A thrombus is defined as an accumulation of platelets, fibrin, and other clotting factors that lodges in an artery or a vein and occludes blood flow. Blood coagulation occurs via both intrinsic and extrinsic pathways (Figure 1). Four conditions can cause a thrombus: venous stasis, vessel damage or injury, inflammation, and hypercoagulability. Deep venous thrombosis causes pain and swelling in the affected extremity, and the thrombus can dislodge and can lead to a potentially fatal pulmonary embolism. Arterial occlusion can lead to pain and ischemia and potentially to amputation because of the lack of arterial blood flow distal to the occlusion.

Because of the seriousness of peripheral vascular occlusions, prompt treatment is critical. Traditionally, patients with deep venous thrombosis have been treated with intravenous infusions of heparin and then with oral warfarin after discharge from the hospital. Patients with arterial occlusions have undergone surgery for removal of the clot or been treated with the thrombolytic agents urokinase or streptokinase. The Food and Drug Administration (FDA) recently rescinded approval for use of urokinase in the United States because of difficulties in manufacturing the drug. Consequently, streptokinase is now the only thrombolytic agent approved by the FDA for treatment of peripheral vascular occlusion. However, because of the low efficacy, poor predictability, and potential for hemorrhagic complications of streptokinase, physicians use other thrombolytic agents such as alteplase and reteplase to treat peripheral vascular occlusion.

The nursing literature provides little information about these medications. In this article, I review catheter-directed thrombolytic therapy with reteplase (Retavase) for peripheral arterial and venous occlusions. Brief descriptions of alteplase and streptokinase are also provided.

The traditional agents used for arterial and venous thrombolysis are streptokinase, urokinase, and alteplase; the primary drug of choice is urokinase. In 1999, as mentioned earlier, the FDA rescinded approval of urokinase because the screening for viral vectors was inadequate.

Streptokinase is currently the only FDA-approved thrombolytic agent for treatment of peripheral vascular occlusion. Streptokinase is a plasminogen activator; cleavage (or activation) of plasminogen

<table>
<thead>
<tr>
<th>Intrinsic</th>
<th>Extrinsic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activation of factor XII</td>
<td>Factor III released</td>
</tr>
<tr>
<td>Factor XI</td>
<td>Factor VII</td>
</tr>
<tr>
<td>Factor IX</td>
<td>Factor V</td>
</tr>
<tr>
<td>Factors V and VIII</td>
<td>Factor X</td>
</tr>
<tr>
<td>X</td>
<td>Prothrombin</td>
</tr>
<tr>
<td>Prothrombin</td>
<td>Fibrinogen</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>Fibrin</td>
</tr>
<tr>
<td>Fibrin</td>
<td>Clot formation</td>
</tr>
</tbody>
</table>

Figure 1 Blood coagulation pathways.
by the enzyme produces plasmin, the enzyme needed for clot lysis. Because the predictability of lysis with streptokinase is low, and the drug tends to cause substantial bleeding and is less effective than are other thrombolytic agents, it is not often used to treat peripheral vascular occlusion. The half-life of streptokinase is 25 minutes, and its lytic action can last 6 hours.

Alteplase is a thrombolytic agent currently being used to treat peripheral vascular occlusion; however, it is not FDA approved. Success has been reported for use of alteplase for catheter-directed therapy, but optimal dosing is unknown. Alteplase is a weak plasminogen activator when fibrin is absent. However, with increased doses of alteplase, plasmin is formed from the circulating plasminogen. The increased levels of plasmin lead to fibrin breakdown and, therefore, clot lysis. The half-life of alteplase is 4 to 6 minutes, with elimination in approximately 35 minutes.

Retaplace has been used to treat coronary thrombosis for several years, and its use in the treatment of peripheral vascular occlusion has recently been investigated. Laird et al studied 2 patients with occlusions of peripheral arteries. After catheter-directed thrombolytic therapy with retaplace, 1 patient had complete thrombolysis (full clot lysis), and the other patient had partial thrombolysis (partial clot lysis).

Comerota et al compared the health-related quality of life between patients who received catheter-directed thrombolytic therapy and patients who received heparin therapy to treat iliofemoral deep venous thrombosis. The patients who received catheter-directed thrombolytic therapy had a better quality of life than did the patients who received heparin therapy.

Davidian et al studied 15 patients with acute peripheral arterial occlusions. Catheter-directed thrombolytic therapy with retaplace had a 73% success rate for thrombolysis. One patient died of a retroperitoneal hemorrhage. Ouriel et al studied 37 patients with venous and arterial peripheral occlusions. Catheter-directed thrombolytic therapy with retaplace resulted in complete thrombolysis in 33 patients (89%) and partial thrombolysis in 4 patients (11%). Patients in that study experienced no adverse effects.

The studies just cited included a total of 54 patients with peripheral vascular occlusions. Total lysis (success) occurred in 83% of the patients, and the complication rate was 11%. All of these studies were limited by the small sample sizes. Further medical and pharmacotherapeutic research must be done to determine the optimal dosage of retaplace, the optimal duration of retaplace infusion, and whether concurrent peripheral infusion of heparin is necessary. None of the published studies described nursing interventions or actions for catheter-directed thrombolytic therapy with retaplace (Table 1).

Retaplace is a plasminogen activator that generates plasmin. Plasmin in turn degrades the fibrin matrix of the thrombus. Unlike other thrombolytic agents, which bind to the fibrin matrix and accumulate on the surface of the thrombus, retaplace penetrates the thrombus and destroys the fibrin matrix, steps that enhance lytic action. The half-life of retaplace is 13 to 16 minutes, with a terminal half-life of approximately 170 minutes.

Retaplace infusions are given at a rate of 0.5 to 2 U/h, for a mean duration of 21 hours. The infusion is given via a catheter that is inserted in the extremity opposite the thrombus during angiographic studies. This technique is called catheter-directed thrombolytic therapy. The catheter is threaded through the opposite extremity to the affected extremity (eg, if the thrombus is in the right popliteal artery, the catheter is threaded through the left femoral artery and is positioned directly above the thrombus). With this placement, the thrombolytic agent can be injected directly into the thrombus, facilitating lysis of the clot. With the catheter-directed approach, the systemic concentration of the thrombolytic agent and the dosage required are decreased, thus decreasing hemorrhagic complications.

The catheter may be a single-lumen or a coaxial (double-lumen) system. The dose of retaplace depends on the type of catheter used. With a single-lumen...
Table 1  Summary of published studies related to use of reteplase for peripheral vascular occlusions

<table>
<thead>
<tr>
<th>Reference/Year</th>
<th>Purpose</th>
<th>Sample</th>
<th>Variables</th>
<th>Findings/Conclusion</th>
</tr>
</thead>
</table>
| Laird et al, 1999<sup>10</sup> | To explore the use of CDTT with reteplase in peripheral arterial occlusions | 2 patients with arterial occlusions  
Case 1: 67-year-old man  
Case 2: 57-year-old man | Case 1: 2-unit loading dose given; infusion rate: reteplase at 0.8 to 1.0 U/h, heparin at 400 U/h  
Case 2: 2-unit loading dose given; infusion rate: reteplase at 1 U/h, heparin at 400 U/h | Case 1: total of 20 units infused, complete lysis occurred, no bleeding complication, discharged home on warfarin therapy  
Case 2: total of 40 units infused, mild hematoma at insertion site, partial lysis occurred with subsequent balloon dilatation |
| Comerota et al, 2000<sup>16</sup> | To determine if CDTT improves health-related quality of life in patients with deep venous thromboses more than traditional heparin therapy does | 98 patients, 68 treated with CDTT and 30 treated with heparin  
CDTT group: 24 men, 44 women; mean age, 53 years  
Heparin group: 14 men, 16 women; mean age, 61 years | Health-related quality-of-life questionnaire, 80 items, self-administered  
Diagnosis of deep venous thrombosis within past 6 months | Patients who received CDTT had a better quality of life  
Patients with CDTT reported better physical functioning; less stigma, less health distress, and fewer postthrombotic signs and symptoms |
| Davidian et al, 2000<sup>9</sup> | To determine efficacy of reteplase in CDTT for lower extremity occlusions | 15 patients with acute ischemia of lower extremities  
11 men, 4 women; mean age, 65.4 years  
2 diabetics, 8 tobacco users | 6 native arterial occlusions  
9 synthetic graft or venous bypass occlusions  
Infusion rate, 0.5-1.0 U/h  
6 received peripheral heparin, 9 did not | Thrombolysis occurred in 11 patients (73%)  
Mean length of infusion, 20.8 hours  
Mean dose of reteplase, 17.7 units  
One death due to retroperitoneal hemorrhage  
One patient with hemoptysis, bypass the next day |
| Ouriel et al, 2000<sup>13</sup> | To determine usefulness of CDTT with reteplase in peripheral arterial and venous occlusions | 26 patients with arterial occlusions  
11 patients with venous occlusions  
Arterial group: mean age, 64.5 years; 50% female, 50% male  
Venous group: mean age, 47.9 years; 75% female, 25% male | Dose 0.5-2.0 U/h  
Loading dose in 17 patients  
Therapeutic dose of heparin in 11 patients, subtherapeutic dose in 14 patients  
Arterial group: 16 native arterial occlusions, 10 prosthetic bypass graft occlusions  
Venous group: 7 iliac segment and femoropopliteal occlusions, 4 brachiocephalic occlusions | Arterial group: mean duration of infusion, 19.3 hours; complete thrombolysis in 23 patients, 3 patients with partial thrombolysis, reocclusion in 2 patients; increased risk of bleeding with loading dose; therapeutic heparin increased thrombolysis, no deaths occurred  
Venous group: mean duration of infusion, 31.1 hours; thrombolysis in 10 patients, 1 patient without lysis; minor bleeding occurred in 2 patients, 1 with decreased hematocrit; no pulmonary embolism occurred, no intracranial hemorrhage, no deaths |

CDTT indicates catheter-directed thrombolytic therapy.
catheter, a full dose of reteplase is infused, whereas with the coaxial system, the dose is split equally between the lumens. A continuous infusion of a low dose or a full dose of heparin may also be used during the reteplase infusion. Many studies have shown that use of heparin facilitates clot lysis and continued lysis after the reteplase infusion is completed. The cost of a 20-unit vial of reteplase is approximately $2150. Contraindications to the use of reteplase are listed in Table 2.

NURSING CONSIDERATIONS

Patients undergoing catheter-directed thrombolytic therapy...
with reteplase are admitted to the intensive care unit for monitoring for hemorrhagic complications. A nurse begins the continuous infusion of reteplase via the catheter immediately after the patient is admitted. A bolus of heparin is given, and a peripheral intravenous infusion of heparin is started.

Because intracranial hemorrhage is a major complication of thrombolytic therapy (with an overall risk of 1%), a neurological examination must be done every hour. Maintaining a blood pressure less than 180/110 mm Hg helps prevent intracranial hemorrhage. Retroperitoneal hemorrhage is also a complication that can lead to hypotension and/or death (with an overall risk of 0.3%). A physician should be notified immediately if the patient complains of severe back pain.

Heparin and reteplase are not compatible and thus should not be administered via the same tubing. Currently, neither the optimal duration nor the optimal dose of reteplase in catheter-directed therapy is known. Table 3 indicates nursing interventions for many of the potential adverse reactions that can occur during catheter-directed thrombolytic therapy with reteplase. Figure 3 is an example of a hospital’s standard order set for patients undergoing catheter-directed thrombolytic therapy with reteplase.

**SUMMARY**

Several studies since 1998 have shown the efficacy of catheter-directed thrombolytic therapy with reteplase. Reteplase is a plasminogen activator that penetrates the thrombus and causes lysis. This catheter-directed approach has been used to treat both arterial and venous occlusions, with a success rate of 72% to 88%. The most serious complication associated with thrombolytic therapy is intracranial hemorrhage. Patients should be admitted to the intensive care unit for monitoring of neurological status, vital signs, laboratory values (hematocrit, hemoglobin level, activated partial thromboplastin time, and fibrinogen concentration), and bleeding or oozing at puncture sites. Staff nurses in the intensive care unit must be aware of this important thrombolytic therapy, its indications, and its implications for nursing interventions.

### Table 2 Contraindications for thrombolytic therapy with reteplase

<table>
<thead>
<tr>
<th>Contraindication</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolutely no use of reteplase</td>
<td>Increased risk of hemorrhage</td>
</tr>
<tr>
<td>Aneurysm, arteriovenous malformation, bleeding, cerebrovascular disease, coagulopathy, head trauma, increased intracranial pressure, intracranial bleeding, intracranial hypertension, intracranial mass, spinal anesthesia, stroke, or surgery</td>
<td></td>
</tr>
<tr>
<td>Cautious use of reteplase</td>
<td>Increased risk of hemorrhage</td>
</tr>
<tr>
<td>Anticoagulant therapy, brain tumor, cardiac arrhythmia, cardiac disease, diabetic retinopathy, advanced age, endocarditis, gastrointestinal bleeding, hypertension, infection, intramuscular injections, mitral stenosis, recent obstetric delivery, organ biopsy, peptic ulcer disease, pericarditis, thrombophlebitis, trauma, and venipuncture</td>
<td></td>
</tr>
<tr>
<td>Hepatic disease, renal disease, and renal failure</td>
<td>Reteplase primarily cleared by liver and kidneys</td>
</tr>
<tr>
<td>Atrial fibrillation and atrial flutter</td>
<td>Risk of cerebral embolism</td>
</tr>
<tr>
<td>Young age (children)</td>
<td>Safety not established</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>FDA pregnancy category “C”. 19</td>
</tr>
<tr>
<td>Breast feeding</td>
<td>Unknown if reteplase excreted in breast milk</td>
</tr>
</tbody>
</table>

**References**

Table 3  Nursing considerations for patients receiving catheter-directed thrombolytic therapy with reteplase

<table>
<thead>
<tr>
<th>Potential adverse reaction</th>
<th>Manifested by</th>
<th>Nursing action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracranial hemorrhage</td>
<td>Change in mental status or level of consciousness</td>
<td>Do neurological examination every hour</td>
</tr>
<tr>
<td></td>
<td>Headache</td>
<td>Monitor vital signs frequently</td>
</tr>
<tr>
<td>Retroperitoneal hemorrhage</td>
<td>Severe back pain</td>
<td>Notify physician immediately if back pain occurs</td>
</tr>
<tr>
<td>Genitourinary hemorrhage</td>
<td>Hematuria</td>
<td>Insert a Foley catheter to monitor urine output (optional)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Notify physician immediately if hematuria noted</td>
</tr>
<tr>
<td>Gastrointestinal hemorrhage</td>
<td>Nausea and vomiting</td>
<td>Provide clear liquid diet</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Famotidine 20 mg intravenously every 12 hours</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Notify physician immediately if gastrointestinal hemorrhage noted</td>
</tr>
<tr>
<td>Hematoma at puncture sites</td>
<td>Hematoma at insertion site of catheter in groin</td>
<td>Apply pressure to all puncture sites</td>
</tr>
<tr>
<td></td>
<td>Hematoma at venous puncture sites</td>
<td>Do not give intramuscular injections</td>
</tr>
<tr>
<td></td>
<td>Excessive bleeding at insertion site of catheter</td>
<td>Insert heparin lock to obtain all blood samples for laboratory tests</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Monitor excess bleeding at puncture sites; notify physician immediately if bleeding does not cease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Log-roll patient to avoid excess movement of catheter in groin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Keep extremity with catheter completely straight to avoid excess bleeding at insertion site</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>Severe shortness of breath</td>
<td>Monitor respiratory rate</td>
</tr>
<tr>
<td></td>
<td>Chest pain</td>
<td>Maintain continuous pulse oximetry</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Notify physician immediately if change in respiratory status occurs or shortness of breath develops</td>
</tr>
</tbody>
</table>

1. Patient to be admitted to ICU for close observation post radiology.

2. Vital signs with distal pulse check q 15 minutes x 2, then q 1 hour. Verify pulse check with a doppler. Monitor for hypertension as a predisposing factor to intracranial hemorrhage.

3. Catheter-directed thrombolytic therapy orders—mark which one is wanted.
   - Katzen wire—Double lumen.
   - Catheter A infuse retavase 5U/250cc NS at 0.5U/hr or 25cc/hr x 10 hours.
   - Single lumen catheter—infuse retavase 10U/250cc NS at 1U/hr or 25cc/hr x 10 hours.
   - Side ports of catheters called introducers—infuse NS at 25cc/hr

4. Continuous Heparin infusion—peripheral
   - Weight based protocol: Patient’s weight in KG ____________
   - Bag concentration of 25,000U/250cc of D 5W
   - Heparin bolus ____________ given at ____________
   - Heparin infusion at 1000U/hr or 10cc/hr.

   aPTT level | Rebolus | Hold drip | Infusion rate | Repeat aPTT
---|---|---|---|---
35-44 seconds | 50U/kg | Do not hold drip | Increase drip by 3U/kg/hr | 3 hours after change drip rate
45-54 seconds | 30U/kg | Do not hold drip | Increase drip by 2U/kg/hr | 3 hours after change drip rate
55-70 seconds | 0U/kg | Do not hold drip | No Change in drip rate | 3 hours after last draw
71-90 seconds | 0U/kg | Do not hold drip | Decrease drip by 2U/kg/hr | 3 hours after change drip rate
> 91 seconds | 0U/kg | Call physician for additional orders | To be determined by physician | 3 hours after change drip rate

5. Labs to be drawn: aPTT, CBC, BUN/creatinine 3 hours after initial heparin bolus given.
   - aPTT and fibrinogen to be drawn every 4 hours while patient is receiving retavase and peripheral heparin infusions.
   - CBC, aPTT, BMP to be drawn in the a.m.
   - Call physician for Hgb < 9.0 g/dl, K+ > 5.5 mEq/L, fibrinogen < 100 mg/dl, aPTT > 90 or < 40 seconds.

6. Insert a venacath into the arm opposite the heparin infusion. This venacath is to be used for all blood draws only. Flush with normal saline only.

7. Insert a Foley catheter.


9. Accurate intake and output.


11. When NPO, start a peripheral IV infusion of D 51/2NS at 50cc/hr.

12. When retavase infusion is complete (after 10 hours), run heparin 1000U/500cc of D 5W at 25cc/hr via all ports of the catheter. Flush all ports with 30cc of normal saline prior to hanging the heparin. Heparin and retavase are not compatible in the same tubing.

13. Continue to infuse the peripheral heparin.

14. Medications:
   - Morphine 2-6mg q 3 hours IV as needed for pain (avoid IM injections).
   - Sedation ____________.
   - Pepcid 20mg IV q 12 hours.

15. Notify physician immediately for any signs of:
   - Bleeding, redness, or edema at any puncture site.
   - Complaints of headache, change in mental status, confusion, (intracranial hemorrhage), backache (retroperitoneal hemorrhage), nausea or vomiting (gastrointestinal hemorrhage), hematuria (genitourinary hemorrhage), respiratory difficulty (pulmonary embolism—especially if patient has a DVT).

**Figure 3** Sample thrombolytic orders

*Heparin titration based on aPTT is approved by St. John West Shore Hospital.

aPTT indicates activated partial thromboplastin time; BMP, basic metabolic panel; BUN, blood (serum) urea nitrogen; CBC, complete blood cell count; D5W, 5% dextrose in water; DVT, deep venous thrombosis; Hgb, hemoglobin; HOB, head of bed; ICU, intensive care unit, IM, intramuscular; IV, intravenous; NPO, nothing by mouth; NS, normal saline; q, every.

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Reteplase: Nursing Implications for Catheter-Directed Thrombolytic Therapy for Peripheral Vascular Occlusions
Michelle E. Bussard

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