

Thrombolytics

Enzymes given to dissolve a clot that has already formed, all of them working by converting plasminogen into plasmin - and separated from one another by how strongly they confine that conversion to the clot itself rather than to the whole circulation.

Online guide: <https://www.medguideglobal.com/pharmacology/cardiovascular/thrombolytics>

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Quick revision

One Liner: Thrombolytics are the only antithrombotic drugs that break down a clot that already exists, and because the enzyme they release cannot tell a dangerous clot from a useful one, everything about their use is governed by bleeding risk and by time.

1. All available thrombolytic agents are serine proteases that cleave plasminogen into active plasmin, which is why they are also called plasminogen activators. [1]
2. Plasmin is the enzyme that actually degrades fibrin, so the drug is one step upstream of the effect it produces. [2][1]
3. The class divides in two: fibrin-specific agents that preferentially activate plasminogen already bound to fibrin, and non-fibrin-specific agents that activate plasminogen anywhere and produce a systemic lytic state. [1]
4. Alteplase, reteplase and tenecteplase are the fibrin-specific agents; streptokinase is the principal non-specific one. [1]
5. Native tissue plasminogen activator is a serine protease made by vascular endothelial cells, and alteplase is a recombinant form structurally identical to it. [2][1]
6. Alteplase has a very short half-life - an initial phase of only a few minutes - and is cleared mainly by the liver, which is why it is given as a bolus followed by an infusion. [3][1]
7. Tenecteplase is an engineered variant of alteplase carrying three amino acid substitutions, which is where the letters T, N and K in its name come from. [4]
8. Those three changes give tenecteplase greater fibrin specificity, more resistance to its natural inhibitor plasminogen activator inhibitor-1, and a longer half-life, so it can be given as a single bolus. [4][1]
9. Reteplase lacks the kringle-1 domain, which slows its clearance and weakens its fibrin binding, so it diffuses through the clot rather than acting mainly on the surface, and it is given as two boluses. [1]
10. Streptokinase is not a direct activator: it must first bind free plasminogen, and that complex then converts further plasminogen into plasmin. [1]
11. Because streptokinase comes from streptococci it is highly antigenic, causing febrile and allergic reactions and dose-dependent hypotension, and repeat treatment within roughly six months is avoided. [1]
12. Urokinase, in contrast, converts plasminogen to plasmin directly and has low antigenicity, so it can be given repeatedly. [1]
13. In acute ischaemic stroke, benefit is greatest when treatment starts early and declines with time, and intravenous alteplase is given within a window of four and a half hours from when the patient was last known well. [1][2]
14. Bleeding is the commonest complication and intracranial haemorrhage the most serious, with risk raised by older age, uncontrolled hypertension, recent stroke, recent surgery, a bleeding tendency and concurrent anticoagulation. [1]
15. Orolingual angio-oedema is a characteristic reaction to alteplase, most often in patients also taking an angiotensin-converting enzyme inhibitor, and it can obstruct the airway. [1][2]
16. The absolute contraindications are dominated by bleeding: recent intracranial haemorrhage, a structural cerebral vascular lesion, recent ischaemic stroke, possible aortic dissection, active bleeding, recent significant head or facial trauma, recent intracranial or spinal surgery, and severe uncontrolled hypertension. [1]

Overview

1. Thrombolytics, also called fibrinolytics, are given to dissolve a clot that is already blocking a vessel, so that blood flow returns before the tissue beyond it dies. That makes them fundamentally different from the rest of the antithrombotic drugs: anticoagulants and antiplatelet agents prevent clots or stop them growing, but neither breaks down fibrin. They are used in acute ischaemic stroke, ST-elevation myocardial infarction, pulmonary embolism, deep vein thrombosis, acute limb ischaemia and selected other occlusions, and they can be given either systemically through a peripheral vein or delivered by a catheter placed at the clot itself. [1]
2. The mechanism is the same for every agent. The body already has a system for clearing fibrin: plasminogen circulates as an inactive zymogen, binds fibrin through loop-shaped kringle domains, changes shape once bound so that it becomes easier to activate, and is then converted into plasmin, the enzyme that cuts the fibrin mesh apart. Tissue plasminogen activator, made naturally by the endothelium lining blood vessels, is what triggers that conversion at the clot. Every thrombolytic drug is a serine protease that does the same job, so the pharmacology is really about accelerating a process the body already performs, in a place and at a speed it would not manage on its own. [5][2][1]
3. What separates the agents is how tightly they confine that conversion to the clot. Fibrin-specific agents - alteplase, reteplase and tenecteplase - preferentially activate plasminogen that is already bound to fibrin. Non-fibrin-specific agents, of which streptokinase is the main example, activate plasminogen anywhere and produce a systemic lytic state. The recombinant agents also differ from one another by design: reteplase lacks one structural domain, which slows its clearance and lets it diffuse into the clot instead of working only on its surface, while tenecteplase carries three point mutations that lengthen its half-life, increase its fibrin specificity and make it resistant to the body's own inhibitor of fibrinolysis. Those engineering choices are what allow bolus rather than infusion administration. [1][4]
4. The limits of the class are set by two things: time and bleeding. Benefit falls as the interval from symptom onset lengthens, which is why treatment windows and door-to-needle targets dominate the practical guidance. And because plasmin cannot distinguish a dangerous clot from one that is holding a healed vessel closed, bleeding is the commonest complication, with intracranial haemorrhage the most serious. The absolute contraindications are almost entirely about bleeding - recent intracranial haemorrhage, a structural vascular lesion in the brain, recent ischaemic stroke, possible aortic dissection, active bleeding, recent significant head or facial trauma, recent intracranial or spinal surgery, and severe uncontrolled hypertension - with the one immunological exception of recent previous streptokinase. [1]

Classification and drug examples

Intro: The clinically decisive division is between agents that concentrate their action on fibrin and agents that do not, because that determines how much of the circulation is affected and therefore how much bleeding risk is incurred for a given amount of clot lysis.

1. Name: Fibrin-specific plasminogen activators

1. Note: Recombinant forms and variants of human tissue plasminogen activator. They preferentially activate plasminogen already bound to fibrin, although some systemic activation still occurs.

1. Name: Alteplase

1. Recombinant tissue plasminogen activator

2. rtPA

1. Route: Intravenous, or instilled locally to clear an occluded catheter

1. Note: Structurally identical to native tissue plasminogen activator and produced by recombinant DNA technology; the agent most often used for ST-elevation myocardial infarction, pulmonary embolism and acute ischaemic stroke, with a very short plasma half-life and no antigenicity. [1][3][2]

2. Name: Tenecteplase

2. Route: Intravenous, as a single bolus

2. Note: A bioengineered variant with three amino acid substitutions - the source of the letters in its name - giving

higher fibrin specificity, resistance to plasminogen activator inhibitor-1 and a longer half-life; efficacy comparable to alteplase with less non-cerebral bleeding, and cleared mainly by the liver. [4][1]

3. Name: Reteplase

1. Recombinant plasminogen activator

2. r-PA

3. Route: Intravenous, as two sequential boluses

3. Note: A second-generation unglycosylated deletion variant made in *Escherichia coli* and lacking the kringle-1 domain; slower clearance supports bolus dosing, and weaker fibrin binding lets it spread through the clot rather than acting mainly on its surface. [1] [1][2]

2. Name: Non-fibrin-specific plasminogen activators

2. Note: These activate plasminogen without needing it to be bound to fibrin, so fibrinolysis occurs throughout the circulation. They are older, cheaper and still widely used outside the United States.

1. Name: Streptokinase

1. Route: Intravenous

1. Note: The first thrombolytic used clinically, isolated from streptococci. It is not a direct activator: it binds free plasminogen first, and the complex then generates plasmin. High antigenicity brings febrile and allergic reactions and dose-dependent hypotension, and it is no longer marketed in the United States. [1]

2. Name: Urokinase

2. Route: Intravenous or catheter-directed

2. Note: A physiological activator originating largely from kidney tissue and purified from human urine, with a recombinant form also available. It converts plasminogen directly, has low antigenicity so it can be repeated, and is used in catheter-directed thrombolysis, catheter occlusion, pulmonary embolism and peripheral vascular thrombosis. [1]

3. Name: Anistreplase

Anisoylated purified streptokinase activator complex

3. Route: Intravenous

3. Note: A pre-formed complex of streptokinase and plasminogen that does not depend on circulating plasminogen; its acyl group hydrolyses spontaneously after administration. Highly antigenic and rarely used now that fibrin-specific agents exist. [1] [1]

Mechanism of action

Summary: Every thrombolytic is a serine protease that cleaves plasminogen into plasmin. Plasmin degrades the fibrin mesh that holds a thrombus together. Whether the drug does this mainly at the clot or throughout the blood is what separates fibrin-specific from non-specific agents, and it is what determines how much systemic bleeding risk accompanies the lysis.

Target: Plasminogen, converted to plasmin, which in turn degrades fibrin within the thrombus

1. Step: 1

1. Title: Thrombin builds the fibrin mesh that has to be removed

1. Detail: During clot formation, the coagulation cascade generates thrombin on the phospholipid surface of activated platelets, and thrombin converts fibrinogen into fibrin. That fibrin matrix is what stabilises the thrombus, and it is the structure a thrombolytic drug must dismantle. [1]

2. Step: 2

2. Title: Plasminogen docks onto fibrin through its kringle domains

2. Detail: Plasminogen circulates as an inactive zymogen. It binds intact fibrin through kringle domains - large loops of amino acids held together by disulfide bonds - which attach to carboxy-terminal lysine residues on the fibrin surface.

This binding is described as the first stage of fibrinolysis. [5]

3. Step: 3

3. Title: Binding changes the shape of plasminogen and makes it easier to activate

3. Detail: Once attached to fibrin, plasminogen adopts a more open conformation that increases its susceptibility to activation. This is the molecular reason fibrinolysis concentrates where fibrin is, rather than occurring uniformly through the plasma. [5]

4. Step: 4

4. Title: The body has a brake on premature lysis

4. Detail: Thrombomodulin on the endothelium binds thrombin and generates carboxypeptidase B, which removes the free carboxy-terminal lysine residues plasminogen needs to bind. That prevents useful haemostatic clots being dissolved and limits activation on large, actively forming thrombi. [5]

5. Step: 5

5. Title: Tissue plasminogen activator converts bound plasminogen into plasmin

5. Detail: Native tissue plasminogen activator is a serine protease secreted by vascular endothelial cells with high affinity and specificity for fibrin. It binds both fibrin and plasminogen, which brings enzyme and substrate together at the clot surface and converts plasminogen into plasmin locally. [2][1]

6. Step: 6

6. Title: Plasmin cuts the fibrin mesh apart

6. Detail: Plasmin binds fibrin within the thrombus and degrades it, releasing fibrin degradation products and reopening the vessel. Plasmin also lyses circulating fibrinogen, which is the source of the systemic effect seen even with fibrin-preferring agents. [1][3]

7. Step: 7

7. Title: Fibrin-specific agents mimic the natural activator; non-specific ones do not

7. Detail: Alteplase, reteplase and tenecteplase preferentially activate fibrin-bound plasminogen. Streptokinase and urokinase generate plasmin with only limited dependence on local fibrin, so fibrinolysis becomes systemic and circulating fibrinogen is consumed. [1]

8. Step: 8

8. Title: Streptokinase works through a complex rather than directly

8. Detail: It binds free circulating plasminogen, and that streptokinase-plasminogen complex is what converts further plasminogen into plasmin. Anistreplase is essentially that complex supplied pre-formed with a protecting acyl group that hydrolyses after administration. [1]

9. Step: 9

9. Title: Protein engineering tunes half-life and fibrin binding

9. Detail: Deleting the kringle-1 domain in reteplase slows clearance and loosens fibrin binding so the drug penetrates the clot. Three point mutations in tenecteplase slow clearance further, raise fibrin specificity and confer resistance to plasminogen activator inhibitor-1, together permitting a single-bolus regimen. [1][4]

Major clinical uses

1. Drug: Alteplase

1. Indication: Acute ischaemic stroke within the treatment window

1. Line: mainstay of intravenous thrombolysis

1. Note: Guidance describes intravenous alteplase as the mainstay for eligible patients presenting within four and a half hours of the time they were last known well, with benefit greatest when treatment begins early and declining as time passes; brain imaging first excludes haemorrhage. [1][2]

2. Drug: Alteplase

2. Indication: ST-elevation myocardial infarction where timely coronary intervention is not available

2. Line: reperfusion strategy when intervention would be delayed

2. Note: Recommended when symptom onset is recent and transfer for primary percutaneous coronary intervention cannot be achieved within the guideline-defined interval; rescue intervention is recommended if reperfusion fails. [2][1]

3. Drug: Alteplase

3. Indication: Acute pulmonary embolism with haemodynamic compromise, and restoration of flow in an occluded central venous catheter

3. Line: systemic in the first case, local in the second

3. Note: Systemic thrombolysis is considered for acute pulmonary embolism with hypotension where bleeding risk is low; a separate low-dose formulation is used purely to clear a blocked central venous access device, where plasma concentrations are unlikely to reach pharmacological levels. [2][3]

4. Drug: Tenecteplase

4. Indication: ST-elevation myocardial infarction, including treatment before hospital arrival

4. Line: commonly preferred fibrinolytic

4. Note: Efficacy comparable to alteplase with less non-cerebral bleeding; single-bolus administration is the stated reason it is often the preferred agent for prehospital fibrinolysis programmes. [1][4]

5. Drug: Tenecteplase

5. Indication: Acute ischaemic stroke

5. Line: increasingly used alternative

5. Note: Not approved by the United States regulator for stroke, but its use is increasing; a meta-analysis in patients with large vessel occlusion reported better recanalisation and clinical outcomes than with intravenous alteplase. [4][1]

6. Drug: Reteplase

6. Indication: Acute myocardial infarction

6. Line: double-bolus alternative

6. Note: Approved for acute myocardial infarction as two sequential boluses given a short interval apart; it must not share an intravenous line with heparin because the two are incompatible in solution. [1]

7. Drug: Streptokinase

7. Indication: Thrombolysis where cost governs availability

7. Line: widely used outside the United States

7. Note: Described as the most widely used fibrinolytic worldwide because of its low cost, despite lower fibrin specificity and lower reperfusion rates than alteplase; it is no longer marketed in the United States. [1]

8. Drug: Urokinase

8. Indication: Catheter-directed thrombolysis, catheter occlusion, pulmonary embolism and peripheral vascular thrombosis

8. Line: established alternative

8. Note: Low antigenicity permits repeated administration, which suits the prolonged catheter-directed treatments where the same agent may be needed again. [1]

9. Drug: Any fibrinolytic by catheter

9. Indication: Acute limb ischaemia that is not immediately limb-threatening, and selected pulmonary embolism

9. Line: catheter-directed rather than systemic

9. Note: Local fibrinolysis typically takes many hours to dissolve a clot, so it suits ischaemia of recent onset that is not immediately threatening; ultrasound-facilitated catheter-directed delivery has improved outcomes in massive and submassive pulmonary embolism while limiting systemic exposure. [1]

Pharmacokinetics

1. Drug: Alteplase

1. Route: Intravenous bolus followed by infusion; also instilled locally into a blocked catheter

1. Absorption: Given directly into the circulation, so there is no absorption phase

1. Metabolism: Cleared primarily by the liver

1. Elimination: Hepatic, with a very rapid initial phase

1. Half Life: An initial half-life of only a few minutes and a terminal half-life of a little over an hour

1. Dose Adjust: Weight-based and indication-specific; regimens differ between stroke, myocardial infarction and pulmonary embolism and belong in a prescribing reference [3][1]
2. Drug: Tenecteplase
2. Route: Intravenous, as a single rapid bolus
2. Absorption: Given directly into the circulation
2. Metabolism: Final clearance occurs primarily through hepatic metabolism
2. Elimination: Hepatic, slowed by the engineered substitutions
2. Half Life: Roughly twenty to twenty-five minutes, substantially longer than alteplase
2. Dose Adjust: Weight-based with a ceiling; a halved dose has been studied in older patients, where a trial reported less intracranial haemorrhage than with the standard dose [4][1]
3. Drug: Reteplase
3. Route: Intravenous, as two sequential boluses
3. Absorption: Given directly into the circulation
3. Metabolism: As an unglycosylated deletion variant it is cleared more slowly than native tissue plasminogen activator
3. Elimination: Slower plasma clearance, attributed to the missing kringle-1 domain
3. Half Life: Longer than alteplase, with a faster onset of action
3. Dose Adjust: Fixed sequential boluses rather than weight-based dosing; it is incompatible with heparin in solution and must not share a line with it [1]
4. Drug: Streptokinase
4. Route: Intravenous
4. Absorption: Given directly into the circulation
4. Metabolism: A bacterial protein that acts by complexing with plasminogen rather than acting catalytically alone
4. Elimination: Cleared as a foreign protein, with neutralising antibodies persisting afterwards
4. Half Life: Not the limiting factor; the practical limit is the antibody response, which persists for months
4. Dose Adjust: Repeat administration within roughly six months of a previous course is avoided because of neutralising antibodies and hypersensitivity risk [1]
5. Drug: Urokinase
5. Route: Intravenous or catheter-directed
5. Absorption: Given directly into the circulation or delivered at the clot
5. Metabolism: A physiological human enzyme originating largely from renal parenchyma, purified from urine or produced recombinantly
5. Elimination: Cleared as an endogenous protein, with no antigenic barrier to repeat dosing
5. Half Life: Short enough that catheter-directed infusion is continued over hours to achieve lysis
5. Dose Adjust: Determined by whether delivery is systemic or catheter-directed and by the clot being treated [1]
1. Route of delivery is a genuine pharmacological choice here, not just a practicality: catheter-directed administration concentrates the drug at the clot and reduces systemic fibrinolytic exposure, which is the same problem fibrin specificity addresses chemically. [1]
2. Half-life determines the shape of the regimen. A very short half-life requires a bolus followed by an infusion, while the engineered variants last long enough to be given as one or two boluses, which is what makes treatment before hospital arrival practical. [3][4][1]
3. Anticoagulants and antiplatelet drugs are withheld for a period after alteplase is given for stroke, because adding them during the window of greatest haemorrhagic vulnerability compounds the risk. [1]
4. This page gives no dose regimens by design. Doses are weight-based, differ by indication and agent, and belong in a prescribing reference used by the treating clinician.

Adverse effects

1. Effect: Bleeding

1. Detail: The most common complication of the whole class. It occurs at vascular access and puncture sites or spontaneously anywhere in the body, and it is the price of generating plasmin that cannot distinguish a pathological clot from a protective one. [1]
 2. Effect: Hypotension
 2. Detail: Listed among the shared adverse effects of the class, and specifically dose-dependent with streptokinase, where it requires careful monitoring during administration. [1]
 3. Effect: Allergic and febrile reactions
 3. Detail: Frequent with streptokinase and anistreplase because both are antigenic; the recombinant tissue plasminogen activators lack antigenicity and cause few allergic reactions. [1]
 4. Effect: Reperfusion arrhythmias
 4. Detail: Rhythm disturbances that follow restoration of flow, particularly when treatment is given for acute myocardial infarction, which is why cardiac monitoring accompanies therapy. [1]
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1. Effect: Intracranial haemorrhage
 1. Detail: The most serious bleeding complication, including haemorrhagic stroke. Risk is raised by advanced age, uncontrolled hypertension, recent stroke, recent surgery, an underlying bleeding tendency and concurrent anticoagulant therapy.
 1. Action: Treatment is stopped immediately if neurological deterioration occurs, and urgent non-contrast brain imaging is obtained to look for haemorrhage. Strict blood pressure control before and after treatment is described as essential to reduce this risk. [1]
 2. Effect: Major systemic haemorrhage
 2. Detail: Bleeding severe enough to threaten life can arise at any site, and the systemic lytic state produced by non-fibrin-specific agents makes it more likely with those drugs.
 2. Action: Fibrinolytic and anticoagulant drugs are stopped at once, and supportive measures follow: stabilising the circulation, replacing volume, and giving blood products such as cryoprecipitate, fresh frozen plasma, platelets or factor replacement as indicated. Protamine is used if unfractionated heparin was also running. [1]
 3. Effect: Orolingual angio-oedema
 3. Detail: Swelling of the tongue and mouth occurring most frequently with alteplase, and particularly in patients also receiving an angiotensin-converting enzyme inhibitor. It can obstruct the airway.
 3. Action: Anticipated as part of preparing for stroke thrombolysis, with readiness to manage the airway rather than treating it as an unexpected event. [1][2]
 4. Effect: Anaphylaxis
 4. Detail: Listed among the potential adverse effects of the class, and the risk is concentrated in the antigenic agents, where prior exposure raises antibody titres.
 4. Action: Managed as an acute allergic emergency; with streptokinase, previous treatment within roughly the preceding six months is itself an absolute contraindication. [1]
 5. Effect: Failed or incomplete reperfusion
 5. Detail: Not an adverse effect of the drug in the usual sense, but a serious clinical outcome: a substantial minority of patients treated with fibrinolysis for myocardial infarction achieve no reperfusion, and a further group achieve it incompletely.
 5. Action: Rapid transfer to a centre able to perform coronary intervention is described, and rescue intervention after failed thrombolysis is associated with fewer cardiovascular events than conservative care or repeating the thrombolytic. [1]
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1. Drug: Streptokinase
 1. Effect: High antigenicity, producing febrile and allergic reactions and dose-dependent hypotension, with neutralising antibodies that persist for months after a course. [1]
 2. Drug: Anistreplase
 2. Effect: Shares streptokinase's antigenicity and, like it, cannot distinguish circulating from fibrin-bound plasminogen,

so it produces a systemic lytic state; it is rarely used now. [1]

3. Drug: Alteplase

3. Effect: Orolingual angio-oedema is its characteristic reaction, and despite its fibrin preference it still produces systemic fibrinolytic activity with circulating fibrin degradation products. [1]

4. Drug: Tenecteplase

4. Effect: Comparable efficacy to alteplase with a lower risk of non-cerebral bleeding; in older patients a halved dose reduced intracranial haemorrhage compared with the standard dose in a randomised trial. [1][4]

5. Drug: Reteplase

5. Effect: Physically incompatible with heparin in solution, so the two must not be given through the same intravenous line - a practical hazard rather than a pharmacological one. [1]

Contraindications, precautions and interactions

1. Recent intracranial haemorrhage. [1]

2. A known structural cerebral vascular lesion. [1]

3. Ischaemic stroke within the preceding few months. [1]

4. Suspected aortic dissection. [1]

5. Active bleeding or a bleeding tendency, with menstruation explicitly excluded from this criterion. [1]

6. Significant head injury or facial trauma within the preceding few months, and recent intracranial or spinal surgery. [1]

7. Severe hypertension that remains uncontrolled despite treatment. [1]

8. Previous streptokinase within roughly the preceding six months, because neutralising antibodies reduce effectiveness and raise the risk of an allergic reaction. [1]

1. A history of severe and poorly controlled hypertension, and marked hypertension at the time of presentation. [1]

2. Prolonged cardiopulmonary resuscitation, or major surgery within the preceding weeks. [1]

3. A previous ischaemic stroke outside the absolute-contraindication window. [1]

4. Internal bleeding within the preceding weeks, and vascular punctures at sites that cannot be compressed. [1]

5. Concurrent anticoagulant therapy that has already prolonged the international normalized ratio or the prothrombin time. [1]

6. Pregnancy, a relative contraindication because of bleeding risk, although guidance allows intravenous alteplase to be considered for stroke where the benefit outweighs the risk of uterine bleeding. [1]

7. A limb that is immediately threatened by ischaemia, where catheter-directed lysis is too slow and urgent revascularisation is generally required instead. [1]

1. With: Anticoagulants and antiplatelet agents

1. Effect: Add substantially to bleeding risk, and concurrent anticoagulation appears among the factors raising the chance of a haemorrhagic event; they are withheld for a period after alteplase is given for stroke. [1]

2. With: Angiotensin-converting enzyme inhibitors

2. Effect: Increase the likelihood of orolingual angio-oedema during alteplase treatment, which is the reason that reaction is anticipated in this group. [1]

3. With: Unfractionated heparin given alongside a thrombolytic

3. Effect: If serious bleeding develops, protamine can be given to reverse the heparin component even though it does nothing for the fibrinolytic itself. [1]

4. With: Heparin in the same intravenous line as reteplase

4. Effect: The two are incompatible in solution and must be given through separate lines. [1]

5. With: Aminocaproic acid

5. Effect: Reverses fibrinolytic activity by inhibiting plasmin-mediated fibrin degradation, but is reserved for life-threatening haemorrhage because suppressing the body's own fibrinolysis can increase thrombotic risk, and caution is advised in disseminated intravascular coagulation. [1]

6. With: Previous exposure to streptokinase or anistreplase

6. Effect: Raises antistreptococcal antibody titres, which both neutralise the drug and increase the likelihood of a hypersensitivity reaction on re-exposure. [1]

Comparison tables

1. Title: The thrombolytic agents side by side

1. Caption: Properties for learning rather than a selection guide. Agent choice, dosing and eligibility are clinical decisions made from current guidelines and a prescribing reference.

1. Key: agent

1. Label: Agent

1. Is Row Header: true

2. Key: origin

2. Label: Origin

3. Key: specificity

3. Label: Fibrin specificity

4. Key: administration

4. Label: How it is given

5. Key: antigenic

5. Label: Antigenic?

1. Agent: Alteplase

1. Origin: Recombinant human tissue plasminogen activator, structurally identical to the native enzyme

1. Specificity: Fibrin-specific, though systemic activity still occurs

1. Administration: Bolus followed by infusion

1. Antigenic: No [1][3]

2. Agent: Tenecteplase

2. Origin: Engineered variant with three point mutations

2. Specificity: Highest fibrin specificity of the group

2. Administration: Single bolus

2. Antigenic: No [4][1]

3. Agent: Reteplase

3. Origin: Deletion variant lacking kringle-1, made in Escherichia coli

3. Specificity: Fibrin-specific but binds fibrin more weakly, so it diffuses into the clot

3. Administration: Two sequential boluses

3. Antigenic: No [1]

4. Agent: Streptokinase

4. Origin: Bacterial protein from streptococci

4. Specificity: Not fibrin-specific; produces a systemic lytic state

4. Administration: Intravenous infusion

4. Antigenic: Yes, highly [1]

5. Agent: Urokinase

5. Origin: Human enzyme from renal parenchyma, purified from urine or made recombinantly

5. Specificity: Limited dependence on fibrin, so activity is largely systemic

5. Administration: Intravenous or catheter-directed

5. Antigenic: Minimally, so it can be repeated [1]

2. Title: Where thrombolytics sit among the antithrombotic drugs

2. Caption: The three families do different jobs. Confusing them is the single most common error in this area.

1. Key: family

1. Label: Drug family

1. Is Row Header: true
2. Key: does
2. Label: What it does to a clot
3. Key: timing
3. Label: When it is useful
1. Family: Antiplatelet agents
 1. Does: Reduce platelet activation so a clot is less likely to form
 1. Timing: Prevention, and long-term secondary prevention [1]
2. Family: Anticoagulants
 2. Does: Interrupt the coagulation cascade so an existing clot does not extend and new fibrin is not laid down
 2. Timing: Treatment and prevention over days to years [1]
3. Family: Thrombolytics
 3. Does: Generate plasmin, which degrades the fibrin already present and reopens the vessel
 3. Timing: A narrow, time-critical window after the occlusion, with benefit falling as delay increases [1][2]

High-yield exam pearls

1. Pearl: Thrombolytics are the only drugs in the antithrombotic family that remove an existing clot.
 1. Why: Anticoagulants stop a clot growing and antiplatelet drugs stop one forming, but neither dissolves fibrin. That distinction is the reason thrombolysis is time-critical while anticoagulation is not, and it is the most commonly tested idea in the whole area. [1]
2. Pearl: Fibrin specificity is relative, never absolute.
 2. Why: Alteplase theoretically acts only on the fibrin surface, but systemic fibrinolytic activity still occurs, producing circulating fibrin degradation products and a real bleeding risk. Treating a fibrin-specific agent as if it were confined to the clot is a mistake. [1]
3. Pearl: The kringle domains are how plasminogen finds fibrin.
 3. Why: They are large disulfide-stabilised amino acid loops that bind carboxy-terminal lysine residues on fibrin, and once plasminogen is bound its shape changes so it becomes far easier to activate. That is why the reaction concentrates at the clot at all. [5]
4. Pearl: Removing a domain and mutating three residues are the two engineering tricks in this class.
 4. Why: Reteplase is a deletion variant lacking kringle-1, which slows clearance and lets it be given as boluses; tenecteplase carries three point mutations that prolong its half-life and increase fibrin specificity. Knowing which trick belongs to which drug answers most comparison questions. [1][4]
5. Pearl: Streptokinase is the only agent with an immunological contraindication of its own.
 5. Why: It is a bacterial protein, so neutralising antibodies persist after exposure. Repeat administration within roughly six months is avoided both because the drug may not work and because hypersensitivity is more likely. [1]
6. Pearl: Tenecteplase resists plasminogen activator inhibitor-1; native tissue plasminogen activator does not.
 6. Why: That inhibitor is the body's own brake on fibrinolysis, so resistance to it is part of why the engineered variant achieves its effect from a single bolus rather than a prolonged infusion. [4]
7. Pearl: Reperfusion after thrombolysis is not guaranteed.
 7. Why: A substantial minority of patients treated for myocardial infarction do not achieve reperfusion at all and a further group achieve it incompletely, which is why guidance directs rapid transfer to a centre capable of coronary intervention and supports rescue intervention after failed thrombolysis. [1]
8. Pearl: Blood glucose is checked before treating a suspected stroke.
 8. Why: Both low and high blood glucose can mimic stroke symptoms, and thrombolysis is not indicated for a non-vascular neurological problem. Non-contrast brain imaging beforehand is what excludes haemorrhage. [2]
9. Pearl: There is a reversal strategy for fibrinolysis, but it is not benign.
 9. Why: Aminocaproic acid inhibits plasmin-mediated fibrin degradation and can be considered in life-threatening

haemorrhage, but suppressing the body's own fibrinolysis raises thrombotic risk, so its use is reserved for severe bleeding. [1]

10. Pearl: Plasminogen deficiency does not cause thrombosis.

10. Why: It causes thickened mucous membranes from fibrin accumulation instead, which is a useful check on the intuition that fibrinolysis is simply the opposite of clotting. [5]

Common exam traps

1. Trap: Calling heparin or aspirin a clot-busting drug.

1. Correction: Neither dissolves fibrin. Only a plasminogen activator generates plasmin, and plasmin is what degrades the fibrin mesh holding a clot together. [1][2]

2. Trap: Assuming streptokinase activates plasminogen the way alteplase does.

2. Correction: Streptokinase is not a direct activator. It first binds free circulating plasminogen, and the resulting complex then converts further plasminogen into plasmin, which is why its action is systemic rather than confined to the clot. [1]

3. Trap: Treating a fibrin-specific agent as free of systemic effect.

3. Correction: Alteplase produces measurable systemic fibrinolysis and circulating fibrin degradation products despite its fibrin preference, and it carries a moderate bleeding risk accordingly. [1]

4. Trap: Reading angio-oedema during stroke thrombolysis as an unrelated allergy.

4. Correction: Orolingual angio-oedema is a recognised reaction to alteplase, occurs most often in patients taking an angiotensin-converting enzyme inhibitor, and can obstruct the airway, so it is anticipated rather than discovered. [1][2]

5. Trap: Assuming thrombolysis is the answer to every acutely ischaemic limb.

5. Correction: Local catheter-directed fibrinolysis takes many hours to dissolve the clot, so it suits non-limb-threatening ischaemia; a limb immediately threatened generally needs urgent revascularisation, alone or combined with catheter-directed treatment. [1]

6. Trap: Believing thrombolysis is obsolete because coronary intervention exists.

6. Correction: Guidance directs transfer for primary intervention when it can be delivered promptly, but fibrinolysis remains the recommended reperfusion strategy when that delay would be too long, and it can be given before hospital arrival. [2][1]

7. Trap: Confusing prourokinase with urokinase.

7. Correction: Prourokinase is a relatively inactive precursor that must be converted to urokinase to work, and that activation step gives it fibrin-selective behaviour that urokinase itself lacks. [1]

Self-test questions

1. Question: What is the shared mechanism of every available thrombolytic agent?

1. Direct inhibition of thrombin
2. Cleavage of plasminogen into plasmin
3. Blockade of the platelet glycoprotein IIb/IIIa receptor
4. Depletion of vitamin K-dependent clotting factors

1. Explanation: All thrombolytic agents are serine proteases that convert plasminogen into plasmin, which is the enzyme that actually degrades fibrin. This is why the class is also called the plasminogen activators. [1]

2. Question: Which agent is non-fibrin-specific and produces a systemic lytic state?

1. Alteplase
2. Reteplase
3. Tenecteplase
4. Streptokinase

2. Explanation: Streptokinase is the principal non-fibrin-specific agent: it activates plasminogen without needing fibrin binding, so fibrinolysis occurs throughout the circulation. The three recombinant tissue plasminogen activators

preferentially activate fibrin-bound plasminogen. [1]

3. Question: Why can tenecteplase be given as a single bolus while alteplase needs a bolus followed by an infusion?

1. Tenecteplase is more potent per milligram
2. Three point mutations prolong its half-life and it resists plasminogen activator inhibitor-1
3. Tenecteplase is not cleared by the liver
4. Alteplase is inactivated by contact with plastic tubing

3. Explanation: Tenecteplase is a bioengineered variant of tissue plasminogen activator with three amino acid substitutions that slow its clearance and increase resistance to the endogenous inhibitor, giving it a substantially longer plasma half-life than alteplase. [4][1]

4. Question: What structural change distinguishes reteplase from native tissue plasminogen activator?

1. It carries an added carbohydrate chain
2. It lacks the kringle-1 domain, which slows clearance and weakens fibrin binding
3. It is a bacterial protein rather than a human one
4. It has no protease activity of its own

4. Explanation: Reteplase is an unglycosylated deletion variant lacking kringle-1. Slower plasma clearance supports bolus administration, and weaker fibrin binding lets it diffuse into the clot rather than acting mainly at the surface. [1]

5. Question: How does streptokinase differ mechanistically from urokinase?

1. Streptokinase must first form a complex with plasminogen, whereas urokinase converts plasminogen directly
2. Streptokinase inhibits plasmin, whereas urokinase activates it
3. Streptokinase acts only on clot-bound plasminogen
4. Urokinase requires antithrombin as a cofactor

5. Explanation: Streptokinase binds free circulating plasminogen and the resulting complex then activates further plasminogen. Urokinase is a direct activator and, being non-antigenic, can be given repeatedly, unlike the bacterial streptokinase. [1]

6. Question: Which of the following is an absolute contraindication to thrombolytic therapy?

1. Age above seventy-five
2. A history of well-controlled hypertension
3. Recent intracranial haemorrhage
4. Menstruation

6. Explanation: Recent intracranial haemorrhage is an absolute contraindication, alongside a structural cerebral vascular lesion, ischaemic stroke within the preceding months, possible aortic dissection, active bleeding or a bleeding tendency, recent significant head or facial trauma, recent intracranial or spinal surgery, and severe uncontrolled hypertension. Menstruation is explicitly excluded from the active-bleeding criterion. [1]

7. Question: A patient given alteplase for stroke develops swelling of the tongue. What is the most likely explanation?

1. Orolingual angio-oedema, most frequent with alteplase and commoner with an ACE inhibitor
2. Extension of the stroke into the brainstem
3. A reperfusion arrhythmia
4. Hypoglycaemia mimicking a stroke

7. Explanation: Orolingual angio-oedema occurs most frequently with alteplase, particularly in patients also receiving an angiotensin-converting enzyme inhibitor, and it can obstruct the airway, so airway readiness is part of preparing for treatment. [1][2]

8. Question: Which agent may be considered to reverse fibrinolytic activity in life-threatening haemorrhage?

1. Protamine sulfate
2. Idarucizumab
3. Aminocaproic acid
4. Vitamin K

8. Explanation: Aminocaproic acid is an antifibrinolytic that inhibits plasmin-mediated fibrin degradation. It is reserved

for severe bleeding because suppressing endogenous fibrinolysis raises thrombotic risk, and blood products such as cryoprecipitate and fresh frozen plasma are used to replace fibrinogen and clotting factors. [1]

9. Question: What happens to the benefit of thrombolysis as time passes after symptom onset?

1. It stays constant until the treatment window closes
2. It increases, because the clot becomes more organised and easier to lyse
3. It declines, so the benefit is greatest when treatment starts early
4. It is unrelated to timing

9. Explanation: Benefit is significant when treatment begins early after onset and declines with delay. This underlies both the treatment window in acute ischaemic stroke and the emphasis on minimising door-to-needle time in myocardial infarction. [1]

Frequently asked questions

1. Question: How is a thrombolytic different from an anticoagulant?

1. Answer: An anticoagulant interrupts clot formation, so it stops an existing clot getting bigger and prevents new ones. It cannot remove fibrin that is already there. A thrombolytic generates plasmin, the enzyme that cuts the fibrin mesh apart, so it actually dissolves the clot and reopens the vessel. That is why one is used over days or years and the other within a window of hours. [1][2]

2. Question: What does fibrin specificity actually mean?

2. Answer: It means the drug preferentially activates plasminogen that is already stuck to fibrin, so plasmin is generated mainly at the clot rather than throughout the blood. It is a preference and not a rule: alteplase still produces systemic fibrinolytic activity and circulating fibrin degradation products, and it still carries a real bleeding risk. [1]

3. Question: Why does the body not just dissolve dangerous clots itself?

3. Answer: Partly because it actively prevents that. Thrombomodulin on the vessel wall binds thrombin and generates an enzyme that clips off the lysine residues plasminogen needs in order to attach to fibrin. That brake protects clots doing a useful job and limits activation on large, actively forming thrombi - which is also why a drug is needed to shift the balance when a clot is doing harm. [5]

4. Question: Why is tenecteplase increasingly preferred over alteplase?

4. Answer: Convenience with equivalent effect. Its three engineered amino acid substitutions prolong its half-life and increase fibrin specificity, so it works from a single rapid bolus instead of a bolus followed by an hour-long infusion. Efficacy in myocardial infarction is comparable to alteplase with less non-cerebral bleeding, and single-bolus delivery is what makes treatment before hospital arrival practical. [4][1]

5. Question: Why can streptokinase not simply be given again if the first course did not work?

5. Answer: Because it is a bacterial protein. Exposure raises antistreptococcal antibody titres that both neutralise the drug and make a hypersensitivity reaction more likely, so repeat treatment within roughly six months is avoided. Urokinase and the recombinant tissue plasminogen activators do not have this problem. [1]

6. Question: What happens if someone bleeds seriously after thrombolysis?

6. Answer: The fibrinolytic and any anticoagulant are stopped immediately, the circulation is stabilised, and blood products are given as needed - cryoprecipitate and fresh frozen plasma to replace fibrinogen and clotting factors, platelets where the count is low. If unfractionated heparin was also running, protamine reverses that component. Aminocaproic acid can be considered to oppose the fibrinolysis itself, but only in life-threatening haemorrhage. [1]

7. Question: Why is the treatment window so strict in stroke?

7. Answer: Because the benefit and the risk move in opposite directions with time. Reopening the artery helps only while brain tissue is still salvageable, and that benefit declines steadily from symptom onset, while the haemorrhagic risk does not fall to match it. Guidance therefore sets a window measured from when the patient was last known to be well, and imaging is obtained first to exclude bleeding. [1][2]

8. Question: Why give a thrombolytic through a catheter rather than a vein?

8. Answer: To get the drug to the clot without exposing the whole circulation to it. Catheter-directed delivery, including

ultrasound-facilitated techniques, has improved outcomes in massive and submassive pulmonary embolism while reducing systemic fibrinolytic exposure and the bleeding that goes with it. The trade-off is that local lysis takes many hours, so it does not suit an emergency where tissue is about to be lost. [1]

References

- [1] Thrombolytic Therapy (StatPearls). StatPearls Publishing / NCBI Bookshelf 2026.
<https://www.ncbi.nlm.nih.gov/books/NBK557411/>
- [2] Tissue Plasminogen Activator Therapy (StatPearls). StatPearls Publishing / NCBI Bookshelf 2025.
<https://www.ncbi.nlm.nih.gov/books/NBK482376/>
- [3] Alteplase (StatPearls). StatPearls Publishing / NCBI Bookshelf 2023. <https://www.ncbi.nlm.nih.gov/books/NBK499977/>
- [4] Tenecteplase (StatPearls). StatPearls Publishing / NCBI Bookshelf 2023. <https://www.ncbi.nlm.nih.gov/books/NBK592420/>
- [5] Physiology, Plasminogen Activation (StatPearls). StatPearls Publishing / NCBI Bookshelf 2022.
<https://www.ncbi.nlm.nih.gov/books/NBK539745/>

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