

Electron Transport Chain

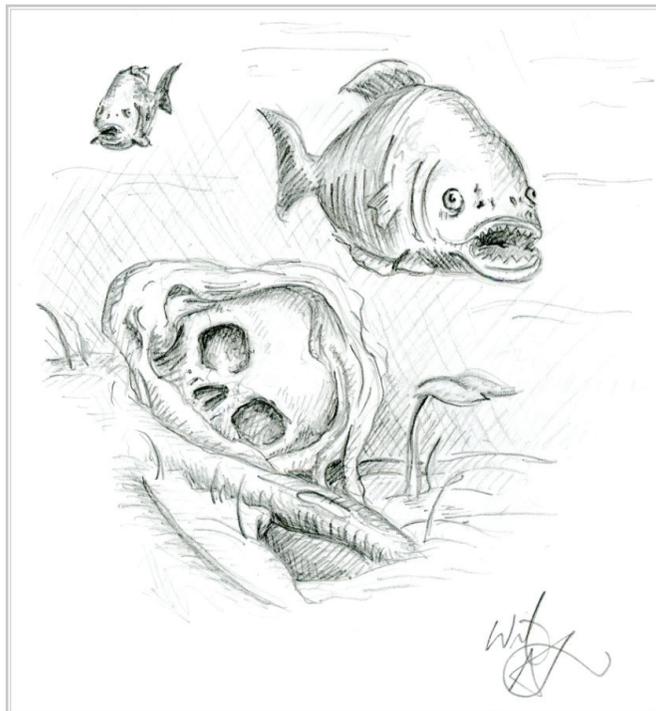
CYANIDE AND THE CASSAVA

It is the end of the 16th century and a group of Spanish explorers are on an expedition into the jungles of South America to find wealth and glory. The men entered the jungle in hopes of finding gold and treasure, but as the hazards of the environment cut them down one by one, dreams of material wealth are abandoned and the only goal is survival.....

The pale, sweating man stumbled and planted both hands in a pile of decaying leaves. The smell of the jungle was all around him. He thought he heard his name, but it must have been a monkey or a bird: none of his companions was alive to say it. Caimans and piranhas had gotten Vasquez on the way across the river. Javier had fallen to the poisonous dart-guns of three men who had not believed his story about being a god from across the sea. A jaguar had leaped on San Germano when he got up to relieve himself in the middle of the night. Now only he, Morales,

was left alive to finish the expedition. But as starvation weakened his body and addled his mind survival had gone from fleeting hope to impossible dream. His fingers scabbled the dirt and felt something like bark. Roots—they might be edible! He dug frantically, pulled the thick brown root out of the ground, and groaned in disappointment: it was the one that the people in the last village had told the foreigners never to eat. “It makes you sick and you lose control of yourself,” they had explained through the interpreter, “and then you die.” Morales learned this first hand as Miguel, another of his companions, had consumed it out of hunger. At first Miguel was fine but soon after growing weak and confused was left behind to die. A quick death due to poisoning seemed much better than being





mauled by animals or murdered by natives. Morales, smiling at the thought of being free of this nightmare and joining his friends, wiped the root on what was left of his tunic and tried a tiny nibble: bitter as jealousy and hard as an old boot. He spat the root out in disgust. Maybe stewing it would help. He could at least die with one last good meal. He had a tinderbox but nothing to cook in—their packs were at the bottom of the river with Vasquez's bones. He took off his iron helmet, dipped water from a nearby puddle, and built a fire under that. When the root

was soft, he took it out and looked at it. If it killed him, his sufferings would be over. If he lived, he would make this miserable land pay. He took a bite—it was bland, but in his starving mouth it tasted better than his mother's home-baked bread. Hunger overcame him and he gobbled the rest of it down. His belly full for the moment, no longer caring if he lived or died, Morales went to sleep at the foot of the tree in a state of peace he had not known since entering the jungle. His first thought when he awoke was glee: I'm still alive! Day after day, Morales continued to make this stew until he was once again at full strength. In time he left the jungle realizing that life was more valuable than any amount of gold and anxious to share with the world the food that had saved his life.

Scientific Connection

The stew that Morales made is known today as tapioca, and this story of disaster and attempted suicide is one of the legends surrounding the discovery of this popular treat. Tapioca is a starch that is extracted from the cassava root. Starches are carbohydrate rich plant extracts that are typically used as thickening agents in cooking, similar to the corn starch that you can find in your local grocery store. However, unlike corn, the cassava can be loaded with cyanide. In many plants, including the cassava, cyanide is bound to chains of glucose forming what are known as cyanogenic glycosides. As long as the cyanide stays bound to those glucose chains you are safe, but if cyanide gets released from those sugars it will poison you. As a general rule, living things don't like

to get eaten and the cassava is no different. When the plant cells of the cassava are crushed—by teeth, for instance—the destroyed cells release proteins that start to cut cyanide away from the sugar molecules, precipitating its toxicity.

Cyanide is a potent inhibitor of cellular respiration and works to inhibit ATP production by blocking the electron transport chain in mitochondria. Electrons are harvested from nutrient molecules (like sugars, fats and amino acids) by the Krebs cycle. These electrons are passed down the electron transport chain where they are finally accepted by oxygen. As electrons are passed through the chain, hydrogen ions are pumped into the space between the inner and the outer mitochondrial membranes. The generation of this hydrogen ion gradient is really the most important part of cellular respiration because the more hydrogen ions you can fit between the inner and outer mitochondrial membrane, the more ATP you can make. ATP synthase is like a little water wheel: as the hydrogen ions pass by it they push the wheel and make it spin. The spinning of the wheel is what generates the energy to make ATP from ADP and inorganic phosphate. Cyanide blocks the electron transport chain, preventing the flux of electrons and the formation of the hydrogen ion gradient, and leading to potentially fatal decreases in ATP production. It is similar to hydroelectric power plants, in which water wheels are pushed by gigantic waterfalls. The force of the waterfall spins the water wheels and the mechanical energy of those spinning wheels can be converted into enough electrical energy to power a town. However, if the powerful waterfall is reduced to a trickle the wheels will stop spinning and then no electricity will be produced.

ATP is stored biological energy that is used to do essential biological work. The harder the tissue must work, the more ATP is needed to keep it functioning. The tissues of the nervous system contain very hard-working cells called neurons that require a significant amount of ATP to function. While you cannot physically see decreases in ATP production, you can observe the effects of a tissue that is not working. Because cyanide inhibits ATP production, tissues like the nervous system that depend on high levels of ATP generation will suffer first. Acute cyanide intoxication, as in Miguel's case, causes confusion, agitation, and disorientation because it impairs the nervous system and prevents normal cognition (thinking). If the nervous system is significantly impaired, then death will follow because it controls the rate of breathing and the beating of the heart. As with the snake venoms in previous stories, when heartbeat and respiration stop, death follows quickly. Morales, on the other hand, seemed to be unaffected. What did he do that Miguel did not?

The secret lies in the making of the stew, Morales crushed the root up, dried it out, and boiled it in a pot. The drying and boiling process destroyed the protein that liberates the cyanide from the glucose chains and facilitated the elimination any of the volatile (easily vaporized)

cyanide that had been liberated during the crushing process. By making the stew, Morales disabled the cyanide defenses of the cassava and made it safe to eat. The proper handling and preparation of cassava is a worldwide health issue, because it is a major crop in the Southern Hemisphere, especially Africa, which produces 30 million tons of cassava root/year. In rural regions of Africa, cassava represents a major portion and occasionally exclusive component of the diet especially in times of war, famine, and drought. Cassava sold in American grocery stores in has low cyanide content and is not nearly as hazardous to eat raw. In places where high-cyanide cassava is grown, improper processing and preparation can lead to outbreaks of serious illness. The chronic cyanide exposure that results from consumption of improperly processed cassava primarily affects the nervous system producing two well known diseases: Konzo and Tropical Ataxic Neuropathy.

PATIENT SKETCH OF KONZO

A young boy needs a cane to walk. Even with the cane he struggles considerably and makes almost a tripod with it as he hobbles along. Both legs are straight and move without a bend in the knees. The legs seem to be very weak.

Konzo means “tired legs” and it is heavily associated with a diet rich in high-cyanide-content cassava in the setting of low dietary protein intake. It results in an irreversible spastic (stiff) paralysis of both legs. It seems to strike children around the age of 2-3 or women of childbearing age. Your body, while not immune to cyanide (CN⁻), can detoxify it by converting it to thiocyanate (SCN⁻) but you need sulfur in your diet to do that, and dietary sulfur comes from foods that are high in protein. Cassava is a carbohydrate-rich food that is very low in protein and thus its exclusive consumption is a setup for this sort of scenario.

PATIENT SKETCH OF TROPICAL ATAXIC NEUROPATHY

A 70-yearold man with poor vision and hearing has a difficult time feeling things touch his skin. He has a hard time feeling pain and has burned himself a few times without even knowing it. He can walk if his eyes are open, but if he closes them and tries to walk he will trip even if there is nothing to trip over. With his eyes closed he is extremely unsteady and is at risk of falling over, but when he opens them he is considerably more stable on his feet.

This is tropical ataxic neuropathy, which is believed to be caused by many years of eating poorly processed cassava in the background of low dietary protein intake. Unlike Konzo, which results from higher amounts of consumption over a short period of time, tropical ataxic neuropathy is believed to result from lower levels of exposure for a much longer period of time. The nervous system is still affected, but in konzo the effect is paralytic and tropical ataxic neuropathy is more or less a destruction of the senses. Associated signs of tropical ataxic neuropathy: sensory neuropathy (the inability to feel physical sensations like being touched or burned), bilateral optic atrophy (serious decreases in the vision of both eyes), bilateral deafness (inability to hear in either ear due to damage to nerves), and sensory ataxia (inability to walk with eyes closed because all other senses that help you coordinate, like, touch are gone due to nerve damage. The ability to see where you are going corrects this).

↪ ***Take Home Message*** ↪

Cyanide inhibits cellular respiration and can cause fatal decreases in ATP production. Cyanogenic glycosides are found in many plants besides cassava, such as apple seeds and peach pits.