Chicago Cyanide Murders: A Case Study in Cellular Respiration

Part 1: Background

Imagine that you work at the medical examiner’s office in Chicago. As Chief Medical Officer, you investigate suspicious deaths and provide toxicology services for the county. Unfortunately, it’s been a busy week. In the past five days, seven people have died, all with similar symptoms. It is your job to examine the data and determine the cause of death for these victims.

The first was a 12-year-old girl. Her parents said that she was awake in the middle of the night complaining of a stuffy nose and sore throat. They gave her an extra strength Tylenol and sent her back to bed. At 7am the next morning, the parents discovered that the girl had collapsed on the bathroom floor. An ambulance rushed the girl to a nearby hospital, where she was pronounced dead.

The same day, paramedics found the second victim unconscious on his kitchen floor after what they thought was an apparent heart attack. Sadly the victim’s brother and his fiancée also collapsed later that night while the family gathered to mourn his passing. Both had taken Tylenol to help them cope with their loss shortly before collapsing; neither survived.

In the next four days, four other similar deaths were reported, all in the same neighborhood and all with similar symptoms.

Are these seven deaths related? What is causing these people to die? It is your job to answer these questions before more deaths are reported.

Symptoms exhibited by each of the victims included:

- weakness, dizziness, sleepiness
- flushed, bright red, skin tone
- headache
- shortness of breath and rapid breathing
- vomiting
- confusion and disorientation

Most deaths were very rapid, occurring within a few hours of symptoms.

1. Are there any similarities or connections between these seven individuals? What additional questions would you need to ask the families to determine if they are connected?
   All seven victims live in the same neighborhood. At least three of the seven took Tylenol. I would ask the four other victims if they took Tylenol, if they knew anyone in common, etc.

2. In your opinion, are these seven deaths connected? Why or why not?
Part 2: Autopsy report

After some investigating, it is concluded that each of the victims had died of hypoxia. **Hypoxia** means that the person suffered from a lack of oxygen, or they were suffocated. The reason for the hypoxia is not always clear at the first examination.

The medical examiner also showed the tissue samples from the heart, lungs, and liver had massive cell death. After staining the samples with specific dies and looking at them under the microscope, it was shown that the tissues had major mitochondrial damage.

Even though the victims died of hypoxia, their level of oxygen in their blood was approximately 110 mm Hg. The normal range is 75-100 mm Hg.

3. Recall your knowledge of the function of organelles. What function of the cells was interrupted in these patients? Could this loss of function lead to the death of these individuals? Why or why not?
   - The process of cellular respiration was probably disrupted in these individuals. If a person does not carry out Cellular Respiration they can die. This is because all cells in the body need energy and the process of cellular respiration creates energy for the cells.

4. Analyze the oxygen levels of the victims. Were the levels higher or lower than normal? How can you explain these results with the cause of death being hypoxia?
   - The oxygen levels were higher than normal. This means that the victims suffocated on a cellular level—as the cells were not using the oxygen that was in the blood stream.

Part 3: Subcellular Metabolite Analysis

Detailed analysis of the damaged cells showed that ATP levels in the mitochondria were very low. Levels of Pyruvate and acetyl-coA were normal. You begin to suspect a malfunction of a specific pathway for ATP production. You request a more detailed analysis of the metabolites found in the affected cells. The levels of key metabolites are reported below:

**Average Metabolite Levels**

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>Average Patient Level</th>
<th>Normal Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>99</td>
<td>100</td>
</tr>
<tr>
<td>Pyruvate</td>
<td>27</td>
<td>25</td>
</tr>
<tr>
<td>NADH</td>
<td>400</td>
<td>50</td>
</tr>
</tbody>
</table>

5. Where are each of the metabolites listed above generated during cellular respiration?
   - **Glucose**—we get it from the food we ingest.
   - **Pyruvate**—comes from breaking down glucose during glycolysis.
   - **NADH**—is created in the Kreb's/Citic Acid Cycle.

6. List the function of each part of cellular respiration below:
   - **Glycolysis**: to break down glucose into pyruvate.
   - **Krebs Cycle**: to create the high energy electron carrier NADH.
   - **Electron Transport Chain**: to create ATP from the electron carrier NADH.
7. Are there any abnormalities in the levels of metabolites found in the victims? What part of cellular respiration do you think is being affected? Why do you think this?

Yes—the levels of NADH are very high. This means that the Electron Transport Chain is being affected because the NADH isn’t being broken down and used to create ATP.

Part 4: Role of Cyanide

Toxicology reports show that the victims had been poisoned with cyanide. The poison was traced back to extra strength Tylenol where the murderer had opened the capsules and replaced acetaminophen (a pain killer) with cyanide. Cyanide acts very quickly, often killing within minutes of ingestion and authorities were slow to identify the cause of the deaths. Once the cause was identified, stores removed Tylenol and other drugs from shelves. While there were many suspects, no one was ever charged with the crime and it is still an ongoing investigation. Since the Chicago Tylenol murders, drug companies have drastically changed how medicines are packaged. Why is cyanide such an effective poison? You might be surprised to learn that it directly interferes with cellular respiration that occurs in the mitochondria.

8. Recall that the mitochondrion is sometimes called the "powerhouse" of the cell. What does this mean? Why is the mitochondrion important?

Mitochondria are important because they create ATP that is required to power all the processes of the cell.

Part 5: Why Do We Need Oxygen?

It seems like a simple question, everyone knows you need to breathe to live. Have you ever thought about why oxygen is so important? The victims of the cyanide poisoning all had high levels of oxygen in their blood, but the poison was interfering with how the cells use that oxygen. To understand, we need to take a very close look at the structure of the mitochondrion.

Inside the mitochondrion, there are several layers of membranes. In fact, these membranes resemble the membrane that surrounds the cell. It has a bilayer of phospholipids and embedded proteins. On the diagram above, the proteins are labeled I, II, III, IV, and Cytochrome C.

The proteins in the membrane pass electrons from one to the other; this is known as the electron transport chain. The passing of these electrons allows ATP (adenosine triphosphate) to be generated. At the end of the electron transport chain, Cytochrome C passes the electron to its final acceptor, oxygen. Oxygen then binds with hydrogen to create...
water. This process is continuous in cells, with ATP constantly being generated and oxygen being used as the final electron acceptor.

Cyanide inhibits cytochrome C, preventing the last protein from doing its job. The electron stops at the end of the chain and cannot be passed to oxygen. The whole chain grinds to a halt and no ATP can be made.

9. Cyanide is an extremely fast acting poison. In fact, it was developed as a suicide pill (called L-pill) during World War II so that British and American spies could avoid being captured alive. Given what you know about ATP and cellular respiration; explain why cyanide is so fast acting.

   The body cannot produce enough ATP without going through the electron transport chain. Therefore, all of the processes of the cell will stop very quickly because they are not getting any energy from cellular respiration.

10. Given what you know about cyanide poisoning, do you think that treating a person with oxygen would be effective? Why or why not?

   Treating a person with Oxygen would not be effective because the cells are not lacking oxygen-they are lacking a way to use that Oxygen.