NATIONAL CENTER FOR CASE STUDY TEACHING IN SCIENCE

Digesting Danger:

Nutrition, Genetics, and Colon Cancer

by

Chandler M. Ciuba, Abigail Rohr, Min-Ken Liao, and Linnea R. Freeman*
Department of Biology
Furman University, Greenville, SC

Part I – Hot Diggity Dog

"Three, two, one, eat!" the MC yelled over the microphone. And so began the annual hotdog eating championship in Wigston County, West Virginia. Three-year record holder Nathan Payne was working hard to defend his title of county champion, which essentially equated to celebrity status in his town. West Virginia was estimated to consume 481 hotdogs per person per year according to the National Hotdog and Sausage Council, with most of the consumption occurring during "hotdog season," the glorious months between Fourth of July and Labor Day.

Just one more, thought Nathan as he swallowed his 74th hotdog at the 9:50-minute mark. One more and he would beat his own personal record and set his third competition record. *Just one more, and it'll all be over...* He forced the last hotdog down.

"Ladies and gentlemen…we have a winner!" the MC shouted into the microphone.

I know I should be thrilled, but something doesn't feel … Nathan turned from the stage and vomited, and the crowd went silent. He looked up at his father, who was staring back with dark, tormented eyes. *Well, here we go again,* thought Nathan.

Nathan's father, and his father's father, had also been hotdog-eating champions. It was a family tradition of sorts. However, both his father and grandfather suffered from colon cancer. Nathan's grandfather tragically died from the disease one year ago to the day, and Nathan's father couldn't bear to see his 35-year-old son afflicted with the same disease. No matter how often Nathan's father begged him to see the doctor, Nathan would not comply. He honestly didn't even believe that eating hotdogs had anything to do with colon cancer; the way Nathan saw it, if both his father and grandfather developed colon cancer, it must be due to bad genes. If he was going to get the disease anyway, he may as well enjoy his life and do what he loved to do: eating hotdogs.

After he cleaned himself up, Nathan shuffled over to his parents. "We need to talk, son," his father said. "I made an appointment for you. It's just a consultation so that you can talk to a doctor about different risk factors that you may be facing. If your grandpa was here, you know he would agree with me."

Way to hit me with that guilt trip Dad, Nathan thought to himself. But deep down, Nathan knew his father was right; it was time to see a professional.

Before he met with the doctor, Nathan was uneasy. *I hate not knowing what the doctor is talking about,* he thought to himself. *It makes me wonder if it's even true*. He decided to take matters into his own hands and do some research about the disease. At the most basic level, Nathan understood that colon cancer occurs when healthy cells in the large intestine become mutated and grow uncontrollably. He read that colon cancer does have a strong genetic component, but also discovered that something known as epigenetics has an impact on the disease. The longer he spent scouring the internet for answers, the more overwhelmed and confused he felt. *Polyps? Adenoma? APC? FAP? HNPCC? What do all these words and letters even mean?! Maybe my dad was right… I do need a professional to explain this to me.*

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*Chandler Ciuba and Abigail Rohr, co-first authors; Linnea Freeman and Min-Ken Liao, co-last authors.

Questions

1. Do you think Nathan's family history of colon cancer is due to genetics or diet, or both? What is the difference between sporadic and hereditary colon cancer?

2. Do you think Nathan should listen to his father and visit the doctor? If not, why? If so, what test would the doctor most likely perform?

3. In order to better understand colon cancer, define the following terms using the NIH National Cancer Institute website dictionary of cancer terms (https://www.cancer.gov/publications/dictionaries).
   - *Polyp:*
   - *Adenoma:*
   - *Carcinoma:*
   - *FAP:*
   - *HNPCC:*
   - *Epigenetics:*

Part II – Just Bad Genes?

As they walked into the triage room, the nurse asked Nathan for his age and weight, questioned him about his general lifestyle habits, and took his blood pressure and pulse. Once he walked into the exam room, Dr. Brown came in and began asking about his family history and dietary habits.

"Now that I know a little bit about you, I'd like to talk with you about colon cancer screenings and let you ask me any questions you might have," the doctor said.

"Well, I looked into the disease before the appointment, but…"

The doctor instantly recognized the overwhelmed look that many new patients have. "I know it's complicated," the doctor assured him,"but let me break it down for you. Most colon cancer is sporadic, but there are also two main inheritable syndromes that can lead to inherited colon cancer. The first is called hereditary nonpolyposis colorectal cancer (HNPCC), also known as Lynch syndrome, and it's responsible for 2–4% of all colorectal cancers. The other one is called familial adenomatous polyposis (FAP), and it's responsible for about 1% of cases. FAP is caused by a mutation in a gene called *APC* that leads to thousands of adenomatous colorectal polyps, which are usually non-cancerous tumors that can develop into colorectal cancer in young adulthood. Individuals with a high risk of having FAP, such as yourself, should undergo the screening process as early as twenty years of age" (Gryfe, 2009).

Dr. Brown continued, "The reason I wanted to explain this to you is because you have a family history of colon cancer. As I said, this can greatly increase your risk of getting colon cancer. Usually we recommend colonoscopies every five to ten years starting at the age of 50. In 2021, the U.S. Preventive Services Task Force even issued a new recommendation to screen folks of average colon cancer risk at age 45. Still, in your case, I highly recommend getting a colonoscopy, even though you're only 35. I also recommend visiting a genetic counselor to test for any of the genetic mutations we have reviewed, but that is ultimately your decision. Finally, I'd like to discuss your dietary habits, especially because of your hobby."

"Now wait a minute," Nathan interjected. "I'm so sick of everyone telling me to stop eating hotdogs. I'm not going to stop."

Dr. Brown nodded. "I understand your hesitation. However, out of concern for your health, I urge you to consider meeting with Ms. Kelly. She's our nutritionist at the clinic, and she can more fully explain these lifestyle risk factors and address your questions."

Questions

1. Which type of risk factor should Nathan address first, genetic or environmental? Why?

2. Most HNPCC cancers result from a mutation in *MLH1, MSH2,* or *MSH6* genes. Using the NIH National Cancer Institute website dictionary of cancer terms (https://www.cancer.gov/publications/dictionaries), see what role these genes play.

3. If Nathan only agrees to make one lifestyle or dietary change to address these risk factors, which do you think it should be and why?

Part III – You Are What You Eat

"Hi Nathan, welcome to my office," Ms. Kelly said, introducing herself. "I wanted to talk to you about the nutritional risk factors that can lead to colon cancer." Ms. Kelly motioned to two chairs trying to make Nathan more comfortable. She continued, "Now luckily you don't use tobacco or alcohol, which are both classified as type 1 carcinogens. A type 1 carcinogen is defined as a substance known to cause cancer in human tissue. But you do eat processed meat and red meat, and they're classified as type 2A carcinogens, which means they're probably carcinogenic to humans; in other words, there's strong evidence to believe this, but we don't have conclusive evidence yet. Processed meat is any meat that has been processed to preserve or add flavor to it and includes things such as hotdogs, ham, sausage, deli meat, and bacon. It also includes pork, beef, lamb, and goat. Recent research shows that eating fifty grams of processed meat every day, which is equivalent to one hotdog per day, increases the risk of colorectal cancer by 18% (Alexander, 2021; Crowe et al., 2019). So, eating seventy-five hotdogs in a day increases your risk dramatically. I understand that you love what you do. However, if you want to avoid this disease, you must begin to seriously consider reducing your consumption of hotdogs and other processed meats or eliminating them."

Nathan looked at Ms. Kelly in bewilderment, "Is this really that serious? I don't understand how eating hotdogs can be that bad for you."

Ms. Kelly patiently let Nathan work through the skepticism and anxiety that is common during consultations like this before beginning again. "Yes, it is that serious. Your family history makes eating processed meats much more concerning than for people with no genetic predispositions." She flashed a wistful smile. "Rather than focusing on the negative effects that meat can have on colon cancer risk, let's focus on the positive effects that plant proteins can have. The substitution of plant protein for red meat is associated with an 11% decreased risk of colon cancer (Liao et al., 2019). Research also recommends at least 50 grams or 1/3 cup of fiber each day (O'Keefe, 2022). This could include foods such as vegetables, oats, brown rice, and fruits (Mayo Clinic, 2023)." Nathan leaned back and huffed from all the information he had just absorbed. Ms. Kelley leaned in from her chair and assured him, "I want to begin with small steps in your journey toward a healthier lifestyle. In between our meetings, I ask that you read this pamphlet about both nutritionally harmful and protective foods so that we can work together to reduce your risk of getting colon cancer."

Nathan let out a huge sigh of relief. "That sounds manageable. I think I need time to 'digest' everything we've talked about before I make any dramatic changes."

"Of course," Ms. Kelly agreed. "I'd like to meet with you next week to follow up on your colonoscopy results, speak more with you about the pamphlet I have suggested, and hear about the healthier foods you have been incorporating into your daily diet. Finally, I plan to further explain the role of the microbiota in colon health. How does that sound?"

Nathan smiled agreeably and left the office feeling much more hopeful than when he first arrived.

Questions

1. In order to better understand certain environmental impacts on colon cancer, define *heterocyclic amine* and *nitrosamine* using the NIH National Cancer Institute website dictionary of cancer terms (https://www.cancer.gov/publications/dictionaries). Why are these a threat to Nathan's health?

2. What are some alternatives that would be a healthier choice than hotdogs? Give one animal-based option and one plant-based option for Nathan to try.

3. There are two "cancer-fighting" compounds you can extract from the diet, phytate and butyrate. Phytate is an antioxidant compound that triggers apoptosis and represses pathways that would otherwise allow defective cells to survive. Phytates are found in foods like whole grain cereal, nuts, and lentils. It is important to also increase fiber intake because any of these carbohydrates that you consume are fermented by your gut microbiota into protective short-chain fatty acids (SCFAs) like butyrate. Butyrate is an intestinal metabolite that can induce apoptosis in cancerous colonocytes through a process known as histone acetylation. To begin to understand these processes, use the NIH National Cancer Institute website dictionary of cancer terms (https://www.cancer.gov/publications/dictionaries) to define the following:
   - *Antioxidant:*
   - *Apoptosis:*
   - *Histone and histone deacetylase:*
   - *Microbiome:*

Part IV – No Guts, No Glory

When Nathan returned to Ms. Kelly's office, he felt nervous that he wasn't as prepared as she might expect him to be. *What if she grills me about not making enough dietary changes? It's only been a week! I'm still trying to make sense of this new information,* he thought, as Ms. Kelly swung open her door.

"Hi Nathan, great to see you again! Come on back." Ms. Kelly began their meeting by asking how the week went and if he had any questions about the pamphlet.

"Well, I don't have any questions per se, but last week, you mentioned something called *microbiota*. I looked it up online, and it was extremely confusing. I'm not sure how these things are connected: colon cancer, eating hotdogs, toxins in my gut, probiotics… It seems a little far-fetched, to be honest," said Nathan.

Ms. Kelley sat down next to Nathan and said, "I'm glad you took the time to look into it and I'm happy to explain. One main reason the colon, diet, and microbiota are related is that the colon's lining is exposed to various compounds consumed in the diet. Some components of a diet can contain procarcinogens, which are substances that can be transformed into carcinogens during metabolism. Other components of the diet can have protective effects on the colon. There is strong scientific evidence that shows that nitrosamines (NA), heterocyclic amines (HCAs), and polycyclic aromatic hydrocarbons (PAHs) are all carcinogenic substances derived from cooking and processing foods. I asked you to reduce your intake of the processed meats you regularly consume because they can damage DNA and are thus associated with cancer risk (Jakszyn et al., 2004)."

Nathan cocked his head to the side and asked, "So how does this tie into the microbiota again?"

Ms. Kelley smiled as she could tell Nathan was beginning to become as interested in his health as she was. "Research suggests that diet can greatly affect the colonic environment by either increasing or decreasing exposure to mutagens through changes in the composition and activity of the gut microbiota. A healthy human gut can be measured by the level of diversity of the microbiota. Dysbiosis, the imbalance in composition and functionality of the gut microbiota, is related to many diseases including colon cancer. In patients with colon cancer, we typically see an increased prevalence of certain pathogenic microbes and a significant decrease in protective microbes. The components of the red and processed meats you've been regularly consuming can get metabolized by gut bacteria and produce carcinogenic metabolites associated with colon cancer (Song et al., 2020)."

Nathan's eyes widened as Ms. Kelly continued. He thought to himself, *I had no idea all of these things were happening in my body. I thought it was all an exaggeration... I can never tell whether diet advice is true or just a marketing ploy. What have I done?* Nathan could feel sweat glistening on his forehead and his lip began to quiver.

Ms. Kelly stopped for a moment to let him regroup. "My intentions are never to cause anxiety in my patients. I just want to give you all the information so that together we can make the healthiest plan for your future," she explained.

"Thank you. I want that too," Nathan replied. "I was in denial for so long. Now that I know just how damaging my habits are, I feel like I can't reverse all the harm I've already caused."

Ms. Kelly assured him that it was completely normal to feel stuck. "We'll take this one step at a time through weekly meetings. You don't have to change your entire life today. Keep making small, realistic changes as we discuss them each week. Reminding yourself that you are doing everything in your power to maintain a healthy lifestyle should bring you some peace of mind."

Nathan smiled. "I'll definitely work on that. Thank you. I'll see you next week."

Questions

1. How are microorganisms classified? (Refer to Pitt & Barer, 2012.)

2. What are the major and subdominant microorganisms found in the gut in order of abundance? What crucial functions do the microorganisms perform in the gut? (Refer to Rinninella et al., 2019.)

3. What does research say about the effect of probiotics on the colon? (Refer to Drago, 2019, or find a recent article.)

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