• Strychnine alkaloid can be found naturally in *Strychnos nux-vomica*, a tree native to tropical Asia and North Australia, and in *Strychnosignatii* and *Strychnos tiente*, trees native to South Asia.
HISTORY

- Strychnine was first introduced as a rodenticide in 1540, and in subsequent centuries was used medically as a cardiac, respiratory, and digestive stimulant, "as an analeptic," and as an antidote to barbiturate and opioid overdoses." Nonketotic hyperglycemia, sleep apnea, "and snake bites" were also once considered indications for strychnine use.
It is an \textit{odorless} and \textit{colorless} crystalline powder that has a bitter taste when dissolved in water.
In addition to the naturally occurring alkaloidal form, strychnine is available from commercial sources in its salt form, usually as nitrate, sulfate, or phosphate.
Currently, strychnine is used mainly as a pesticide and rodenticide (for moles, gophers, and pigeons), "and a research tool for the study of glycine receptors, Most commercially available strychnine-containing products contain about 0.25% to 0.5% strychnine by weight."
Strychnine poisoning has resulted from deliberate exposure with suicidal and homicidal intent, from unintentional poisoning by a Chinese herbal medicine (Maqianzi), "a Cambodian traditional remedy (slang nut) and adulteration of street drugs."
The bitter taste and lethality of strychnine allow it to be substituted for heroin" and cocaine, There are also reports of strychnine poisoning from adulterated amphetamines, "ecstasy ( [MDMAJ), Spanish fly," and from the ingestion of gopher bait.
TOXICOKINETICS

• Standard references list the lethal dose of strychnine as approximately.

• However, mortality resulting from doses as low as 5 to 10 mg and, alternatively, survival following ingestions of 1 to 15 g of strychnine are reported.
Protein binding is minimal and strychnine is rapidly distributed to peripheral tissues' with a large volume of distribution (13 L/kg).
• Strychnine is metabolized by hepatic P450 microsomes: producing **strychnine-N-oxide** as the major metabolite, and this metabolism is increased by P450 induction.
• Glycine, one of the major inhibitory neurotransmitters in the spinal cord, opens a ligand-gated chloride channel, thus allowing the inward flow of Cl⁻. As Cl⁻ moves inward the cell becomes hyperpolarized or inhibited.
Strychnine competitively inhibits the binding of glycine to the a-subunit of the glycine-ergic chloride channel.
• Although strychnine affects all parts of the central nervous system in which glycine receptors are found, the most significant effect is in the spinal cord.
• With loss of the glycine inhibition to the motor neurons in the ventral horn, there is a loss of inhibitory influence on the normally suppressed reflex arc.
CLINICAL MANIFESTATIONS

- Strychnine poisoning is characterized by a rapid onset of signs and symptoms beginning within 15 to 60 minutes of ingestion.
• The **typical** symptoms of poisoning are involuntary, generalized muscular contractions resulting in neck, back, and limb pain.
- The contractions are easily triggered by trivial stimuli (such as turning on a light) and each episode usually lasts for 30 seconds to 2 minutes."
- Recurrent episodes may last as long as 12 to 24 hours.
Differences in the strength of various opposing muscle groups result in the classic signs of opisthotonus, facial trismus, and risus sardonicus, with flexion of the upper limbs and extensions of lower limbs predominating.
Because strychnine affects glycine inhibition mainly in the spinal cord, the patient typically remains fully alert until metabolic complications arise.
The combination of convulsive motor activity involving both sides of the body in the conscious patient has often resulted in imprecise descriptions such as:

- "conscious seizure"
- "spinal seizure."
Hemodynamically, both hypotension, or hypertension, in the presence of bradycardia, or tachycardia has been reported.
Hyperthermia, presumably from increased muscular activity, is typical, and temperatures as high as 109.4°F (43°C) are reported.
Early in the course of strychnine poisoning, mortality is mainly due to hypoventilation and hypoxia secondary to muscular contractions.
Later, life-threatening complications include rhabdomyolysis with subsequent myoglobinuria and acute renal failure, "hypoxia or hyperthermia-induced multiorgan failure, aspiration pneumonitis, "anoxic brain injury, and pancreatitis.
Ddx

- The diagnosis of strychnine poisoning is mainly established on clinical grounds, based on exposure history and compatible clinical manifestations, but can be confirmed by detection of strychnine in biological specimens.
**DIAGNOSTIC TESTING**

- **Respiratory and metabolic acidosis** both commonly occur in strychnine-poisoned patients. Metabolic acidosis correlates with serum lactate concentrations," whereas respiratory acidosis is secondary to hypoventilation resulting from diaphragmatic and respiratory muscle failure.
Survival of patients with serum pHs in the range of 6.5 to 6.6 is well documented.

Thus, profound acidemia in strychnine poisoning is not necessarily associated with a poor prognosis.
Orogastric lavage should be considered on an individual basis after evaluating potential benefits and risks. When orogastric lavage is thought to be indicated, it may be important to protect and secure the airway with an endotracheal tube before attempting lavage.
• Activated charcoal (AC) binds strychnine effectively at a ratio of approximately 1:1; 1 g of AC will bind 950 mg of strychnine.
Currently, there is no evidence to recommend the use of multiple dose AC or whole-bowel irrigation for strychnine poisoning.
• **Supportive treatment** remains the **most important** aspect of management in the majority of cases. The focus of care is to stop the muscular hyperactivity as soon as possible to prevent the metabolic and respiratory complications.
• Benzodiazepines remain the first line treatment for strychnine-induced muscular hyperactivity.
In addition to benzodiazepines, barbiturates and propofol are also effective, although considered secondary therapies, in stopping the strychnine-induced hyperactivity.
If these measures fail to control the muscular hyperactivity, a non-depolarizing neuromuscular blocker (NMB) should be administered. **Only nondepolarizing NMBs** should be used, as succinylcholine itself, a depolarizing NMB, induces muscle contractions.
• Hyperthermia should be treated aggressively by active cooling
• with ice water immersion, cooling blanket, or mist and fan, depending
• on the magnitude of temperature elevation
• Means to prevent rhabdomyolysis-induced acute renal failure include adequate fluid administration to ensure good urine output (greater than 1 mL/kg/h), the potential use of urinary alkalinization with sodium bicarbonate, "and temporary renal replacement therapy, if acute renal failure occurs."
• Effective management in the first few hours of strychnine poisoning is crucial for survival.

• If the patient can be supported adequately for the first 6 hours, this may be considered a good prognostic sign.
SUMMARY

• A "conscious seizure" is the *characteristic presentation* of strychnine toxicity, and is rapidly followed by life-threatening metabolic and respiratory consequences.
• The **mainstay** of treatment is **supportive** care with the goal of rapidly terminating muscular contractions, providing adequate airway management, and rapidly treating hyperthermia and/or metabolic abnormalities.
• Strychnine, an alkaloid found in the seeds of the tree *Strychnos nux-vomica*, increases the level of neuronal excitability by selective antagonism at glycine receptors.
The strychnos plant (*Strychnos nux-vomica*) is associated with violent seizures, paralysis, and death. Strychnos is a native plant of India and Southeast Asia.
• The strychnine alkaloid is a reversible and competitive inhibitor of glycine receptors in the spinal cord and cerebral cortex.
• Although rare most strychnine poisonings today result from adulteration of street drugs (cocaine & heroin) as well as from small amounts found in herbal medications & homeopathic remedies and rarely rodenticides.
Differential Diagnosis

- Tetanus
- Epilepsy
- Dystonic Drug Reactions
- Infections of the neck
- Hypocalcemia
- Picrotoxin Exposure
- Psychogenic Disorders
LAB

- Rapid lab tests for detecting & qualifying strychnin are unavailable in most clinical settings.

- The main value of lab analysis lies in confirmation of the exposure & identification of complications such as rhabdomyolysis.
• Aggressive control of muscle rigidity is the cornerstone to successful management.

• High dose benzodiazepines are the mainstay for controlling muscle activity. (Grade 2c)
If more than 0.5 mg/kg of diazepam are given without significant improvement in the patient's condition, we suggest the addition of a barbiturate to further control muscle activity.
• Most deaths result from respiratory compromise, and the emergent airway management is often necessary with a significant acute ingestion.
• Sedation, paralysis & endotracheal intubation are necessary in the setting of:
  • Uncontrollable motor activity
  • Severe Acidosis (PH<7.1)
  • Significant Hyperthermia
  • (core T>40)
RSI

- Etomidate 0.3 mg/kg
- Propofol & midazolam: good Alternative induction agents
- We prefer rocuronium 1 mg/kg or another non depolarizing NMBA.
• BZD or Propofol may be used for sedation following intubation.
• Long acting non depolarizing agents (vecuronium 0.010 to 0.015 mg/kg with a duration of 15 minutes) particularly in the setting of hyperthermia.
• Paralysis is the most rapid & effective means for reversing hyperthermia & acidosis in these patients.
• Succinylcholine has no role in the long term of these patients, given its potential to cause hyperkalemia and hyperthermia, & to worsen rhodomyolysis.
• There is no role for gastric lavage.
• MDAC may be beneficial as high strychnine concentration found in the hepatobiliary system suggests enterohepatic recirculation, but benefit is unproven.
Pediatric consideration

- As with adults, the key to management is controlling involuntary muscle activity, administering supportive care and treating complications.

- The starting dose of diazepam is 0.1 mg/kg with rapid titration to effect.
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• Vigilance for signs for fatigue is essential.

• End Tidal co2 monitoring may be a useful adjunct for early identification of hypo ventilation.
Pediatric exposures to strychnine occur worldwild, often in developing countries where use of strychnine as a pesticide continues.

Some rodenticide formulations are sold as bright pink tablets, making them appealing to small children.