the hospital,

19 patients had postmortem examinations. Fifty-eight patients were diabetic (in addition to obvious clinical diabetes our definition included those not known to be diabetic who required supplemental insulin while on TPN). A malignant process was responsible for the referral in 44 cases. Congestive heart failure on clinical grounds was present in 33 patients. The average age of the patients was 57 years. Thus, the population is unique and seriously ill, with many cases of chronic disease and multiple-organ failure.

Catheters

The great majority of the insertions were subclavian, and performed with a standard eight inch, 16-gauge polyvinylchloride catheter. During the 18 months, 323 central catheters were placed. Of these, 175 were involved in the administration of parenteral nutrition. There were 145 subclavian and 20 internal jugular venipunctures performed by the nutrition service. Approximately three out of every five catheters were inserted on the right side (Table 2). This same ratio was observed in terms of the number of catheter days. The internal jugular vein was infrequently used for nutritional purposes. Central venous catheters, for purposes other than feeding, were placed in essentially equal numbers between the subclavian and internal jugular veins. The antecubital fossa was occasionally used for central venous pressure catheter placement, and on one occasion for TPN. Those catheters not constructed of polyvinylchloride included five of silicone elastomer and 19 of heparin-impregnated hydrophilic polymers.[7] The average TPN cannula remained in place for 19 days. In comparing the average duration *in situ* of the various catheter materials or the different sites of insertion, no significant differences were observed (Table 2).

Complications of Placement

Of the more serious complications reported in the literature, pneumothorax, hemothorax, and mediastinal hematoma are represented here. Although less dramatic, improperly placed catheter tips and unsuccessful venipunctures were not infrequent. There were no air or catheter emboli and no lymphatic fistulas, nor were there any catheter-related deaths.

The incidence of major complications from catheter placement in this series was 4.8%—eight of 165 attempted subclavian or internal jugular catherizations. There were five pneumothoraces, for an incidence of 3.0%. Two of these resolved without chest tubes.

Catheter misdirection was a fairly common problem occurring in 19 out of 165 insertions (11.5%). There were 13 subclavian catheters whose tips initially terminated in the internal jugular vein; ten of these were from the right. Four catheters coiled in the vein and required straightening. Two right subclavian catheters terminated in the left innominate or the left subclavian veins.

There were 20 unsuccessful attempts at cannulation. In the majority of these patients, a later attempt was usually successful, although the site may have varied. In only one patient was a peripheral nutritional regimen established, due to failure to achieve central venous cannulation. No one choice of site was particularly prone to result in failure.

Catheters and Infection

Of the 175 catheters used to deliver 3291 days of TPN, there were 11 with positive cultures, for an incidence of 6.4%. Five of the catheters (2.8%) were believed to be a source of sepsis—one occurrence of septicemia for every 658 catheter days. Fifty-five per cent of the patients were septic or had demonstrated bacteremia from other sources.

Forty-one catheters were removed for suspicion of sepsis; of these, six (15%) had positive cultures. The earliest positive culture was observed at three days. All but two of these catheters were colonized with staphylococci (six coagulase negative and three coagulase positive). The exceptions were *Serratia liquifaciens* and *diptheroids* species.

One of the 11 catheters was the only femoral TPN catheter in this series. Two of the remaining catheters were internal jugular, and the remainder subclavian catheters.

Fourteen of the 175 catheters were inserted by other services for nonfeeding purposes, and were "taken over" by the nutrition support service. Two of these

TABLE 2. *Distribution of Catheters Used for Delivery of TPN*

	Subclavian	Internal Jugular	Other	Totals	Catheter Days	Per Cent	Average Duration*
Right	89	11	3	103	1941	59%	18.8 ± 1.5
Left	56	9	7	72	1350	41%	18.9 ± 1.5
Total	145	20	10	175	3291	100%	18.8 ± 1.5

* Standard error of the mean.

were eventually colonized, for an incidence of 14% in this rather small group. There were 20 patients who had their TPN delivered via a cycled regimen; 22 more received Intralipid® "piggy back" into their TPN lines. Three catheters from each group returned positive cultures (15% and 14%, respectively), but these patients also had a number of other complicating factors predisposing them to colonization.

Venous Thrombosis

There were nine patients with indwelling venous devices who developed venous thrombosis, for an incidence of 8.6%. Five of these patients presented clinical evidence of thrombosis. Four of the patients presented, initially, with left subclavian thromboses, two of which progressed to superior vena caval thromboses. The fifth patient also had thrombosis of the superior vena cava, but did not have unilateral findings.

Four other patients were shown to have thrombosis at autopsy examination. Two of these had mural thrombi noted in the superior vena cava; one patient had undergone cardiac surgery, and both patients, had required at least seven days of pulmonary arterial monitoring.

Another patient had a right subclavian catheter misplaced into her left subclavian vein. She received several weeks of TPN via left subclavian catheters, both preceding and following this catheter. At autopsy examination, an organizing thrombus was identified in the subclavian vein; it had not been recognized clinically and was not occlusive.

The fourth patient represented the only experience with a femoral catheter. He developed an iliofemoral thrombus and had several positive catheter cultures as well, emphasizing the necessity to avoid this site.

Discussion

Delivery of total parenteral nutrition is safe and has provided a significant therapeutic advance, since its clinical introduction. The morbidity and mortality rates associated with insertion and maintenance of the access system can strongly influence the acceptability of this treatment. The most significant of these problems relates to catheter placement, infection, and venous thrombosis.

Catheter Placement

The potential threats of major pleural and mediastinal complications are self-evident. The incidence of these has been inversely correlated with experience in technique, and positively correlated with emergency placement.[8] Adequate prior hydration and a standard technique make successful, uncomplicated venipuncture more certain. A necessity for active assisted ventilation increases the severity and significance of pleural transgression during the procedure. Fortunately, diagnosis and treatment of potential complications are generally straightforward, especially when these problems are anticipated. The significance of abnormal coagulation is underlined by the report of a death that was secondary to mediastinal hemorrhage.[3] In the central locations, mechanical considerations may make it very difficult to control bleeding, necessitating reliance on normal blood coagulation to avoid problems. Careful selection of patients is, therefore, important.

For patients in whom insertions does not succeed on the first attempt, special caution is needed. The incidence of serious complications in this group was quite high, and included all three hemorrhagic problems. On the basis of this data, no particular side or site appears to be particularly prone to these complications.

Because it has been notoriously difficult to maintain adequate dressings for jugular catheters, this site has been unpopular for long-term catheterization. Benotti et al.[9] have described a satisfactory technique, the subcutaneous tunnel, for moving the exit site to the infraclavicular skin, thus avoiding this problem. The technique was also used to isolate the entry site from open cervical or tracheotomy wounds. There were no mechanical or bacteriologic complications associated with the catheters so placed.

Catheter Misdirection

Nutritional catheters terminating in veins other than the superior vena cava have previously been associated with thrombosis,[3,10] as have those which have been allowed to remain coiled within the lumen.[10,11] The most frequent site associated with catheter misdirection was the right subclavian (Table 3). Approximately one in ten catheters passed into the right internal jugular vein; coiling was also three times more likely to occur on the right. Inappropriately placed cannulae were redirected into the superior vena cava using stainless steel guidewires, under fluoroscopic control, prior to administration of hypertonic dextrose.

Accidental or premature removal of the catheter can best be prevented by a proper suturing technique. This involves immobilization of the proximal, external portion of the catheter to prevent side-to-side motion, which can gradually lever it out of position. Occlusion secondary to clotting within the plastic tube can generally be corrected by flushing it with saline soon after this occurs. Obviously, a break in

TABLE 3. *Complications of Insertion (165 Subclavian and Internal Jugular Venipunctures)*

				Number Involved	Per Cent
Pleural and Mediastinal Complications				8	4.9
pneumothorax				4	
hemo-pneumothorax				1	
pleural effusion				1	
mediastinal hematoma				2	
Failure-to-place				20	12.1
	Subclavian	Internal Jugular	Other		
Right	8	2	0	10	
Left	8	1	1	10	
Misdirection				19	11.5
	Ipsilateral Internal Jugular	Coiled in Vein	Contra-lateral Sub-clavian		
Right	10	3	2	15	
Left	3	1	—	4	

the integrity of the catheter itself requires changing the device to prevent bacterial colonization, air embolus, or loss or solution.

Catheters and Infection (Table 4)

The 2.8% incidence of sepsis from a catheter focus in this series closely parallels current reports from other institutions. Copeland et al.,[12] in 1977, reported a 1.6% incidence of infection in a series of cancer patients, specifically evaluated because of a high expectation of sepsis from other sources. Ryan[3] reported a 7% incidence of infections, the majority coming from that subgroup of catheters with observed protocol violations, and a 3% incidence of catheter sepsis among those that are properly maintained. In a review of a number of reports on TPN catheter related sepsis, Maki[5] cited an overall average incidence of 7%.

Catheter colonization is a practical and easily applied clinical concept, defining a group of catheters which require therapeutic action (removal), and which may be held responsible for septicemia. Colonization may occur either as seeding from distant sources of bacteremia or as a significant accumulation of organisms along the subcutaneous tract. Maki's technique[13] of selective semiquantitative culture should provide for more accurate definition of colonization, the mechanism of its development, and catheter-related sepsis.

Of the five patients who became septic in this series, three died after prolonged septic illness. No patient died as a direct result of catheter-related sepsis; although one patient's death may have been hastened. Only one patient in the entire population was noted to have a white blood cell count of less than 1500 cells/mm^3 at the outset of nutritional therapy; only two of the patients with colonized catheters had reactivity to a standard battery of intradermal recall antigens. This is in comparison with the 70% incidence of reactivity seen in the referral population.[14]

A predominance of coagulase-negative staphylococci was observed. The more virulent coagulase-positive staphylococcus was associated with catheter-related sepsis in each of three patients. There was no fungi cultured from the catheters. These bacteriologic findings are consistent with Maki's[13] premise that the organisms involved are basically skin flora. Therefore, close monitoring and care of these catheters should minimize the incidence of colonization. However, bacteriologic seeding of intravenous foreign bodies may also occur, and detection can be expected to occur more frequently with established protocols for satisfactory maintenance of the insertion site. In fact, two of the five septic catheters had well documented sources for such seeding and are presumed to have become colonized by this mechanism.

TABLE 4. *Catheter Related Infection (175 Catheters Successfully Placed)**

	Number of Patients	Positive Cultures	Per Cent Incidence of Positive Cultures	Sepsis
Organisms				
staphylococcus, coagulase positive	3	3		3
staphylococcus, coagulase negative	5	6		2
serratia liquificiens	1	1		0
diptheroids	1	1		0
fungi	0	0		0
Sites of insertion				
subclavian vein	145	9	6.2	4
internal jugular vein	20	2	10	0
femoral vein	1	1	100	1
Subgroups				
catheters "taken over"	14	2	14	0
cycled TPN	20	3	15	2
"piggyback" fat emulsion	22	3	15	1
tunnelled catheters	8	0	—	—
changed over guide wire	11	0	—	—

* Colonized catheters: 11 catheters, 6.4%. Catheter related sepsis: 5 catheters, 2.8%.

TABLE 5. *Venous Thrombosis*

Clinically apparent		5	4.8%
left subclavian	2		
left subclavian—progressed to superior vena caval occlusion	2		
superior vena cava	1		
Diagnosed postmortem		4	3.8%
superior vena cava—mural thrombus	2		
left subclavian	1		
left iliofemoral	1		
Total (104 patients)		9	8.6%

Of the catheters removed because of unexplained sepsis, fully 85% were not colonized. On the other hand, all five septic catheters were removed, and the diagnosis was established because of this suspicion. All of the colonized catheters removed for this reason were eventually shown to be septic. Thus, the value of changing the catheter and culturing it cannot be overemphasized.

None of the patients with subcutaneous tunneling, or who had catheters changed over a wire, developed positive cultures, supporting the acceptability of these procedures. Although there appeared to be a moderately increased risk of colonization with internal jugular catheters, the outstanding risk was with femoral venipuncture.

Femoral catheters have been avoided for many years because of an increased incidence of both thrombus formation and infection, complications which were corroborated here. Allowing the use of a femoral site for TPN resulted in two septic catheters, one apparently seeded by the other.

Dividing the catheters into subgroups, several conclusions are suggested. Interpretation of the data must take into account the statistical implications of the relatively small numbers involved.

Three subgroups of patients with an increased incidence of bacteriologic complications were identified. As might be expected, a high incidence was found in the group of catheters which were "taken over." Although their average duration *in situ* as TPN cannulae was shorter, the standard insertion and maintenance precautions would not have been observed during the initial time of their use.

The patients treated with "piggyback" fat emulsions or cyclic regimens demonstrated a moderately increased incidence of colonization. Although this suggests a slightly greater risk from these "controlled" violations of standard protocol, other factors need to be considered as well. For example, two of the three positive catheter cultures associated with intravenous fat were from the patient with the femoral catheter.

Venous Thrombosis (Table 5)

Clearly, five of the patients developed thrombosis secondary to their TPN catheters. In an additional four patients, other invasive devices may also have contributed to the presence of thrombi. A host of factors have been related to venous thrombosis in the past, several of which were prominent in this group of nine patients. Especially notable were prolonged bed rest (all nine patients), sepsis (six patients), congestive failure (five patients), and malignant disease (four patients). In addition, all patients underwent prolonged exposure to an intravenous foreign body delivering potentially irritating solutions. It is probable that the reported incidence is falsely low since autopsy examinations were performed on only one-half of the patients who died. In addition, four thrombi observed at autopsy examinations were not clinically apparent. If one were to extrapolate the occult autopsy incidence (four in 19) to the clinical population, a 21% incidence of inapparent thrombotic phenomena would result.

For what is described as a relatively unusual clinical condition, this complication appears in a remarkable number of patients. In fact, its incidence was greater than that of significant infection or major complications of placement. It is worth noting that so-called "effort" (or "spontaneous") axillary or subclavian vein thrombosis occurs 66% of the time on the right side.[15] The remarkable initial left-sided incidence of subclavian thrombosis is even less attributable to chance, in light of the predominance of right-sided catheterization (Table 2). The increased risk of thrombosis with left-sided cannulation is significant at $p < 0.01$ by chi square analysis using a two tailed test.

Prevention of this complication can be achieved in several ways. The use of less thrombogenic heparin-impregnated[7] or silicone[16] catheters should be encouraged. Assiduous avoidance of the femoral site should continue. At our institution 6000 units of heparin per 24 hours is routinely added to the nutritional solutions of some patients and appears to reduce this complication. When a choice is available, nutritional catheterization should be preferentially performed on the right side. While there is a greater chance of misdirection from the right side this seems a small price to pay for decreasing the incidence of thrombosis. Misdirected catheters are easily rerouted but subclavian thrombosis is permanent.

In summary, insertion of a central venous catheter for parenteral nutrition can be a safe and effective procedure with minimal risk of complications and death. The progressive decline of infectious prob-

lems[3,12,17] emphasizes the need for a precise protocol delivered by an experienced team. Thus, the patient can benefit from the prevention or treatment of hospital malnutrition, with a minimum of complications.

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