- Systemic adverse events and theophylline serum concentrations are directly related.
- When serum concentration is 10 mg/L or less, adverse events are minimal but may include nausea, vomiting, and diarrhea.
- When the serum concentration is greater than 10 mg/L, patients often experience tachycardia, tremors, and metabolic abnormalities (electrolytes and glucose).
- Significant toxicity may occur if the serum theophylline concentration is greater than 25 mg/L.
- Cardiac toxicity, the most common acute manifestation, is evident by the appearance of tachycardia and arrhythmias. Profound hypotension and cardiovascular collapse have been reported with serum concentrations greater than 80 mg/L.
- Seizures are rare unless the serum concentration is greater than 80 mg/L.

- The methylxanthines, theophylline and its water-soluble derivative, aminophylline, have been used in the treatment of acute and chronic asthma for decades.
- Clinical studies suggest that theophylline offers minimal additional benefit to inhaled bronchodilators and results in a greater frequency of adverse events. More recent data propose that theophylline may have a role in the treatment of acute asthma in critically ill asthmatic patients with impending respiratory failure and in the treatment of severe acute exacerbations of chronic obstructive pulmonary disease (COPD).
- Caffeine, also a methyl-xanthine and metabolic derivative of theophylline, is indicated in the prevention of neonatal apnea and is a commonly utilized agent in the neonatal ICU.

- On initial presentation, standard acute overdose therapy should be applied. Initial gastric lavage may be useful.
- Supraventricular arrhythmias and tachycardia may be managed by β-adrenergic blockers or calcium antagonists, and hypotension with fluids that expand vascular volume. β-Adrenergic blockers should be used cautiously in patients with underlying COPD or asthma.
- Seizures should be treated with benzodiazepines; if they are refractory, phenobarbital may be effective. Phenytion may worsen theophylline-induced seizures and should be avoided.
- Metabolic abnormalities, including hypokalemia, hypomagnesemia, hypercalcemia, and hyperglycemia, are common and may complicate the treatment of cardiovascular and neurologic adverse events.
- Theophylline's half-life varies widely (3.4 to 30 hours), depending on age and underlying physiologic factors.

- Theophylline is regarded as having a narrow therapeutic spectrum, and toxicity develops when therapeutic serum concentrations are exceeded.
- If theophylline is administered intravenously, there usually is a lag of 15 to 60 minutes between achievement of therapeutic serum concentrations and detection of pulmonary airway responses.
- Theophylline distributes readily into fat tissue in both adults and children (mean volume of distribution, 0.45 L/kg). Therefore, total body weight should be used for calculating loading doses and initial intravenous infusion rates.
- All methylxanthines are eliminated by hepatic metabolism; renal elimination accounts for up to 10% to 15% of the overall excretion in adults.
- The primary route of metabolism is mediated via the cytochrome P450 system.

- Significant toxicity may occur if the serum theophylline concentration is greater than 25 mg/L.
- Cardiac toxicity, the most common acute manifestation, is evident by the appearance of tachycardia and arrhythmias. Profound hypotension and cardiovascular collapse have been reported with serum concentrations greater than 50 mg/L.
- Seizures are rare unless the serum concentration is greater than 80 mg/L.
- Seizures should be treated with benzodiazepines; if they are refractory, phenobarbital may be effective. Phenytion may worsen theophylline-induced seizures and should be avoided.
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- Theophylline serum concentration should be monitored every 2 hours until declining values are confirmed.
- When life-threatening conditions such as refractory seizures, hypotension, or arrhythmias are present or the serum concentration is greater than 80 mg/L, hemodialysis or hemoperfusion with charcoal should be initiated.
- CVVHDH results in a rapid reduction of the theophylline serum concentration and is an acceptable alternative to haemoperfusion.
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