

PHARMACOLOGY / RESPIRATORY / METHYLXANTHINES / HIGH-ALERT DRUG

Theophylline.

A narrow-window bronchodilator that walks a tightrope between therapy & toxicity.

GENERIC NAME	BRAND NAMES	DRUG CLASS	BODY SYSTEM	THERAPEUTIC RANGE
Theophylline	Theo-24, Theochron, Elixophyllin	Methylxanthine Bronchodilator	Respiratory · CNS · Cardiac	10–20 mcg/mL
RISK PROFILE				
⚠ HIGH-ALERT · Narrow Therapeutic Index				



§ 01 • Drug Overview

BRONCHODILATOR



Why we give it

A second- or third-line bronchodilator reserved for stubborn obstructive disease — used when first-line agents (SABAs, LABAs, ICS) aren't enough.

Primary Indications

- ▶ **Chronic asthma** — long-term maintenance (not for acute attacks)
- ▶ **COPD & chronic bronchitis** — bronchospasm prevention
- ▶ **Apnea of prematurity** (caffeine preferred today)
- ▶ Status asthmaticus (as IV **aminophylline**, rare today)

High-Yield Clinical Use

- ▶ Adjunct in moderate-to-severe persistent asthma when symptoms persist despite inhaled steroids
- ▶ Improves diaphragmatic contractility in COPD
- ▶ Mild CNS & respiratory stimulant — caution in vulnerable patients
- ▶ **NOT a rescue drug.** Slow onset; never used for acute bronchospasm



How it changes the body

*Two-punch action: relaxes airway smooth muscle and stimulates the CNS — which explains both the bronchodilation **and** the toxicity.*

1 Inhibits phosphodiesterase (PDE)



2 ↑ Intracellular cAMP in smooth muscle



3 Bronchial smooth muscle relaxation → bronchodilation



4 Blocks adenosine receptors → CNS stimulation, ↑ HR, ↑ diaphragm strength



5 Mild diuretic + cardiac & respiratory stimulation

QUICK LOGIC

Theophylline is a chemical cousin of **caffeine**. Picture an "espresso for the lungs" — it opens airways but also revs the heart, brain, and GI tract. Every adverse effect = a too-strong cup of coffee.



What "working" looks like

✓ RESPIRATORY IMPROVEMENT

- ▶ Decreased wheezing & SOB
- ▶ Improved breath sounds bilaterally
- ▶ Increased peak expiratory flow rate (PEFR)
- ▶ Improved FEV₁ on PFTs
- ▶ ↓ Use of rescue inhaler

✓ FUNCTIONAL IMPROVEMENT

- ▶ Improved exercise tolerance
- ▶ Fewer nighttime awakenings from dyspnea
- ▶ ↓ Frequency of exacerbations & ED visits
- ▶ Pink, dry mucous membranes; SpO₂ ≥ 95%
- ▶ Theophylline level **10–20 mcg/mL**

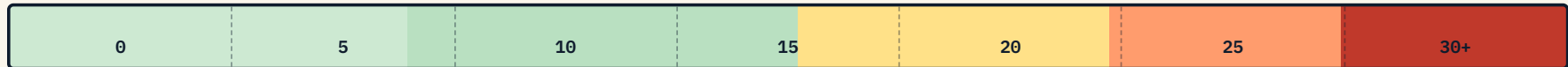
When the espresso goes too far

COMMON EFFECTS DOSE-RELATED

- ▶ **GI:** Nausea, vomiting, anorexia, abdominal pain, GERD
- ▶ **CNS:** Headache, restlessness, irritability, insomnia, tremor
- ▶ **Cardiac:** Tachycardia, palpitations
- ▶ **GU:** Diuresis (mild), hyperglycemia
- ▶ Often the *earliest* warnings of approaching toxicity

SERIOUS / TOXIC EFFECTS

- ▶ **Seizures** — often the **FIRST** sign of severe toxicity in adults
- ▶ **Cardiac dysrhythmias** — sinus tach → SVT → VT → V-fib
- ▶ **Severe hypotension & cardiac arrest**
- ▶ Hyperthermia, hypokalemia, hyperglycemia, metabolic acidosis
- ▶ Hematemesis, severe agitation, cardiovascular collapse
- ▶ **Death** at high serum levels (>30–40 mcg/mL)



Serum theophylline (mcg/mL) — therapeutic window 10–20 · toxicity ≥20 · severe ≥30

EARLY VS LATE TOXICITY SIGNS

EARLY (≥20 mcg/mL):

- ▶ Nausea, vomiting (often first)
- ▶ Restlessness, insomnia, tremor
- ▶ Tachycardia, palpitations
- ▶ Headache, irritability

LATE / SEVERE (≥30 mcg/mL):

- ▶ **Seizures** (may be presenting sign)
- ▶ Ventricular dysrhythmias
- ▶ Severe hypotension, shock
- ▶ Cardiac arrest, death



Assess • Monitor • Hold • Notify

ASSESS & MONITOR

- ▶ **Serum theophylline level** (target 10–20 mcg/mL)
- ▶ Vital signs — esp. HR & BP, every shift & PRN
- ▶ Respiratory status: rate, effort, breath sounds, SpO₂, PEFR
- ▶ I&O (mild diuretic effect)
- ▶ CNS: tremor, restlessness, seizure activity
- ▶ GI: nausea, vomiting, epigastric pain
- ▶ EKG for any palpitations or HR >100

HOLD & NOTIFY HCP IF...

- ▶ **HR > 100 bpm** in adults (or above pt baseline)
- ▶ **Serum level > 20 mcg/mL** (toxicity range)
- ▶ New tremor, restlessness, insomnia, persistent N/V
- ▶ Any seizure activity — **priority emergency**
- ▶ New dysrhythmia or palpitations
- ▶ Patient starts/stops smoking (alters metabolism)

CONTRAINDICATIONS & CAUTIONS

- ▶ Active **peptic ulcer disease** — worsens GI irritation
- ▶ Uncontrolled **seizure disorder**
- ▶ Underlying **cardiac dysrhythmias**
- ▶ Severe hepatic impairment (drug metabolized by liver)
- ▶ Hyperthyroidism — amplified cardiac stimulation
- ▶ Caution: pregnancy (Cat. C), elderly, neonates

⚡ High-Yield Drug Interactions

↑ THEOPHYLLINE LEVEL

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Cimetidine → ↑ **tox risk**

↑ THEOPHYLLINE LEVEL

Erythromycin / clarithromycin → ↑ **tox**

↓ THEOPHYLLINE LEVEL

Smoking / nicotine → ↓ **effect**

△ SYNERGY

Beta-agonists (albuterol) → ↑ tachycardia

Ciprofloxacin & other fluoroquinolones → ↑ **tox**

↑ TOXICITY

Caffeine (coffee, tea, cola, chocolate, energy drinks)

↓ THEOPHYLLINE LEVEL

Phenytoin, rifampin, phenobarbital, carbamazepine

△ RISK

St. John's Wort ↓ levels | **Charcoal-broiled food** ↓ levels



The numbers that matter

LAB / TEST	REFERENCE RANGE	WHAT ABNORMAL MEANS
Serum Theophylline	10–20 mcg/mL (therapeutic) <10 = subtherapeutic >20 = TOXIC	Highest priority lab. Draw trough (right before next dose). Rising level + new symptoms → hold & notify.
Heart Rate / EKG	HR 60–100 bpm	Tachycardia, SVT, VT, V-fib all signal toxicity. Continuous EKG if level > 20.
Serum Potassium	3.5–5.0 mEq/L	Toxicity → hypokalemia (drives K ⁺ into cells) → worsens dysrhythmias
Serum Glucose	70–110 mg/dL fasting	Toxicity may cause hyperglycemia
ABG / SpO₂	SpO ₂ ≥ 95%; pH 7.35–7.45	Severe toxicity → metabolic acidosis
LFTs	AST/ALT < 40 U/L	Hepatic impairment ↓ metabolism → ↑ levels → toxicity risk
PEFR / FEV₁	Compare to personal best	Below 80% personal best = poor response or worsening disease

TIMING OF THE LEVEL

- ▶ **Oral immediate-release:** draw level just before next dose (trough)
- ▶ **Sustained-release:** draw mid-dose interval per hospital protocol
- ▶ **IV aminophylline:** level 30 min after loading dose, then steady-state at 12–24 h
- ▶ Any change in dose, smoking status, or interacting drug → recheck level



Route, timing, & high-alert handling

ROUTES & FORMS

- ▶ **PO immediate-release** tablet/elixir — q6–8 h
- ▶ **PO sustained-release** (Theo-24, Theochron) — q12–24 h
- ▶ **IV aminophylline** (theophylline ethylenediamine, 80% theophylline) for acute use
- ▶ No inhaled or IM forms

TIMING & TECHNIQUE

- ▶ Take at the **same time daily** with a full glass of water
- ▶ SR tablets: **do NOT crush, chew, or split**
- ▶ Avoid taking with high-fat meals (alters absorption of SR forms)
- ▶ IV: **administer slowly** via pump; rapid push → cardiac arrest
- ▶ Loading dose typically 5 mg/kg IV over 20–30 min

HIGH-ALERT PRECAUTIONS

- ▶ Verify dose with **2 nurses** per facility protocol (high-alert classification)
- ▶ Continuous cardiac monitoring for IV aminophylline
- ▶ Have **activated charcoal & IV diazepam/lorazepam** available for overdose
- ▶ Rapid IV push = **seizures, dysrhythmias, sudden death**
- ▶ Never abruptly increase dose — small changes cause large level shifts (zero-order kinetics at high levels)



What the patient must know

✓ Daily Habits

- ▶ Take at **the same time every day** — consistency keeps blood levels stable
- ▶ Limit **caffeine**: coffee, tea, cola, chocolate, energy drinks (additive toxicity)
- ▶ Avoid **charcoal-grilled foods** & sudden diet changes (can ↓ levels)
- ▶ Do not crush or chew sustained-release tablets
- ▶ Keep **scheduled labs** for theophylline level checks

🚭 Smoking & Lifestyle

- ▶ **Tell HCP if you start or stop smoking** — smoking ↑ metabolism & ↓ levels; quitting can rapidly raise levels into toxic range
- ▶ Tell every provider/dentist about theophylline before any new prescription
- ▶ Avoid OTC cold medicines with stimulants (pseudoephedrine, ephedra)
- ▶ Wear a **medical alert** bracelet/ID

📞 CALL HCP / SEEK HELP IMMEDIATELY IF YOU HAVE...

- ▶ **Persistent nausea/vomiting** — earliest toxicity warning
- ▶ **Rapid or pounding heart, palpitations**
- ▶ **Tremor, restlessness, can't sleep, headache that won't stop**
- ▶ **Seizure** — call 911 immediately
- ▶ Blood in vomit, fainting, severe weakness
- ▶ This drug is **NOT for an asthma attack** — use rescue inhaler (albuterol) and follow asthma action plan



⚠ Where students lose points

- ▶ **Trap #1 — Rescue confusion:** Theophylline is NEVER for an acute attack. The right answer in an attack is a **SABA (albuterol)**.
- ▶ **Trap #2 — Caffeine isn't "just food":** Patient drinking coffee + on theophylline → additive stimulation → dysrhythmias. Counsel *limit caffeine*.
- ▶ **Trap #3 — Smoking direction is opposite of intuition:** Smokers need *higher* doses (smoking induces CYP1A2). When a patient *quits*, levels rise and toxicity appears.
- ▶ **Trap #4 — N/V is not "just GI upset":** Persistent nausea/vomiting in a patient on theophylline = **toxicity until proven otherwise**. Hold drug, draw level.
- ▶ **Trap #5 — Seizure can be the first sign:** In adults, severe toxicity may present with seizures *without* earlier GI warning. Don't wait for "classic" symptoms.
- ▶ **Trap #6 — Crushing SR tablets:** Crushing Theo-24 or Theochron releases the full 24-hour dose at once → instant toxicity.
- ▶ **Trap #7 — Drug interactions cluster:** Cimetidine, ciprofloxacin, erythromycin, fluvoxamine ALL ↑ levels. Memorize these.
- ▶ **Trap #8 — Therapeutic range is tight:** 10–20 mcg/mL. A level of 21 is "abnormal," not "almost normal." Treat as toxic.
- ▶ **Trap #9 — Priority assessment:** Tachycardia + tremor + N/V on theophylline = toxicity → check serum level → hold drug → notify provider. Do NOT just "monitor."
- ▶ **Trap #10 — IV aminophylline ≠ IV bolus:** Always given as a slow infusion. Rapid push causes seizures and cardiac arrest.



Mnemonics that stick

"TEA"

- T** achycardia & **tremor** — early toxicity
- E** arly: **emesis** (nausea/vomiting) is the first sign
- A** rrhythmias & agitation as level climbs → seizures

"THEO"

- T** en to **twenty** — therapeutic range mcg/mL
- H** eart rate > **100** = HOLD
- E** limination changed by smoking, cipro, cimetidine
- O** verdose = seizures + arrhythmias → activated charcoal + diazepam

"CAFFEINE COUSIN"

If it would happen from too much coffee, theophylline can do it: jittery → nauseated → tachycardic → arrhythmic → seizing.
Reverse-engineer side effects from a strong cup of espresso.

"5 C's of Drug Interactions"

- C** imetidine ↑
- C** iprofloxacin ↑
- C** larithromycin / erythromycin ↑
- C** affeine ↑ effects
- C** igarettes ↓ levels (induce metabolism)

★ Bonus • Most Tested in This Class

CLASS COMPARISON

Methylxanthines side-by-side

DRUG	ROUTE & FORM	PRIMARY USE	THERAPEUTIC LEVEL	NCLEX PEARL
Theophylline Theo-24, Theochron	PO IR & SR	Chronic asthma, COPD maintenance	10–20 mcg/mL	Narrow window; check level & HR before each dose
Aminophylline	IV (slow infusion)	Acute severe asthma / COPD exacerbation	10–20 mcg/mL theophylline	~80% theophylline. Never IV push — risk seizures & cardiac arrest. Loading dose then maintenance.
Caffeine citrate	PO / IV	Apnea of prematurity (drug of choice)	5–25 mcg/mL	Wider safety margin than theophylline; preferred in neonates. Watch for tachycardia & feeding intolerance.
Dyphylline	PO / IM	Bronchospasm (rare today)	~12 mcg/mL	Renally excreted (vs. theophylline = hepatic). Not converted to theophylline. ↓ dose in renal failure.

KEY CLASS DIFFERENCES

- ▶ All work via **PDE inhibition + adenosine blockade** — same mechanism, different routes & clearances
- ▶ **Theophylline** = oral chronic; **aminophylline** = IV acute; **caffeine** = neonatal apnea
- ▶ All share **narrow therapeutic index** — except caffeine, which is the safest of the group
- ▶ All cause the same toxicity pattern: **GI** → **CNS** → **cardiac**



Think like the NCLEX

When a question stem mentions theophylline, the examiner is almost always testing one thing: **can you recognize toxicity and act on it?**

#1

PRIORITY RISK

Toxicity-induced seizures & lethal cardiac dysrhythmias. The narrow therapeutic window (10–20 mcg/mL) means a small level change can cross into life-threatening territory.

#2

WHAT HARMS FIRST

The CNS & heart. Look for tachycardia >100, tremor, restlessness, persistent N/V, then progression to seizures and ventricular arrhythmias. GI symptoms = early warning bell.

#3

FIRST NURSING ACTION

HOLD the next dose, then assess HR, recognize signs, draw a serum theophylline level, place on continuous cardiac monitoring, and **notify the provider**. Have charcoal & IV benzodiazepines ready.

🧠 THE "IF/THEN" FRAMEWORK (NCJMM)

- ▶ **If** patient has new tachycardia > 100 → **then** hold dose, check serum level
- ▶ **If** patient reports new N/V + tremor → **then** assume toxicity, hold, notify HCP
- ▶ **If** patient is starting cipro / cimetidine / erythromycin → **then** anticipate level rise & recheck
- ▶ **If** patient quits smoking → **then** theophylline level may rise → recheck within 1 week
- ▶ **If** patient is having an acute asthma attack → **then** theophylline is NOT the answer — give the SABA
- ▶ **If** patient has a seizure on theophylline → **then** it's toxicity. Protect airway, IV benzo, stop drug, get level

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