



Clinical Pharmacology & Toxicology Pearl of the Week

Hydroxocobalamin - Cyanide Antidote

Hydroxocobalamin is the preferred antidote for cyanide toxicity. It binds to cyanide to make cyanocobalamin (Vit. B12). Hydroxocobalamin **can interfere with all spectrophotometric and colorimetric-based laboratory investigations**. Consult PADIS if considering cyanide toxicity and treatment with hydroxocobalamin.

Mechanism of Hydroxocobalamin

- ✓ Contains a central cobalt cation that acts as electrophilic moiety that undergoes nucleophilic substitution by the cyanide anion
- ✓ Combines with cyanide in an equimolar (1:1 molecular) ratio to form cyanocobalamin (Vitamin B12)
 - Standard dose of 5g can combine with 96 mg of cyanide, or 111 mmol/L in an 80 kg adult
- ✓ Can also combine with structurally similar nitric oxide (NO)

Elimination

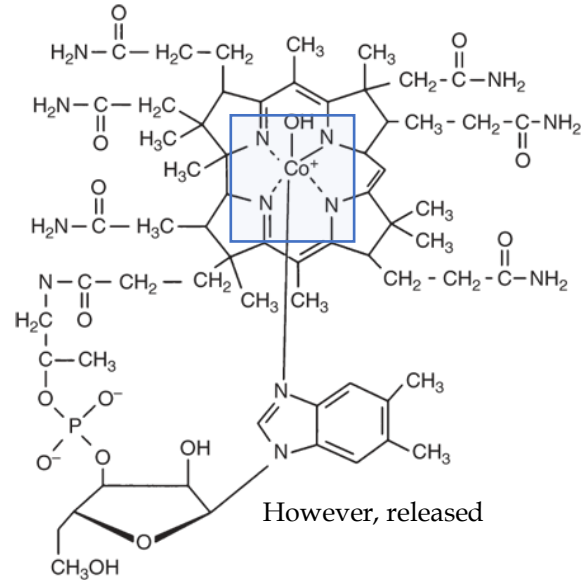
- ✓ Eliminated by the **kidneys**
- ✓ Half-life of hydroxocobalamin and cobalamin-complexes up to 31 hours
- ✓ Small fraction of cyanocobalamin decomposes, releasing free cyanide. cyanide is metabolised by intrinsic rhodanase activity

Adverse Effects


- ✓ Adverse Effects rare. Large therapeutic index
 - Anaphylaxis and allergic reactions rare
 - **Hypertension** is a common adverse reaction likely due to combining with NO, preventing vasodilation
 - Typically limited to 4 hours in duration
- ✓ Red discoloration of skin, serum, and urine common. Lasts 12 hours to several days
 - **Chromaturia** (red urine) is near universal, & can last 30 days

Laboratory Interference

- ✓ Intense red colour of serum and urine can affect colorimetric and spectrophotometric laboratory tests
 - Degree and direction of measurement error unpredictable
 - **Contact Clinical Biochemist on call** for details on your specific laboratory methods
 - Commonly affects co-oximetry. Increases total Hgb measured, **increases or decreases carboxyhemoglobin**, increases methemoglobin, and decreases oxyhemoglobin
 - Other labs often affected include liver enzymes, bilirubin, lipase, calcium, magnesium, phosphorus, glucose, triglycerides, uric acid, coagulation panel, lactate, and creatinine
- ✓ Can **interfere with pulse oximetry** decreasing saturation measurement up to 10 to 15%
- ✓ Red discoloration can trigger "blood leak" alarm on hemodialysis machines
- ✓ Draw blood immediately prior to hydroxocobalamin administration - effects on laboratory tests can last 2-3 days



 The Calgary Clinical Pharmacology physician consultation service is available Mon-Fri, 9am-5pm. The on-call physician is listed in ROCA. Click [HERE](#) for clinical issues the CP service can assist with.

 The Poison and Drug Information Service ([PADIS](#)) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414, and select option 1.

References:

1. Lewis S. Nelson et al, Goldfrank's Toxicologic Emergencies. 11th ed. New York: McGraw Hill Medical; c2019
2. Beckerman N et al. Laboratory interferences with the newer cyanide antidote: hydroxocobalamin. Semin Diagn Pathol 2009; 26: 49-52
3. Lee J et al. Potential interference by hydroxocobalamin on cooximetry hemoglobin measurements during cyanide and smoke inhalation treatments. Ann Emerg Med. 2007;49:802-805

4. Pamidi P. V. A., DeAbreu M., Kim D., Mansouri S. Hydroxocobalamin and cyanocobalamin interference on co-oximetry based hemoglobin measurements. *Clinica Chimica Acta*. 2009;401(1-2):63-67. doi: 10.1016/j.cca.2008.11.007
5. "Therapeutic Drugs and Antidotes." *Poisoning & Drug Overdose*, 7e Eds. Kent R. Olson, et al. New York, NY: McGraw-Hill, ,c2018