

## PERSPECTIVES IN RENAL MEDICINE

# The hemodialysis catheter conundrum: Hate living with them, but can't live without them

**STEVE J. SCHWAB and GERALD BEATHARD***Duke University Medical Center, Durham, North Carolina, and Austin Diagnostic Clinic, Austin, Texas, USA***The hemodialysis catheter conundrum: Hate living with them, but can't live without them.**

**Background.** Hemodialysis requires reliable recurrent access to the circulation. On a chronic basis, this has been best provided by the use of arteriovenous fistulae and arteriovenous grafts. In recent years, hemodialysis catheters have come to play an increasingly important role in the delivery of hemodialysis. The use of both temporary as well as cuffed hemodialysis catheters has emerged as a significant boon for both patients and practicing nephrologists. The complications, however, associated with each of these hemodialysis catheters, both in terms of anatomic, thrombotic, and infectious issues, have emerged as a major problem with their continued use. This significant morbidity and complication rate has forced many nephrologists to face a basic conundrum: they have come to hate having to deal with the problems inherent in catheter usage, but the enormous utility of these devices have forced physicians to accept the fact they cannot live without them in their current practice.

**Methods.** We used a comprehensive literature review to describe the types, use and dilemmas of hemodialysis catheters.

**Results.** This article provides a comprehensive review of both the benefits inherent with the use of these hemodialysis catheters while cataloging their complications and offering some possible solutions.

**Conclusion.** Hemodialysis vascular access catheters are essential in the maintenance of hemodialysis vascular access. However, they have a significant infectious, thrombotic, anatomic complication rate that are detailed with proposed problem-solving guidelines.

Hemodialysis requires reliable, recurrent access to the circulation. On the chronic basis, this has generally been provided by either an arteriovenous (AV) fistula or by a prosthetic bridge graft (AV Graft) composed of polytetrafluorethylene (PTFE). In recent years catheters have

come to play an increasingly important role in the delivery of hemodialysis. These catheters are of great value in situations where an immediate vascular access is required and have come to be increasingly used in patients with chronic renal failure. Clinical practice has led to the emergence of two distinct classes of catheter access: (1) temporary or acute catheters and (2) chronic or tunneled cuffed catheters. Data collected by the United States Renal Data System indicate that in 1996, 18.9% of all new hemodialysis patients were being dialyzed with a tunneled cuffed catheter and 12.9% were still using a catheter 60 days after starting dialysis [1]. This number has been progressively increasing; in 1993 only 9.7% of patients were using a tunneled cuffed catheter 30 days after the initiation of dialysis.

While some catheter use is inappropriate, there is no doubt that dialysis access catheters have come to be an important tool in the management of patients requiring hemodialysis. The primary reason for this is that catheters can be used in virtually any patient, they are easily inserted, and they are suitable for immediate use following insertion. Table 1 illustrates the variety of instances in which catheters are used.

Unfortunately, as we have learned all too well, the dialysis access catheter is a double-edged sword. The tremendous advantages that it brings can also carry a tremendous cost. This has forced many nephrologists to face a basic conundrum. They have come to hate having to deal with the problems inherent with catheter usage, but have had to accept the fact that they can't live without them. Our purpose is to review the problems related to catheter use and to present some possible solutions to these problems.

## TEMPORARY CATHETERS

Originally, acute vascular access for hemodialysis was provided by the use of venous and arterial trocars. This was replaced by the use of either a single lumen dialysis catheter that required an intermittent flow device or two

**Key words:** dialysis, renal replacement therapy, arteriovenous fistula, thrombosis, infection, vascular access.

Received for publication July 16, 1998

and in revised form November 20, 1998

Accepted for publication December 21, 1998

Updated January 28, 1999

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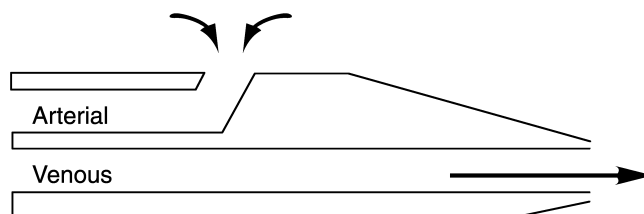
**Table 1.** Uses of the tunneled-cuffed catheter

Temporary catheters
Acute renal failure
Maturing AV access (3 weeks or less)
Intoxication
Plasmapheresis
Chronic catheters (tunneled cuffed)
Same as temporary catheter, but requiring more than 2–3 weeks of dialysis
Anticipated living-related donor transplantation
Maturation of peritoneal dialysis access
Maturing AV access
Failure of AV vascular access
Bridge following infection and removal of access

separate dialysis catheters for simultaneous inflow and outflow [2]. Subsequent design modifications and improvements have led to a near universal standard for acute hemodialysis catheters. This design is characterized by dual lumens arranged coaxially in a single catheter (Fig. 1). To minimize recirculation of blood and allow a continuous blood path, the catheter is designed with the arterial port proximal to the venous and separated from it by 2 to 3 cm (Fig. 1).

Temporary catheters are characteristically composed of rigid materials such as polyurethane or polyvinyl. These materials are relatively stiff at room temperature to allow for ease of insertion over a guidewire without requiring a sheath. They become more pliant and flexible at body temperature within the bloodstream, and this serves to minimize the risk of vessel damage [2]. Temporary catheters are characteristically non-cuffed and are not tunneled at the time of placement to allow rapid access to the circulation with minimal patient trauma. They are available in a variety of lengths, adaptable for use in any accessible central vein. These devices are suitable for use for a period of days to weeks. These characteristics that emphasize simplicity and ease of insertion allow rapid access to the circulation at the bedside without requiring flouroscopy or other radiologic support [2].

Temporary catheters offer the advantages of ease of placement. They can be inserted at the bedside using a sterile Seldinger technique. While blood flow is limited with most of these catheters, they generally provide a blood flow (200 to 250 ml/min) that is adequate for short-term usage. Newer temporary catheter designs have utilized silicone and have incorporated a larger diameter that is said to provide blood flow of 400 ml/min or greater. Because of the flexibility of these silicone temporary catheters they must be inserted using a disposable trocar or a peel-away sheath substituting complexity for an increase in blood flow.



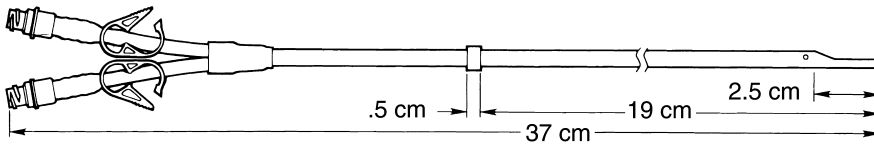
**Fig. 1. Acute catheter schematic showing catheter and distal tip.** (Adapted from Fan [2]; used with permission of the author and W.B. Saunders Company.)

## TUNNELED CATHETERS

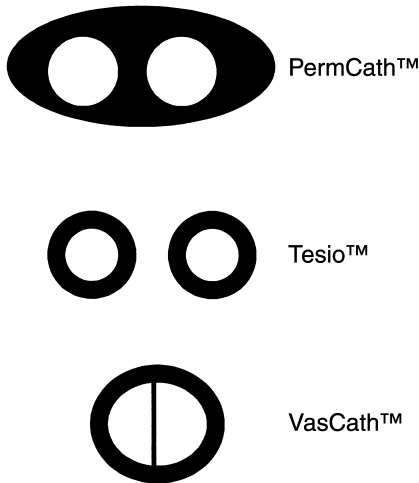
Cuffed, tunneled hemodialysis catheters were developed in 1987 as an alternative to acute hemodialysis vascular access (Fig. 2) [3, 4]. These catheters are usually constructed of silicone or silastic elastomer, which is much softer and pliable than the material generally used for acute hemodialysis catheters. For this reason, these catheters are usually inserted using a peel-away sheath that has been placed into the vein using the Seldinger technique. The use of a tunnel and a bonded cuff serve to anchor the dialysis catheter in the tunnel, and presumably, prevent migration of bacteria down the outer surface of the catheter. The soft silastic elastomer allows the use of larger lumen size and placement of these catheters with their tip in the right atrium. A larger lumen permits greater blood flows than is possible with the smaller temporary catheters. To achieve the blood flow benefits of the larger lumen, flouroscopy is required to assure positioning in the right atrium. The cannulation hole in the vein is also larger because the peel away sheath is larger than the catheter.

The original tunnel hemodialysis catheter was marketed by Quinton Instrument Co (Perm Cath™, Quinton Instrument Company, Seattle, WA, USA) and was a large oval catheter with two distinct circular lumens (Fig. 3). Subsequent designs utilized a round catheter with a central septum to facilitate easier peel-away introducer insertion (Vas Cath; Bard, Salt Lake City, UT, USA; and others; Fig. 3). The third popularized design included the use of two separate single lumen catheters with the inflow catheter in the proximal superior vena cava and the return catheter with one tip in the right atrium (Tesio™; Medcomp, Harleysville, PA, USA; and others; Fig. 3). Modifications of the Tesio™ design to fuse the two separate catheters at some point along its length to allow insertion in a single sheath has become popular (ASH Catheter, Medcomp, Harleysville, PA, USA). The most recent design modification is to connect the catheters to totally subcutaneous ports (LifeSite; VascA, Topsfield, MA; and Dialock; Biolink Inc., Boston, MA, USA). This design avoids complications associated with a transcutaneous device (Fig. 4).

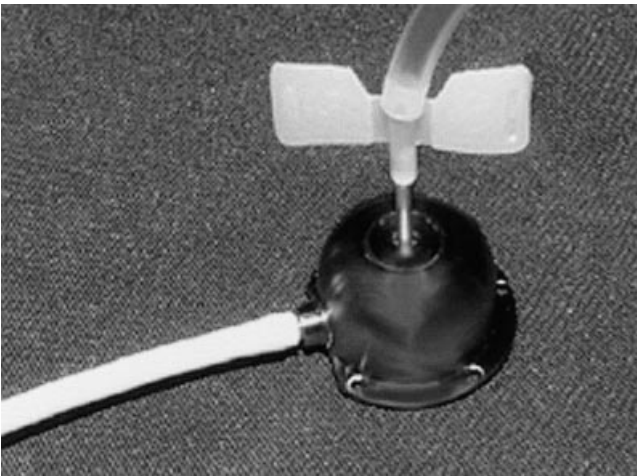
Initially intended as a bridge device to provide pro-



**Fig. 2. Schematic of a cuffed tunneled catheter.** (From Schwab et al [3], used with permission of W.B. Saunders Company.)



**Fig. 3. Cross sectional schematic of three commonly used catheters.** (From Athirakul et al [7]; used with permission from *Nephrology, Dialysis Transplantation*.)



**Fig. 4. Lifesite port (VasCA, Topsfield, MA, USA) constructed of a titanium alloy.** This port is designed to be placed subcutaneously. It is entered using a standard 14-gage dialysis needle. Two ports are placed, one to serve as the arterial and the other the venous access. The 12 French catheters are placed into the right internal jugular vein.

longed periods of temporary access, cuffed tunneled catheters have emerged to fill a much greater role (Table 1).

Regardless of the type of catheter, temporary or tunneled, or its design, there are certain complications that are associated with all catheter usage (Table 2). In general these complications are the same. The major difference

**Table 2. Complications of catheter usage**

Limited ability to provide adequate dialysis
Related to size of catheter
Diameter
Length
Recirculation
Placement problems
Complications of placement
Tip location
Thrombosis
Extrinsic
Intrinsic
Infection
Exit site
Tunnel
Catheter-related bacteremia

**Table 3. Poiseuille's Law**

Laminar blood flow = $k(P \times D^4)/(L \times V)$
P – pressure
D – diameter
L – length
V – viscosity
K – proportionality constant

is that when a problem occurs with a temporary catheter, the alternative of disposing of the catheter is more likely to be possible. The success of any plan to use a catheter, either short-term or prolonged, is largely dependent upon how well these complications can be managed.

## CATHETER FLOW

The primary determinants of catheter blood flow are catheter size dimensions and tip placement. As with flow through any tubular structure, blood flow through a catheter is related to the diameter and length of the device. This relationship between these variables is expressed in *Poiseuille's Law* (Table 3). The major catheter-related determinant of flow is its diameter. Flow increases in direct proportion to an increase in diameter raised to the fourth power. This relationship dictates that by increasing the diameter by only 19%, the flow will be increased by a factor of two. There is an inverse relationship between flow and catheter length, but it is not as important a determinant as diameter. Actually, increasing the diameter by only 19% can compensate for a doubling of length. Because resistance to pumped blood flow is generally higher when a catheter is used as the vascular

access, pre-pump (dialyzer inflow) pressures are likely to be lower (more negative) than with either an arterio-venous (AV) fistula or a prosthetic bridge graft [5]. Negative pre-pump pressures result in a partial collapse of the blood line pump segment, rendering the pump RPM meter highly inaccurate as a measure of dialyzer blood flow. Depner, Rizwan and Stasi reported a decrease of 8.5% in blood flow measured volumetrically compared to the blood pump meter reading when a pressure of  $-200$  mm Hg was applied to the tubing [6]. This difference increased to 33% when a negative pressure of  $-400$  mm Hg was applied. Thus, when pre-pump pressures fall below  $-200$  to  $250$  mm Hg the pump read flow readings become progressively more inaccurate. This explains the significant falls in dialysis efficiency despite near equivalent blood pump flow readings and dialysis times when catheters are substituted for AV access.

Elevated venous (dialyzer outflow) pressure occurs in a subset of patients. This usually reflects placement in a smaller vessel or placement near a venous bend with the catheter tip placed up against the vessel wall. An alternative explanation is a partial venous out flow lumen thrombus.

In the past, temporary or acute catheters have adhered to a small diameter design, 10 to 12 French, to facilitate ease of bedside insertion. As a result of this design, these catheters have characteristically provided blood flows of only 200 to 250 ml/minute. Design compromises were developed to maximize ease and safety of insertion at the cost of dialysis efficiency. When used for relatively short periods of time these compromises were well reasoned and readily apparent. Recently, larger caliber temporary catheters have been produced with diameters of 14 French, said to be capable of faster blood flows but at the cost of ease of insertion. In selecting a temporary catheter for general use these compromises must be understood. Longer treatment times at lower blood flows are required to deliver an adequate dose of dialysis. Temporary catheters are generally inserted without the use of real-time fluoroscopy. Blind placement of a relatively stiff device through the right internal jugular vein has created the necessity of using a short catheter to avoid atrial perforation. The tip of these catheters comes to be located in the proximal superior vena cava, and this tip location in smaller blood vessels does not allow for as great a blood flow as catheters located in the distal superior vena cava and the right atrium.

Tunneled cuffed catheters were introduced to provide for longer periods of use than temporary catheters but require fluoroscopy for placement to use their full blood flow potential [2–4]. These cuffed tunneled catheters vary in configuration and size, both diameter and length (Figs. 2 and 3). As a consequence, the flow that can be expected from the use of various catheters will vary. In a prospective study, the mean blood flow of the various

designs placed in the internal jugular position with right atrial tip placement is shown in Table 4 (Fig. 3) [7]. The poor performance of the central septum catheter (Vas Cath™) was based on lumen diameter. The relatively small size of the central septum catheter, in contrast, made it the easiest to insert. Larger diameter central septum catheters would be expected to flow better but be more difficult to insert. Ultrasound dilution determination of catheter blood flow under these circumstances determined that mean flow under these conditions for all tested catheter types was 10 to 15% less than the blood pump predicted. When pre-pump pressure exceeded (that is, were more negative than) 200 mm Hg (as was almost always the case when the blood pump was set for 350 to 400 ml/min; Table 4) blood flow, measured by ultrasound dilution, averaged 20 to 30% less than pump read blood flow (Table 4). Thus, increasing blood pump speed when pre-pump pressure exceeds negative 200 to 300 mm Hg leads to a limited improvement in actual net blood flow. Patients will almost always require an increase in dialysis duration when the access is changed from an AV access to a dialysis catheter.

As with the temporary catheter, there appears to be an inverse relationship between ease of placement and catheter flow capability. Nevertheless, the primary determinant used to select a catheter for chronic use should be the flow that it can provide. Ease of placement must be a secondary issue for temporary catheters unless the patient and the physician are willing to significantly increase treatment duration to compensate for the diminished flow. The DOQI guidelines define sufficient extracorporeal blood flow as 300 ml/min [8]. However, this should be regarded as a minimum criterion, not the optimum. In practice, when using hemodialysis catheters a true blood flow of 300 ml/min may require a pump read flow of 350 to 400 ml/min.

With the use of catheters, recirculation is dependent upon two factors: the location of the catheter tip and the status of the patient's central circulation. Catheters with their tips placed in smaller blood vessels are more prone to recirculation than catheters placed in larger blood spaces. Thus, there is a greater likelihood of recirculation when a femoral catheter is used versus an internal jugular or subclavian. Soft right atrial catheters are least likely to show recirculation. Kelber, Delmer, and Windus reported recirculation rates of 4%, 5% and 10% for internal jugular, subclavian and 24 cm femoral catheters, respectively [9]. They reported an 18% recirculation rate with a 15 cm femoral catheter. Other investigators reported negligible recirculation in right atrial catheters [7]. This changes dramatically if the lumens are reversed, approaching 20% [7]. The more centrally the tip is located, the less likely recirculation is to occur. In placing tunneled catheters in the femoral vein with real-time fluoroscopic guidance, we (GAB) have found that in



**Table 4.** Catheter blood flow capabilities

	Catheter type		
	Perm Cath™	Tesio™	VAS Cath “Soft Cell”™
Mean blood pump QB ml/min	384 ± 28.5	396 ± 45.1	320 ± 62
Mean QB ml/min Ultrasound dilution	301 ± 21	307 ± 28	229 ± 40
Pre-pump pressure (mean)	320 mm Hg	330 mm Hg	360 mm Hg

**Table 5.** Complications of initial catheter placement

Arrhythmias
Pneumothorax
Bleeding
Hematoma formation
Arterial puncture
Hemothorax
Air embolism
Hemomediastinum
Recurrent laryngeal nerve palsy
Cardiac arrest
Atrial perforation
Improper tip placement

most patients a 45 to 50 cm catheter is required for the tip to lie within the inferior vena cava.

## CATHETER PLACEMENT

### Complications of placement

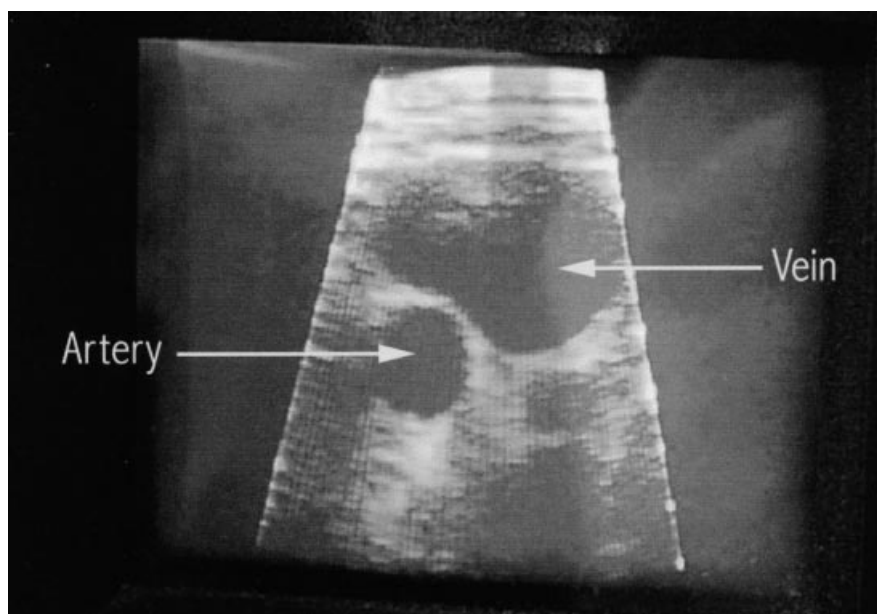
As listed in Table 5, a variety of complications can occur at the time of catheter placement. The major determinant for problems at the time of insertion is the experience of the operator [10] and whether real-time visualization techniques are used. Even in the hands of experienced surgeons in the operating room, blind insertion results in complication rates as high as 5.9% [11, 12]. These complications include: pneumothorax (0 to 1.8%), hemothorax (0 to 0.6%), hemomediastinum (0 to 1.2%), recurrent laryngeal nerve palsy (0 to 1.6%), and bleeding that required re-exploration and/or transfusion (0 to 4.7%) [3, 4, 11–19]. This contrasts with the series reported by Trerotola et al using real-time ultrasound guidance [20]. Their complication rate was limited to 2 cases (0.8%) of small, clinically silent air embolism in 250 catheter placements.

The use of ultrasound-guided cannulation has resulted in an substantial decrease in procedural complications [21, 22]. Randolph et al performed a meta-analysis of the literature and concluded that ultrasound guidance decreased central venous catheter placement failure (relative risk of 0.32), decreased complications from catheter placement (relative risk of 0.22), and decreased the need for multiple catheter placement attempts (relative risk of 0.60) when compared to landmark cannulation tech-

niques [23]. The reason that even very experienced operators have problems with blind central vein cannulation is the variability that exists in the venous anatomy. In an ultrasonic evaluation of 104 patients, Lin et al found that 27% of the cases had internal jugular vein anatomical variations that would have contributed to difficulty in external landmark-guided cannulation [24]. In the chronic hemodialysis population it is not at all unusual to discover the absence of an internal jugular vein when the patient is evaluated with ultrasound (at Duke University 18% of patients referred for catheter insertion had thrombosed, occluded or absent right internal jugular veins). Real-time ultrasound guided cannulation was strongly recommended by the DOQI committee on vascular access [25]. This is probably too conservative, it should be considered a standard part of the procedure (Fig. 5). The availability of small inexpensive ultrasound cannulation machines makes ultrasound observation and confirmation of vessels to be cannulated prior to cannulation possible even for bed side cannulation (SITE RITE™, Pittsburgh, PA, USA). Experienced physicians who dislike the added complexity of real time cannulation are still well served by confirming vessel location and patency prior to cannulation.

Long-term complications of catheter placement are also important. For over a decade the relationship between central venous catheters, particularly subclavian catheters, and central venous stenosis has been recognized [26–29]. This has been a serious problem with the use of temporary catheters (Fig. 6). The incidence of subclavian stenosis following catheter placement has been reported to be in the range of 42 to 50%. In contrast, the rate of innominate stenosis following use of the internal jugular vein has been reported to be 0 to 10% [30, 31]. In these reports, the catheters were not tunneled and were placed without imaging guidance. Thus, the DOQI guidelines recommended that subclavian vein cannulation should be avoided except as a last resort [8].

When a temporary catheter is left in place for a prolonged period, progressive vascular erosion can occur and lead to perforation. This is related to the length and relative rigidity of these devices. Improper catheter positioning or migration of the tip out of the proximal superior vena cava increases the risk of this occurrence.



**Fig. 5. Ultrasound appearance of right internal jugular vein (Vein) and carotid artery (Artery).** With visualization of this type, cannulation of the internal jugular is easily accomplished.

This can result in a hemothorax or atrial perforation and pericardial tamponade [2]. In general, temporary non-cuffed catheters inserted in the femoral position may be left in place in bed bound patients for three to five days prior to needing removal and replacement. Temporary catheters placed in the internal jugular position characteristically have a use life of no more than two to three weeks because of the increasing risk of catheter related bacteremia [2, 3].

### Selection of site of placement

The right internal jugular is the preferred initial access site for cuffed tunneled catheter placement because of the relative direct path to the superior vena cava (SVC) and the right atrium, and the relative low incidence of central vein stenosis. The second choice for placement of a catheter is not clear. The left internal jugular is a less desirable access site. In order for the catheter to reach the right atrium it must traverse two curves, in contrast to the single curve required of the subclavian catheter. Not only does a catheter in this position risk stenosis, it also has a higher malfunction rate [24]. The subclavian site allows excellent function but has a high rate of central vein stenosis and should therefore be avoided [26–30]. In cases in which all easily accessed sites have been depleted, translumbar [32], transhepatic [33] and femoral catheters [34] have been used for the placement of tunneled catheters. These sites have higher dysfunction and infection rates than the other insertion sites.

For single use or in patients confined to the bed, femo-

ral placement of a temporary dialysis catheter offers a convenient means for short-term vascular access. In general, patients with a femoral temporary catheter should not be allowed to ambulate. Femoral placement of a tunneled catheter is an attractive alternative in patients in the intensive care unit, especially when the patient is on a respirator. In patients with head and neck trauma, patients with multiple central venous lines around the neck and chest and patients with a tracheostomy, moving the dialysis access to the lower extremity makes it more convenient and more easily managed.

### Placement of catheter tip

Improper tip placement is a common cause of poor flow. The tip of a temporary non-cuffed catheter placed in the neck or chest should extend to the superior vena cava. Shorter catheters may be plagued by excessive recirculation and catheters that are longer present the risk of atrial perforation. The optimal length for an internal jugular catheter is 15 cm. Femoral placement demands a longer length catheter in order to minimize recirculation. Optimally, these catheters should reach the inferior vena cava. Unfortunately, the longest lengths of temporary catheters (25 cm) in common usage are not quite long enough to do this. Rigid temporary catheters should never be placed in the right atrium because of the risk of vessel puncture and catheter induced arrhythmia.

Because the cuffed tunneled catheter is constructed of soft material (silicone, silastic elastomer), there is little risk of atrial perforation. Therefore these catheters can be, and if fact should be, longer. Placing the tip of the

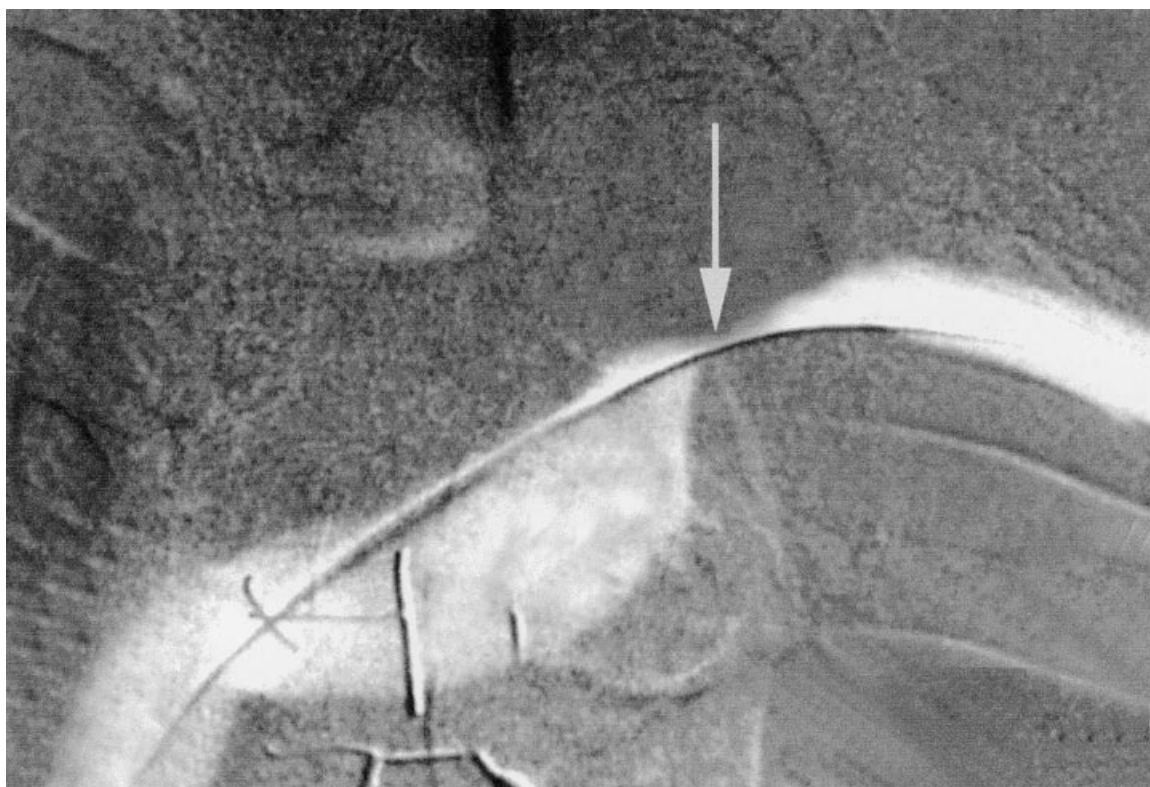


Fig. 6. Venogram of left subclavian showing area of severe stenosis (arrow).

catheter into the atrium is safe and minimizes the risk of recirculation. There is also the problem of catheter retraction. The tunneled catheter usually does not become attached to the tissue except at the cuff. The catheter moves back and forth within the tunnel in association with changes in anatomic position. The chest wall tissues move downward when the supine patient (as at the time of catheter placement) assumes an erect position (as at the time of dialysis). Since the catheter cuff is anchored in this tissue, it retracts. At times, this retraction can be considerable (Fig. 7). Thus, change in patient position can materially affect catheter flow. The tip of a tunneled catheter should be placed within the atrium at the time of insertion and should span the caval-atrial junction on an erect inspiratory film (Fig. 7B). A catheter positioned with the tip at the caval-atrial junction may not work in the dialysis unit, especially in obese patients and patients with large breasts as the catheter when the patient is sitting may retract well above the atrial caval junction. Fluoroscopy is required to optimize cuffed tunneled catheter placement.

The optimum orientation of the catheter tip is important for proper function and good flow. First, with double lumen catheters, the red hub (arterial lumen) should be turned medially, away from the vessel wall. This will prevent it from adhering to the wall when suction is

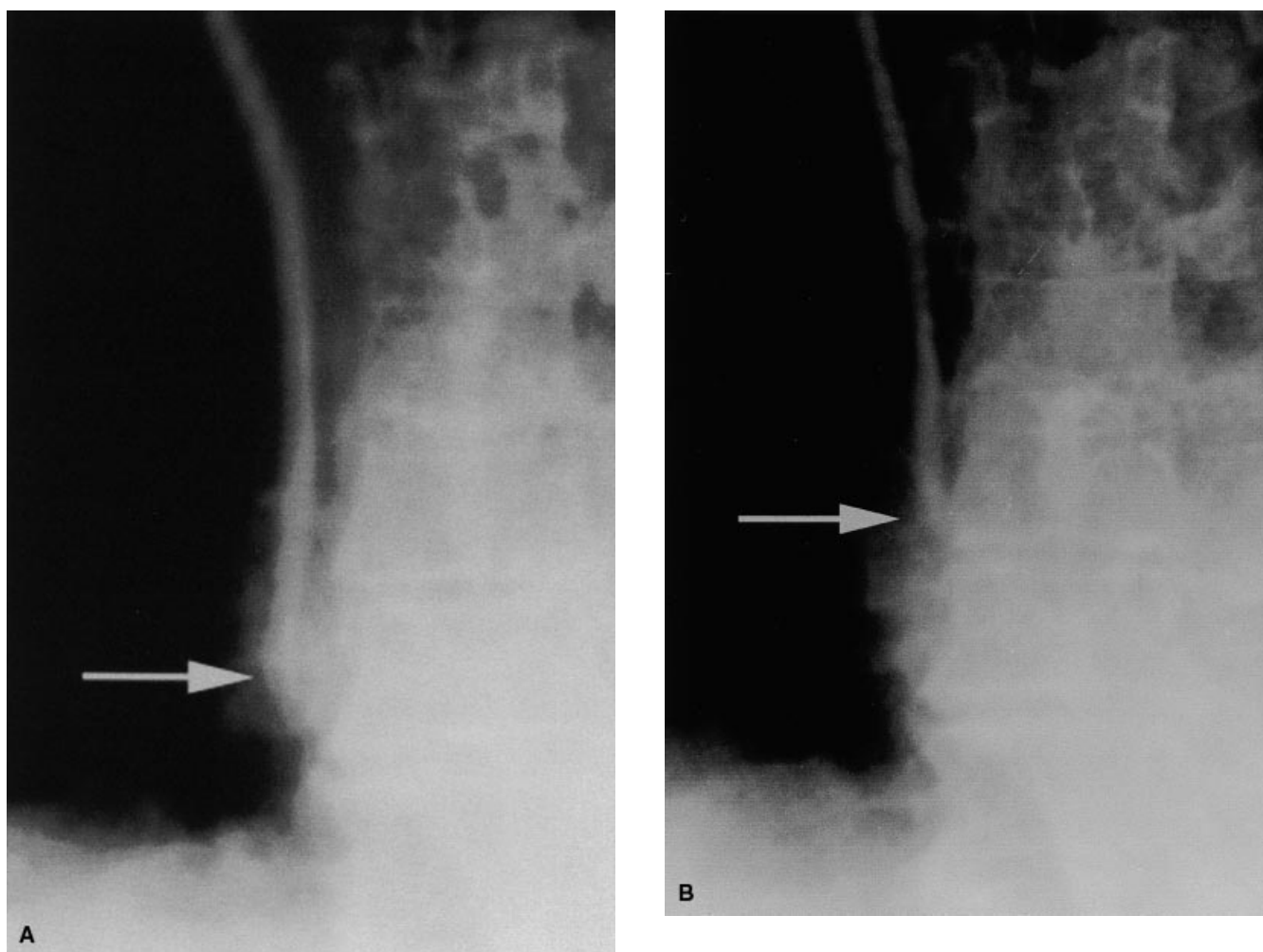
applied. With twin catheters, tip positioning is not a factor, however, the venous element should extend 3 to 4 cm beyond the arterial one to minimize recirculation.

#### **Catheter thrombosis: Patency**

In general, catheter blood flow problems that occur early after placement are related to catheter position while those that occur late are related to thrombosis. Thrombosis is a common problem with both temporary and cuffed tunneled catheters, and the problems encountered with these two types of catheters are similar. The major difference lies in the fact that when flow problems occur with the temporary catheter, it is often easier to just exchange it over a guidewire than deal with the range of solutions offered for its cuffed tunneled cousin. The mean primary patency rate (time to first required therapeutic intervention) for tunneled catheters has been reported to range from 73 to 84 days [35, 36]. Reported cumulative patency rates (time from placement to catheter site failure) vary widely. The DOQI panel concluded that a 12 month patency was a believable estimate [8]. Catheter associated thrombosis can be classified as extrinsic and intrinsic (Table 6).

#### **Extrinsic thrombosis**

*Central venous thrombosis.* The presence of a catheter within the central veins can precipitate thrombosis of



**Fig. 7. (A) Appearance of tunneled cuffed catheter with patient supine.** Contrast has been injected to facilitate visualization of the catheter. The arrow indicates the position of the tip. Note that it is in the lower atrium. **(B)** The same patient as shown in A. This film was taken with the patient erect. Notice the difference in the position of the catheter tip as indicated by the arrow. Note the degree of retraction that has occurred. This catheter position is considered optimum.

**Table 6.** Classification of catheter thrombosis

Extrinsic
Mural thrombus
Central vein thrombosis
Atrial thrombus
Intrinsic
Intraluminal
Catheter tip thrombus
Fibrin sheath

the vein. How often this occurs is not clear. Agraharkar et al suggested that it is not common [37], and reported an incidence of only 2% in a series of 101 percutaneously inserted catheters. Karnik et al, in a study of 63 patients with central venous catheters (not dialysis), found an incidence of 63.5% [38]. It is certainly clear that symptomatic central vein thrombosis is not common, but when

it does occur the symptoms can be dramatic. Diagnosis is based primarily upon the clinical picture presented by the patient. The patient presents with swelling of the ipsilateral extremity, which may also be tender and painful. The presence of central vein thrombosis may be confirmed by the use of ultrasound evaluation of venography. Treatment consists of catheter removal and anticoagulation. In cases in which the potential sites for vascular access are depleted or extremely limited, it may be possible to preserve the catheter. These patients must be systemically anticoagulated and observed very closely. Some investigators have reported success with direct urokinase infusion [39]. The catheter must be left in place to prevent bleeding from the catheter site if this therapy is attempted.

*Mural thrombus.* This is a thrombus that is attached to the wall of the vessel or the atrium at the point of



contact by the tip of the catheter. It is presumed that catheter tip movement causes damage that results in thrombus formation. The tip of the catheter is frequently attached to this mural thrombus, and when this occurs, it can interfere with catheter function. Most of these thrombi are not recognized unless there is catheter malfunction, at which time they may be recognized at the time of angiographic evaluation. When recognized, removal of the catheter accompanied by 3 months of anticoagulation is indicated, and in our experience represents adequate treatment. A large mural thrombus raises the risk of a significant embolism when the catheter is removed. A suitable therapy for this problem has not been developed, and our practice is to remove these catheters under real time observation so that immediate lytic therapy can be employed if indicated.

**Atrial thrombus.** Rarely, a large intra-atrial thrombus may develop in association with a dialysis catheter and present as a mass within the right atrium as seen angiographically or with an echocardiogram [40]. This probably represents a variant of the mural thrombus. Removal of the catheter, anticoagulation and echocardiographic follow-up have been used in these cases. Real time catheter removal with lytic therapy on standby in case a large pulmonary embolism develops is probably warranted.

### **Intrinsic thrombosis**

This type of thrombosis represents the major complication associated with dialysis access catheters.

**Intraluminal thrombus.** Intraluminal thrombosis occurs when a thrombus forms within the catheter lumen. It results from either an inadequate volume of heparin being placed within the catheter lumen, heparin being lost from the catheter between dialysis treatments, or from the presence of blood within the catheter. Urokinase instillation characteristically resolves these thromboses. The vascular access DOQI provides two urokinase instillation or lock techniques. One technique involves placing urokinase (1 ml/5000  $\mu$ ) in a volume sufficient to fill the catheter followed by aspiration in 20 minutes. The alternate technique is similar but uses small injections of saline to advance the urokinase to the catheter tip at 5 to 10 minute intervals.

Heparin of 1 ml/5000  $\mu$  or 1 ml/10,000  $\mu$  should be placed in the catheter at the conclusion of each hemodialysis treatment. The catheter should be filled to its capacity; capacity of the catheter is labeled on the catheter for each lumen. The catheter should have tape labels marked with the date of instillation describing the type of quantity of heparin instilled on each lumen with a warning "do not flush."

**Catheter tip thrombus.** Many catheters have side holes at the tip of the arterial limb. Unfortunately, the portion of the catheter from the side holes to the tip will not retain heparin and a thrombus can form. A tip thrombus

may be occlusive, or it may act as a ball valve. Preventative measures that are commonly used to avoid intraluminal thrombosis are largely subverted by the presence of the side holes. It is probable that forcible flushing before and after dialysis does aid in clearing poorly attached catheter tip thrombi. Urokinase instillation (lock) usually resolves this thrombosis.

**Fibrin sheath thrombus.** This is the most difficult to treat of the intrinsic conditions. In fact, this could equally well be considered an extrinsic condition, but is discussed here to facilitate a step-wise evaluation of the problem. The term fibrin sheath refers to a sleeve of fibrin that surrounds the catheter starting at the point where it enters the vein. This sheath is only loosely attached to the catheter. It is probable that all central venous catheters become encased in a layer of fibrin within a few days of insertion. Hoshal, Ause and Hoskins reported a fibrin sheath in 100% of 55 patients with central venous catheters at autopsy [41]. These are not always symptomatic. The incidence of catheter dysfunction secondary to fibrin sheath has been reported to be 13 to 57% [35]. When a catheter is removed, gentle angiography of the catheter can demonstrate a "wind sock" of residual fibrin sleeve (Fig. 8) in approximately 40% of cases [42]. As the sheath extends downwards, it eventually closes over the tip of the catheter. In this position, it can be disrupted by inward pressure to create a flap-valve that will allow injection but prevents withdrawal of blood and fluid.

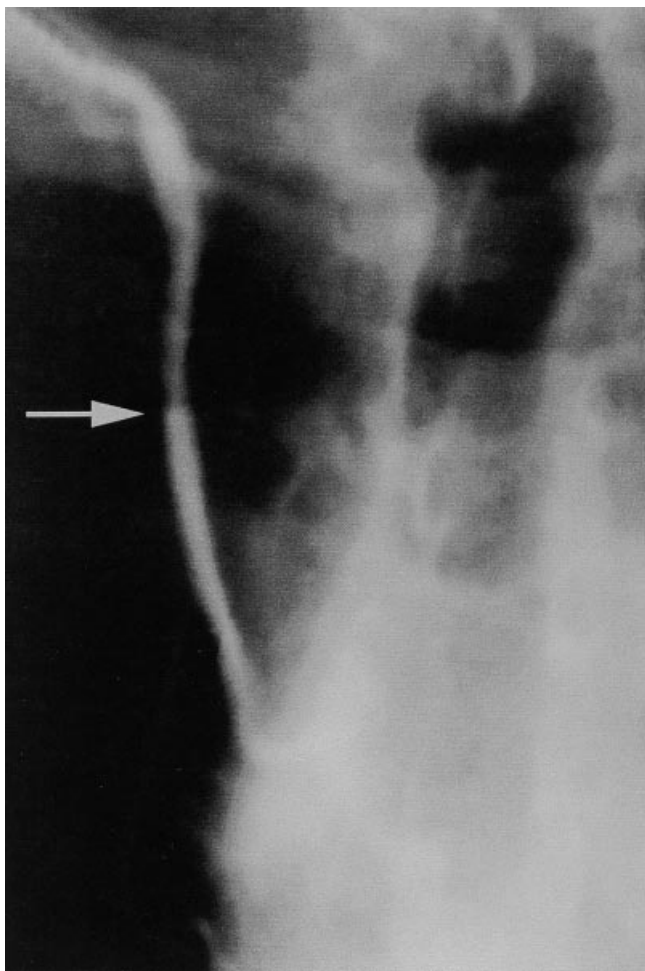
Fibrin sheath formation generally causes catheter dysfunction weeks or months after catheter placement; however, it may be seen as early as 48 hours. It is not clear whether or not prevention of the formation of a fibrin sheath is possible. There is anecdotal experience to suggest that chronic systemic anticoagulation with warfarin is beneficial, at least in selected patients. There are multiple treatment regimens discussed below. However, patients who form a fibrin sheath are likely to reform a sheath.

### **Prevention of catheter malfunction**

Chronic anticoagulation with either warfarin or low molecular weight heparin has garnered anecdotal support for preventing both lumen thrombus and fibrin sheath formation on hemodialysis catheters. To date no prospective clinical trials have been published. Currently clinical trials are underway in the U.S. and Canada to test partial and systemic anticoagulation with both classes of agents in a prospective controlled format. Similarly, prospective trials of urokinase as an alternate to heparin locked in the catheter between treatments as a means of diminishing both lumen thrombus and fibrin sheathing are underway.

### **Treatment of catheter malfunction**

The first step in the management of catheter malfunction is the recognition of the problem. Early malfunction



**Fig. 8. The appearance of a fibrin sheath.** The arrow indicates the tip of the catheter that has been partially removed in preparation for a catheter exchange. The fibrin sheath can be seen hanging below the catheter in its original position.

is usually due to improper placement with poor tip positioning or subcutaneous kinking of the catheter. With temporary catheters, repetitive bending of the relative stiff device will eventually lead to fatigue of the material and kinking due to collapse. This may be confused with thrombosis. Although it is possible for a tunneled catheter to become displaced after it has been in satisfactory use for a period of time, later cases of malfunction are generally due to thrombosis.

Catheter malfunction is defined as a failure to attain and maintain an extracorporeal blood flow sufficient to perform hemodialysis without significantly lengthening the hemodialysis treatment. Sufficient extracorporeal blood flow is considered to be 300 ml/min [8]. Once catheter malfunction is recognized it should be immediately treated. The approach to treatment may be different for temporary catheters versus tunneled catheters. The expense and difficulty of some of the treatment

methods for acute or temporary catheters may be considered excessive in view of the ease that these devices can be exchanged over a guidewire. Treatment can be categorized as primary and secondary.

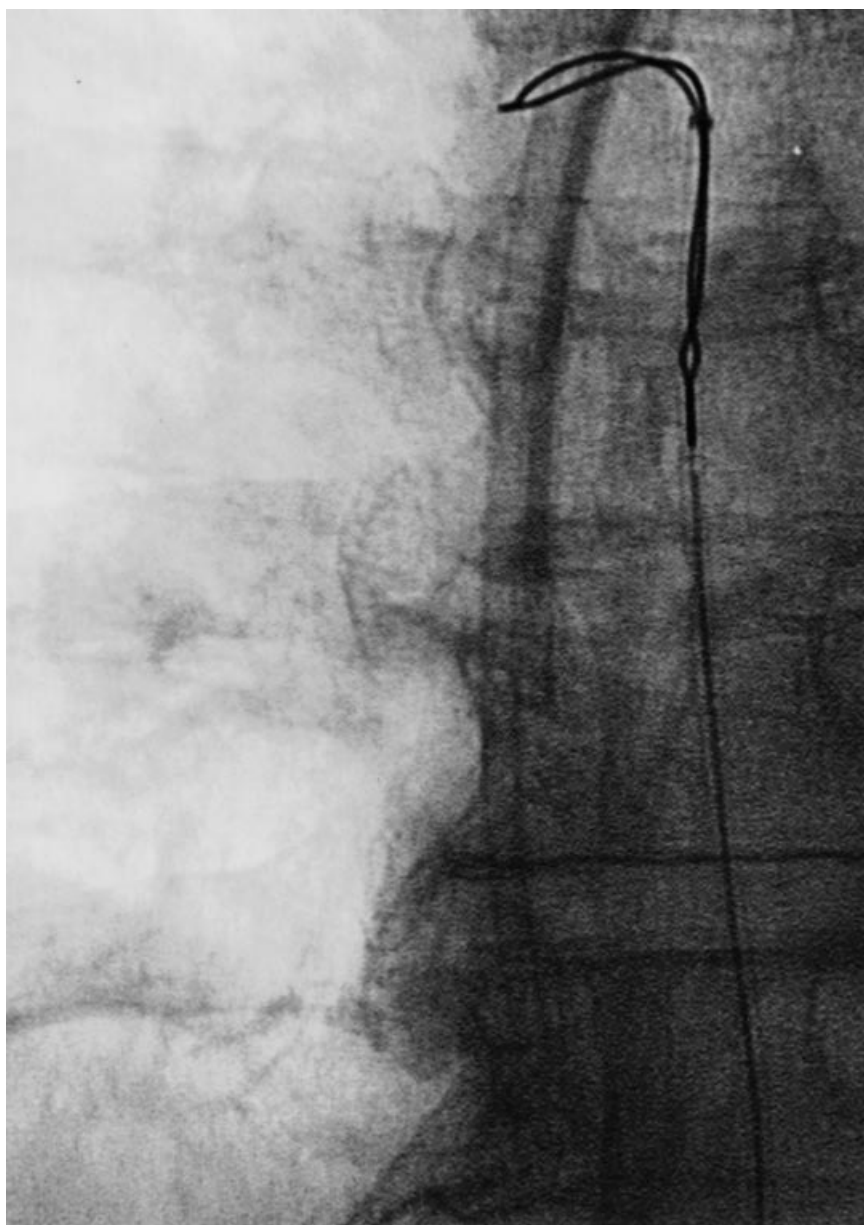
*Primary treatment of catheter malfunction.* Primary treatment of catheter malfunction refers to the treatment that can be immediately applied in the hemodialysis facility.

*Urokinase.* Numerous protocols for urokinase administration or urokinase catheter lock are in use. Two effective examples are provided in the Vascular Access DOQI Guidelines. Proper use of intraluminal urokinase has been shown to be successful in restoring catheter function in 74 to 95% of cases [3, 35]. The advantages of the urokinase technique are that it has a high rate of success in treating intraluminal thrombus, produces no systemic effect and is therefore safe, and can be performed by a trained nurse in the hemodialysis facility.

Urokinase catheter lock is not a good solution for the treatment of a fibrin sheathing. Thrombolysis only occurs within the catheter and at its tip. There is no systemic effect and no mechanism by which the enzyme can come into contact with the major portion of the sheath. At Duke University preliminary results of a 30 minute infusion of 20,000 units of urokinase in to the affected catheter lumen has been 70% effective in restoring function after failure of the urokinase lock technique. This low dose protocol is affordable and can be performed in the hemodialysis unit. Recently, Twardowski has reported a series of high dose urokinase infusions for catheter dysfunction performed during the hemodialysis treatment itself [43]. These urokinase infusion protocols hold promise and are undergoing clinical trials at several centers. Whether the low dose (20,000 to 40,000 units) or the higher dose 125,000 to 250,000 units) will be equally successful or whether one is able to open the catheter well enough to perform another infusion during the treatment awaits the results of the trials. In a similar fashion the value of slow infusion versus rapid injection is under study. Regardless, the current problem of the unreimbursed expense of urokinase in the hemodialysis unit represents a current barrier to consideration of the high dose urokinase intradialytic protocols in the United States.

*Secondary treatment of catheter malfunction.* If the primary treatments are unsuccessful or if the problem quickly recurs, a radiographic study using contrast should be performed. Further secondary treatment should be performed based upon the radiographic findings. These treatments are usually not performed in the hemodialysis facility. Appropriate treatments include:

(a) *Fibrin sheath stripping.* The fibrin sheath can be stripped using a snare catheter (Fig. 9). The snare is introduced through the femoral vein from where it is advanced up to the level of the dialysis catheter. The



**Fig. 9. Snare around a fibrin sheath prior to catheter fibrin sheath stripping.** (From Su-hocki [35], used with permission by the author and W.B. Saunders Co.)

reported success of this procedure ranges from 92 to 98% [35, 42, 44], and the reported duration of patency has varied from a mean of 20 days to a mean of 90 days. Fibrin sheath stripping generally results in asymptomatic embolization of the fibrin sheath.

Advantages of this technique are high success rate, safety, it preserves the catheter and the duration patency is reasonable.

(b) *Catheter exchange over guidewire.* This technique can be effectively used to eliminate the problem of catheter thrombosis (abstract; Duszak et al, *Radiology* 197: 284, 1995). This can be done using a technique that preserves both the exit site and the venotomy site. It is important that the patient be checked for a fibrin sheath

prior to inserting the new catheter. It is possible to place the new catheter back into the retained sheath and have the same problem within a short time. To avoid this complication, the sheath can be removed (embolized) using an 80-cm Fogarty embolectomy balloon.

Advantages of this procedure are that it preserves the exit and venotomy site and has a low reported complication rate, is less expensive than fibrin sheath stripping, and it has a high rate of success. Disadvantages of this technique are that a new catheter exit wound is created with its associated risks of bleeding and infection.

(c) *Urokinase infusion.* Treatment of catheter thrombosis by prolonged administration of urokinase has been used. This involves the administration of 20,000 units of



urokinase per hour for four to six hours. Lund et al reported a success rate of 79.5% with this technique [36]. This dose of urokinase is not large enough to result in systemic effects and does not require hospital admission. Other urokinase protocols both published and under investigation were discussed previously for use in the hemodialysis unit.

Advantages of these urokinase infusion techniques are that they appear safe, preserve the catheter and are less expensive than either fibrin sheath stripping or catheter exchange. The primary disadvantage lies in the fact that it requires four to six hours of hospital observation to facilitate payment for the urokinase. In countries or areas where time of observation in the hemodialysis unit or urokinase reimbursement are not barriers these protocols can be adapted to the hemodialysis unit.

## CATHETER RELATED INFECTION

Infection associated with hemodialysis catheters has emerged as the most prominent and most serious complication that is encountered. Tunneled cuffed catheters have a much lower bacteremia rate than that of temporary catheters [2, 3, 45, 46]. The incidence of tunneled catheter related bacteremia was recently described by Marr et al in a large prospective trial as being one episode per 252 catheter days [47]. Kovalik and associates demonstrated a significant increase in metastatic infection in patients with dialysis catheters versus AV grafts [48]. Robinson and coauthors demonstrated that endocarditis occurred at a much higher rate in patients with catheters as opposed to patients with AV access [49]. Marr and colleagues noted four episodes of endocarditis in patients with cuffed tunneled catheters followed for 16,000 catheter days [47].

Secondary complications of hemodialysis catheter related bacteremia (CRB) and sepsis such as septic arthritis, endocarditis, and epidural abscess have dire consequences and can result in death [15, 37–49]. Kovalik and associates [48] and Marr and colleagues [47] showed that *Staphylococcus aureus* was much more likely to adhere to valve and bone than other organisms. Careful evaluation for possible metastatic infection is needed when this organism is identified.

The most commonly reported isolate in cases of CRB has been *Staphylococcus aureus* [15, 47–50]. In a series of 123 cases of CRB, it was observed that 104 cases (84.5%) had Gram positive cocci, 41 (33.3%) had a Gram negative organism, and 2 (1.6%) had an acid-fast organism [51]. Thirty-seven percent of the cases were secondary to *Staphylococcus aureus*. Multiple organisms were isolated in 17% of the cases.

## Risk factors

In addition to the foreign body effect of the tunneled cuffed catheter (TCC), there are a number of factors

that have been identified as risk factors for the development of CRB [51–54]. These include skin and nasal colonization with staphylococcus, catheter hub colonization, duration of catheterization, thrombosis, frequency of catheter manipulation, diabetes mellitus, iron overload, immunoincompetency, use of a transparent dressing and the conditions of catheter placement.

## Prevention of infection

Prevention of catheter associated infection involves three areas: technique of catheter placement, daily catheter exit site care and catheter management in the hemodialysis facility. It is critically important that maximal barrier precautions be used when a catheter is placed. If not done in an operating room, the environment should stimulate an operating room.

Care given to the catheter after placement is of equal importance. The use of either mupirocin or providone-iodine or other antibiotic ointment at the exit site until it is healed has been advocated [55]. The use of a transparent dressing occlusive dressing has been indicated as a risk factor for CRB [52], since it promotes skin colonization. Nevertheless, the question as to whether it is best to use gauze or a plastic dressing remains unresolved and controversial [54–56]. We adopted the approach of keeping of catheter exit site covered with sterile gauze at all times and using providone-iodine ointment or other antibiotic ointment, in keeping with the DOQI recommendations. Some polyurethane catheters have developed mechanical breakdown after prolonged exposure to antibiotic ointments (BARD Inc., Salt Lake City, Utah, USA). In these catheters the manufacturer's recommendation should be followed.

Most cases of catheter associated infection occur at a point in time distant from the time of insertion. This suggests that factors related to pathogenesis are most likely to be located within the hemodialysis facility, and it appears that bacterial colonization plays an important role. Colonization of the patient's nares, the patient's skin and the catheter hub have been examined. Zimakoff et al found that catheter-related staphylococcal infection occurred most often in patients who had nasal colonization, and in more than half of the cases it was with the same strain [56]. Nasal carriage can be eliminated [57] but it is not permanent, and continuous treatment is necessary.

The strategy applied in the hemodialysis facility should be to minimize the effects of bacterial colonization by minimizing the chances of exposure to these sources of potential contamination. Analysis of our cases of CRB revealed that 2/3 of them had no associated exit site or tunnel infection [50]. This and the fact that the infections were delayed more than two months on average from the time of placement caused us to conclude that contamination of the catheter hub or lumen at the time of manipulation in the dialysis unit was a major risk factor.



## Treatment of infection

Infection associated with a dialysis catheter has the potential for being a very serious problem. There are two issues that must be addressed: the infection and what to do about the catheter. Conservatively the catheter should be removed and should not be replaced until the infection is clear. Unfortunately, continuing demand for dialysis may preclude the total abandonment of vascular access. What to do with the catheter as an alternative to permanent removal must be addressed. The answer to this question will depend upon the type of catheter, the character of the infection and the patient's continuing dialysis requirements. Catheter related infection can be classified into three categories; exit site infection, tunnel infection (only with tunneled catheters), and catheter related bacteremia (CRB). The therapeutic approach to each of these is somewhat different.

**Exit site infection.** This is defined as infection localized to the catheter exit site (external to the anchoring cuff in cuffed catheters), and is characterized by localized redness, crusting, and exudate. If the patient has systemic symptoms and a positive blood culture, the case should be managed as a CRB below. An exit site infection is a local infection. With a temporary catheter, removal of the catheter is warranted with replacement at an alternate site. Exit site infections associated with a tunneled catheter should be treated with local measures (cleaning with a topical disinfectant and use of a topical antibiotic) in a salvage attempt if there is continued need for its use [58]. Systemic antibiotics are necessary in more severe cases or in cases that fail to respond to topical therapy. Antibiotics with anti-staphylococcal properties are preferred. Cases that fail to respond quickly to local measures and antibiotics necessitate catheter removal to prevent bacteremia.

**Tunnel infection.** By definition, tunnel infections occur only with tunneled catheters. This category of infection is defined as involvement within the catheter tunnel internal to the anchoring cuff. Involvement of the tunnel external to the cuff is commonly seen as part of the exit site infection. When the tunnel is infected internal to the cuff, it is a serious problem because the catheter moves back and forth within this portion of the tunnel and there is often direct communication with the blood stream. When it appears that the patient has a tunnel infection, the blood cultures are often found to be positive, thus, it is actually a tunnel mediated CRB. Appropriate treatment consists of parenteral antibiotics according to culture results and catheter removal. The catheter should not be replaced at this site.

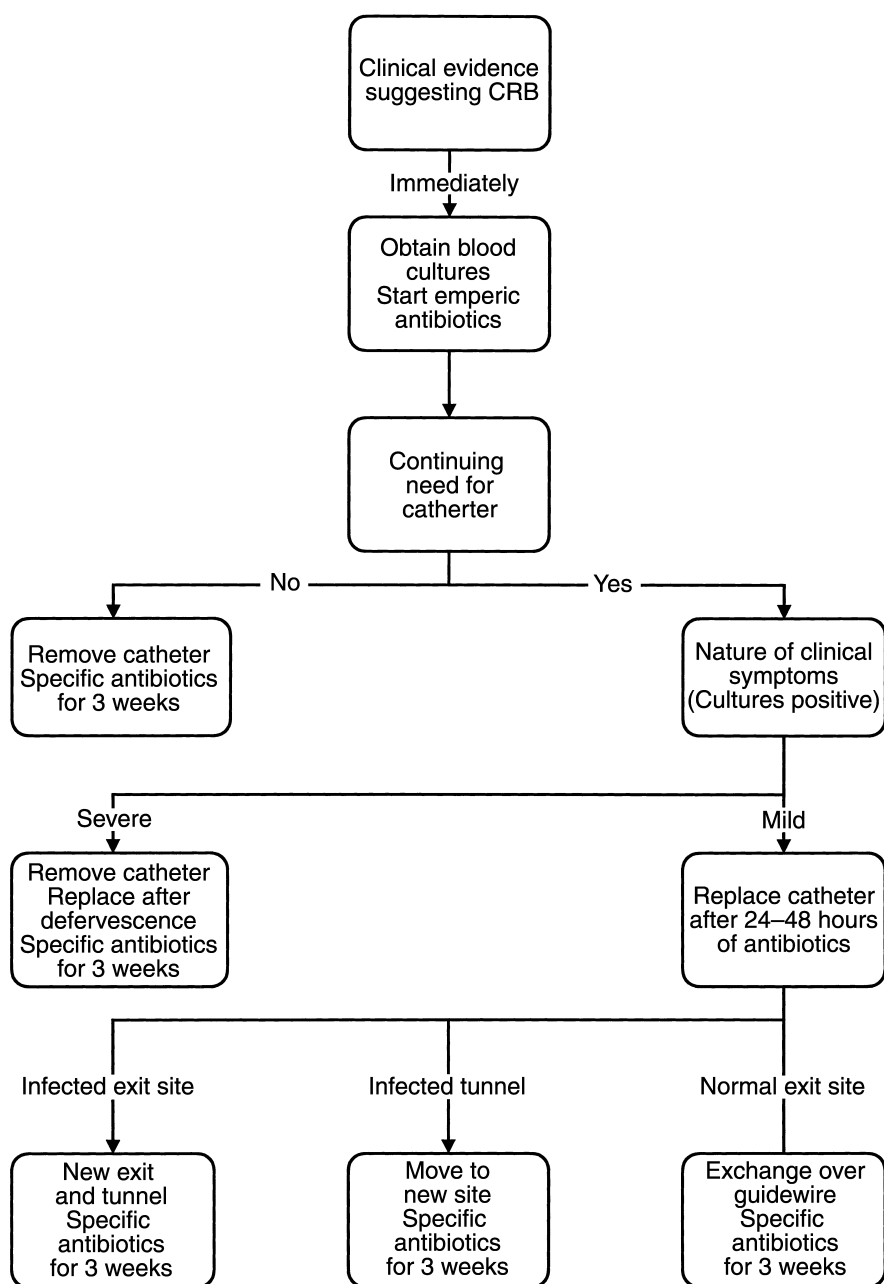
**Catheter related bacteremia.** When a catheter patient presents with a positive blood culture, immediate and prolonged antibiotic treatment is essential. The antibiotic used must be based upon culture and sensitivity

data. The prolonged empiric use of vancomycin should be avoided because of the risk of inducing vancomycin resistant enterococcus. Initial therapy with vancomycin and an amino glycoside antibiotic until culture results are available is prudent. Rapid conversion to appropriate antibiotics based on culture sensitivities is needed not only to prevent emergence of resistant organisms, but also to avoid ototoxicity. Antibiotic therapy should be continued for a minimum of three weeks [47–59]. Blood cultures should be repeated a week following therapy to assure that the infection has been eradicated. Routine evaluation for valvular vegetations by echocardiography should be considered. Fowler et al have suggested that transesophageal echocardiography is essential to establish the diagnosis of endocarditis and should be considered part of the early evaluation of any patient with bacteremia due to *Staphylococcus aureus* [59]. Appropriate management of the catheter must also be addressed. There are several choices: leave the catheter in, change the catheter over a guidewire, change the catheter over a guidewire with a new tunnel and exit site, or remove the catheter and delay replacement until the infection has been treated. There are several issues that affect this choice.

The presence of a biofilm on the inner or outer surface of the catheter may play an important role in catheter related bacteremia [60, 61]. Bacteria adhere and become embedded in the glycocalyx of the biofilm making them more resistant to antibiotics than those floating in the circulation [60, 62]. Passerini et al demonstrated the presence of a biofilm on the surface of 100% of the central venous catheters removed from 26 ICU patients [63]. Some of these catheters had been in place for only one day. Bacteria were demonstrated within 88% of these biofilms.

From a purely infectious disease viewpoint, removal of the catheter appears to be important [63–69] and where possible, this course of action should be followed. However, in the dialysis patient the issue is complicated by the fact that the patient must continue to receive dialysis treatments. Removal of a tunneled catheter creates a requirement for the use of temporary catheters and the risk of their associated complications. It mandates multiple procedures, a period of hospitalization and increased costs. Additionally, removal of the catheter may be associated with a loss of the central venous entry site because of stenosis or thrombosis. Unnecessary loss of a central venous site should be avoided if salvage of the site does not jeopardize the patient's health.

Saltissi and Macfarlane suggested treating the patient with the catheter in place [64]. However, in an attempt to do this, Marr et al observed a failure rate of 68% even with prolonged antimicrobial therapy [47]. This study indicates that this approach should not be considered as a therapeutic option.



**Fig. 10. Management of catheter related bacteremia (flow diagram).**

Shaffer, however, demonstrated encouraging results in a small series of patients treated with guidewire catheter exchange, new tunnel creation and antibiotic therapy for catheter related bacteremia in cuffed tunneled catheters [45]. Robinson et al reported a series of 23 hemodialysis tunneled catheter patients with CRB who were treated with catheter exchange over a guidewire combined with three weeks of antibiotic therapy [70]. These were patients with no evidence of tunnel infection who had defervescenced within 48 hours of beginning empiric antibiotic therapy. They defined technique failure as a repeat infection with any organism within 90 days of the catheter

exchange. They reported a success rate of 82%. In a series of 49 patients with minimal symptoms and no exit site infection, an 87% cure rate for CRB was obtained utilizing catheter exchange over a guidewire 24 to 48 hours after initiation of empiric antibiotics followed by three weeks of continued specific antibiotic treatment [50]. These studies confirm that catheter exchange over a guidewire combined with three weeks of specific antibiotic therapy is a viable treatment option for a subset of patients with CRB. Failure to respond rapidly to antibiotic therapy or an inflamed tunnel track require immediate catheter removal combined with antibiotic therapy [71].

In patients who have exit site or tunnel infections, the catheter must be removed and a new tunnel and exit site must be created when it is replaced. To do otherwise exposes the patient to unacceptable risks. In one report, a series of 37 cases of CRB in tunneled catheter patients with severe symptoms of septicemia were treated by removing the catheter, starting antibiotics and replacing the catheter at a new site as soon as the patients had become afebrile [50]. Specific antibiotic therapy was continued for a total duration of three weeks. A cure rate of 87% was obtained in these patients. Thus, replacing the catheter at a new site 24 to 48 hours after the patient has become afebrile is successful in the vast majority of patients. Removal of the catheter during an episode of infection is always the correct option if there is any doubt about the status of the patient or the catheter tunnel track. It is practice at our institution to require that the patient be afebrile and blood cultures be negative during antibiotic therapy prior to catheter replacement. These two requirements lead to catheters not being replaced before 48 to 72 hours following removal of the previous catheter. We routinely treat with intravenous antibiotics for three weeks following an episode of catheter mediated bacteremia and always perform cultures one week following antibiotic therapy.

Several European investigators have used antibiotics locked into the catheter in lieu of catheter removal. Capdevila and associates reported this in their 1993 pilot study and recently other investigators have also explored this option (abstract; Sodermann et al, *J Am Soc Nephrol* 8:173A, 1997).

We have not been as successful as yet with this technique. Prospective trials locking antibiotics and urokinase into the catheter between treatments to both prevent and treat catheter mediated bacteremia are underway. When the catheter is removed in the face of a CRB the DOQI guidelines recommend that a new permanent catheter not be placed until the patient has negative cultures with antibiotic therapy and has been afebrile for 48 to 72 hours.

These studies demonstrate that catheter related bacteremia can be effectively managed while paying proper attention to both the effective treatment of the infection and the proper management of the catheter that is necessary for continuing dialysis therapy. Antibiotic therapy must be specific, based upon the results of cultures, and prolonged. Treatment should be continued for a minimum of three weeks. Disposition of the catheter should be based upon the clinical presentation of the patient and the appearance of the tunnel and exit site. It is possible for many patients to preserve the exit site, tunnel and venotomy entry site (Fig. 10).

## SUMMARY

Our ability to care for the dialysis-dependent patient with chronic renal failure has been considerable enhanced by the development and availability of catheters, both temporary and chronic. There is no question that the development of these devices has been a tremendous asset to the nephrologist. However, it is equally obvious that their use carries a price measured in patient morbidity and physician frustration. They truly represent a double-edged sword. It is important that we develop a catheter usage strategy based upon an understanding of the complications that can occur with the use of these devices, and the appropriate preventive and therapeutic measures necessary to address these complications. It is also important that we come to grips with the fact that a catheter is inferior to and not a substitute for a peripheral access, not for an AV bridge graft and certainly not for an arteriovenous fistula. Early elective placement of an AV fistula is the best way to avoid the complications of hemodialysis catheters.

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