Hold ourselves accountable to the standard of care

Use evidence-based guidelines to deliver quality care to pediatric patients with central lines
Central Venous Access Devices (CVADs) deliver life-sustaining therapies

“CVADs are integral to infants and children requiring intermittent or continuous infusion therapy. In many health care settings, young patients require a reliable CVC for safe delivery of infusion therapy.”
AVA Best Practice Guidelines in the Care and Maintenance of Pediatric Central Venous Catheters, 2015, page 7

Catheters can be used either short or long term for the infusion of:
- Antibiotics
- Parenteral nutrition
- Medication/solutions in patients with limited peripheral access
- Chemotherapy or other vesicant or irritating solutions
- Blood and blood products
- Therapy that is ongoing or continued at home

AVA=Association for Vascular Access.

Why is it important to ensure central line patency?

An occluded line may complicate patient care by:
- Disrupting therapies or delaying procedures
- Interrupting administration of medications and solutions
- Delays in discharge
- Additional procedures, such as catheter replacement

“Foster a just culture and individual accountability through a focus on improving systems and processes by clinicians and leaders.”
INS Infusion Therapy Standards of Practice, 2016, page S21, standard 6A

“Catheter salvage is preferred over catheter removal for management of CVAD occlusions.”
INS Infusion Therapy Standards of Practice, 2016, page S104, standard 48.3

INS=Infusion Nurses Society.
CVADs provide access to central venous circulation

**Pediatric catheter insertion sites**
Appropriate CVAD site selection should be based on\(^1\)\(^8\)
- Diagnosis
- History of vascular access devices
- Anatomical variances
- Type and length of therapy
- Patient and/or caregiver preference
Vessel location is relatively similar in adults and children, but children have smaller bodies and fewer veins, making it more difficult to successfully achieve access.\(^1\)\(^8\)

**CVAD insertion and tip sites\(^9\)**

<table>
<thead>
<tr>
<th>Location</th>
<th>Tip Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUBCLAVIAN</td>
<td>SUPERIOR VENA CAVA</td>
</tr>
<tr>
<td>CEPHALIC</td>
<td>TIP LOCATION</td>
</tr>
<tr>
<td>BASILIC</td>
<td>INFERIOR VENA CAVA</td>
</tr>
<tr>
<td>BRACHIAL</td>
<td>(ALTERNATE TIP LOCATION)</td>
</tr>
<tr>
<td>FEMORAL</td>
<td></td>
</tr>
</tbody>
</table>

**Types of CVADs**

**Peripherally inserted central catheters (PICCs)\(^1\)\(^4\)**
- Can be used for a variety of IV therapies
- Indicated for therapies of 5 to 7 days or more
- Less expensive when compared with surgically placed CVADs

**Nontunneled catheters\(^1\)\(^2\)\(^4\)**
- Also called subclavian, percutaneous, or short-term catheters
- Typically used for short-term therapy for all types of IV therapy, to draw blood, and to monitor central venous pressure
- Can be single or multilumen and is inserted at the bedside or in the operating room

**Tunneled catheters\(^2\)\(^4\)**
- Designed for long-term use and frequent venous access
- Used for extended courses of antibiotics, chemotherapy, and total parenteral nutrition (TPN)
- Require surgical procedure for insertion

**Implanted ports\(^2\)\(^4\)**
- Preferable for frequent or long-term access
- Consist of 2 attached parts: the catheter and the portal body with reservoir
- Long-term dwell capacity, requiring little maintenance when not in use
- Useful for cyclically infused therapies, such as chemotherapy
- Blood draws may be done through the port
- Surgically inserted

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(A) © 2012 C. R. Bard, Inc. Used with permission. Bard is a registered trademark of C. R. Bard, Inc.  
(B) Please be advised, the port shown is manufactured by VADA but is not for implantation in humans or animals and is only supplied non-sterile. Port is for use in simulation training/practice only.

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One in 3 pediatric catheters may become occluded\(^1\)

Occlusions occur in up to 36% of CVADs within 2 years of placement\(^1\)
- Occlusion is the most common noninfectious complication in the long-term use of CVADs\(^2\)
- May occur soon after insertion of a device or develop at any time\(^10\)

Causes of catheter occlusions*\(^\)
- About 58% of catheter occlusions are thrombotic, resulting from the formation of a thrombus within, surrounding, or at the tip of the catheter\(^10,11\)
- About 42% of catheter occlusions are due to nonthrombotic causes, including precipitates, malpositioning, mechanical obstructions, and other factors\(^10,11\)

Nonthrombotic catheter occlusions

Mechanical occlusions\(^11\)
- Mechanical occlusions may result from malposition during insertion and use, or catheter migration
- Factors influencing the incidence of malposition include an increase in intrathoracic pressure from coughing, sneezing, or vomiting; arm movements; forceful flushing of the catheter; and thrombus formation

Precipitates\(^11\)
- Precipitates can form as a result of drug crystallization, drug-drug incompatibilities, or drug-solution incompatibilities
- Drug precipitates in the catheter may occur in conjunction with thrombus formation and should always be considered during assessment of an occlusion, since this may have implications for how the occlusion should be managed

Lipid residue\(^11\)
- Lipid residue can accumulate in central venous catheters, often following the administration of lipid-containing, three-in-one total parenteral nutrition admixtures or drugs with oleaginous vehicles

Salvaging catheters with nonthrombotic occlusions\(^11\)
- In many instances, mechanical problems, such as kinked tubing or clogged in-line filters, can be identified and corrected
- Possible interventions to reposition catheters include patient positioning, rapid flushing of the catheter guidewire catheter exchange, fluoroscopic catheter guidance, or partial catheter withdrawal
- Catheters occluded by calcium-phosphate precipitates can be treated with 0.1 N hydrochloric acid
- Sodium bicarbonate (1 mEq/mL) is used for substances known to dissolve in an alkaline environment
- Lipid occlusions have been treated with ethanol (70%) or sodium hydroxide (0.1 mmol/mL)
- The use of incompatible drugs or solutions should be avoided

"Catheter occlusions are categorized as thrombotic or nonthrombotic, and an accurate diagnosis of the type of occlusion is essential for appropriate treatment."\(^1\)
AVA Best Practice Guidelines in the Care and Maintenance of Pediatric Central Venous Catheters, 2015, page 12

*Data in this section derived from a study of 200 dysfunctional catheters in 172 adult patients.
When introduced into the body, all catheters begin to accumulate fibrin
This is the body’s natural attempt to protect itself against a foreign body. The fibrin starts to form a layer around the outside of the catheter within minutes of insertion, beginning at either the line entry site or where the tip contacts the vein.\(^{6,12}\)

**Fibrin tail, or flap\(^{6,13}\)**
- Extends from the catheter tip but is drawn inward, blocking the opening of the catheter lumen on aspiration attempts
- Results in an inability to infuse fluids but inability to withdraw blood

**Intraluminal thrombus\(^{13}\)**
- Occurs when blood refluxes inside the catheter lumen
- Common causes of reflux include coughing, inadequate flushing after blood draws or after checking for blood return, or improper use of flush syringes

**Mural thrombus\(^3,6,13\)**
- Forms where the catheter touches or “rubs” the vein wall
- Common sites are the entry site, anywhere along the catheter path, and the catheter tip

**Fibrin sheath\(^6,13\)**
- Forms when fibrin adheres to the external catheter surface, often beginning at the entry site, and may encase all or part of the catheter like a sock
- May completely cover the opening of the catheter tip

**Thrombotic catheter occlusions**

**Catheter occlusions can be partial or complete\(^9\)**

- **Partial occlusion**: ability to infuse but not withdraw fluids, or the presence of sluggish flow*  
- **Complete occlusion**: inability to infuse or aspirate

**Partial occlusion**

- Fibrin tail allowing infusion
- Beginning to flap back with start of withdrawal

**Complete occlusion**

- Fibrin sheath encases a completely occluded catheter

**Aspirating for positive blood return may reveal a partial occlusion**

- Flushing the line is not enough—you must be able to withdraw blood to rule out a partial occlusion before administering critical therapies.\(^7\)

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\*One quantitative measure for sluggish flow is a blood return of less than 3 mL in 3 seconds, as recommended by the Oncology Nursing Advisory Board.\(^{13}\)
Recognizing signs of CVAD occlusion

A catheter is dysfunctional

- When there is an inability to freely flush or obtain a brisk blood return

Signs of a CVAD occlusion include

- Inability to aspirate or infuse through the CVAD
- A change in the ability to flush or aspirate
- Infiltration/extravasation or swelling/leaking at the infusion site
- Frequent pump occlusion alarms

A CVAD that exhibits any of these signs requires further assessment and possible treatment.

CVADs should be flushed

- Before and after medication administration
- Before and after blood sampling
- After an infusion has been discontinued
- When a catheter is not in use and is locked

"With the smaller catheter sizes, lower infusion rates, and significantly smaller lumen volumes in pediatric patients, the risk of occlusion is higher [than in adults]."\(^1\)

AVA Best Practice Guidelines in the Care and Maintenance of Pediatric Central Venous Catheters, 2015, page 12

Recommended routine assessment of catheter patency in pediatric patients

“Prior to administering an infusate or solution, the CVC should be assessed for patency. This includes flushing and aspirating the lumen of the CVC for a brisk blood return for 3F [3 French] or larger CVCs.”\(^1\)

AVA Best Practice Guidelines in the Care and Maintenance of Pediatric Central Venous Catheters, 2015, page 16

Prior to the administration of any medications or solutions, the nurse should always

- For 3F or larger CVCs, aspirate for a positive blood return that is the color and consistency of whole blood
- Check for other indications of an occlusion
- Attempt to flush to determine resistance, flushing with an adequate volume of saline or appropriate solution
- Palpate the insertion site to determine tenderness
- Assess the patient for any pain or discomfort

Documentation of CVAD patency is a clinical practice standard and should include

- Device patency
- Absence of signs and symptoms of complications
- Lack of resistance when flushing
- Presence of a blood return upon aspiration

*CVC=central venous catheter.

*Data compiled from studies in JAMA Pediatrics and Journal of Vascular Interventional Radiology.*
**Recommended algorithm for assessing and treating occluded catheters**

- **Sluggish flow or inability to withdraw blood or infuse fluid through the catheter**
  - **Flow restored**: Check for presence of nonthrombotic obstruction
  - **Obstruction remains**: Suspect thrombotic occlusion
  - **Function restored**: Instill appropriate dose of Cathflo Activase (alteplase) based on patient weight
  - **Obstruction remains**: Repeat Cathflo dose
  - **Function restored**: Consult with medical team to consider alternative etiologies and additional management strategies

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**Indication**

Cathflo Activase (alteplase) is indicated for the restoration of function to central venous access devices as assessed by the ability to withdraw blood.

**Important Safety Information**

**Contraindications**

Cathflo Activase should not be administered to patients with known hypersensitivity to alteplase or any component of the formulation.

**Precautions**

**General**

Certain causes of catheter dysfunction should be considered before treatment with Cathflo Activase (e.g., catheter malposition, mechanical failure, constriction by a suture and lipid deposits or drug precipitates within the catheter lumen). These types of conditions should be considered before treatment with Cathflo Activase.

Excessive pressure should be avoided when Cathflo Activase is instilled into the catheter. Such force could cause rupture of the catheter or expulsion of the clot into the circulation.

**Bleeding**

The most frequent adverse reaction associated with all thrombolytics in all approved indications is bleeding. Cathflo Activase has not been studied in patients known to be at risk for bleeding events that may be associated with the use of thrombolytics. Caution should be exercised with patients who have any condition for which bleeding constitutes a significant hazard.

Should serious bleeding in a critical location (e.g., intracranial, gastrointestinal, retroperitoneal, pericardial) occur, treatment with Cathflo Activase should be stopped and the drug should be withdrawn from the catheter.

**Infections**

Cathflo Activase should be used with caution in the presence of known or suspected infection in the catheter. Using Cathflo Activase in patients with infected catheters may release a localized infection into the systemic circulation. As with all catheterization procedures, care should be used to maintain aseptic technique.

Please see select Important Safety Information throughout and the accompanying full Prescribing Information.

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**Cathflo is the standard of care for treatment of thrombocytically occluded catheters**

Cathflo is the only FDA-approved thrombolytic agent for the restoration of function to CVADs as assessed by the ability to withdraw blood

Cathflo is the only thrombolytic recommended by clinical practice standards

- Infusion Nurses Society (INS)
- Association for Vascular Access (AVA)
- American Association of Critical Care Nurses (AACN)
- Oncology Nursing Society (ONS)

**Cathflo—a fibrin-specific MOA**

The fibrin-specific mechanism of action addresses the root cause of thrombotic occlusions.

Cathflo binds to fibrin in the thrombus, converting entrapped plasminogen to plasmin, initiating local fibrinolysis.

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**Important Safety Information (cont’d)**

**Hypersensitivity**

Hypersensitivity, including urticaria, angioedema and anaphylaxis, has been reported in association with use of Cathflo Activase. Monitor patients treated with Cathflo Activase for signs of hypersensitivity and treat appropriately if necessary.

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*The clinical significance of fibrin specificity is unknown.*
**Cathflo Activase (alteplase) safety and efficacy profile in pediatric patients**

**Cathflo Pediatric Study (CAPS)**

**CAPS (N=310): Serious adverse events**

<table>
<thead>
<tr>
<th>Event</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catheter-related complications</td>
<td>1.3%*</td>
</tr>
<tr>
<td>Sepsis</td>
<td>1.0%</td>
</tr>
<tr>
<td>Fever</td>
<td>&lt;1.0%</td>
</tr>
<tr>
<td>Intracranial hemorrhage</td>
<td>0.0%</td>
</tr>
<tr>
<td>Major hemorrhage</td>
<td>0.0%</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>0.0%</td>
</tr>
<tr>
<td>Embolic event</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

Adapted from Blaney M, et al. *At least 1 due to catheter rupture.

- Largest study of thrombolytic therapy in pediatric patients
- Designed to evaluate the safety profile of Cathflo in 310 pediatric patients between the ages of 2 weeks and 17 years
  - 55 patients <2 years of age
  - The smallest patient weighed 2.2 kg
- Cathflo is not expected to reach pharmacologic levels in systemic circulation
- No reports of intracranial hemorrhage or embolic events with Cathflo in clinical trials

CAPS was an open-label, single-arm trial that evaluated the safety of Cathflo in 310 patients between the ages of 2 weeks and 17 years. Cathflo was evaluated in a maximum of 2 doses at ≤2 mg per dose. The primary objective was to evaluate safety, as measured by the incidence of intracranial hemorrhage (ICH). Secondary objectives included assessing restoration rates at 30 minutes and at 120 minutes, and serious adverse events within 48 hours.

Please see select Important Safety Information throughout and the accompanying full Prescribing Information.

**Cathflo is integral to evidence-based practices for treating thrombotically occluded catheters**

**CAPS (N=310): Clinical efficacy in pediatric patients**

- **Cumulative efficacy**
  - Cathflo restored function in 83% (257/310) of central lines after up to 2 doses using a 120-minute dwell time for each.

- **Rapid restoration**
  - Cathflo restored function within 30 minutes in 54% (166/310) of central lines.

- **First-dose efficacy**
  - Cathflo restored function after 1 dose in 75% (233/310) of central lines after up to 120 minutes of dwell time.

"If a thrombotic occlusion is suspected, the treatment is timely administration of alteplase (Cathflo Activase), a thrombolytic that is the only FDA-approved agent for treatment of dysfunctional catheters."

AVA Best Practice Guidelines in the Care and Maintenance of Pediatric Central Venous Catheters, 2015, page 14

**Important Safety Information (cont’d)**

**Drug Interactions and Drug/Laboratory Test Interactions**

The interaction of Cathflo Activase with other drugs has not been formally studied. Concomitant use of drugs affecting coagulation and/or platelet function has not been studied. Potential interactions between Cathflo Activase and laboratory tests have not been studied.

**Carcinogenesis, Mutagenesis, Impairment of Fertility**

Long-term studies in animals have not been performed to evaluate the carcinogenic potential or the effect on fertility.

**Pregnancy**

There are no adequate and well-controlled studies in pregnant women. Cathflo Activase should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
Dosing and administration of Cathflo Activase (alteplase)

Administration

After WASHING hands and applying gloves:

1. After reconstitution using 2.2 mL sterile water for injection and aseptic technique, performing hand hygiene, and donning gloves, INSPECT solution for foreign matter and discoloration.

2. INSTILL the appropriate dose of Cathflo into the occluded catheter using a 10-mL syringe (see dosing chart on the following page).

3. After 30 minutes of DWELL time, assess catheter function by attempting to aspirate blood. If the catheter is functional, go to step 5; if not functional, go to step 4.

4. ASSESS catheter function after a total of 120 minutes of dwell time by attempting to aspirate blood. If the catheter is functional, go to step 5; if catheter is still occluded, a second dose of equal amount may be instilled. Repeat steps 1 through 3.

5. If catheter function has been restored, ASPIRATE 4 mL to 5 mL of blood in patients ≥10 kg or 3 mL in patients <10 kg to remove Cathflo and residual clot. Then discard aspirate, and flush catheter with 0.9% Sodium Chloride, USP. Any unused solution should be discarded.

Important Safety Information (cont’d)

Adverse Reactions

In clinical trials, the most serious adverse events reported after treatment were sepsis, gastrointestinal bleeding, and venous thrombosis. You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at (888) 835-2655.

Please see select Important Safety Information throughout and the accompanying full Prescribing Information.

FDA-approved dosing with Cathflo

- Cathflo is available in a single-use, 2-mg vial and it is not recommended that it be compounded, frozen, or thawed.
- If catheter function is not restored at 120 minutes after 1 dose of Cathflo, a second dose may be instilled.*

*Clinical Practice.

Measure the internal lumen volume to determine the Cathflo dose for pediatric patients

Device

<table>
<thead>
<tr>
<th>Device name</th>
<th>Device ranges</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripherally inserted central venous catheter (PICC)</td>
<td>Device priming volume ranges from 0.06 to 0.6 mL. Check manufacturer guidelines.</td>
</tr>
<tr>
<td>Tunneled and nontunneled</td>
<td>Device priming volume ranges from 0.12 to 1.3 mL. Check manufacturer guidelines.</td>
</tr>
<tr>
<td>Implanted port</td>
<td>Device priming volume ranges from 0.8 to 2 mL. Check manufacturer guidelines.</td>
</tr>
</tbody>
</table>

References:

4. Miller VL. Appropriate CVAD site selection should be based on anatomy and patient needs.
5. Refer to the Appropriate CVAD site selection should be based on anatomy and patient needs.
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*Studies only evaluated up to two 2-mg doses.
Is your hospital delivering the standard of care for patients with central lines?

- Utilize the highest level of evidence available for central line care and maintenance
- Include patency checks in central line care protocols and maintenance bundle
- Develop a culture of accountability using CVAD quality metrics and EHR documentation

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**Please see accompanying full Prescribing Information for additional Important Safety Information.**

To learn more about the management of thrombocytically occluded catheters, please visit www.cathflo.com or call Genentech Customer Service at 1-800-551-2231 to locate your local Genentech clinical specialist.

www.cathflo.com

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