Histamine & Anaphylaxis — Paramedic Field Reference

Recognition, the epinephrine ladder, adjuncts that do not rescue, and the traps

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The core idea. Histamine is the fastest mediator out of the mast cell — **not the only one, and not the most dangerous one**. Mast cells also release tryptase, leukotrienes, prostaglandins and **platelet-activating factor**, which tracks severity better than histamine. That is why an antihistamine relieves hives and **cannot** reverse airway edema or shock. **Epinephrine is the only drug that reverses both.**

RECEPTORS — WHY THE PICTURE LOOKS THE WAY IT DOES

Rec	Effects	Clinical meaning
H1	Vasodilation (NO), capillary leak, bronchoconstriction, mucus, itch/sneeze	Most of the visible disease — hives, swelling, wheeze, hypotension
H2	Gastric acid, some vasodilation, chronotropy	Famotidine helps flushing/hives only
H3 / H4	Presynaptic CNS autoreceptor / immune cell chemotaxis	H4 amplifies and prolongs the reaction

Non-IgE triggers (no allergy needed): MRGPRX2 — vancomycin, opioids, neuromuscular blockers, iodinated contrast; complement C3a/C5a; direct activation by cold, exercise, alcohol.

RECOGNITION — 2025 AHA / 2026 WAO CRITERIA

Skin/mucosa + one of:	Respiratory compromise (dyspnea, wheeze, stridor, hypoxemia) · hypotension or end-organ signs (collapse, syncope, incontinence) · severe GI symptoms (cramping, repeated vomiting)
Or without skin:	**Hypotension alone** or **bronchospasm alone** after a known exposure — the presentation that gets missed
Timing:	Minutes to hours; **alpha-gal (tick-bite red meat) and immunotherapy up to 10 hours**
Mimics:	Vasovagal · panic · septic shock · severe asthma · hereditary angioedema (bradykinin — no urticaria, epi ineffective) · scombroid fish poisoning (histamine in spoiled fish, responds to antihistamines)

EPINEPHRINE — THE LADDER

Route / situation	Dose	Notes
IM — first line always **1 mg/mL (1:1,000)**	**Adult 0.3–0.5 mg** **Peds 0.01 mg/kg, max 0.3 mg**	Lateral mid-thigh. Repeat q5 min PRN. Autoinjector 0.3 mg adult / 0.15 mg small child. **No absolute contraindication.**
IV — shock or airway compromise **1:10,000**	**0.1 mg** slow IV over 1–2 min, repeat per protocol	**One-tenth of a milligram. Giving 1 mg of 1:1,000 IV is tenfold and kills.**
Refractory — after 2 IM doses + fluids	Infusion **1–10 mcg/min** titrated, or **0.05–0.2 mcg/kg/min** by protocol	Pump, monitored. No pump? Push-dose **10 mcg/mL** (1 mL of 1:10,000 + 9 mL NS), **10–20 mcg** boluses
Intranasal (neffy)	**2 mg** per device, adults and peds ≥30 kg	Removes the needle barrier. Not a substitute for IV in shock

EVERYTHING ELSE — AND WHAT IT CANNOT DO

Drug	Dose	Truth
Isotonic crystalloid	1–2 L adult 20 mL/kg peds	**Half of shock treatment.** Reassess after each bolus. AHA 2025: isotonic IV fluids may be used for fluid resuscitation in anaphylaxis arrest
Albuterol	2.5–5 mg neb	Bronchospasm only. Does nothing for edema or leak. Never a substitute for epi
Glucagon	1–5 mg IV	Works through adenylate cyclase **downstream of the beta receptor** — for beta-blocked patients. AHA 2025: reasonable in refractory with suspected beta-blocker
Diphenhydramine	25–50 mg	Itch/flush/hives only. Does not reverse edema, pressure, or progression
Famotidine	20 mg IV	Modest, adjunct only
Methylprednisolone **Hydrocortisone**	125 mg 200 mg	**Hours to act.** Current evidence does not show they prevent biphasic reactions

Position first. Supine and **flat**. Sitting is allowed only if the patient is in respiratory distress and cannot lie down. **Do NOT elevate the legs** — leg elevation is not a valid treatment for anaphylaxis. **Never let them stand or walk** — standing empties the dilated venous capacitance and the heart has nothing to pump; sudden deaths in anaphylaxis have been reported from exactly that.

ARREST AND AIRWAY

- **Arrest from anaphylaxis (AHA 2025):** CPR with **IV epinephrine 1 mg q3–5 min**, aggressive isotonic volume. The standard autoinjector or IM anaphylaxis dose **may not offer benefit** in arrest. Anaphylaxis is listed among reversible causes where **ECLS/VA-ECMO** may support a peri-arrest patient.
- **Airway edema** gets harder every minute: voice change, stridor, drooling, tongue swelling. Suction, difficult-airway plan, surgical backup, and caution with induction agents that drop sympathetic tone — **ketamine is usually kinder**.
- **Observation:** 4–6 h floor, longer if severe, repeated epi or hypotension. Antihistamines and steroids do not buy a shorter stay. Tryptase supports the diagnosis afterward; it never changes acute care.