RESTORING PATENCY TO CENTRAL VENOUS ACCESS DEVICES
Indications

- Venous access is poor
- Intravenous therapy involves venous sclerosants
- Ambulatory chemotherapy given as an outpatient
- Repeated sampling, or venesection
- Prolonged intravenous chemotherapy and/or total parenteral nutrition (TPN), or for repeated administration of blood products
Contraindications

There is not absolute contraindications

Thrombocytopenia and platelet dysfunction: The platelet count $< 50 \cdot 10^9/l$

The clotting factors abnormality: the INR $> 1.5$

Neutropenia: A neutrophil count $< 1,000/\mu L$

• may have septic episodes

Active infection

• who require long-term antibiotic treatment, a temporary percutaneous CVA catheter or a peripherally inserted central venous catheter is preferable
Choice of catheter

- **Nontunnelled catheter**
  - Short term use

- **Skin-tunnelled catheter**
  - Complex insertion and removal

- **Ports**
  - Patient can swim, bath as normal

- **PICC**
  - Don’t require platelet support and correction of clotting
Choice of catheter

Non-Tunneled Central Venous Access Device

- Collar Bone
- Vein Entry
- Exit Site out of Skin
- Catheter Tail
- Cap

Tunneled Central Venous Access Device

- Vein Entry
- Exit Site out of Skin
- Catheter Tail
- Cap
Choice of catheter

- PICC
- PORTS
Management of complications

- Catheter-related infection
- Catheter malfunction
- Catheter-related thrombosis
Figure 4. A Large-Scale Analysis of Central Venous Access Device Complications in Individuals Receiving Central Infusions on an Outpatient Basis

*Note.* Based on information from Moureau et al., 2002.
Note. Fibrin deposits, as well as fully formed thrombi, can produce a plug residing within the lumen of a catheter (an intraluminal thrombus) or can form a sock-like sheath that covers the exterior of the catheter tip. The insoluble material can also form a “tail” at the catheter tip, interfering with blood withdrawal. Thrombi forming along the wall of the vein but exterior to the catheter (mural thrombi) also can interfere with fluid flow through the central venous access device.

Figure 6. Classes of Thrombotic Occlusion
Note. Images courtesy of Genentech, Inc. Used with permission.

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Note. Alteplase is a recombinant form of the normal blood component tissue-type plasminogen activator (t-PA), which causes thrombolysis as shown here. t-PA binds to and activates plasminogen, producing plasmin. Plasmin cleaves fibrin, releasing fibrin degradation products and causing the clot to dissolve.

Figure 7. Degradation of an Intraluminal Blood Clot (Thrombolysis)
Note. Image courtesy of Genentech, Inc. Used with permission.
Streptokinase → Plasminogen → Plasmin

α2 macroglobulin → Alfimeprase → Fibrin

Plasminogen activator inhibitor

Urokinase, Alteplase, Reteplase, r-UK, Anistreplase, & Tenecteplase

Fibrin clot dissolved

Fibrin degradation products
Clinical Evidence

In a head-to-head trial, t-PA (alteplase) was shown to be more effective at clearing thrombotic occlusions than nonrecombinant u-PA (Haire, Atkinson, Stephens, & Kotulak, 1994). A newer, recombinant form of u-PA (Abbokinase®, Microbix Biosystems Inc.) has been developed and is expected to be similar to the nonrecombinant form but without the potential contamination risks (Haire et al., 2004). Other agents that could be used for that purpose are being studied (Liu, Jain, Shields, & Heilbrun, 2004; Moll et al., 2006). Alteplase is approved in Canada and the United States for restoring CVAD patency (Genentech, Inc., 2003). Therefore, all recommendations for thrombolytic treatment in this article relate to alteplase.

![Graph showing cumulative efficacy](image)

**Note.** In the Cardiovascular Thrombolytic to Open Occluded Lines-2 Trial, one to two standard doses of alteplase were used to restore patency to occluded peripherally inserted central lines and other types of central venous access devices.
Efficacy in Central Venous Access Device Clearance

The efficacy of alteplase in clearing occluded CVADs has been reported to be 87%–90% (Deitcher et al., 2002; Journey-cake & Buchanan, 2006; Ponec et al., 2001). In the various efficacy studies, treatment was applied as many as two times, for one to two hours at each application. The largest of the studies was the Cardiovascular Thrombolytic to Open Occluded Lines–2 (COOL-2) interventional trial (N = 995), which showed 87% efficacy (Deitcher et al.). A subanalysis of the COOL-2 data focusing on the 242 patients with PICCs showed still higher levels of treatment success—93% on a cumulative basis when treated as many as two times (see Figure 8) (Ng, Li, Tu, & Semba, 2004).

The published clinical trials with alteplase have excluded patients with complete CVAD occlusions, when instilling the specified volume of fluid to treat the occlusion was not possible. However, a recent trial of recombinant u-PA has been reported in which totally occluded lines were treated successfully with a variation on the normal CVAD instillation procedure (Haire et al., 2004; Horne, 2004; Kerner et al., 2006). The alternate procedure, requiring a three-way stopcock, is used widely in infusion clinics and has been described extensively (Hamilton, 2006b; Infusion Nurses Society, 2006; Ottawa Hospital, 2006).
Figure 12. Algorithm for Restoring Patency to a Central Venous Access Device

1. **Sluggish blood withdrawal (< 3 ml in three seconds) or resistance to fluid instillation**
   - Is there evidence of venous thromboembolism?
     - No
     - Yes, consult physician.
   - Is there evidence of mechanical or chemical occlusion?
     - No
     - Yes, treat per institutional procedure.
   - Secure order for thrombolytic treatment.
   - Can fluid be instilled directly into line?
     - No
     - Yes, begin standard alteplase instillation.
   - Begin alternative (stopcock) alteplase instillation.
   - Is patency restored after a 30-minute dwell?
     - No
     - Yes

2. **Reinstill first dose of alteplase for an additional 90 minutes (for a total of 120 minutes).**
   - Is patency restored?
     - No
     - Yes, aspirate 5–10 ml blood. Flush and continue normal treatment of lock CVAD per manufacturer's recommendations.
   - Instill second dose of alteplase.
   - Is patency restored?
     - No
     - Yes
   - Reinstill second dose of alteplase for an additional 90 minutes (or overnight, depending on institute protocol).
   - Is patency restored?
     - No
     - Consult physician.

3. **If the line remains blocked but not completely occluded, repeat instillation of alteplase using the standard instillation method. Removing the three-way stopcock (if present) is not necessary.**
Recombinant urokinase is safe and effective in restoring patency to occluded central venous access devices: a multiple-center, international trial.

- **BACKGROUND:**
  - The treatment of choice for central venous access device (CVAD) occlusion is intracatheter thrombolysis, which has been reported to reestablish patency in up to 80% of cases.

- **OBJECTIVE:**
  - This multiple-center, open-label study was performed to test the hypothesis that a new recombinant urokinase (r-UK, urokinase alfa) is safe and effective in reestablishing patency in a large unselected cohort of occluded CVADs.

- **METHODS:**
  - Pediatric and adult patients with any type of CVAD occlusion of any duration were treated with 5000 IU/mL intracatheter r-UK. Lumen patency was assessed after 5, 15, and 30 mins; a second dose of r-UK was instilled if the catheter remained occluded after 30 mins.

- **RESULTS:**
  - A total of 903 r-UK instillations were performed in 878 patients (age range, 16 days to 96 yrs). Overall, instillation of r-UK successfully restored total catheter patency (all treated lumens) to 75% of CVADs (681 of 902).
  - Patency was restored to at least one occluded lumen in 79% of devices (712 of 902).
  - Patency was restored equally in catheters with total occlusion (76%) as in catheters with only withdrawal occlusion (75%).
  - The median +/- sd time to patency was 15 +/- 20.8 mins (range, 5-203 mins).
• Recombinant tissue plasminogen activator (alteplase) for restoration of function to occluded central venous catheters in pediatric patients.
  • **Shen V¹, Li X, Murdock M, Resnansky L, McCluskey ER, Semba CP; COOL Investigators.**

**PURPOSE:**
• To evaluate the safety and efficacy of alteplase for restoring function to occluded central venous catheters in a pediatric population.

**PATIENTS AND METHODS:**
• A phase III, open-label, single-arm, multicenter trial was performed in 995 adult and pediatric patients with dysfunctional nondialysis catheters and ports.
  • 2 and 18 years of age N = 122
  • Alteplase (2 mg/2 mL) 30 and 120 minutes.
  • Subjects weighing ≥30 kg received 2 mL of alteplase; subjects <30 kg received 110% of the internal lumen volume (not exceeding 2 mL).
  • Alteplase dosing was repeated once after 120 minutes if the catheter remained dysfunctional.
  The primary safety endpoint was the rate of intracranial hemorrhage (ICH) within 5 days of treatment.

**RESULTS:**
• The overall efficacy following up to two instilled doses of alteplase was 87%. In 70 patients (57%), restoration of catheter flow occurred by 30 minutes following a single dose of alteplase. Restoration of function was related to the duration of occlusion (P = 0.04). For catheters with occlusions of 0, 1 to 14, and >14 days duration, the efficacy was 91%, 78%, and 60%, respectively. Success was independent of the patient’s age, sex, body weight, CVC type, or catheter age. There were no cases of death, ICH, major bleeding episodes, or embolic events attributable to treatment.

**CONCLUSIONS:**
• An alteplase regimen of up to two 2-mg doses is safe and effective for restoration of function to occluded central venous catheters in a pediatric population.
Thrombolytic therapy for central venous catheter occlusion

Design and Methods

Efficacy of thrombolytic therapy, central venous catheter clearance rates and time to clearance were assessed.

Results

Conclusions
Thrombolytic agents successfully clear central venous catheter occlusions in most cases. Newer agents may act more rapidly and effectively than currently utilized therapies, but randomized studies with direct comparisons of these agents are needed to determine optimal management for catheter obstruction.

PURPOSE:
This study was undertaken to evaluate the safety and efficacy of alteplase in the treatment of CVAD occlusions in a pediatric population.

MATERIALS AND METHODS:
A prospective, multicenter, open-label, single-arm study evaluating a maximum of two doses (< or =2 mg per dose) of alteplase was performed in pediatric patients.
- Patient age less than 17 years with an occluded CVAD (single-, double-, and triple-lumen catheter or implanted port).
- Hemodialysis catheters, mechanical occlusion, considered at high risk for bleeding or embolization
- Assessment of function was made 30 and 120 minutes (if required) after each dose. The primary objective of the study was to evaluate the safety of alteplase as measured by the incidence of intracranial hemorrhage (ICH); secondary objectives included the evaluation of specific targeted serious adverse events and efficacy of alteplase in the restoration of catheter function.

RESULTS:
- A total of 310 patients (174 male patients, 136 female patients; mean age, 7.2 years; range, 0.04-18.3 y) were treated; 55 of the patients (17.7%) were younger than 2 years of age. No patients experienced ICH (95% CI, 0%-1.2%). Nine serious adverse events were noted in eight patients (2.6% incidence), two of which were attributed by the investigator to study drug administration (one case of sepsis and one case of a ruptured catheter lumen).
- The cumulative rate of restoration of CVAD function after serial administration of a maximum of two instillations of alteplase, each with a maximum dwell time of 120 minutes, was 82.9% (95% CI, 78.2%-86.9%). Similar rates of catheter function restoration were seen among all catheter types studied; there were no clinically meaningful differences among age or sex subgroups.

CONCLUSION:
The administration of alteplase is safe and effective for the restoration of function to CVADs in pediatric patients.
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<th>RECOMMENDATION</th>
<th>LEVEL OF EVIDENCE</th>
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<tr>
<td>Take appropriate steps to prevent central venous access device (CVAD) occlusion and to salvage dysfunctional CVADs. Attempt thrombolytic treatment to restore the patency of devices occluded by blood clots. Apply thrombolytic treatment with caution in patients with known or suspected CVAD infection.</td>
<td>II: strong evidence from at least one properly designed, randomized, controlled trial of appropriate size</td>
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<td>Use locking solution or positive pressure device, as directed by device manufacturer, to prevent thrombotic occlusions. Apply thrombolytic treatment as soon as possible after complete or partial thrombotic occlusion has been identified (may require diagnostic imaging).</td>
<td>III: evidence from well-designed trials such as nonrandomized trials, cohort studies, time series, or matched case-controlled studies</td>
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<td>Select CVAD type based on expected duration of therapy and the least invasive procedure available. Before attempting thrombolytic treatment, review record and, if necessary, consult with pharmacy to identify possible chemical blockage and determine appropriate clearing solution. Use turbulent flow while flushing lines properly to prevent thrombotic occlusions. Attempt thrombolytic treatment on an empirical basis if no mechanical or chemical causes of CVAD dysfunction can be identified. Apply thrombolytic treatment with caution in patients with active internal bleeding, recent surgery, or hemostatic abnormalities.</td>
<td>V: opinions of respected authorities, based on clinical evidence, descriptive studies, or reports of expert committees</td>
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Long – term care catheter

Flushing with the correct solution and technique is essential to maintain catheter patency, and only single-dose solutions should be used.

Infections can be minimized by careful hand washing and catheter site care.

Plain X-ray or a catheter contrast study may be helpful in confirming the diagnosis of catheter malfunction.
Removal of catheter

- Catheter-related infection
- Persistent catheter occlusion
- Damaged catheter
- The end of treatment
- Catheter-related thrombus
THANK YOU FOR YOUR ATTENTION