NATIONAL CENTER FOR CASE STUDY TEACHING IN SCIENCE

Who Killed Yew? Murder and Mitosis

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Part I – The Intruder

The intruder entered the kitchen of the upscale restaurant at 2:43am. All was quiet. All was dark.

The intruder moved quickly, but he was not in a rush. He knew that the baker would not arrive until 4:00am, as she did most mornings. Most of the meal for the private lunch to be catered later that day had already been prepped. He peered over the stainless steel countertops and into bowls of chopped vegetables, rising dough, and homemade marinades until he found what he was looking for—the dessert prep. Pecan pie was the dessert of choice for the lunch party. He smiled. He could not have chosen a better dessert to carry out his plan!

The intruder reached into his pocket with a gloved hand and produced a small bag with what appeared to be chopped pecans. These were not pecans, however. The bag contained the chopped seeds of a *Taxus baccata* tree.

The intruder swiftly dumped the contents of the bag into the bowl of chopped pecans. He stirred the mixture with his hand. Satisfied that no one would notice his addition of the extra ingredient, the intruder made his way out of the kitchen and into the night.

Questions

1. What type of plan could be carried out by adding the seeds of *Taxus baccata* to a pecan pie?

2. What are taxines?

Part II – The Lunch

At lunch that Thursday afternoon, Governor Adrienne Baker sat with her aide Benji, Lieutenant Governor Graham Fitzpatrick, and physician Dr. Kathy Beckham, a trusted advisor and best friend. Over the course of the lunch, the diners munched on a pre-determined menu of marinated artichoke salad and rosemary encrusted lamp chops with roasted potatoes and carrots, and discussed the major issue of the governor's term. The closing of the largest state-supported hospital had been a lightning rod for controversy, and Dr. Beckham was nervous for her friend. This was a highly contentious issue, and people with a lot of power and money had a lot to lose if the governor announced the closing of the hospital, as she was planning to do the following Tuesday during a press conference. While Dr. Beckham hated to see the hospital close, she was not worried about being able to find a new job. Dr. Beckham locked eyes with her friend and gave the governor a reassuring smile.

When the dessert finally came out, Governor Baker was thrilled. Pecan pie was her absolute favorite, and after the stress of discussing the hospital issue, she wanted some comfort food. The governor, the lieutenant governor, and Benji the aide had no trouble polishing off their entire slices of pie. Dr. Beckham, who did not like pecans and who was feeling rather full, had one small bite of the pie in order to be polite, but placed her fork down across her plate, signaling the end of the meal.

Questions

1. Most of the governor's lunch party just ate pecan pie filled with taxines, a potent mixture of poisons, one of which is actually a powerful mitotic inhibitor. What is a mitotic inhibitor?

2. Which specific cytoskeletal element is most susceptible to mitotic inhibitors?

3. Describe the function of mitosis in animal cells. Why is mitosis important?

Watch the video of mitosis at **http://youtu.be/C6hn3sA0ip0** and then answer the following:

4. In the table below, draw the six major stages of the cell cycle. Be sure to *label* the following in each of your drawings where appropriate: *chromosomes/chromatin/sister chromatids, mitotic spindle, asters, centromeres, microtubules, kinetochore, cleavage furrow,* and *nuclear membrane.*

5. In each stage, note the role of the microtubules.

Interphase	Prophase
Notes:	Notes:
Prometaphase	Metaphase
Notes:	Notes:
Anaphase	Telophase & Cytokinesis
Notes:	Notes:

Part III – The Hospital

Later that afternoon, from the local hospital, Dr. Kathy Beckham called her friend, Governor Adrienne Baker, to thank her again for lunch and to check in, as she often did. Adrienne did not answer her phone, which was not unusual. The governor was a busy woman after all and would at least send a text within an hour or so if she missed Kathy's call.

While making her rounds, Dr. Beckham began to feel ill. She was nauseous and a little dizzy. Her heart was beating quickly. She checked her cell phone. Adrienne still had not returned her call, nor sent a text. Kathy began to feel uneasy. It wasn't like Adrienne to not even shoot her a quick text to let her know how her day was going.

Dr. Beckham moved into the next patient's room. The TV was on in the background—a soap opera. The patient was sleeping and as the doctor leaned forward to wake him, she glanced up at the television. Her mouth dropped open as the news flashed across the screen.

> *BREAKING NEWS: Governor Adrienne Baker found dead in her home. Lieutenant Governor Graham Fitzpatrick and aide Benji Williams rushed to local hospital unconscious and in critical condition. Police suspect foul play.*

Dr. Beckham stared at the screen in shock and disbelief. She jumped when she felt a hand on her shoulder. It was a police officer. "Ma'am," the police officer said sternly, "I'd like you to come with me."

Question

1. Why did Dr. Beckham have only mild symptoms (dizziness, nausea, racing heart beat) as compared to the others?

Part IV—The Interrogation

Back at the station, while being grilled about her possible motive for killing her friend, Dr. Kathy Beckham described her friendship with the governor as well as the events leading up to the controversial hospital decision, and gave an account of her movements and whereabouts for the last 24 hours. She became sick to her stomach and threw up during the interrogation. Her heart was racing. She was overwhelmed with grief and shock, but there was something else going on and she couldn't put her finger on it. A new detective entered the interview room.

"Dr. Beckham, I am Detective Perry. I am sorry to have had to bring you here and sorry for the loss of your friend. At this point, we don't believe you had anything to do with the murder. Sources tell us you were out to lunch with the governor and her aide as well as the lieutenant governor today. Could you tell us what you all ate for lunch?"

"We all had the same salad, lamb chops, and dessert. Pecan pie. Well, come to think of it, I only ate a small bite of the pie while the others ate their entire piece. I am not particularly fond of pecans." She paused. Her eyes widened. "Do you think someone poisoned us, Detective?!" asked Dr. Beckham. Pieces of the puzzle were beginning to fit together.

"The pathologist just called," began the detective, "and initial toxicology reports indicate traces of a compound called paclitaxel. Have you heard of it?"

"Yes," replied Dr. Beckham, "I distribute it in my hospital to breast cancer patients as a chemotherapy drug."

Questions

As mentioned previously, taxines from the yew tree are a mixture of poisons. When parts of the yew tree are ingested, the taxines include the compounds paclitaxel and taxine B. The taxine B is actually what causes death (within hours) of those poisoned. It interferes with calcium channels in the heart and causes cardiac arrest, which can be fatal, as it was in the case of the governor. Paclitaxel is also a poison that can be fatal, but its mechanism of action takes longer.

Watch the video at **http://youtu.be/o8wVJonsnJw** how paclitaxel affects cells undergoing mitosis and answer the following questions.

1. Based on the video you just watched, explain how paclitaxel exerts its effect and why that could be deadly. Specifically discuss the role of microtubules during mitosis and how that is impacted when a cell is exposed to paclitaxel.

2. Generally speaking, what is cancer? Why would the discovery of paclitaxel's mechanism of action be exciting for scientists studying cancer?

3. There are three major types of cancer treatments: surgery to remove cancerous tissue, chemotherapy, and radiation. Which treatment would paclitaxel be considered?

4. List at least two organs in the body with rapidly dividing cells.

5. Chemotherapeutic drugs are toxic to any rapidly dividing cell and are typically administered into the circulatory system. Paclitaxel has been converted to a powerful and commonly prescribed chemotherapy known as Taxol®. What would be side effects on healthy tissue, particularly those discussed in Question 4 (above), after being exposed to Taxol ?

6. Why does ingesting parts of the yew tree cause death while administration of the chemotherapy drug Taxol does not? Do you think cancer patients could be given chemotherapeutic drugs indefinitely?

Part V—The Intruder Revisited

Detective Perry's patrol car turned down the street of the Chairman of the Board of Trustees of the hospital the governor had plans to shut down. He had been an outspoken critic of her policies, and his brother owned the upscale restaurant where the governor and her team had been poisoned. Detective Perry pulled in the driveway and from his car could see a huge yew tree in the backyard.