

SAXITOXIN

History: Saxitoxin and saxitoxin-like substances are naturally occurring toxins produced by the dinoflagellates, *Alexandrium tamarense* (formerly *Gonyaulax tamarensis*) and *Alexandrium catenella* (formerly *Gonyaulax catenella*). Generally, these toxins are produced in greatest abundance between the months of May and August. *A. catenella* and *A. tamarensis* are among those organisms responsible for harmful algal blooms (the so called “red tide” phenomenon). Saxitoxin is one of several toxins that cause paralytic shellfish poisoning (PSP). Under ordinary conditions, humans are exposed to saxitoxin through ingestion of bivalve mollusks (e.g., oysters) that accumulate dinoflagellate toxins during feeding. In biological/chemical warfare, saxitoxin could become an agent of mass destruction through dissemination of aerosolized toxin recovered from mass-produced laboratory cultures. In this instance, the respiratory tract would be the principal route of exposure. Other ways to deliver the agent include loading it into projectiles or by contaminating food and water. Contamination of food and water supplies with saxitoxin is, however, an inefficient way to deliver the toxin to large numbers of people.

Mechanism of Action: Saxitoxin is odorless and tasteless. It is heat and acid resistant; and it cannot be easily detected nor removed by food preparation procedures. The toxin, being lipid soluble, is readily absorbed from the gastrointestinal (GI) and respiratory tracts. Saxitoxin is a potent neuroparalytic agent that binds to the sodium channels of nerve and muscle tissue, preventing propagation of action potentials in excitable cells and, ultimately, causing blockade of depolarization at the neuromuscular junction. This ultimately leads to neuromuscular dysfunction, the most serious of which is respiratory paralysis that, in severe cases, may result in death from respiratory failure.

Signs and Symptoms: The classic presentation of saxitoxin intoxication is that of recent shellfish ingestion followed closely in time by an acute gastrointestinal illness with neurological symptoms. Although in classic saxitoxin exposure, signs and symptoms may occur from minutes to hours after exposure, aerosolized saxitoxin acts rapidly (within minutes). After respiratory exposure with aerosolized saxitoxin, the patient may have only the neurological syndrome. GI signs and symptoms may be absent or attenuated. Initial symptoms include numbness and tingling of the lips, tongue, and fingertips, followed by numbness of the neck and extremities and motor incoordination. Cranial nerve involvement can result in diplopia, speech, and swallowing difficulties. Other symptoms may include light-headedness, dizziness, weakness, confusion, memory loss, and headache. Nausea, vomiting, abdominal pain and diarrhea may be prominent after ingestion of saxitoxin. Flaccid paralysis and respiratory failure are life-threatening complications occurring 2 to 12 hours after ingestion. With respiratory exposure, the timeframe may be significantly shortened. Few patients remain significantly symptomatic for more than 24 hours following exposure to saxitoxin and usually recover completely with supportive care. Complete neurological recovery may require 7 to 14 days.

Diagnosis: Diagnosis of saxitoxin poisoning is by history and clinical signs and symptoms. Detection of the antigen (toxin) by radioimmunoassay or by indirect enzyme-linked immunoadsorbent antibody test (ELISA) or by mouse bioassay confirms the diagnosis. Clinical specimens that may be tested for saxitoxin include stomach contents,

serum, and, after respiratory exposure, respiratory secretions. Toxin samples taken directly from a weapon or from environmental surfaces are often easier to test than biological samples because they do not contain body proteins and other interfering materials. The best early diagnostic sample for most aerosolized toxins is a swab of the nasal mucosa. In general, the more toxic toxins are more difficult to detect in tissues and body fluids, because so little toxin needs to be present to exert its effect. The agent may be quantified with high-pressure liquid chromatography. Definitive laboratory diagnosis could take up to 72 hours, and, thus, is not useful in the clinical setting. Radioimmunoassay of serum IgM and IgG titers within two to three weeks of exposure may confirm or indirectly identify the agent.

Supportive Laboratory Tests: Routine clinical laboratory findings are not helpful in diagnosing saxitoxin poisoning, but may be helpful in ruling out saxitoxin poisoning. Cardiac conduction disturbances may develop but electrocardiographic findings are nonspecific.

Differential Diagnosis includes ciguatera (ciguatera toxin) and pufferfish poisoning (tetrodotoxin). Ciguatera occurs following ingestion of large-finned reef fish but, in contrast to saxitoxin, results in more severe GI symptoms (nausea, vomiting, diarrhea). Ciguatera poisoning is characterized by a peculiar reversal of temperature sensation: hot feels cold, cold feels hot. The differential diagnosis of acute gastrointestinal illness following recent ingestion of shellfish also includes bacterial or viral gastroenteritis. Manifestations of aerosolized saxitoxin poisoning are likely to be more similar to neurotoxic shellfish poisoning (NSP) or pufferfish poisoning – or even recent organophosphate pesticide or nerve gas poisoning – than viral or bacterial gastroenteritis. Botulism may be suspected, but, in contrast to botulinum toxin, saxitoxin intoxication causes sensory and CNS symptoms in addition to the motor effects characteristic of botulism.

Treatment: Treatment of saxitoxin poisoning is supportive. Particular attention must be given to the patient's ventilatory status. Temporary mechanical ventilation may be required. Activated charcoal to adsorb toxin from the gut may be effective if given within 1 to 2 hours of ingestion. Lavage, emesis or catharsis may be helpful if instituted early in the course of poisoning via the GI tract. Although emesis has fallen into disfavor as a treatment for poisoning, the technique may be useful during treatment of mass casualties, as it requires little medical supervision. GI treatments are not useful after respiratory exposure to aerosolized saxitoxin.

Prophylaxis and Antidotes: No vaccines or effective prophylactic treatments exist for Saxitoxin. There is no antidote for this poison.