

A Fatal Bite: Investigating a Malaria Outbreak in Sub-Saharan Africa

by

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Introduction

The following fictional storyline is intended to provide an opportunity to gain a deeper understanding behind various determinants of malaria, explore the mechanisms of popular malaria tests, and attempt to address and solve barriers relating to malaria outbreaks within Sub-Saharan Africa. Through a discovery-oriented case study approach, you will need to integrate the information from this story with the sources provided in order to adequately answer the questions. At times, you may also be challenged to conduct your own literature search to help you answer the questions.

Before you begin, take a look at the following article, which can be useful if you find that you need to search for specific topics relating to malaria that are not provided in the storyline or suggested resources.

- Martin, S., Hussain, Z., & Boyle, J. G. (2017). A beginner's guide to the literature search in medical education. *Scottish Medical Journal* 62(2): 58–62. <<https://doi.org/10.1177/0036933017707163>>

Part I – The Cycle Begins Again

Mr. Okoro lifted his seven-year-old daughter, Ada, and carried her in his arms as he began a long journey to the nearest medical center in Enugu, first on foot, then by bus. Judging by the look of desperation on his daughter's face, he knew that time was desperately short, but luckily Mr. Okoro was seen by a doctor within minutes upon their arrival.

During the physical examination of Ada, Dr. Famuyiwa noticed symptoms of fever, chills, headache, and abdominal pain, all of which looked too familiar. Since the malaria outbreak began in July, this was already the 56th case he had documented. Dr. Famuyiwa was used to experiencing these outbreaks during the rainy season when mosquito populations peaked. Patients regularly demonstrated the same symptoms as Ada, in addition to muscle aching and general weakness, vomiting, coughing, and diarrhea.

After examining the physical condition of Ada, Dr. Famuyiwa decided to perform further testing. He first considered a blood smear examination. This test would allow for the parasite *Plasmodium* to be identified in a drop of blood. However, due to limited testing equipment in the area, Dr. Famuyiwa did not have access to a microscope to review the blood smear. Also, the blood smear test would need to be taken at multiple timepoints every 12–24 hours over a period of two to three days in order to accurately verify a positive result and examine the progress of the parasitic load within the blood. Although the lack of equipment posed a problem, Dr. Famuyiwa remembered that a lab technician was making his way to the center and would bring the testing equipment with him to view the blood smears. Dr. Famuyiwa thus decided to proceed with the test, as he recalled from his previous medical training that blood smear examinations are the gold standard for malaria diagnosis. After taking a sample of Ada's blood, he handed it over to the nurse, who stored it in a temperature-controlled freezer until it could be examined by the trained lab technician.

Dr. Famuyiwa also conducted a rapid diagnostic test (RDT), also called a “dipstick test.” This immunologic test could be completed within 15 minutes and identify the presence of *Plasmodium* parasite. Knowing that the RDT test results would take about 15 minutes, Dr. Famuyiwa sought to gather the medical history of Ada by interviewing Mr. Okoro in order to accumulate more information on the events leading up to the ailment.

When asked about home life, Mr. Okoro explained that because it was the rainy season in Enugu, he had been needing more help at his farm. He took his two sons and Ada with him to work so they could plant more seeds. His two sons were 15 and 18 years of age, making Ada the youngest. During the past few weeks, Ada had been taking more responsibility around the house as her mother was pregnant and seemed to be getting paler and weaker each day. In the mornings, Ada would wake early with her father and brothers to go work on the farm, and her mother walked to the farm to pick her up in the afternoon. The two brothers were left behind with the father, while Ada helped her mother for the remainder of the day. Ada had been taught to fetch water from a local well and to hunt small fish in a nearby shallow river using the malaria bed net given to her, as her mother watched her from afar. Mr. Okoro also mentioned that at night after Ada finished helping her family, she enjoyed going outside and playing in front of the family’s compound. She would dance and skip around until she became tired and went to bed. While his daughter was in safe hands, Mr. Okoro used the opportunity to call his pregnant wife to give her an update on their arrival to the medical center and to see how his sons were doing on the farm.

Reflecting on what Mr. Okoro had told him, Dr. Famuyiwa recognized that malaria prevalence was high in young children because their immune system was still developing, which could explain why Ada was the only family member experiencing symptoms. Hearing the activities that Ada completed each day, Dr. Famuyiwa acknowledged how risk factors such as working in wet farmland fields and shallow water reservoirs were potential contact points where Ada could have been exposed. With seven minutes left until the completion of the RDT test, Dr. Famuyiwa recalled that in the years of his medical practice he had experienced several outbreaks of this disease in this village. He knew that the disease outbreak was malaria, which is caused by the parasite *Plasmodium*. Malaria can be a difficult disease to treat and depending on the severity of the illness, a patient could die. He did not want this to be Ada’s fate.

When the 15 minutes were up, Dr. Famuyiwa examined the RDT strip. The test strip was positive, indicating that indeed Ada had malaria. Dr. Famuyiwa quickly arranged for immediate care for Ada with her father by her side.

Questions

1. In his years of training, Dr. Famuyiwa had both seen and treated multiple forms of malaria. To help refresh his memory, what are the four different types of malaria? Which type is most common across Sub-Saharan Africa? Why is one type more prevalent in this area of Africa?
2. As Dr. Famuyiwa completed a sample patient history form, he documented that Ada was in several high-risk contact points for malaria. What were the risk factors that Dr. Famuyiwa noted that increased the possibility of Ada contracting malaria? List the possible points of contact where the daughter may have encountered the vector that increased her risk of being infected with malaria. Aside from this story and the risk factors that Ada encountered, can you think of any other high-risk factors that can lead to a person being exposed to and developing malaria?

3. When Mr. Okoro finished his phone call, he feared that Ada might pass the malaria to another family member. Is malaria contagious? Explain your answer. What would you say to Mr. Okoro in response to his fear?

4. After reading this section, what ecological conditions make malaria prevalent in this region? (*Hint*: think about temperature and precipitation.)

5. Interestingly, the only member of the family who presented malarial symptoms was Ada. Who is at greatest risk for contracting malaria? Why do you think this may be? Why is this disease not contagious person-to-person? What does it mean for a disease to be vector-borne?

6. The symptoms of malaria are very similar to symptoms of the flu, such as fever, headache, chills, muscle aching, and general weakness. How could Dr. Famuyiwa correctly diagnose malaria? How might other colleagues, such as the lab technician making his way to the medical center with special equipment (including microscopes and staining material), help him with this?

Part II – The Ghostbusters of Disease

It was 10 a.m. when Dr. Fabian received a phone call. It was the Africa Centers for Disease and Control and Prevention (CDC) in Addis Ababa, Ethiopia where Dr. Fabian worked as an epidemiologist in the Division of Surveillance and Disease Intelligence. During the phone call, Dr. Fabian was asked if she would travel to Enugu, Nigeria and take the lead on investigating a potential malaria outbreak within the community. Excited for a new challenge, Dr. Fabian accepted the assignment and began to pack her bags.

That same morning Dr. Fabian was on a plane heading to meet with Dr. Famuyiwa and a lab technician to learn more about the potential outbreak. She was assigned the task of creating a progress report on the current situation and to debrief the Surveillance and Disease Intelligence division upon her return. While snacking on the plane, she opened her laptop to see an unread email sent to her from the lab technician, explaining he was trained in identifying malarial species by morphology from microscopic examination of thin blood smears. He said he was looking forward to investigating the blood smears with her when she arrived. The lab technician had also attached several files for Dr. Fabian to examine and gain familiarity on the morphology of the different malarial species. Dr. Fabian decided to spend the rest of her flight examining these files.

- Diagnostic procedure and morphology detection for *P. Falciparum*.
<https://www.cdc.gov/dpdx/resources/pdf/benchAids/malaria/Pfalciparum_benchaidV2.pdf>
- Diagnostic procedure and morphology detection for *P. Vivax*.
<https://www.cdc.gov/dpdx/resources/pdf/benchAids/malaria/Pvivax_benchaidV2.pdf>
- Diagnostic procedure and morphology detection for *P. Ovale*.
<https://www.cdc.gov/dpdx/resources/pdf/benchAids/malaria/Povale_benchaidV2.pdf>
- Diagnostic procedure and morphology detection for *P. Malariae*.
<https://www.cdc.gov/dpdx/resources/pdf/benchAids/malaria/Pmalariae_benchaidV2.pdf>

Towards the end of her flight, Dr. Fabian created an action plan of what to do when she arrived. She would first meet with Dr. Famuyiwa to discuss how this medical center had been caring for patients. Second, she would gather and review the samples with the lab technician. She would then be able to generate her report for the Surveillance and Disease Intelligence division on which species of *Plasmodium* was likely causing the latest outbreak of malaria in Enugu.



Before continuing the story, review the resources below to learn more about malaria:

- Centers for Disease Control and Prevention. (2020). About malaria: biology [webpage]. Global Health, Division of Parasitic Diseases and Malaria. <<https://www.cdc.gov/malaria/about/biology/index.html>>
- Khan Academy. (2015). The basics of malaria [video]. Running time: 9:59 min. <<https://www.khanacademy.org/science/health-and-medicine/infectious-diseases/malaria/v/the-basics-of-malaria>>



As soon as Dr. Fabian's plane touched down, she visited the local medical center to which Ada had been brought. There, she was whisked away by Dr. Famuyiwa into a crowd of concerned citizens outside the center who had heard rumors of a malaria outbreak in a nearby village. As a villager anxiously asked if her son could be infected with malaria, Dr. Fabian looked to Dr. Famuyiwa and suggested that they present the epidemiological triangle of malaria transmission to inform the gathered crowd. An epidemiological triangle, she explained, would help to visually map out how an agent, host, and environment connect in order to impact health. Dr. Famuyiwa agreed it was a good idea.

Dr. Fabian then turned and addressed the crowd: “There are four components to the epidemiological triangle. The first is the *agent*, which is the pathogen. The second is the *host*, which is the species the pathogen infects and resides within; you should also know that sometimes there can be several hosts for a given pathogen. The third component is the *environment*, which consists of the physical and social structures that exist in the surrounding society. The fourth and final component is the *vector*, which transmits the infection of the pathogen from one host to another, without suffering the actual disease itself.”

Questions

After Dr. Fabian's brief presentation, the concerned citizens had many questions they wanted to ask. If you had been presenting alongside Dr. Fabian and Dr. Famuyiwa, what responses would you have given to the questions below?

1. How can the epidemiological triangle be used to understand the malaria outbreak in Enugu?
2. Can all mosquitoes transmit malaria?
3. Can a single mosquito bite cause malaria?
4. Will a person exhibit clinical symptoms during the liver stage or the blood stage within the malaria transmission cycle?
5. In addition to the four mentioned species of *Plasmodium* (i.e., *P. falciparum*, *P. vivax*, *P. ovale*, and *P. malariae*), there is a fifth species, *P. knowlesi*, that infects people. What animal is this type of malaria naturally found in? Is malaria caused by *P. knowlesi* considered to be a zoonotic disease? Explain why or why not.

Part III – Ready, Set, Microscope!

After Dr. Fabian met with the lab technician, they agreed to first examine the blood samples that had already been stained to detect the parasites, and then examine the RDT kits, which are rapid immunological tests used to quickly detect malaria. Since the lab technician was trained to identify the malarial species through microscopic examination from the blood smears, he decided to share with Dr. Fabian the process of his work.

The lab technologist first examined the thick smears as it is useful when screening for parasites and detecting mixed infections (Figure 1). He began by screening the entire smear at a low magnification using the 10× objective lens to detect any large parasites. After seeing several parasites, he increased magnification with the 100× objective lens. He selected an area well stained that had around 15 white blood cells (WBC) so that his examination would be reliable.

After viewing the parasites on the thick smears, he then examined the thin smears to identify the species of malaria (Figure 2). As before, he first examined the thin smear at a low magnification of 10×, then at 100× view. As he continued, he noticed key characteristics, such as the gametocytes (the precursor cells that mediate the transmission of the parasite from mosquito to human) were crescent or sausage shaped, and the blood cells were within normal size and not enlarged. These characteristics fit the description for *Plasmodium falciparum*.

The technician directed Dr. Fabian to take a look at the microscope and told her the species he had found based on the morphology. Dr. Fabian took note of this and made a chart on her computer of which samples corresponded to which species of malaria in order to help her create the debrief report upon her return.

After examining the stained blood samples, Dr. Fabian and the lab technician examined the results from the RDT kits. RDT kits for malaria employ immunochromatographic methods to detect malarial antigens. Before examining the RDTs, Dr. Fabian and the lab technician reviewed the resource below to refresh their memory of how they work.

- World Health Organization (WHO). How malaria RDTs work. <<https://www.who.int/teams/global-malaria-programme/case-management/diagnosis/rapid-diagnostic-tests/how-malaria-rdts-work>>

After examining the blood samples and RDT results, they realised that the majority of cases they had looked at had acquired *P. falciparum*, the most lethal among the five *Plasmodium* species that affect humans. After Dr. Fabian added this information to the notes for her report that she would present to the Division of Surveillance and Disease Intelligence, she and the lab technician relayed this information to Dr. Famuyiwa so that he could administer an appropriate treatment regimen to his patients.

Having acquired all the information she had been assigned to find, Dr. Fabian was ready to return home and prepare her report. Before leaving, Dr. Famuyiwa shared with her his concern about seeing many mosquito bed nets (which were provided by non-profit organizations to help reduce the risk of being bitten by mosquitoes) misused by community members. Rather than using them for their intended purpose, Dr. Famuyiwa described seeing people cast

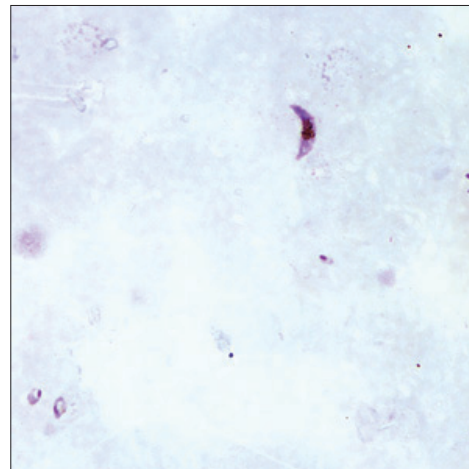


Figure 1. Gametocyte of *P. falciparum* in a thick blood smear; many ring-form trophozoites also present. Credit: DPDx, CDC <<https://www.cdc.gov/dpdx/malaria/index.html>>.

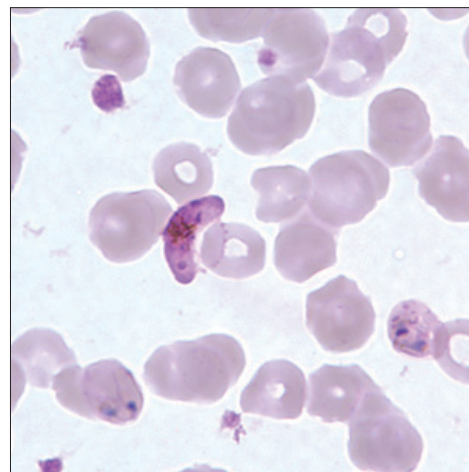


Figure 2. Gametocyte of *P. falciparum* in a thin blood smear; ring-form trophozoites exhibiting Maurer's clefts also present. Credit: DPDx, CDC <<https://www.cdc.gov/dpdx/malaria/index.html>>

their bed nets into the local rivers, collecting fish and bringing them back to shore to eat and sell in the markets. In addition, he had seen some villagers wash their bed nets too often and had even witnessed a few neighbours use them as wedding dresses. Hearing this, Dr. Fabian recognized how the misuse of bed nets could be a contributing factor in the number of cases and blood samples of positive results she had seen during her visit. She decided to include this information in her report and discuss why prevention methods of bed nets are not always successful.



Use the following resources to learn more about malaria diagnosis and treatment before answering the questions further below.

Resources

Unless otherwise indicated, the following resources are provided by the Centers for Disease Control and Prevention (CDC) or the World Health Organization (WHO).

How RDTs Work

- [1] “How malaria RDTs work.” <<https://www.who.int/teams/global-malaria-programme/case-management/diagnosis/rapid-diagnostic-tests/how-malaria-rdts-work>>
- [2] “Blood specimens: microscopic examination.” <<https://www.cdc.gov/dpdx/diagnosticprocedures/blood/microexam.html>>

Identifying Different Malarial Species Through Microscopic Identification

- [3] “Blood specimens: molecular diagnosis.” <<https://www.cdc.gov/dpdx/diagnosticprocedures/blood/moleculardx.html>>

Morphology Differences of Malarial Blood Smears

- [4] “Diagnostic procedure and morphology detection for *P. Falciparum*.” <https://www.cdc.gov/dpdx/resources/pdf/benchAids/malaria/Pfalciparum_benchaidV2.pdf>
- [5] “Diagnostic procedure and morphology detection for *P. Vivax*.” <https://www.cdc.gov/dpdx/resources/pdf/benchAids/malaria/Pvivax_benchaidV2.pdf>
- [6] “Diagnostic procedure and morphology detection for *P. Ovale*.” <https://www.cdc.gov/dpdx/resources/pdf/benchAids/malaria/Povale_benchaidV2.pdf>
- [7] “Diagnostic procedure and morphology detection for *P. Malariae*.” <https://www.cdc.gov/dpdx/resources/pdf/benchAids/malaria/Pmalariae_benchaidV2.pdf>

Malaria Treatment Regimen

- [8] “Treatment of malaria: guidelines for clinicians (United States).” <https://www.cdc.gov/malaria/diagnosis_treatment/clinicians1.html>

Misused Bed Nets

- [9] “A tragic choice: fight malaria or starve.” [Video]. Produced by Ben C. Solomon, *The New York Times*. Running time: 3.22 minutes. <<https://youtu.be/dJvooI1Ec9o>>

Vaccines in Development for Malaria

- [10] “Vaccines.” <https://www.cdc.gov/malaria/malaria_worldwide/reduction/vaccine.html>

*** Internet references accessible as of November 29, 2021. ***

Questions

1. As Dr. Fabian examined the blood smears under the microscope, what criteria for a determination of “no parasites found” (NPF) under thick smear examination should she have kept in mind while going through the samples? (*Hint: Resource 2.*)
2. Imagine you were responsible for taking the blood smears from the participants in this village. Why would you need to gather both thick and thin blood smears for malaria testing? What is the purpose of each one? (*Hint: Resource 2.*)
3. What is the significance of finding out that the majority of cases are *P. falciparum*? How does this impact treatment? (*Hint: Resource 8.*)
4. If you were helping Dr. Fabian read the results of the RDT kits, would these kits be able to detect all four species of malaria? What antigens can RDT detect? How does the limited capability of this test method compromise the correct identification of malarial parasites? (*Hint: Resource 1.*)
5. After watching “A Tragic Choice: Fight Malaria or Starve” (Resource 9), what do you think the consequences are of not using the malaria bed nets for their intended purpose? What are some of the challenges associated with adopting malaria bed nets? How would this impact the epidemic within this village?
6. Not all malaria drug treatments are given out for free by non-profit organizations, making it hard for some to purchase them out-of-pocket. Imagine another family in a nearby village that has a father, mother, and two sons. The father and one of the sons have both tested positive for malaria. Since the household budget is scarce, the father can only afford to purchase one antimalaria drug packet, but each packet is intended only for one person. Given this family’s circumstance, the father decides to split one treatment packet between him and his son. What

implications might this have on drug resistance? Also, what implication might this have on everyone else in this village? (This brief scenario introduces the topic of *drug resistance*. This term is used when there is a reduction in effectiveness of a medication used to treat a disease or condition. Drug resistance occurs when a pathogen, such as the malaria parasite, changes and acquires resistance to the medication, rendering it no longer effective or reducing its effectiveness. A cause of drug resistance can occur when the full dosage of a specific medication is not taken as instructed. (*Hint*: Think of the malaria lifecycle. If a mosquito has bitten the father or son who now has a drug resistant form of malaria, and then the same mosquito goes on to bite other people, what implications does this create?)

7. Thinking beyond the video (Resource 9), what other social determinants have an impact on malaria transmission within villages such as Enugu? (*Hint*: Think about political climate, distance to closest hospital or medical center (access and availability), poverty, and socioeconomic status.)

8. What are the unique challenges to developing a vaccine against a malaria parasite compared to vaccines for typical pathogens such as the smallpox virus? Why would the task of developing a preventive vaccine for malaria be a relatively more complex process compared to other vaccines? (*Hint*: Resource 10.)

9. As Dr. Fabian flew on her plane back home, she pondered the idea of why parasites primarily have one host species, and yet have the ability to “jump the species barrier” and infect humans. If you were able to have a discussion with her, what input would you give to Dr. Fabian? (*Hint*: Think about the importance of ecological and evolutionary relationships between the agent, vector and host, and how they have co-evolved alongside each other for decades.)

10. After reviewing this case study, discuss whether you think malaria can be eradicated.