**Introduction: Acute aortic aneurysm dissection**

Acute aortic aneurysm dissection is a life-threatening cardiovascular emergency that requires prompt recognition and management. It occurs when a tear develops in the innermost layer of the aortic wall, allowing blood to enter the middle layer and split the layers apart. This creates a "false lumen" and can impair blood flow. With its increasing prevalence and high mortality if untreated, acute aortic dissection is a critical diagnosis for physicians and pharmacists to rapidly identify and manage collaboratively.

**Epidemiology**

The incidence of acute aortic dissection ranges from 2 to 3.5 cases per 100,000 person-years. The mean age at presentation is 63 years old, with a male predominance of 3:1. The most common predisposing risk factor is hypertension, present in 60-80% of patients. Other risk factors include connective tissue disorders like Marfan syndrome and Ehlers-Danlos syndrome, bicuspid aortic valve, coarctation of the aorta, family history of aortic disease, atherosclerosis, and prior cardiac surgery. The Stanford classification categorizes dissections involving the ascending aorta as type A, present in 60-70% of cases, while dissections limited to the descending aorta are type B, accounting for 30-40% of cases. Type A dissections have higher in-hospital mortality, reported as high as 1-2% per hour after symptom onset if left untreated. Overall mortality of untreated ascending dissections approaches 50% within the first 48 hours.

**Pathophysiology**

* The pathophysiology involves an initial tear in the intimal layer of the aortic wall, allowing pulsatile blood flow to penetrate the media and propagate distally or proximally. The pulsatile shear stress contributes to separation of the medial layers and enlargement of the false lumen. Dissections can be complicated by compromising flow in aortic branch vessels, obstruction of coronary ostia, pericardial effusion and tamponade, aortic valve insufficiency, and aortic rupture. Uncontrolled hypertension is the major factor driving propagation and adverse complications. Medical management aims to minimize shear forces while definitive repair is planned.

**Clinical Presentation**

The clinical presentation of acute aortic aneurysm dissection encompasses a range of signs and symptoms that require prompt recognition for timely diagnosis and management. Key signs and symptoms include:

* Sudden-onset severe chest or back pain:
  + The hallmark symptom of acute aortic aneurysm dissection is intense and often excruciating pain. Patients commonly describe the pain as tearing or ripping, which can be debilitating.
* Radiation of pain:
  + The pain may radiate to various areas, including the neck, jaw, or abdomen. The location of the pain can provide clues about the extent and involvement of the dissection.
* Hypertension:
  + High blood pressure is frequently observed in patients with acute aortic aneurysm dissection. The elevation in blood pressure may be related to the release of stress hormones or impaired blood flow due to compromised aortic branches.
* Syncope or altered mental status:
  + In some cases, aortic dissection can lead to decreased blood flow to the brain, resulting in syncope (fainting) or altered mental status.
* Focal weakness or neurologic deficits:
  + Depending on the location and extent of the dissection, patients may experience symptoms such as focal weakness, paralysis, or changes in sensation due to compromised blood flow to specific regions of the brain.
* Signs of cardiac tamponade:
  + When the dissection involves the aortic root, bleeding into the pericardium can occur, leading to cardiac tamponade. Signs of cardiac tamponade include jugular venous distention, muffled heart sounds, tachycardia, and hypotension.
* Pulse deficits or discrepancies in blood pressure between limbs:
  + Involvement of branch vessels or obstruction of blood flow to the arterial system can lead to pulse deficits or variations in blood pressure between the upper and lower extremities.
* Symptoms suggestive of organ malperfusion:
  + Aortic dissection can compromise blood flow to various organs, resulting in symptoms such as mesenteric ischemia (abdominal pain, nausea, vomiting), renal failure (decreased urine output, flank pain), or limb ischemia (pain, pallor, pulselessness).

**Risk Factors**

Several risk factors contribute to the development of acute aortic aneurysm dissection. Hypertension is the most common risk factor associated with this condition.

Other risk factors include:

* Connective tissue disorders: Patients with conditions such as Marfan syndrome and Ehlers-Danlos syndrome have an increased risk of aortic dissection due to weakened connective tissue in the aortic wall.
* Bicuspid aortic valve: Individuals with a bicuspid aortic valve, a congenital abnormality where the aortic valve has two instead of three leaflets, are at higher risk of aortic dissection.
* Family history: A positive family history of aortic dissection increases the risk of developing the condition.
* Aging: The incidence of aortic dissection increases with age.
* Atherosclerosis: Although less common, atherosclerosis can contribute to the development of aortic dissection.
* Trauma or prior cardiac surgery: Blunt trauma or previous cardiac surgery can weaken the aortic wall and increase the risk of dissection.

A high index of suspicion is required, especially in patients >60 years old presenting with sudden-onset chest, back or abdominal pain and history of hypertension. Pain is the most common symptom but clinical presentations vary based on extent of dissection. Aortic regurgitation, pulse deficit, hypotension and cardiac tamponade indicate ascending (type A) dissection.

**Diagnostic Approach**

The diagnostic approach for patients presenting with acute aortic aneurysm dissection involves a combination of clinical assessment, imaging studies, and laboratory tests. Prompt and accurate diagnosis is essential to guide appropriate management and prevent potential complications.

1. Clinical Assessment:
   * Obtain a detailed medical history, including symptoms, risk factors, and prior cardiac or vascular conditions.
   * Perform a thorough physical examination, including blood pressure measurements in both arms and assessment for pulse deficits or discrepancies.
2. Imaging Studies:
   * Computed Tomography Angiography (CTA): This is the imaging modality of choice for diagnosing acute aortic aneurysm dissection. CTA provides detailed images of the aorta, allowing visualization of the dissection, the location of the entry tear, and the extent of involvement. It can also identify complications such as branch vessel involvement, aortic regurgitation, or pericardial effusion.
     1. CTA chest: Sensitivity 83-94%, specificity 87-100%. Gold standard test, defines entire dissection.
   * Magnetic Resonance Angiography (MRA): MRA is an alternative to CTA, especially in patients with contraindications to iodinated contrast media. MRA provides high-resolution images of the aorta and can help evaluate the extent of dissection and involvement of branch vessels.
   * Transthoracic Echocardiography (TTE): TTE is useful for initial evaluation and can provide information about aortic regurgitation, pericardial effusion, and the proximal extent of the dissection. However, its sensitivity for detecting distal dissections is limited.
3. Laboratory Tests:
   * Complete Blood Count (CBC): To assess for anemia, thrombocytosis, or other blood abnormalities.
   * Basic Metabolic Panel (BMP): To evaluate renal function and electrolyte imbalances.
   * Coagulation Profile: To assess coagulation status and exclude any coagulopathies.
   * D-Dimer: Elevated levels of D-dimer can suggest the presence of an acute aortic aneurysm dissection, although it is not specific and false positives can occur.
   * Genetic Testing: In patients with a strong family history or suspected genetic connective tissue disorder, genetic testing may be considered to identify underlying genetic mutations.
4. Differential Diagnosis:
   * Other conditions that can present similarly to acute aortic aneurysm dissection should be considered and excluded. These include acute coronary syndrome, pulmonary embolism, aortic rupture, aortic intramural hematoma, and other causes of acute chest or back pain.

Immediate imaging is required, with CTA chest the gold standard to delineate the dissection. TEE provides rapid evaluation, especially of ascending dissection and complications. Initial management should not wait for confirmatory imaging if suspicion is high.

**Management - Overview**

Immediate imaging is required, with CTA chest the gold standard to delineate the dissection. TEE provides rapid evaluation, especially of ascending dissection and complications. Initial management should not wait for confirmatory imaging if suspicion is high.

1. Medical Management:
   * Blood Pressure Control: The reduction of blood pressure is crucial to minimize shear forces on the aortic wall and prevent further dissection
   * Pain Management: Acute aortic aneurysm dissection is associated with severe pain.
   * Anti-Impulse Medications: Additional medications may be used to control blood pressure in cases where beta-blockers alone are insufficient.

1. Surgical Intervention:
   * Type A Dissection: Type A dissections involving the ascending aorta, aortic arch, or proximal descending aorta typically require emergent surgical intervention.
   * Type B Dissection: Type B dissections involving the descending thoracic aorta are initially managed with medical therapy unless complications or malperfusion are present. In selected cases, endovascular repair with stent graft placement (thoracic endovascular aortic repair, or TEVAR) may be considered to seal the entry tear and promote false lumen thrombosis.

1. Surveillance and Follow-up:
   * Long-term management includes regular surveillance and follow-up imaging studies to monitor the size and progression of the aortic aneurysm, identify complications, and guide further interventions if necessary.
   * Lifestyle modifications, including blood pressure control, smoking cessation, and regular exercise, are recommended to reduce the risk of disease progression and complications.

**Therapeutic Goals**

The priority pharmacotherapy goals include:

* Minimize shear forces on dissected aorta by controlling heart rate and blood pressure
* Alleviate severe pain and anxiety
* Prevent further propagation of dissection
* Avoid agents causing reflex tachycardia or inotropy
* Facilitate smooth postoperative recovery after surgical repair

**Pharmacotherapy**

**Medical Management**

The priority is to rapidly reduce shear forces on the dissected aorta by controlling heart rate and lowering blood pressure. This requires careful selection of pharmacologic agents that reduce aortic wall tension without increasing shear stress by excessive reflex tachycardia or inotropy.

Goals of Medical Therapy:

* Heart rate <60 bpm
* Systolic BP 100-120 mm Hg
* Mean arterial pressure 60-80 mm Hg
* Avoid increased dP/dT or reflex tachycardia

**First Line Agents:**

Intravenous Beta Blockers:

* Esmolol: Short-acting beta-1 selective blocker. Loading dose 500 mcg/kg over 1 minute followed by infusion at 50-200 mcg/kg/min titrated to heart rate goal. Has very short half-life if adverse effects occur.
* Labetalol: Combined alpha/beta blocker. Bolus dosing of 20 mg IV push every 10 minutes (up to 300 mg) until heart rate goal achieved, then infusion 1-2 mg/min titrated up to 200 mg/hr.
  + The alpha antagonism causes peripheral vasodilation to complement the beta effects of lowering heart rate and contractility. Labetalol does not have active metabolites so effects dissipate quickly after stopping the infusion.
* Metoprolol: Beta-1 selective blocker. 5 mg IV every 5 minutes (up to 15 mg total) then 25-50 mg orally every 6 hours.

Beta blockers reduce shear stress by decreasing heart rate, contractility, and dP/dT. They are first line agents and the cornerstone of medical management. Continuous IV infusions allow titration to prompt heart rate control. The choice among these agents depends on the clinical scenario, need for very short-term control, and contraindications. Esmolol provides the most rapid onset and titratability but requires a continuous infusion. Labetalol has the advantage of combined alpha and beta effects. Metoprolol can be transitioned easily to oral therapy. The beta blockade should continue for at least 72 hours after surgery or until the dissection is stabilized on imaging.

**Second Line/Adjunctive Agents:**

* Nicardipine: Intravenous dihydropyridine calcium channel blocker. Initial infusion at 5 mg/hr, increasing by 2.5 mg/hr every 5 minutes (max 15 mg/hr) to achieve BP target. Useful if beta blocker contraindicated or additional agent needed.
* Clevidipine: Rapid-acting intravenous dihydropyridine calcium channel blocker with very short half-life. Starting dose 1-2 mg/hr, doubling every 90 seconds until BP approaches goal, then increasing by less than double to finely titrate. Useful for perioperative blood pressure management.
* Sodium nitroprusside: Direct vasodilator. 0.25-0.5 mcg/kg/min infusion, increase by 0.5 mcg/kg/min every 5 minutes, maximum 8 mcg/kg/min. Often used in combination with beta blocker for severe hypertension.
  + Requires invasive arterial monitoring during infusion.
* Hydralazine: Direct vasodilator. Intermittent IV bolus dosing of 5-20 mg every 4-6 hours as needed for BP control. May cause reflex tachycardia.

These agents provide additional options for blood pressure control in patients inadequately responsive to beta blockade. They should be used cautiously and with concurrent beta blocker to prevent reflex tachycardia and increased shear stress. Calcium channel blockers, specifically the intravenous dihydropyridine agents nicardipine and clevidipine, provide options for additional blood pressure management when beta blockers alone are insufficient. They reduce systemic vascular resistance through arteriolar dilation. Key considerations when using these agents:

* They do not treat the underlying pathophysiology or provide rate control, so should not be used as monotherapy
* Reflex tachycardia is common, requiring concurrent beta blockade

Pain Management:

* Morphine: 0.1 mg/kg IV bolus followed by 2-4 mg IV every 5-15 minutes titrated for pain relief.
* Fentanyl: 1-2 mcg/kg IV bolus followed by 1 mcg/kg IV every 30-60 minutes for pain control.

Adequate analgesia helps control pain, anxiety, and catecholamine surges that increase shear stress. It allows smoother titration of antihypertensive therapy. Careful monitoring for respiratory depression is needed.

**Other Pharmacotherapy Considerations**

* Avoid inotropic or chronotropic agents like dopamine, dobutamine, and epinephrine which increase shear stress.
* Manage volume status carefully, as aggressive volume resuscitation can worsen dissection.
* Attentive monitoring is required during transitions of care such as postoperative period.
* Provide in-depth patient education regarding medications, goals of therapy, adherence, and follow-up needs.

**Surgical and Endovascular Management**

Type A Dissections

* Require emergency surgical repair to prevent propagation, fatal complications, and rupture
* Surgery involves ascending aortic replacement with possible arch reconstruction

Indications for surgery:

* All type A dissections
* Type B dissections involving ascending aorta (DeBakey type I)
* Dissection complications: tamponade, coronary occlusion, uncontrolled pain or hypertension

Type B Dissections

* Initially managed medically unless complicated
* Endovascular repair with TEVAR may be used for malperfusion or other complications
* Uncomplicated type B dissections have 5-year survival around 75% with medical therapy alone

TEVAR may be considered if:

* Refractory pain, hypertension, or end-organ malperfusion
* Early aortic expansion >5mm diameter increase
* Large entry tear >10mm
* False lumen thrombosis <25% of total lumen

Surveillance/Follow-Up

* Serial imaging (CT or MRI) to monitor dissection healing and assess complications
* Repeat imaging at 1, 3, 6, and 12 months, then annually
* Monitor BP control and medication adherence
* Counsel on lifestyle modification and risk factor control
* Assess indications for surgical or endovascular intervention

**Tips for Board Exam Questions:**

* Know the specific BP/HR goals and how to achieve them with correct drug selection and dosing
* Recognize importance of controlling shear stress and avoiding reflex tachycardia
* Beta-blockers are first-line, know their strengths/weaknesses and how to combine other agents

**Key Guidelines and Evidence**

1. American College of Cardiology/American Heart Association (ACC/AHA) Guidelines for the Diagnosis and Management of Patients with Thoracic Aortic Disease:
   * Provides comprehensive recommendations for the diagnosis and management of thoracic aortic diseases, including aortic dissection.
   * Key Recommendations
     1. Intravenous beta blockers (esmolol, labetalol, metoprolol) are recommended as first-line agents to control heart rate and blood pressure.
     2. Intravenous vasodilators (nicardipine, clevidipine, nitroprusside) are recommended to rapidly control blood pressure when beta blockers are inadequate or contraindicated.
     3. **Goal is to reduce heart rate to 60-80 bpm and systolic blood pressure <120 mm Hg.**
     4. Intravenous opioids are recommended for pain control, as pain can increase heart rate and blood pressure.
     5. Oral beta blockers should be continued at hospital discharge to improve long-term outcomes.

1. Landmark Trials:
   * The INSTEAD-XL Trial:
     1. Investigated the long-term outcomes of patients with uncomplicated type B aortic dissection treated with medical therapy versus thoracic endovascular repair (TEVAR).
     2. Provided evidence supporting the use of TEVAR in certain patients with uncomplicated type B dissections to reduce disease progression and improve outcomes.
   * Ulici et al 2017
     1. A single-center retrospective chart review evaluated patients diagnosed with aortic dissection. The primary outcome measure was time to reach patient specific systolic blood pressure with clevedipine compared to nitroprusside
     2. Clevidipine administration during initial medical management of aortic dissection showed similar efficacy compared to SNP when used as adjunct therapy to esmolol.

**Clinical Scenarios**

1. Scenario 1:
   * A 62-year-old male with a history of poorly controlled hypertension presents to the emergency department with sudden-onset severe chest pain radiating to the back. On physical examination, blood pressure is 160/90 mmHg in the right arm and 140/80 mmHg in the left arm. The patient appears diaphoretic and anxious. ECG shows ST-segment elevation in leads V2-V4. Given the suspicion of acute aortic dissection, what is the most appropriate immediate management for this patient?

* Immediate Management:
  + The most appropriate immediate management for this patient suspected of having acute aortic dissection is to ensure a controlled blood pressure while minimizing shear forces on the aortic wall. The following steps should be taken:
    - Administer intravenous labetalol or esmolol to reduce blood pressure and heart rate, aiming for a systolic blood pressure target of 100-120 mmHg.
    - Provide adequate pain relief with intravenous opioids, such as morphine, to alleviate the severe chest pain.
    - Avoid treatments that increase blood pressure or heart rate, such as vasopressors or inotropic agents.
    - Consult a cardiovascular surgeon or transfer the patient to a facility capable of performing emergent surgical intervention if necessary.

**Summary: Acute Aortic Aneurysm Dissection Summary**

In summary, acute aortic aneurysm dissection is a life-threatening cardiovascular emergency that requires prompt recognition and management. Clinical pharmacists play a critical role in the management of this condition by ensuring appropriate pharmacotherapy, monitoring for potential drug interactions or adverse effects, and providing patient education.

Acute aortic aneurysm dissection presents with sudden-onset severe chest or back pain, often described as tearing or ripping. The clinical presentation includes hypertension, pulse deficits, and symptoms suggestive of organ malperfusion. Risk factors for aortic dissection include hypertension, connective tissue disorders, bicuspid aortic valve, family history, aging, atherosclerosis, and trauma or prior cardiac surgery.

The management of acute aortic aneurysm dissection involves a multidisciplinary approach. Immediate goals include blood pressure control, pain management, and preventing further propagation of the dissection. Surgical intervention is often required for type A dissections, while medical management is the mainstay for type B dissections. Long-term management includes surveillance, lifestyle modifications, and regular follow-up to monitor disease progression and prevent complications.

Clinical pharmacists with a strong understanding of the clinical presentation, diagnostic approach, pharmacotherapy, and key guidelines can contribute significantly to optimizing patient care and improving outcomes in acute aortic aneurysm dissection.

**References**

* Ledrle FA, Powell JT, Nienaber CA: Does intensive medical treatment improve outcomes in aortic dissection? BMJ 349:g5288, 2014.
* Nienaber CA, Clough RE. Management of acute aortic dissection. Lancet. 2015 Feb 28;385(9970):800-11. doi: 10.1016/S0140-6736(14)61005-9. Epub 2015 Feb 6. PMID: 25662791.
* Gudbjartsson T, Ahlsson A, Geirsson A, Gunn J, Hjortdal V, Jeppsson A, Mennander A, Zindovic I, Olsson C. Acute type A aortic dissection - a review. Scand Cardiovasc J. 2020 Feb;54(1):1-13. doi: 10.1080/14017431.2019.1660401. Epub 2019 Sep 23. PMID: 31542960.
* Siegal EM. Acute aortic dissection. J Hosp Med. 2006 Mar;1(2):94-105. doi: 10.1002/jhm.69. PMID: 17219479.
* Hiratzka LF, Bakris GL, Beckman JA, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease. J Am Coll Cardiol. 2010;55(14):e27-e129.doi:10.1016/j.jacc.2010.02.015
* Erbel R, Aboyans V, Boileau C, et al. 2014 ESC guidelines on the diagnosis and treatment of aortic diseases. Eur Heart J. 2014;35(41):2873-2926. doi:10.1093/eurheartj/ehu281
* Hagan PG, Nienaber CA, Isselbacher EM, et al. The International Registry of Acute Aortic Dissection (IRAD). JAMA. 2000;283(7):897–903. doi:10.1001/jama.283.7.897
* Tsai TT, Fattori R, Trimarchi S, et al. Long-term survival in patients presenting with type B acute aortic dissection: insights from the International Registry of Acute Aortic Dissection. Circulation. 2006;114(21):2226-2231. doi:10.1161/CIRCULATIONAHA.106.622340
* Trimarchi S, Tolenaar JL, Tsai TT, et al. Influence of clinical presentation on the outcome of acute B aortic dissection: evidences from IRAD. J Cardiovasc Surg (Torino). 2012;53(2):161-168.
* Wheatley GH 3rd, Gurbuz AT, Rodriguez-Lopez JA, Ramaiah VG, Olsen D, Williams J, Diethrich EB. Midterm outcome in 158 consecutive Gore TAG thoracic endoprostheses: single center experience. Ann Thorac Surg. 2006;81(5):1570-1577. doi:10.1016/j.athoracsur.2005.11.003
* Fattori R, Montgomery D, Lovato L, et al. Survival after endovascular therapy in patients with type B aortic dissection: a report from the International Registry of Acute Aortic Dissection (IRAD). JACC Cardiovasc Interv. 2013;6(8):876-882. doi:10.1016/j.jcin.2013.03.013
* Nienaber CA, Rousseau H, Eggebrecht H, et al. Randomized comparison of strategies for type B aortic dissection: the INvestigation of STEnt Grafts in Aortic Dissection (INSTEAD) trial. Circulation. 2009;120(25):2519-2528. doi:10.1161/CIRCULATIONAHA.109.886408
* Daily PO, Trueblood HW, Stinson EB, Wuerflein RD, Shumway NE. Management of acute aortic dissections. Ann Thorac Surg. 1970;10(3):237-247. doi:10.1016/s0003-4975(10)65594-4