Emma O'Reilly, Yinka Lamikanra & Samuel Maunsell

Case Study #7: Ratatouille Revenge
BC 362, Medical Biochemistry

Case Background

Ben, a 47-year-old male, was brought to your emergency department by his coworker after collapsing suddenly while working as an exterminator. On arrival, Ben appeared disoriented and incoherent. He was noted to be hyperventilating, with a rapid respiratory rate, and complained of nausea. Physical examination revealed muscle weakness and reduced sensation in his hands and feet. His occupational history as an exterminator raised concerns for possible exposure to neurotoxic agents or metabolic toxins, prompting further investigation and laboratory analyses, like the anion gap and blood tests. Luckily, Ben's coworker Melissa drove to the ED in the company van which allowed for analysis of their rodenticide "Tail-Trap", which notably contained thallium malonate, a known inhibitor of ATP production.

Table 1. Test Results

	Patient	**Normal Ranges**
Anion Gap	28mM	8-16mM
Succinate	70 mcg/mg creatine	0-20 mcg/mg creatine
Malonic Acid	9 µM	<0.9 µM
White Blood Cells	8,000 cells/uL	4500-11,000 cells/uL
β-hydroxybutyrate	39 µg/mL	0-44 µg/mL
Blood pH	7.2	7.35-7.45

Discussion Question 1. What abnormal values were found in Ben's blood and Anion Gap Test? What is notable about the results that may suggest what is happening biochemically?

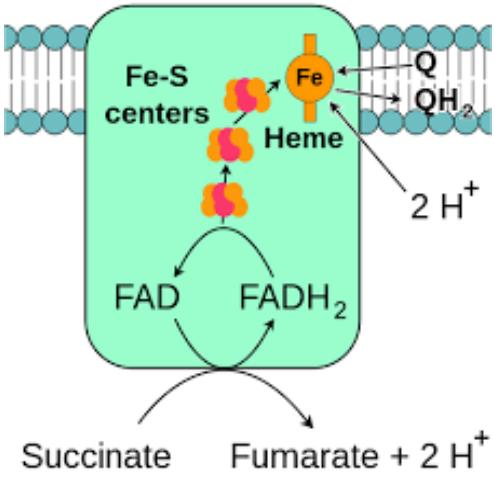

Figure 1. Oxidation of succinate to fumarate in Complex II of the electron transport chain.

Emma O'Reilly, Yinka Lamikanra & Samuel Maunsell

Biochemistry

Complex II in the electron transport chain, also known as succinate dehydrogenase (SDH), is responsible for converting succinate to fumarate. When succinate is oxidized, FAD accepts 2 electrons from it that are later released into the intermembrane space in order to generate ATP. When any part of the electron transport chain is inhibited, the cell is no longer able to produce ATP, causing an increase in anaerobic respiration in order to keep up with the body's demand for oxygen. Increased anaerobic respiration will result in higher levels of lactic acid, causing blood pH to decrease.

Vocabulary: Thallium malonate, succinate, succinate dehydrogenase

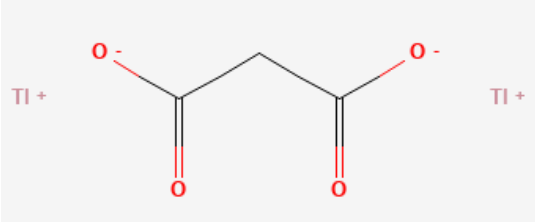

Figure 2. Structure of thallium malonate.

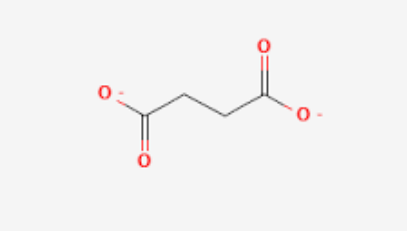

Figure 3. Structure of succinate.

Discussion Question 2. Looking at the structure of succinate and thallium malonate, how is the thallium malonate impacting the ETC?
Discussion Question 3. What is a potential clinical intervention for metabolic acidosis in Ben's situation?

References:

Malonate - an Overview. Science Direct, Accessed 18 Nov. 2025, www.sciencedirect.com/topics/neuroscience/malonate

New Jersey Department of Health and Senior Services. (2000, September). Hazardous Substance Fact Sheet: Thallous Malonate. https://nj.gov/health/eoh/rtkweb/documents/fs/2813.pdf

PubChem. (2025). Compound Summary: Malonate. Accessed 18 Nov. 2025, https://pubchem.ncbi.nlm.nih.gov/compound/2757-18-8#section=Absorption-Distribution-and-Excretion

PubChem. (2025). Compound Summary: Succinate. Accessed 18 Nov. 2025, https://pubchem.ncbi.nlm.nih.gov/compound/Succinate

Answers:

1. **Elevated levels of succinate, malonic acid and a decrease of pH. These results point towards acidosis.**
2. **Malonate competitively inhibits succinate dehydrogenase by binding to its active site, blocking the conversion of succinate to fumarate. This prevents FAD reduction and electron flow from Complex II to CoQ, reducing ATP production. Complex I electrons still enter the chain, so ATP synthesis continues but at a reduced rate. The inhibited TCA cycle causes cells to increase glycolysis, leading**

to lactate buildup and metabolic acidosis. This results in ATP deficiency, fatigue, and increased lactic acid.

3. **Administration of intravenous bicarbonate may help buffer excess acid, providing temporary relief while the toxins are flushed out of the body over time.**