**Introduction**

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.
  + 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.
  + 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.

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:
2. Imaging Studies:
3. CTA chest: Sensitivity 83-94%, specificity 87-100%. Gold standard test, defines entire dissection.
4. * 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.
   * 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.
   * 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.
5. Laboratory Tests:
6. Differential Diagnosis:

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  of Salicylate Toxicity

* ABCs: Airway protection, breathing support, circulation
* GI decontamination: Activated charcoal, whole bowel irrigation
* IV fluids: Replaces losses from vomiting, sweating, renal excretion
* Bicarbonate: Alkalinizes serum and urine to enhance elimination
* Dextrose: Reverses neuroglycopenia despite normal serum glucose
* Electrolytes: Replete potassium, calcium, magnesium
* Hemodialysis: Extracorporeal removal for severe toxicity
* Avoid sedation/intubation if possible given risks
* Frequent monitoring: Salicylate levels, ABG, electrolytes

### Pharmaoctherapy

#### Gastrointestinal Decontamination

**Activated charcoal**

* Single or multiple dose activated charcoal can be administered within 1-2 hours of ingestion to reduce absorption of salicylate from the gut. Multi-dose regimens are preferred over single dose charcoal for large overdoses and sustained-release preparations. Each dose of charcoal can bind 100-300 mg of salicylate. The use of cathartics is no longer recommended given lack of enhanced efficacy and increased adverse effects.

**Whole Bowel Irrigation**

* Whole bowel irrigation with polyethylene glycol electrolyte solution may have additional benefits compared to activated charcoal following massive ingestions, especially if an enteric coated or extended release product was ingested. It can help evacuate drug-containing bowel contents and combat delayed absorption from pharmacobezoars. However, aspiration risk with altered mental status warrants careful consideration.

#### **Alkalinization Therapy**

**Sodium Bicarbonate Administration**

* Alkalinization with intravenous sodium bicarbonate remains a mainstay of therapy to increase renal clearance and prevent salicylate redistribution into tissues. An initial bolus of 1-2 mEq/kg is administered, followed by an infusion of 150 mEq sodium bicarbonate in 1 liter of D5W at 1.5-2 times maintenance infusion rate. The goal is to achieve a urine pH of 7.5-8.0 while maintaining the serum pH under 7.55.
* Oral bicarbonate administration is contraindicated as it can increase absorption across the gastric mucosa. Overly rapid boluses can cause metabolic alkalosis. Prolonged therapy risks volume overload and electrolyte depletion. Common adverse effects include hypokalemia, hypocalcemia, hypoxemia, and paradoxical cerebral acidosis. Frequent monitoring helps minimize complications while achieving optimal alkalinization.

**Monitoring Response to Alkalinization**

* Close monitoring is required to ensure adequate alkalinization while avoiding complications. Serum electrolytes, renal function, urine pH and serial salicylate concentrations should be evaluated every 2-4 hours initially. The frequency can be reduced as the patient stabilizes. The anion gap helps assess the degree of metabolic improvement.
* Hypokalemia is a particular concern as it prevents achieving alkaluria and can cause dysrhythmias. Potassium repletion to 4-5 mEq/L is key. When the urinary pH is sustained above 7.5-8.0 and salicylate concentrations clearly decline in an asymptomatic patient, alkalinization therapy can be discontinued.

#### Extracorporeal Removal

#### **Indications for Hemodialysis**

* Hemodialysis effectively removes salicylate and corrects acid-base disorders. It is indicated for concentrations **exceeding 100 mg/dL in acute ingestions. Hemodialysis is also warranted in chronic toxicity with levels above 60-80 mg/dL depending on renal function.**Regardless of the salicylate concentration, hemodialysis should be performed for serious signs like altered mental status, seizures, ARDS, kidney failure, circulatory collapse or clinical deterioration despite standard therapy.

#### **Timing and Duration Considerations**

* The decision to start hemodialysis should be made early in the clinical course to prevent avoidable morbidity and mortality from delays. Appropriate consultation, coordination of hemodialysis access and patient transportation takes several hours. Clinical decline can be rapid, making it preferable to initiate plans for possible hemodialysis proactively.
* Duration depends on the severity of toxicity. Hemodialysis is generally continued until clinical improvement is apparent, adequate clearance has been achieved and the concentration trends below 20 mg/dL. Longer or repeated sessions may be needed in massive ingestions if absorption from the gut continues. Close monitoring is maintained post-hemodialysis to ensure levels remain low as acidemia improves redistribution into tissues.

#### **Alternative Extracorporeal Modalities**

Hemodialysis is the preferred extracorporeal treatment based on efficacy for clearing salicylate and correcting acidemia. However, alternative modalities can be used when hemodialysis is not readily available. Sustained low-efficiency dialysis (SLED), continuous venovenous hemofiltration (CVVH), extracorporeal membrane oxygenation (ECMO) and exchange transfusion in pediatric patients are reported alternatives. The availability of these modalities depends on the care setting.

### ****Summary of Key Pharmacologic Interventions****

* Sodium Bicarbonate
  + Mechanism: Alkalinizes blood and urine to ionize salicylate for enhanced clearance and reduced tissue redistribution.
  + Dose: 1-2 mEq/kg IV bolus, then 150 mEq in 1L D5W infusion.
  + Adverse Effects: Hypokalemia, hypocalcemia, hypoxemia, volume overload, paradoxical cerebral acidosis.

* Activated Charcoal

* Mechanism: Binds to salicylate in the gastrointestinal tract reducing absorption.
* Dose: 1 g/kg PO every 2-4 hours for several doses.
* Adverse Effects: Vomiting, constipation, aspiration pneumonia.

* Dextrose
  + Mechanism: Reverses neuroglycopenia by providing substrate for glycolysis despite normal serum glucose.
  + Dose: 0.5-1 g/kg IV bolus, then infusion as needed.
  + Adverse Effects: Hyperglycemia, phlebitis, hypokalemia.

Disposition and Follow Up

* Patients warrant admission for at least 24 hours of observation after acute ingestion to ensure concentrations remain low and no clinical deterioration occurs as absorption continues. Discharge is appropriate once the patient is asymptomatic, salicylate levels clearly downtrend, and psychiatric concerns have been addressed.
* Following discharge, outpatient follow up should be arranged to confirm complete resolution, provide toxicity education and limit future access to salicylates in high risk patients. After significant toxicity, survivors should avoid or limit salicylate use given susceptibility to adverse reactions.
* Overall, managing salicylate toxicity requires meticulous monitoring, tailored supportive care, enhanced elimination techniques and targeted pharmacologic interventions. An interdisciplinary approach with pharmacy, nephrology and toxicology guidance is ideal to deliver effective treatment and optimize patient outcomes.

### Key Guidelines and Evidence for Salicylate Toxicity Management

Guidelines for Salicylate Toxicity Management

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| --- | --- | --- |
| **Recommendation** | **Level of Evidence** | **Strength of Recommendation** |
| Serum alkalinization with IV sodium bicarbonate | A | Strong |
| Renal replacement therapy if serum salicylate >100 mg/dL | B | Strong |
| Repeated doses of activated charcoal | B | Weak |
| Aggressive dextrose administration | C | Weak |
| Avoid urine alkalinization in presence of hypokalemia | C | Strong |
| Serum alkalinization with IV sodium bicarbonate | A | Strong |

\*Level of Evidence: A = High quality randomized trials or diagnostic studies; B = Moderate quality evidence from observational studies; C = Expert opinion or case reports

\*Strength of Recommendation: Strong = Benefits clearly outweigh risks/burdens; Weak = Uncertainty in the estimates of benefits, risks and burden; recommendation may change as more information becomes available

1. Effect of Alkalinization on Salicylate Kinetics

Proudfoot AT, Krenzelok EP, Vale JA. Position Paper on urine alkalinization. J Toxicol Clin Toxicol. 2004;42(1):1-26.

* Population: Patients with acute salicylate poisoning
* Intervention: Intravenous sodium bicarbonate to alkalinize urine
* Comparator: None
* Results: Urine alkalinization (pH >7.5) increased urinary salicylate clearance compared to acidic urine pH.

1. Multiple-Dose Activated Charcoal in Salicylate Poisoning

Kirshenbaum LA, Mathews SC, Sitar DS, Tenenbein M. Does multiple-dose charcoal therapy enhance salicylate excretion? A randomized controlled trial. Arch Intern Med. 1990;150(6):1281-1283.

* Population: Healthy volunteers given aspirin 2.8 g
* Intervention: Multiple-dose activated charcoal
* Comparator: No charcoal
* Results: Multiple-dose AC increased total salicylate elimination by 9-18% compared to no AC.

### Clinical Scenarios

Scenario 1:

A 72-year-old woman with a history of rheumatoid arthritis presents after taking an unintentional double dose of her aspirin regimen 2 days ago. She appears fatigued and confused, with shallow rapid breathing. Serum salicylate level is 22 mg/dL, creatinine is 1.8 mg/dL, and arterial blood gas shows pH 7.27, pCO2 32 mmHg, bicarbonate 15 mEq/L.

This patient is exhibiting signs of chronic salicylate toxicity even though the level is only mildly elevated. Her age, pre-existing renal dysfunction, and acid-base disorder increase her risk for adverse effects at lower exposures. Despite the moderate salicylate concentration, aggressive intervention with intravenous fluids, hourly dextrose boluses, and intravenous sodium bicarbonate is indicated given her clinical status and elevated baseline creatinine. Consultation for hemodialysis would be appropriate if she does not respond promptly to maximized medical management. Frequent monitoring of her mental status, serum levels, and acid-base status is essential.

Scenario 2:

A suicidal 17-year-old male is brought to the emergency department after ingesting 40 aspirin tablets approximately 90 minutes ago. He is drowsy with shallow breathing, and admitted taking the pills with vodka. Vital signs show BP 90/52 mmHg, HR 120 bpm, RR 28/min, SpO2 94% on room air, and temperature 37.9°C. Initial management should focus on protecting his airway, assessing mental status, and checking serum glucose to guide dextrose administration for possible ethanol induced hypoglycemia. Obtaining a serum salicylate level, electrolytes, and venous blood gas are also high priority. Activated charcoal could be considered if he is able to protect his airway. Given his critical presentation, preparations should be made for aggressive IV fluid resuscitation, emergent hemodialysis, and ICU monitoring of his unstable status.

### Tips for Answering Exam Questions on Salicylate Toxicity

- Recognize that chronic toxicity occurs more often in older patients at lower serum levels compared to acute ingestions.

- An elevated anion gap metabolic acidosis is expected, but co-ingestants may result in alternate presentations.

- Alkalinization of the urine and serum increases clearance and reduces redistribution into the CNS.

- Dextrose administration is essential for neuroglycopenia despite normal serum glucose levels.

- Hemodialysis is indicated for significant CNS and respiratory depression or acidosis refractory to standard measures.

### Summary

In summary, salicylate toxicity remains a major concern given the prevalence of aspirin and readily available salicylate-containing products. A high index of suspicion is essential to detect toxicity in presentations mimicking other conditions, especially in older adults. Management relies on stabilizing the patient while enhancing elimination through alkalinization techniques. However, deterioration can be rapid, and early extracorporeal removal must be considered in severe toxicity. Overall, pharmacists play pivotal roles in preventing toxicity and improving outcomes when it does occur through prompt recognition, antidote therapy, monitoring, and interdisciplinary care coordination.

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