

Mount Auburn Hospital  
Department of Emergency Medicine

**Chest Pain Orders**

IMPRINT PATIENT DATA

Time patient arrived:

Time ECG performed:

Target is ECG completion within ten minutes.  
Use synchronized clock(s) for all times.

**Physician Triage**

Based on initial ECG (and clinical information), check one of the following initial patient categories:

- Routine risk       Low risk       High risk (possible  catheterization  fibrinolysis)

**Standing Orders**

Date / Time

Nurse initials

- Oxygen saturation, room air.  
 Oxygen, two to four liters by nasal cannula.  
 Four 81 mg chewable aspirin       Contraindication \_\_\_\_\_  
 If aspirin allergy, give clopidogrel 75 mg orally (prior aspirin today is not a contraindication)  
Intravenous access and blood for tests checked:  hold tubes       PT/PTT       CBC/basic metabolic panel  
 cardiac enzymes       digoxin level       other \_\_\_\_\_  
 Nitroglycerin sublingual, 0.4 mg q5min up to 3 as needed. When pain relieved, apply paste as directed below.  
 Nitroglycerin paste       half       one       one and one-half       two inches to chest wall  
 Acetaminophen, 1 g orally, as needed for headache.  
 Radiograph, portable upright chest (history: chest pain; reason: dissection, pneumothorax, pneumonia, heart failure)  
 Repeat ECG after interventions above.

**Optional**

Fibrinolysis

Date / Time

Nurse initials

- Streptokinase infusion by protocol  
 Recombinant tPA by front-load protocol  
 TNK-tPA by single-dose protocol

Time fibrinolytic therapy is begun:

Target is start of fibrinolytic therapy, if indicated,  
within 30 minutes of arrival.

Nitroglycerin IV

Date / Time

Nurse initials

Begin drip at:  10       20       40       80 mcg/minute

Titrate to eliminate chest pain, keeping systolic blood pressure >90 mmHg

Beta-blockade

Date / Time

Nurse initials

- Contraindications?  none       CHF present       LVEF known <35%  
 SPB <100       heart block       pulse <50       COPD or asthma history  
If none, give metoprolol, 15 mg IV, in 5 mg increments q5min. Stop if target pulse reached (50 to 60 bpm).  
After final IV dose, give 50 mg metoprolol orally.

Antithrombotics

Date / Time

Nurse initials

- Heparin by weight-based protocol (80 U/kg IV bolus, then 18 U/kg/hr). Bolus  Infusion   
 Dalteparin by weight-based protocol (120 IU/kg SC q12h, max 10,000 IU). Dose

Physician Signature: \_\_\_\_\_

RN Signature: \_\_\_\_\_

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**MYOCARDIAL INFARCTION**

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**General guidelines**

Patients arriving with signs or symptoms suspicious for myocardial infarction should be moved immediately to a patient care area. Such symptoms include not only chest pain but syncope, dyspnea, nausea, diaphoresis, upper abdominal pain, and upper body pain not clearly musculoskeletal in origin. The triage interview should be conducted together with immediate electrocardiogram (ECG) in a manner which does not delay rapid diagnosis of acute myocardial infarction (AMI). ECG is the *only* method that such a diagnosis can be made early in the course of AMI. Thus, if beds are short, any available space should be used to obtain an ECG. Ideally, time of patient presentation to ECG should be less than ten minutes. The ECG should be shown to an emergency physician in order to immediately determine eligibility for advanced cardiac salvage techniques including fibrinolysis and angioplasty. Once seen, the emergency physician should initial and time the ECG, noting the presence or absence of changes indicative of acute myocardial infarction.

For all patients, the standardized emergency chest pain order sheet should be brought to the emergency physician at the same time as the ECG, so treatment and further diagnostic tests can be quickly begun. Emergency nurses should be familiar with the orders on this sheet, and should initiate the treatment and diagnostic evaluation at their discretion. For example, all patients with suspected angina or myocardial ischemic equivalents should be immediately placed on a cardiac monitor, given supplemental oxygen following room air pulse oximetry, have intravenous access placed with blood tubes drawn, and have a portable chest radiograph performed.

Except in rare circumstances, such patients should also have aspirin administered, even if on warfarin or aspirin already. Aspirin, a relatively benign treatment, has been demonstrated to reduce death from acute MI by 23 percent when used in a dose of 160 to 325 mg daily. In contrast, fibrinolysis, a much riskier treatment, reduces death by 25 percent.<sup>1</sup> The only patients who should have aspirin withheld are those with severe concurrent bleeding or who have had anaphylaxis to aspirin in the past. Patients with anaphylaxis to aspirin may receive ticlopidine (250 mg twice daily), which has been demonstrated to reduce conversion from unstable angina to infarction by 46 percent.<sup>2</sup>

Nitrate use, due to inconclusive studies of mortality benefit, is ordered at the discretion of the emergency physician. Use of nitrates is contraindicated in right ventricular infarction and in patients taking sildenafil (Viagra)

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<sup>1</sup> ISIS-2 Collaborative Group: Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction. *Lancet* 1988;2:349.

<sup>2</sup> Fuster V, Verstraete M: Hemostasis, thrombosis, fibrinolysis, and cardiovascular disease, in Braunwald E (ed), *Heart Disease: A Textbook of Cardiovascular Medicine*, vol 2. Philadelphia: Saunders, 1997:1809-1842.

due to associated case fatalities with this combination. The interval between last use of sildenafil and safe use of nitrates has not been determined.

These ECG criteria suggest AMI:

- Contiguous limb lead ST elevation  $\geq 1$  mm
- Contiguous precordial lead ST elevation  $\geq 2$  mm
- New left bundle branch block (LBBB) with anginal equivalent
- Old LBBB with anginal equivalent and either a deflection of the J point (and ST segment) in the direction of the major QRS complex or an elevation of the ST segment of more than 7 mm opposite the direction of the major QRS complex<sup>3</sup>
- Signs of posterior infarction (R>S in V1, ST depression in V1 and V2, V8 or V9 lead ST elevation  $\geq 1$  mm)

The following criteria are further helpful in determining cardiac ischemia:

- ECG differences on comparison with previous tracings
- ECG changes on right-sided and posterior tracings (V1<sub>R</sub>-V6<sub>R</sub>, V8, V9)
- ECG changes following emergency treatment

If AMI is suggested by the ECG, the patient should be immediately assessed for fibrinolysis or angioplasty. Angioplasty is usually only available weekdays during regular cardiology hours: 7 AM to 5 PM weekdays. Thus, the emergency physician may proceed directly to fibrinolysis if the patient presents after hours, although case-by-case consultation with cardiology is acceptable to determine angioplasty after-hours availability. In cases where angioplasty is considered, the cardiologist on-call for the interventional team, rather than the routine cardiology consultant, should be notified.

Angioplasty is strongly indicated in patients with AMI who have contraindications to fibrinolysis, who are in cardiogenic shock, who have large anterior infarctions, or who do not improve within an hour following fibrinolytic therapy.

**Contraindications to fibrinolysis<sup>2,4,5,6</sup>**

ABSOLUTE CONTRAINDICATION	Active internal bleeding CVA within 6 months Cranial or spinal surgery within 2 months Cerebral or spinal tumor or arteriovenous malformation Severe bleeding diathesis (moderate, such as von Willebrand's, acceptable) BP >200/120 not amenable to emergency department therapy Allergy to fibrinolytic agent
RELATIVE CONTRAINDICATION	Cerebrovascular disease Gastrointestinal or urologic bleeding within 10 days Significant surgery or trauma within 10 days, including puncture of noncompressible vessels BP >180/110 Suspected left heart thrombus (such as mitral stenosis with atrial fibrillation) Suspected aortic dissection or pericarditis Subacute bacterial endocarditis Known coagulation defect (including severe liver dysfunction) Pregnancy (Category C) Active hemorrhagic ophthalmic disease Septic thrombophlebitis or occluded arteriovenous cannula at infected site Warfarin use (manufacturer's recommendation, no data)

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<sup>3</sup> Fesmire FM: ECG diagnosis of acute myocardial infarction in the presence of left bundle-branch block in patients undergoing continuous ECG monitoring. *Ann Emerg Med* 1995;26:69-82.

<sup>4</sup> Aufderheide TP, Gibler WB: Acute ischemic coronary syndromes, in Rosen P, Barkin R (eds), *Emergency Medicine*, vol 2. St. Louis: Mosby, 1998:1700-1716.

<sup>5</sup> Fibrinolytic Therapy Trialists' Collaborative Group: Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomized trials of more than 1000 patients. *Lancet* 1994;343:311-322.

<sup>6</sup> BeDell LS (ed), *Physicians GenRx*. St. Louis: Mosby, 1997:II-72 and II-1907.

For tPA, age over 75 years, small infarctions, or MI onset >6 hours (no advantage over streptokinase)  
 For streptokinase, streptococcal infection or streptokinase use within 1 year

NO  
 CONTRAINDICATION

Angina between 6 and 12 hours  
 Stuttering angina between 12 and 24 hours  
 Hypotension and congestive heart failure  
 Simple diabetic retinopathy  
 Cardiopulmonary resuscitation  
 Previous myocardial infarction  
 Previous coronary artery bypass grafting  
 Menstruation  
 Concurrent heparin use

### Informed consent

Patients who are eligible to undergo fibrinolysis for myocardial infarction should consent for such therapy based on expected risks and benefits. Data from previous studies shows that the risk of death from acute myocardial infarction without treatment is approximately 1 patient in 8. This risk of death is reduced to approximately 1 in 15 patients with fibrinolysis, corresponding to an odds reduction of 39 to 51 percent.<sup>2</sup>

Four major risks are entailed with use of fibrinolysis: death, stroke, bleeding, and for SK, anaphylaxis. Risk of death from complications of fibrinolysis is much lower than the risk of death from untreated myocardial infarction, though exact numbers are impossible to extract from current studies due to ethical prohibitions of performing fibrinolysis on healthy patients. Total risk of stroke with tPA administered to MI patients is approximately 1 in 70. For SK, risk of stroke is approximately 1 in 100 patients. About half of such strokes are hemorrhagic, and not all result in death. Risk of significant (>250 ml blood loss) extracranial hemorrhage with either tPA or SK is approximately 1 in 20 patients, the most common being gastrointestinal and genitourinary sites. For SK, anaphylaxis occurs in less than 1 in 1,000 patients.

### Fibrinolytic administration guidelines

Speed is essential since infarction is irreversible and progresses with time. Efforts should be directed toward beginning therapy as rapidly as possible. The standardized order sheet for emergency chest pain patients has been developed to make the process of evaluation to administration of fibrinolytic therapy as efficient as possible. General guidelines are as follows:

- Blood pressures should be performed manually, due to excessive pressures generated by automatic cuffs which may lead to subcutaneous bleeding in patients receiving fibrinolytic agents.
- Patients who are eligible for fibrinolysis should have all vascular punctures minimized.
- Patients should have at least two 18 gauge or larger peripheral intravenous (IV) catheters placed prior to initiation of fibrinolytic therapy. Central venous access should be avoided unless absolutely necessary. If central access is needed, placement via the external jugular system is recommended, since this vessel is easily compressed should bleeding occur with fibrinolytic therapy. At least one cannula should be in the antecubital fossa, in order to allow rapid central circulation of life-saving medications should the patient experience cardiac arrest.
- Four IV catheters are ideal. (If twin-port peripheral catheters are available, two should be placed, allowing four ports for use.) One port or IV site should be reserved for the fibrinolytic agent alone, one for heparin and nitrates, one for intermittent medication administration, and one (a distal port or separate IV should be reserved for blood draws, in order to reduce recurrent venipunctures.
- Draw the following bloodwork: CBC, BMP, cardiac enzymes, PT, PTT, fibrinogen, and type and hold.

#### TPA ADMINISTRATION

- Reconstitute the tPA vial according to the manufacturer's instructions. The resulting concentration of tPA is 1 mg/mL. Gently swirl to mix. Shaking should be avoided. After spiking the bottle of reconstituted tPA, prime the tubing to the needle hub, being careful not to waste any of the fluid.

- Administer a bolus of tPA in the dose ordered by the emergency physician. A typical bolus is 15 mg regardless of patient weight. The bolus should be administered as rapidly as possible; if an infusion pump is used for this purpose, the bolus should be given in 60 seconds or less. This can be done by programming the infusion pump to deliver 15 mL at the initiation of the infusion using a rate of 900 mL/hour for 60 seconds.
- Administer the remaining two doses of tPA, determined from the weight-based nomogram, over 30 minutes and 60 minutes in sequence. Typical doses for these two doses are 50 mg and 35 mg and are based on a dosage of 0.75 mg/kg and 0.50 mg/kg, respectively.
- At the conclusion of the infusion, flush the infusion line with 50 mL of saline to ensure administration of the entire dose.

TPA WEIGHT-BASED NOMOGRAM

Patient's weight (kg)	Infusion rate first 30 min (mL/hour)	Infusion volume first 30 minutes (mL)	Infusion rate final 60 min (mL/hour)	Infusion volume final 60 min (mL)
30-32	45	23	15	15
33-34	50	25	16	16
35-36	52	26	18	18
37-39	56	28	18	18
40-42	60	30	20	20
43-44	64	32	22	22
45-46	68	34	22	22
47-49	70	35	24	24
50-52	75	38	25	25
53-54	80	40	26	26
55-56	82	41	28	28
57-59	86	43	28	28
60-62	90	45	30	30
63-64	94	47	32	32
65-66	98	49	32	32
67-69	100	50	34	34
>69	100	50	35	35

STREPTOKINASE ADMINISTRATION

- If ordered when appropriate, pretreat with diphenhydramine and hydrocortisone.
- Reconstitute the streptokinase 1.5 mU vial with 5 mL of normal saline. Gently swirl to ensure complete dissolution. Do not shake.
- Withdraw and discard 5 mL from a 50 mL bag of normal saline. Inject the contents of the streptokinase vial to give a final concentration of 1.5 mU in 50 mL saline.
- After spiking the container of streptokinase, prime the tubing to the needle hub, being careful not to waste any of the solution.
- Set the intravenous infusion pump to 50 mL/hour, and deliver the streptokinase solution over 1 hour.
- At the conclusion of the infusion, flush the infusion line with 50 mL of saline to ensure administration of the entire dose.

POST-FIBRINOLYSIS CARE

- Cardiac enzymes should be drawn every 6 hours for 24 hours.
- Serial PTTs should be checked every 6 hours.
- Serial ECGs should be performed at 0, 6, 12, and 24 hours post-infusion, and as needed.
- Patients should be closely monitored for reperfusion dysrhythmias.
- Even after completion of the fibrinolysis infusion, all vascular punctures should be avoided.
- For minor bleeding (e.g. at site of failed IV attempt or radial artery puncture), use direct compression.
- For major bleeding complications, both the fibrinolytic agent and heparin should be halted. Bloodwork should be resent for fibrinogen and a coagulation profile (PT/PTT), and the physician should consider rescue infusions of blood, fresh frozen plasma, cryoprecipitate, and protamine. Exact doses are found elsewhere,<sup>7</sup> but guidelines are given here. For treatment of fibrinolytic-induced hypofibrinogenemic

<sup>7</sup> Bakerman S: Blood component therapy, in *ABC's of Interpretive Laboratory Data*. Myrtle Beach: IRD, 1994:98,99.

hemorrhage, each unit of fresh frozen plasma will elevate coagulation factors by about 8 percent; fibrinogen levels will rise about 13 mg/dL. If cryoprecipitate is available, each bag per 6 kg will raise fibrinogen levels 75-100 mg/dL. Thus in adults, about ten bags of cryoprecipitate are equivalent in fibrinogen replenishment to a unit of fresh frozen plasma. For treatment of heparin-induced hemorrhage, protamine may be used. Dose is 1 mg per each 100 units of active circulating heparin, given slowly over 10 minutes.

## **PULMONARY EMBOLISM**

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### **General guidelines**

Patients with pulmonary embolism (PE) less than two weeks old are candidates for fibrinolytic therapy. Patients with strong clinical suspicion of PE should receive heparin immediately, prior to diagnostic confirmation.

Indications for fibrinolytic therapy are evolving. Currently, three main indications for such use in PE are widely recognized:<sup>8</sup>

- Patients with hypotension or other signs of hemodynamic instability.
- Patients with exhausted cardiopulmonary reserves. This includes patients who have hypoxia, a single lung, multiple large emboli, right ventricular failure, pulmonary hypertension, or preexisting cardiomyopathy. These criteria apply even in the absence of frank hypotension.
- Patients at special risk for recurrent pulmonary embolism. This includes patients with preexisting coagulopathy, permanent immobilization, or previous thromboembolism.

Empiric fibrinolysis may be necessary in patients with suspected PE who are rapidly deteriorating, prior to confirmation of diagnosis by radiographic means. However, when possible, PE should be confirmed prior to initiation of fibrinolytic therapy. Unlike fibrinolytic therapy for AMI, heparin is not given concurrently with a fibrinolytic agent when used for PE, but can be given following completion of the fibrinolytic infusion. Bleeding complications are treated as previously discussed.

Choice of fibrinolytic agent and timing of administration are at the discretion of the emergency physician. Recent literature shows similar short and long term improvement using either tPA or streptokinase in a two hour infusion.<sup>9</sup>

### **Contraindications to fibrinolysis**

These are the same as for myocardial infarction discussed previously.

### **Informed consent**

Patients who are eligible to undergo fibrinolysis for pulmonary embolism should consent for such therapy based on expected risks and benefits. Risk of death from untreated pulmonary embolism is approximately 1 in 3. Approximately 1 in 10 patients with acute pulmonary embolism die within the first hour. Of the remainder, 2 in 9 patients who are untreated will eventually die as a result of the embolism.<sup>10</sup> Of patients who are candidates for fibrinolytic treatment but who only receive heparin, an additional 1 in 9 will die. Of the subcategory of patients who are candidates for fibrinolytic treatment due to shock, all will die without such treatment. For patients who are not in shock, fibrinolysis prevents death in approximately 1 in 15 patients treated (6.4 percent). For those in shock, the rate is much greater. One study of such patients was terminated early after all patients who received fibrinolytic therapy survived, and all who did not die. Fibrinolytic therapy also prevents recurrence of pulmonary

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<sup>8</sup> Feied C: Pulmonary embolism, in Rosen P, Barkin R (eds), *Emergency Medicine*, vol 2. St. Louis: Mosby, 1998:1795.

<sup>9</sup> Meneveau N, et al: Comparative efficacy of a two-hour regimen of streptokinase versus alteplase in acute massive pulmonary embolism: immediate clinical and hemodynamic outcome and one-year follow-up. *J Am Coll Cardiol* 1998;31:1057-1063.

<sup>10</sup> Feied, 1771.

embolism. This occurs in about 1 in 5 patients who are treated with heparin alone, and is reduced to about 1 in 12 when fibrinolytic therapy is given, an absolute reduction of 11 percent.<sup>11,12</sup>

Four major risks are entailed with use of fibrinolysis: death, stroke, bleeding, and for SK, anaphylaxis. Risk of death from complications of fibrinolysis is lower than the risk of death from untreated pulmonary embolism, though exact numbers are impossible to extract from current studies due to ethical prohibitions of performing fibrinolysis on healthy patients. Total risk of stroke with tPA administered to patients with pulmonary embolism is roughly 1 in 80 (1.2 percent). For SK, risk of stroke is roughly 1 in 100 patients, with data extrapolated from studies of patients with myocardial infarction. About half of such strokes are hemorrhagic, and not all result in death. Risk of significant (>250 ml blood loss) extracranial hemorrhage with either tPA or SK is approximately 1 in 20 patients, the most common being gastrointestinal and genitourinary sites. For SK, anaphylaxis occurs in less than 1 in 1,000 patients.

### Fibrinolytic administration guidelines

As for the patient with myocardial infarction, speed in administering fibrinolytic therapy for pulmonary embolism is essential. Efforts should be directed toward beginning therapy as rapidly as possible. General guidelines are as follows:

- Blood pressures should be performed manually, due to excessive pressures generated by automatic cuffs which may lead to subcutaneous bleeding in patients receiving fibrinolytic agents.
- Patients who are eligible for fibrinolysis should have all vascular punctures minimized.
- Patients should have at least two 18 gauge or larger peripheral intravenous (IV) catheters placed prior to initiation of fibrinolytic therapy. Central venous access should be avoided unless absolutely necessary. If central access is needed, placement via the external jugular system is recommended, since this vessel is easily compressed should bleeding occur with fibrinolytic therapy. At least one cannula should be in the antecubital fossa, in order to allow rapid central circulation of life-saving medications should the patient experience cardiac arrest.
- Draw the following bloodwork: CBC, BMP, cardiac enzymes, PT, PTT, fibrinogen, and type and hold.

#### TPA ADMINISTRATION

- The physician may choose to substitute the MI tPA administration guidelines for the ones below. Either is acceptable.
- Reconstitute the tPA vial according to the manufacturer's instructions. The resulting concentration of tPA is 1 mg/mL. Gently swirl to mix. Shaking should be avoided. After spiking the bottle of reconstituted tPA, prime the tubing to the needle hub, being careful not to waste any of the fluid.
- Unlike tPA for AMI, a bolus is not always indicated, but may be ordered at the discretion of the physician. Bolus therapy is appropriate for patients with hypotension or otherwise in states of extremis. If ordered, administer the bolus as rapidly as possible; if an infusion pump is used for this purpose, the bolus should be given in 60 seconds or less.
- Administer the remaining tPA over 120 minutes (rate 50 mL/hour). A typical dose of tPA is 100 mg over this time period.
- At the conclusion of the infusion, flush the infusion line with 50 mL of saline to ensure administration of the entire dose.

#### STREPTOKINASE ADMINISTRATION

- If ordered when appropriate, pretreat with diphenhydramine and hydrocortisone.
- Reconstitute the streptokinase 1.5 mU vial with 5 mL of normal saline. Gently swirl to ensure complete dissolution. Do not shake.
- Withdraw and discard 5 mL from a 50 mL bag of normal saline. Inject the contents of the streptokinase vial to give a final concentration of 1.5 mU in 50 mL saline.
- After spiking the container of streptokinase, prime the tubing to the needle hub, being careful not to waste any of the solution.
- Set the intravenous infusion pump to 25 mL/hour, and deliver the streptokinase solution over 2 hours.

<sup>11</sup> Konstantinides S, Geibel A, Olschewski M, et al: Association between thrombolytic treatment and the prognosis of hemodynamically stable patients with major pulmonary embolism: results of a multicenter registry. *Circulation* 1997;96:882-888

<sup>12</sup> Jerjes-Sanchez C, Ramirez-Rivera A, de Lourdes Garcia M, et al: Streptokinase and heparin versus heparin alone in massive pulmonary embolism. *J Thromb Thrombolys* 1995;227-229.

- At the conclusion of the infusion, flush the infusion line with 50 mL of saline to ensure administration of the entire dose.

#### POST-FIBRINOLYSIS CARE

- Patients should be closely monitored and admitted to an intensive care setting.
- Even after completion of the fibrinolysis infusion, all vascular punctures should be avoided.
- For minor bleeding (e.g. at site of failed IV attempt or radial artery puncture), use direct compression.
- For major bleeding complications, both the fibrinolytic agent and heparin should be halted. Bloodwork should be resent for fibrinogen and a coagulation profile (PT/PTT), and the physician should consider rescue infusions of blood, fresh frozen plasma, cryoprecipitate, and protamine. Exact doses are found elsewhere,<sup>7</sup> but guidelines are given here. For treatment of fibrinolytic-induced hypofibrinogenemic hemorrhage, each unit of fresh frozen plasma will elevate coagulation factors by about 8 percent; fibrinogen levels will rise about 13 mg/dL. If cryoprecipitate is available, each bag per 6 kg will raise fibrinogen levels 75-100 mg/dL. Thus in adults, about ten bags of cryoprecipitate are equivalent in fibrinogen replenishment to a unit of fresh frozen plasma. For treatment of heparin-induced hemorrhage, protamine may be used. Dose is 1 mg per each 100 units of active circulating heparin, given slowly over 10 minutes.

## ACUTE ISCHEMIC STROKE

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### General guidelines

Patients with acute ischemic strokes are candidates for fibrinolytic therapy. Strict inclusion and exclusion criteria for use of such therapy are warranted by the observation that four previous studies of fibrinolytic therapy for stroke showed unacceptably high iatrogenic death rates due to intracranial hemorrhage induced by this treatment. This observation was so compelling that three of the trials were halted prematurely. Patients who meet all criteria and who consent to treatment must have fibrinolytic therapy initiated within 3 hours of onset of symptoms, not simply following their arrival to the ED. Even if all criteria are met, the emergency physician may choose to forego such treatment if he or she believes the risk to the patient outweighs any expected benefit.<sup>13,14,15</sup> Guidelines for use of tPA in acute ischemic stroke are taken from the single study showing efficacy.<sup>16</sup> Indications for use of tPA in stroke are as follows

- Patient has an acute neurologic insult measurable using the NIH stroke scale
- Onset of symptoms has occurred within past 3 hours and began at a clearly definable time
- Head CT scan performed after symptom onset shows no evidence of either intracranial hemorrhage or large (over third MCA distribution) ischemic infarction
- Neurologic symptoms are not minor but are also not massively debilitating
- Symptoms are not improving
- Symptoms do not suggest subarachnoid hemorrhage
- Symptoms are not associated with seizure
- Patient is not acutely hypertensive (systolic >185 or diastolic >110)
- Patient does not otherwise have hypertension requiring "aggressive treatment" to control
- Glucose level is between 50 and 400 mg/dL
- PTT is not elevated (exact guidelines not given in original paper)
- PT is not elevated >15 seconds
- Platelet count is not <100,000
- Patient has never at any time had previous intracranial hemorrhage
- Patient has not had head trauma within 3 months
- Patient has not had a stroke within 3 months
- Patient has not had a gastrointestinal hemorrhage in the past 3 weeks
- Patient has not had a urologic hemorrhage in the past 3 weeks
- Patient has not had surgery in the past 2 weeks

<sup>13</sup> Li J: Questioning thrombolytic use for cerebrovascular accidents. *J Emerg Med* 1998;16:757-758.

<sup>14</sup> D'Addesio J: Thrombolysis for acute ischemic stroke. *Ann Emerg Med* 1998;32:389-390.

<sup>15</sup> Schrager DL, Kalafut M, Starkman, S, et al: Cranial computed tomography interpretation in acute stroke. *JAMA* 1998;279:1293-1297.

<sup>16</sup> NINDS rt-PA Stroke Study Group: Tissue plasminogen activator for acute ischemic stroke. *N Engl J Med* 1995;333:1581-1587.

- Patient has not had an arterial puncture in the past week
- Patient has had no heparin use within past 2 days
- Patient is not currently undergoing treatment with anticoagulants

### Contraindications to fibrinolysis

These are the same as for myocardial infarction discussed previously.

### Informed consent<sup>13,16</sup>

Patients who are eligible to undergo fibrinolysis for ischemic stroke should consent for such therapy based on expected risks and benefits. At the three month point, 1 in 8 more patients who receive fibrinolysis for ischemic stroke (13 percent) will show neurologic improvement when compared to patients who did not receive treatment. However, spontaneous neurologic improvement will occur in 3 of 7 patients (42 percent) even without treatment. In the initial 24 hours following onset of stroke, no difference in improvement has been demonstrated in patients who do or do not receive fibrinolytic treatment.

A major risk of fibrinolytic therapy is presented when a disease mimicking stroke is misdiagnosed as stroke, and when a hemorrhagic stroke is misdiagnosed as an ischemic stroke due to disagreement in interpretation of the CT scan. Risk of the first is approximately 1 in 5 patients, even when expert stroke teams are involved in suspected stroke evaluation.<sup>17</sup> The risk of CT misdiagnosis is approximately 1 in 5 patients, regardless of whether radiologists, neurologists, or emergency physicians are interpreting the scan.<sup>15</sup>

One month following symptom onset, the risk of death from stroke is approximately 1 patient in 6 (16 percent). Treatment with fibrinolysis does not reduce this risk of death. Risk of intracranial hemorrhage induced by treatment is 1 in 15 (6.4 percent), and 1 in 30 more patients (2.9 percent) will die within 36 hours as a result of treatment when compared to patients not treated. Risk of significant (>250 ml blood loss) extracranial hemorrhage with tPA is approximately 1 in 20 patients, the most common being gastrointestinal and genitourinary sites.

### Fibrinolytic administration guidelines

Due to the necessity of beginning fibrinolytic therapy within 3 hours of symptoms onset, efforts should be directed toward beginning therapy as rapidly as possible. In all cases, the neurologist on call should be consulted and be directly involved in the patient's care. Due to the expertise involved in determining whether a patient meets criteria for fibrinolytic therapy, it may be appropriate for patient care to be turned over directly to the neurologist involved. General guidelines are as follows:

- Draw the following bloodwork: CBC, BMP, cardiac enzymes, PT, PTT, fibrinogen, and type and hold.
- Results of the CBC, glucose, PT, and PTT *must* be obtained before beginning therapy.
- Blood pressures should be performed manually, due to excessive pressures generated by automatic cuffs which may lead to subcutaneous bleeding in patients receiving fibrinolytic agents.
- Patients who are eligible for fibrinolysis should have all vascular punctures minimized.
- Patients should have at least two 18 gauge or larger peripheral intravenous (IV) catheters placed prior to initiation of fibrinolytic therapy. Central venous access should be avoided unless absolutely necessary. If central access is needed, placement via the external jugular system is recommended, since this vessel is easily compressed should bleeding occur with fibrinolytic therapy. At least one cannula should be in the antecubital fossa, in order to allow rapid central circulation of life-saving medications should the patient experience cardiac arrest.

#### TPA ADMINISTRATION

- Reconstitute the tPA vial according to the manufacturer's instructions. The resulting concentration of tPA is 1 mg/mL. Gently swirl to mix. Shaking should be avoided. After spiking the bottle of reconstituted tPA, prime the tubing to the needle hub, being careful not to waste any of the fluid.
- Administer a bolus of tPA in the dose of 0.09 mg/kg. Using the weight-based nomogram, administer the bolus in 60 seconds.

<sup>17</sup> Libman R, Wirkowski E, Alvir J, et al: Conditions that mimic stroke in the emergency department. *Arch Neurol* 1995;52:1119-1122.

- Administer the remaining dose of tPA in the dose of 0.81 mg/kg, determined from the weight-based nomogram, over 60 minutes. The maximum acceptable dose of the combined bolus and infusion is 90 mg.
- At the conclusion of the infusion, flush the infusion line with 50 mL of saline to ensure administration of the entire dose.

TPA WEIGHT-BASED NOMOGRAM

Patient's weight (kg)	Bolus rate (mL/hour)	Bolus volume in 60 seconds (mL)	Infusion rate over 60 minutes (mL/hour)	Infusion volume in 60 minutes (mL)
30-32	180	3	25	25
33-34	180	3	27	27
35-36	180	3	29	29
37-39	180	3	31	31
40-42	240	4	33	33
43-44	240	4	35	35
45-46	240	4	37	37
47-49	240	4	39	39
50-52	300	5	41	41
53-54	300	5	43	43
55-56	300	5	45	45
57-59	300	5	47	47
60-62	360	6	49	49
63-64	360	6	51	51
65-66	360	6	53	53
67-69	360	6	55	55
70-72	360	6	57	57
73-75	420	7	60	60
76-78	420	7	62	62
79-81	420	7	65	65
82-84	420	7	67	67
85-87	480	8	70	70
88-90	480	8	72	72
91-93	480	8	75	75
94-96	540	9	77	77
97-99	540	9	79	79
>99	540	9	81	81

POST-FIBRINOLYSIS CARE

- Patients should be closely monitored and admitted to an intensive care setting.
- Even after completion of the fibrinolysis infusion, all vascular punctures should be avoided.
- For minor bleeding (e.g. at site of failed IV attempt or radial artery puncture), use direct compression.
- For major bleeding complications, both the fibrinolytic agent and heparin should be halted. Bloodwork should be resent for fibrinogen and a coagulation profile (PT/PTT), and the physician should consider rescue infusions of blood, fresh frozen plasma, cryoprecipitate, and protamine. Exact doses are found elsewhere,<sup>7</sup> but guidelines are given here. For treatment of fibrinolytic-induced hypofibrinogenemic hemorrhage, each unit of fresh frozen plasma will elevate coagulation factors by about 8 percent; fibrinogen levels will rise about 13 mg/dL. If cryoprecipitate is available, each bag per 6 kg will raise fibrinogen levels 75-100 mg/dL. Thus in adults, about ten bags of cryoprecipitate are equivalent in fibrinogen replenishment to a unit of fresh frozen plasma. For treatment of heparin-induced hemorrhage, protamine may be used. Dose is 1 mg per each 100 units of active circulating heparin, given slowly over 10 minutes.







