Pharmacist's Role in the Management of Acute Stroke

A presentation for HealthTrust Members
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Conflict Disclosure Statements

- Patrick Pauls - There are no relevant financial interest to disclose for myself or my spouse/partner from within the last 12 months
- Patrick J Bridgeman - There are no relevant financial interest to disclose for myself or my spouse/partner from within the last 12 months
- This program may contain the mention of drugs or brands presented in a case study or comparative format using evidence-based research. Such examples are intended for educational and informational purposes and should not be perceived as an endorsement of any supplier, brand, or drug.

Learning Objectives

1. Define the benefits of having a pharmacist as care providers for stroke patients
2. Identify roles and responsibilities of the pharmacist when assisting the team in the management of an acute ischemic or hemorrhagic stroke
3. Formulate a plan for management and monitoring of a patient presenting with an acute ischemic stroke

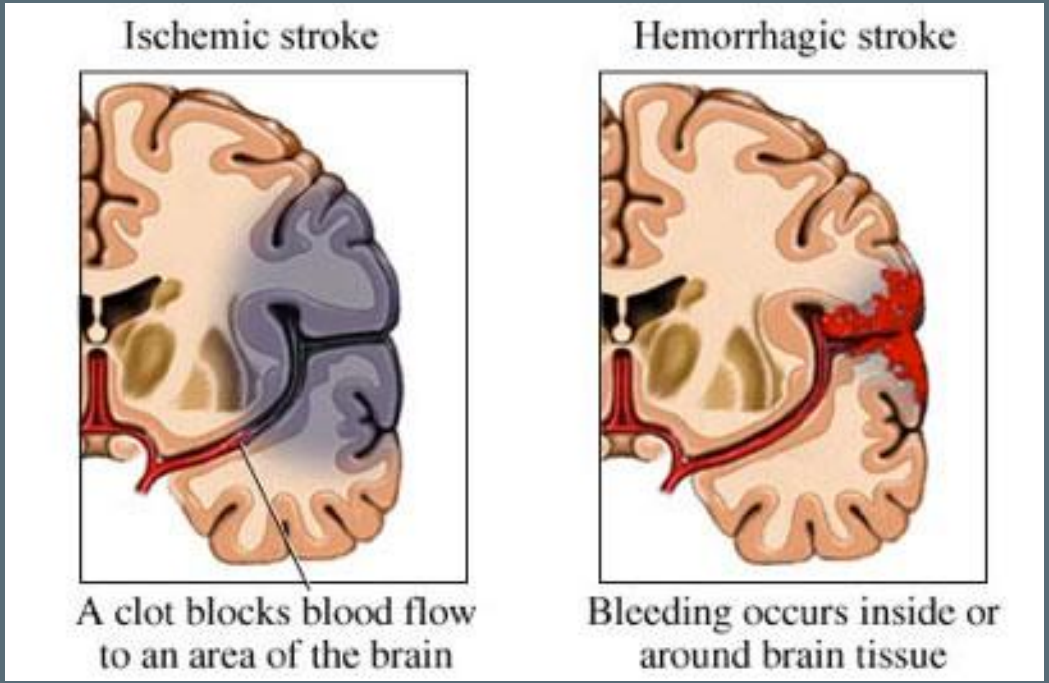
Epidemiology and Impact of Stroke

- 5th leading cause of death in US
  - 2nd leading cause world-wide
- A stroke occurs every 40 seconds in the US
- Death every 4 minutes
- Leading cause of serious long-term disability
- Stroke related costs ~$46 billion between 2014 and 2015

Source: CDC.gov. 2020. Accessed 3/30/21

Definitions

Stroke - interruption or reduction of blood flow to the brain causing tissue necrosis from lack of oxygen and glucose



Transient ischemic attack (TIA) - form of ischemic stroke where the blood flow is temporarily blocked/reduced without tissue necrosis

Sources: CDC.gov. 2021. Accessed 3/30/21
Stroke.org. AHA. 2021. Accessed 3/30/21

B E F A S T

Balance

Does the person have a sudden loss of balance?

Eyes

Has the person lost vision in one or both eyes?

Face

Does the person's face look uneven?

Arms

Is one arm weak or numb?

Speech

Is the person's speech slurred? Does the person have trouble speaking or seem confused?

Time

Call 9-1-1 now!

Source: https://www.dukehealth.org/blog/know-signs-of-stroke-be-fast. Accessed 3/30/21

Management of Ischemic Stroke

Goals of Therapy

- Improve neurological outcome
- Reduce mortality
- Prevent recurrence
- Prevent complications

Source: Powers WJ, et al. *ACC*. 2019; 50:e344–e418.

Benefits of Pharmacists in Management of Stroke

Benefits of Pharmacists in Stroke Management

- Emergency Department (ED)
- Inpatient Setting
- Outpatient Setting
  - Ambulatory Care
  - Community Pharmacy

Source: Basaraba JE, et al. *Can J Neurol Sci*. 2018; 45(1):49-55.

Benefits of Pharmacists in Stroke Management

- Emergency Department (ED)
  - Adding pharmacist to stroke pager and participation in assessment, dose verification, and patient education

Sources: Basaraba JE, et al. *Can J Neurol Sci*. 2018; 45(1):49-55.
Lee E. *P T*. 2011; 36(3):159-161.
Ferguson K, et al. *Crit Care Med*. 2019;47(1):656.

Benefits of Pharmacists in Stroke Management

- Emergency Department (ED)
  - Adding pharmacist to stroke pager and participation in assessment, dose verification, and patient education

Resulted in a **reduction of decision-to-needle times for thrombolytic therapy**

- Zero minute decision-to-needle: 0% to 78%

Sources: Basaraba JE, et al. *Can J Neurol Sci*. 2018; 45(1):49-55.
Lee E. *P T*. 2011; 36(3):159-161.
Ferguson K, et al. *Crit Care Med*. 2019;47(1):656.

Benefits of Pharmacists in Stroke Management

- Inpatient Setting
  - Medication reconciliation
  - Participation in stroke team rounds
  - Communication with community pharmacy and primary care provider (PCP)

Source: Basaraba JE, et al. *Can J Neurol Sci*. 2018; 45(1):49-55.

Benefits of Pharmacists in Stroke Management

- Inpatient Setting → **increased:**
  - **Identification of drug therapy problems**
  - **Patient follow-up** 4 weeks post discharge
  - **Medication adherence** 3 months post discharge
  - Adherence to stroke guideline performance indicators
  - Patient satisfaction with educational sessions

Source: Basaraba JE, et al. *Can J Neurol Sci*. 2018; 45(1):49-55.

Benefits of Pharmacists in Stroke Management

- Outpatient Setting
  - Ambulatory Care
    - Stroke prevention/bridge clinic
    - Prescriptive authority/collaborative practice agreement
  - Community Pharmacy
    - Medication reviews and education
    - Resolved drug therapy problems

Source: Basaraba JE, et al. *Can J Neurol Sci*. 2018; 45(1):49-55.

Benefits of Pharmacists in Stroke Management

- Outpatient Setting
  - Ambulatory Care
    - **Reduced readmission rates** (14.5% → 2.2%)
    - **Significantly more patients reached goal:**
      - **Blood pressure** (83% vs. 40%)
      - **Lipid levels** (40% vs. 13%)
      - **Glucose levels** (75% vs 50%)
  - Community Pharmacy
    - Prevented reduction in HRQoL scores post-stroke
    - Reduced days to pickup of antihypertensives (11 vs. 2 days)

Source: Basaraba JE, et al. *Can J Neurol Sci*. 2018; 45(1):49-55.

Assessment Question 1

Which of the following is not a benefit of having a pharmacist involved in the management of a stroke?

a. Improved medication adherence
b. Reduced decision-to-needle time for thrombolysis
c. Reduced readmission rates
d. Reduced treatment costs

Assessment Question 1 Response

Which of the following is not a benefit of having a pharmacist involved in the management of a stroke?

a. Improved medication adherence
b. Reduced decision-to-needle time for thrombolysis
c. Reduced readmission rates
d. Reduced treatment costs

Get With The Guidelines® - Stroke Achievement Measures

Upon Admission	• Arrive by 3.5 hours, tPA by 4.5 hours • Reversal agent initiation for ICH
By End of Day 2	• Early antithrombotics • VTE prophylaxis
Before Discharge	• Anticoagulation for AFib/Aflutter • Intensive statin • Stroke education

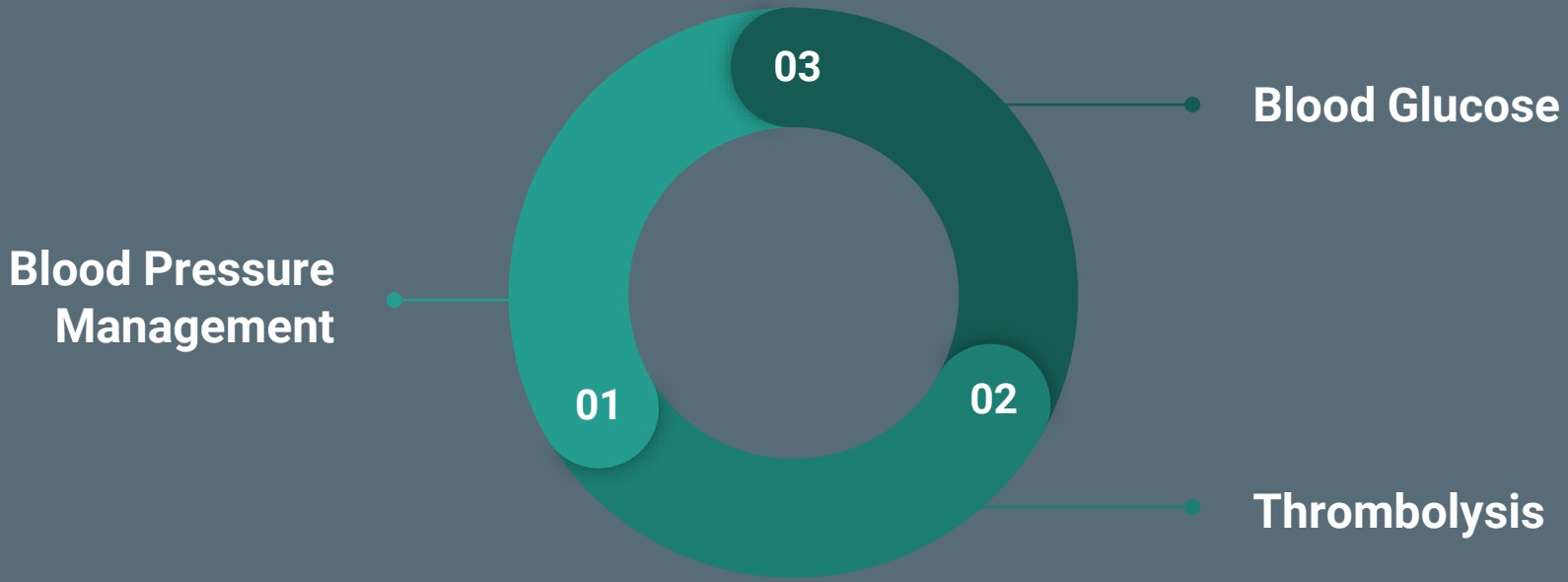
Source: https://www.heart.org/en/professional/quality-improvement/get-with-the-guidelines/get-with-the-guidelines-stroke/ get-with-the-guidelines-stroke-recognition-criteria. Accessed 3/31/21

Patient Case

JM is a 45 year old male who was brought in by his wife because he was feeling dizzy, slurring his words, and was having left sided weakness in his arms and legs

Management of Acute Ischemic Stroke

ED Management of Ischemic Stroke



Source: Powers WJ, et al. *ACC*. 2019; 50:e344–e418.

Blood Pressure Management for Ischemic Stroke

Thrombolysis

BLOOD PRESSURE GOALS:

Before thrombolysis	During & after thrombolysis
SBP ≤ 185 mmHg	SBP ≤ 180 mmHg
DBP ≤ 110 mmHg	DBP ≤ 105 mmHg

No Thrombolysis

Not eligible if SBP > 220 mmHg -OR- DBP > 120 mmHg

- Allow permissive hypertension
- Goal = 15% reduction in SBP over 24 hours

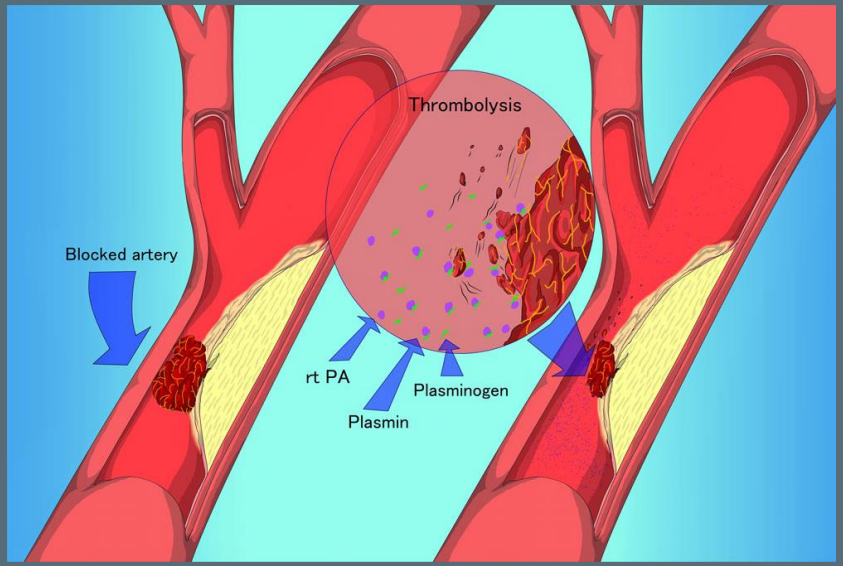
Source: Powers WJ, et al. *ACC*. 2019; 50:e344–e418.

1st Line Options to Treat HTN Prior to tPA

Drug	Dosing
Labetalol	10-20 mg IV push over 1-2 min; may repeat x 1 dose
Nicardipine	5 mg/h IV infusion; Titrate by 2.5 mg/h q5-15mins, max 15 mg/h
Clevidipine	1-2 mg/h IV; double dose q2-5mins, max 21 mg/h

Source: Powers WJ, et al. *ACC*. 2019; 50:e344–e418.

Thrombolysis:
Tissue Plasminogen Activator (tPA)



Source: https://ivcnorthwest.com/treatment/catheter-directed-thrombolysis-thrombectomy/. Accessed 3/30/21

Summary of Thrombolysis Clinical Data

1. **Time is brain!** → goal door-to-needle time < 1 hour
2. tPA improves neurological outcomes, not mortality
3. 4.5-9 hour window not recommended

Sources: Marler JR, et al. *N Engl J Med*. 1995; 333(24):1581-7.
Hacke W, et al. *N Engl J Med*. 2008; 359:1317-1329
Ma H, et al. *N Engl J Med*. 2018; 380:1795-1803

Blood Glucose

Hypoglycemia (BG < 60 mg/dL) should be corrected **prior** to use of tPA

- Hypoglycemia could mimic a stroke
- Goal BG 140-180 mg/dL

Source: Powers WJ, et al. *ACC*. 2019; 50:e344–e418.

Hemorrhagic Stroke

Management of Hemorrhagic Stroke

- Anticoagulant reversal agents
- Blood pressure control

Source: Hemphill JC, et al. *AHA*. 2015;46:2032–2060

Management of Hemorrhagic Stroke

Anticoagulant reversal if currently taking:

Warfarin	Vitamin K + 4F-PCC (or FFP)
DOAC	4F-PCC or Andexanet Alfa
Dabigatran	Idarucizumab

4F-PCC = four-factor prothrombin complex concentrate, DOAC = direct oral anticoagulant, FFP = fresh frozen plasma

Source: Hemphill JC, et al. *AHA*. 2015;46:2032–2060

Management of Hemorrhagic Stroke

Blood pressure control

Initial SBP	Goal SBP
SBP 150-220 mmHg	< 140
SBP > 220 mmHg	Consider aggressive reduction of BP

Source: Hemphill JC, et al. *AHA*. 2015;46:2032–2060

Roles and Responsibilities of the Pharmacist in Acute Stroke:

Evaluating Appropriateness of Thrombolysis

Indications for Thrombolysis with tPA

- Age ≥ 18 years
- Last known normal < 4.5 hours
- Diagnosis of acute ischemic stroke w/neurological deficits

Source: Powers WJ, et al. *ACC*. 2019; 50:e344–e418.

Contraindications for tPA

- **Severe head trauma or prior stroke in the previous 3 months**
- Symptoms suggest subarachnoid hemorrhage
- **Previous ICH**
- Recent intracranial or spinal surgery in previous 3 months
- Intracerebral neoplasm
- Infective endocarditis
- Aortic arch dissection
- **Elevated blood pressure (SBP > 185 mmHg or DBP > 110 mmHg) that cannot be lowered safely**
- Active internal bleeding
- Acute bleeding diathesis (PLT < 100, **heparin within previous 24 hours, warfarin w/INR > 1.7, DOAC)**
- CT demonstrates infarction > one-third of cerebral hemisphere
- **CT demonstrates acute ICH**

Source: Powers WJ, et al. *ACC*. 2019; 50:e344–e418.

Relative Contraindications for tPA

- **Mild and non-disabling or rapidly improving stroke symptoms**
- **Very severe neurologic deficits (NIHSS score > 25) within 3 to 4.5 hour window**
- Pregnancy
- Seizure at onset
- **Recent major surgery or serious trauma within previous 14 days**
- **Recent gastrointestinal or urinary tract hemorrhage within previous 21 days**
- Ischemic stroke within previous 3 months
- Recent ST-elevation acute MI within previous 3 months
- **Blood glucose concentration < 50 mg/dL**

Source: Powers WJ, et al. *ACC*. 2019; 50:e344–e418.

Roles and Responsibilities of the Pharmacist in Acute Stroke:

Evaluating Appropriateness of Reversal

Indications for Anticoagulant Reversal in ICH

01	4F-PCC	• VKA if unknown INR or elevated INR • Bleeding associated with DOAC use
02	Andexanet alfa	• Bleeding associated with DOAC use

VKA = vitamin K antagonist

Sources: [Andexanet alfa]. Alexion Pharmaceuticals Inc. 2021.
[Prothrombin Complex Concentrate (Human)]. CSL Behring. 2020.

Contraindications for Anticoagulant Reversal in ICH

01	4F-PCC	• History of HIT • DIC • Hypersensitivity to any component
02	Andexanet alfa	• No contraindications

DIC = Disseminated intravascular coagulation
HIT = heparin-induced thrombocytopenia

Sources: [Andexanet alfa]. Alexion Pharmaceuticals Inc. 2021.
[Prothrombin Complex Concentrate (Human)]. CSL Behring. 2020.

Roles and Responsibilities of the Pharmacist in Acute Stroke:

Order Entry/Verification of Thrombolysis or Reversal Agent

tPA Dosing

- Alteplase 0.9 mg/kg (max dose of 90 mg)
  - Administered over 1 hour:
    - Bolus: 10% over 1 minute
    - Infusion: The rest over the following 59 minutes
- Tenecteplase 0.25 mg/kg (max dose of 25 mg)
  - Administered IV push over 5 seconds

Source: Powers WJ, et al. *ACC*. 2019; 50:e344–e418.

Reversal Dosing: 4F-PCC

Warfarin →

Pre-treatment INR	2 to < 4	4 to 6	> 6
Dose (units Factor IX/kg)	25	35	50
Max dose (units Factor IX)	2500	3500	5000
Fixed dose (units Factor IX)	1500-2000		

DOAC → 50 mg/kg (max of 5000 units Factor IX)

Sources: [Prothrombin Complex Concentrate (Human)]. CSL Behring. 2020.
Tellor KB, et al. *Blood Transfus*. 2018;16(4):382-386.

Reversal Dosing: Andexanet alfa

DOAC	Last Dose	< 8 hours or unknown	≥ 8 hours
Apixaban	≤ 5 mg	Low dose	Low dose
	> 5 mg/unknown	**High dose**	
Rivaroxaban	≤ 10 mg	Low dose	
	> 10 mg/unknown	**High dose**	

Source: [Andexanet alfa]. Alexion Pharmaceuticals Inc. 2021.

Reversal Dosing: Andexanet alfa

DOAC	Last Dose	< 8 hours or unknown	≥ 8 hours
Apixaban	≤ 5 mg	Low dose	Low dose
	> 5 mg/unknown	High dose	
Rivaroxaban	≤ 10 mg	Low dose	
	> 10 mg/unknown	High dose	

	Initial IV Bolus	Follow-On IV Infusion
Low dose	400 mg at target rate 30 mg/min	4 mg/min for up to 120 minutes (480 mg)
High dose	800 mg at target rate 30 mg/min	8 mg/min for up to 120 minutes (960 mg)

Source: [Andexanet alfa]. Alexion Pharmaceuticals Inc. 2021.

Roles and Responsibilities of the Pharmacist in Acute Stroke:

Patient Education for Thrombolysis

Patient Education for Thrombolysis

- What tPA is and when it is used
- Who qualifies for tPA
- Risks and benefits of tPA
- What to monitor for and report to team
- Follow-up care and prescription counseling

Source: Powers WJ, et al. *ACC*. 2019; 50:e344–e418.

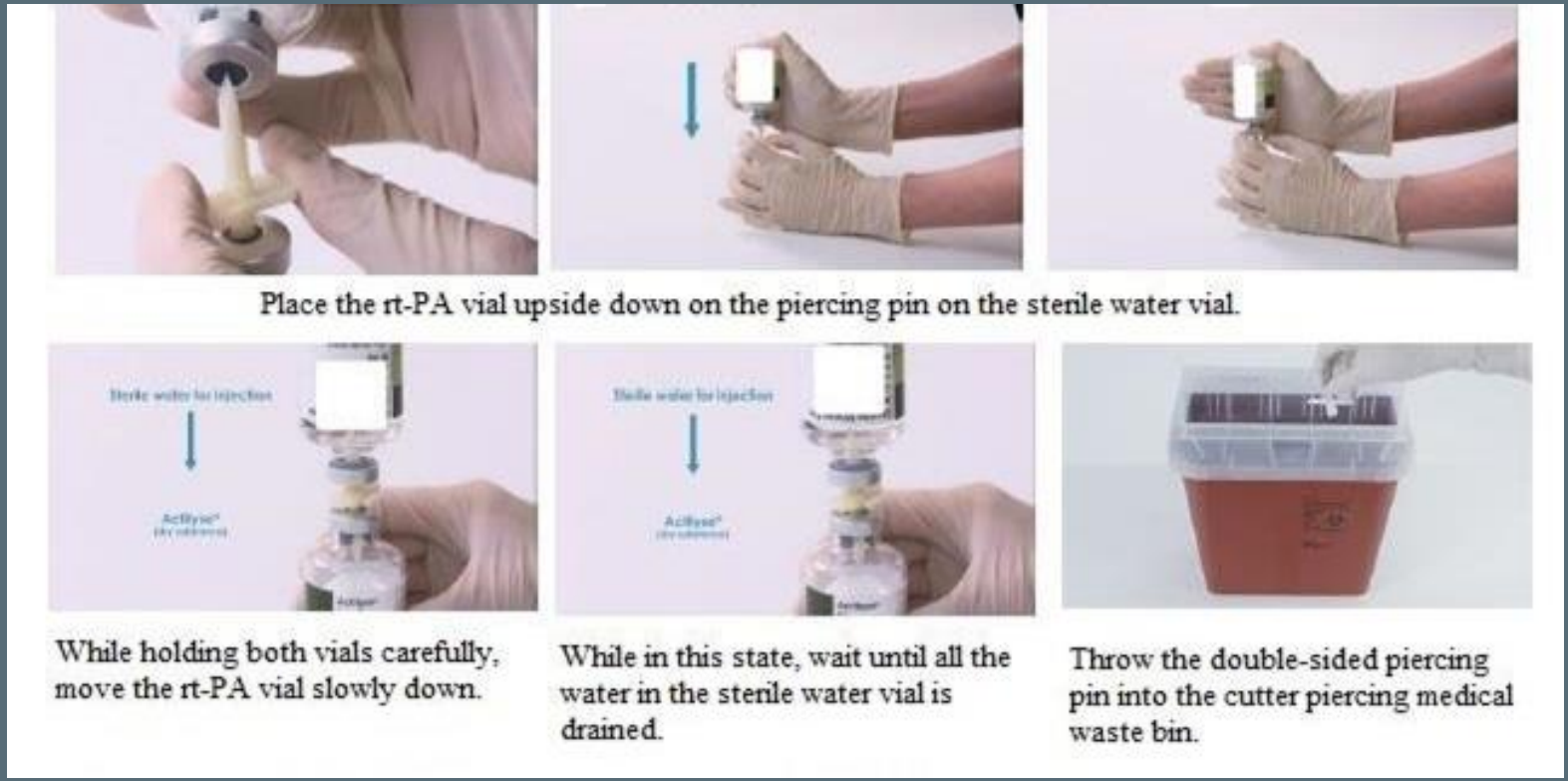
Roles and Responsibilities of the Pharmacist in Acute Stroke:

Preparation of tPA

Alteplase Preparation

Source: https://www.researchgate.net/figure/tPA-preparation-steps-and-details-Turkish-Journal-of-Cerebrovascular-Diseases-2020_fig1_341096225. Accessed 3/30/21

Alteplase Preparation



Source: https://www.researchgate.net/figure/tPA-preparation-steps-and-details-Turkish-Journal-of-Cerebrovascular-Diseases-2020_fig1_341096225. Accessed 3/30/21

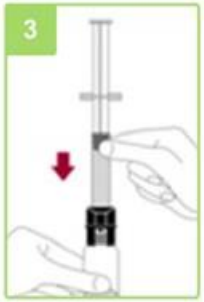
Tenecteplase Preparation

Open the box of the vial-adapter

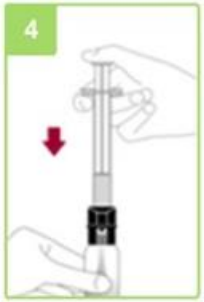
Remove tip cap from syringe.

Remove the flip-off cap from the vial.

Crew prefilled syringe on the vial-adapter **tightly**.

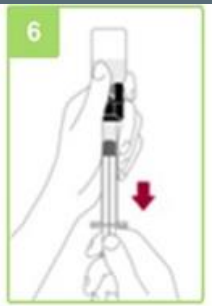


Penetrate the vial stopper in the middle with the spike of the vial-adapter.



Add the water for injections by pushing the syringe plunger **slowly** down to avoid foaming.

Reconstitute by swirling **gently.**



Invert vial/syringe and transfer appropriate volume of solution into syringe according instructions.

Disconnect syringe from the vial-adapter. Now solution is ready for i.v. Bolus injection.

Source: https://www.stemi-care.com/metalyse/administration-and-posology. Accessed 3/30/21

Roles and Responsibilities of the Pharmacist in Acute Stroke:

Monitoring Post-Thrombolysis/Reversal

Post-Thrombolysis Monitoring

01	BP and Neuro	• Every 15 minutes x 2 hours • Every 30 minutes x 5 hours • Every 1 hour x 24 hours
02	Bleeding	• Hold antiplatelets/anticoagulants x 24 hrs • Signs or symptoms of bleeding • Concerns for ICH → hold tPA + CT head
03	Angioedema	• Discontinue tPA • Treat similar to anaphylaxis

Sources: Powers WJ, et al. *ACC*. 2019; 50:e344–e418.
Alteplase [package insert]. Genentech, Inc. 2015.
Tenecteplase recombinant [package insert]. Hoffmann-La Roche Limited. 2018.

Post-Reversal Monitoring

- Clinical response
- Signs of thromboembolism
- Signs of hypersensitivity
- 4F-PCC for warfarin → INR (baseline and 30 minutes after)

Sources: [Andexanet alfa]. Alexion Pharmaceuticals Inc. 2021.
[Prothrombin Complex Concentrate (Human)]. CSL Behring. 2020.

Assessment Question 2

Which of the following is not a task that the pharmacist could assist with in the setting of an acute stroke?

a. Preparation of tPA
b. Identifying need for reversal of anticoagulants
c. Consenting patient for thrombolysis
d. Order entry and/or verification
e. Ensuring patient meets inclusion and exclusion criteria

Assessment Question 2 Response

Which of the following is not a task that the pharmacist could assist with in the setting of an acute stroke?

a. Preparation of tPA
b. Identifying need for reversal of anticoagulants
c. Consenting patient for thrombolysis
d. Order entry and/or verification
e. Ensuring patient meets inclusion and exclusion criteria

Pharmacist Involvement/Impact at RWJUH

Responsibilities:

- Respond to all code strokes
- Evaluate patients and review medications
- Identify contraindications to tPA/reversal agents
- Prepare and deliver tPA/reversal agents
- Monitoring BP and toxicities

Impacts:

- Patient safety: contraindications and appropriate dosing
- Improved Get With The Guidelines® stroke criteria
    - Door-to-needle time

Back to JM

JM is a 45 year old male who was brought in by his wife because he was feeling dizzy, slurring his words, and was having left sided weakness in his arms and legs

- PMH: hypertension and type II diabetes
- Last known normal was 15 minutes ago
- Medications: Lisinopril 20 mg daily, metformin 1000 mg BID
- Vitals: BP 194/100, HR 104, RR 18, Glucose 135 mg/dL, Weight 87 kg

JM is evaluated quickly before being taken to obtain a head CT

Assessment Question 3

The neurologist orders tPA for JM. Which of the following would be appropriate interventions for the pharmacist? Select all that apply

a. Review medication list for anticoagulants
b. Preparation of tPA
c. Administration of alteplase bolus
d. Preparation of 4F-PCC
e. Ensure appropriate dosing of tPA
f. Ensuring BP at goal before starting tPA

Assessment Question 3 Response

The neurologist orders tPA for JM. Which of the following would be appropriate interventions for the pharmacist? Select all that apply

a. **Review medication list for anticoagulants**
b. **Preparation of tPA**
c. Administration of alteplase bolus
d. Preparation of 4F-PCC
e. **Ensure appropriate dosing of tPA**
f. **Ensuring BP at goal before starting tPA**

Summary

- There are several benefits of having a pharmacist as care providers for stroke patients across several different care locations
- Pharmacists play a vital role in the management of an acute ischemic or hemorrhagic stroke
  - Ensuring appropriateness of therapy
  - Improving door-to-needle times
  - Rapid preparation of tPA/reversal agents

Sources: Basaraba JE, et al. *Can J Neurol Sci*. 2018; 45(1):49-55.; 45(1):49-55.
Lee E. *P T*. 2011; 36(3):159-161.
Ferguson K, et al. *Crit Care Med*. 2019;47(1):656.. 2019;47(1):656.

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Thank You for Listening

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