iGEM
SEPSIS

A Trip to the Hospital

Randall’s Lesson on Sepsis

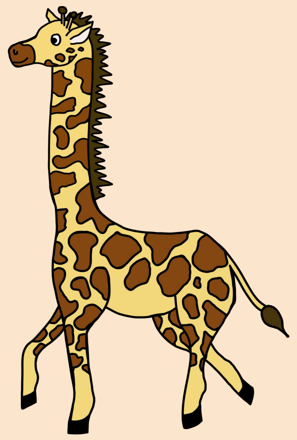
By 2021 iGEM teams OhioState and Rochester Bio-Spire

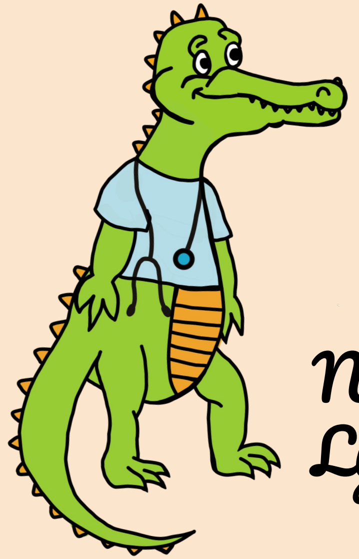
Cast

Perri Panda

Randall Red Panda

Mama Giraffe



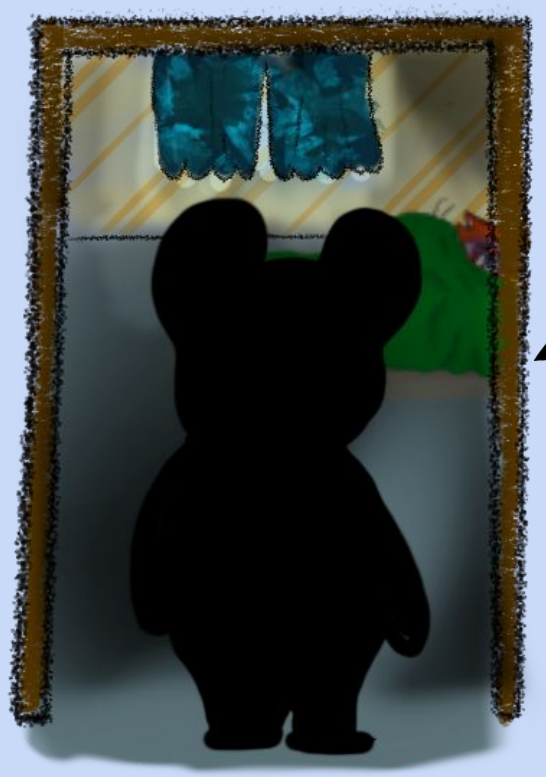

Nurse Lyle Crocodile

AGENT MACROPHAGE

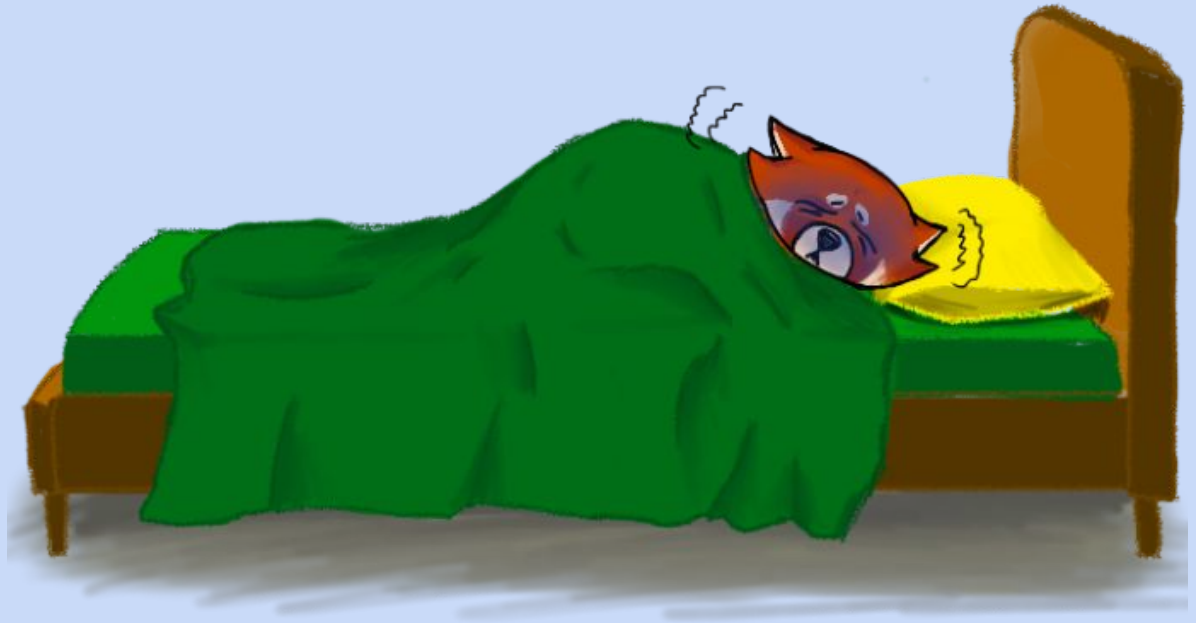
Dr. Slowpoke Sloth

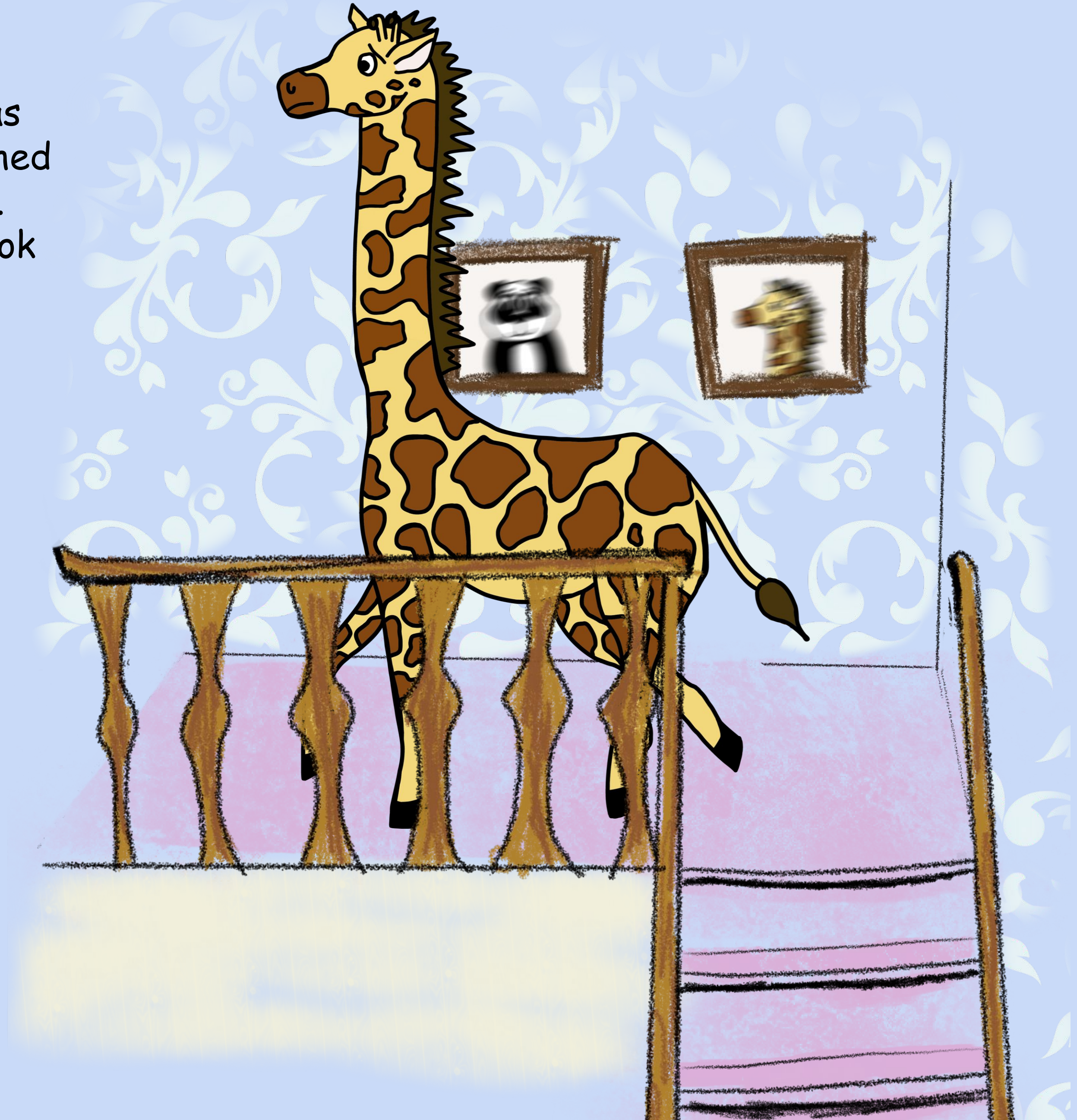
Perri did not want to go to school today. Perri's brother Randall got to miss school several days in a row because he was sick!

She thought: *It's not fair, I wish I were sick too!* But then, Perri thought about how bad her brother must feel, and she went to his room to check on him.

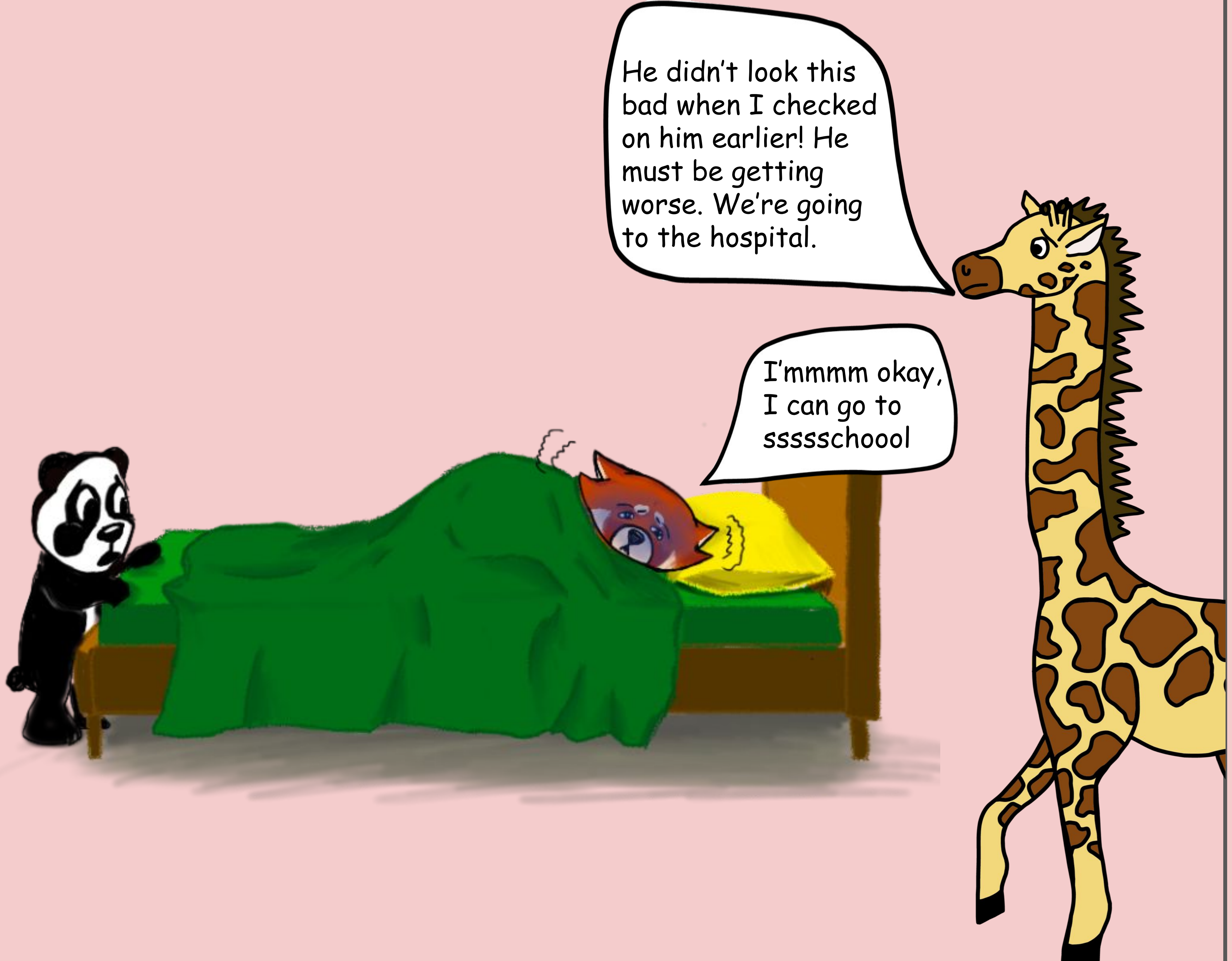

I hope you feel better soon, Randall.

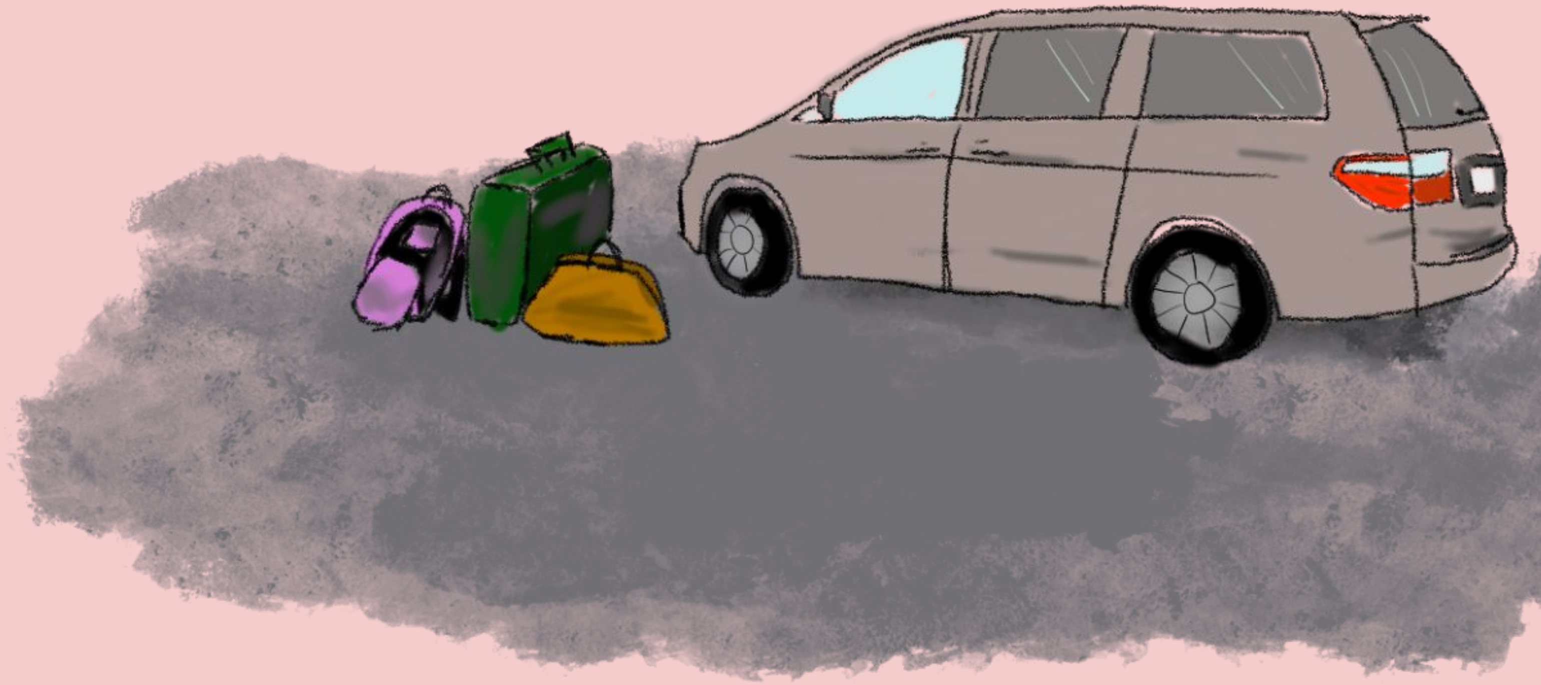
Perri whispered. When she didn't hear a response, she turned on the light to find Randall shivering under the covers.



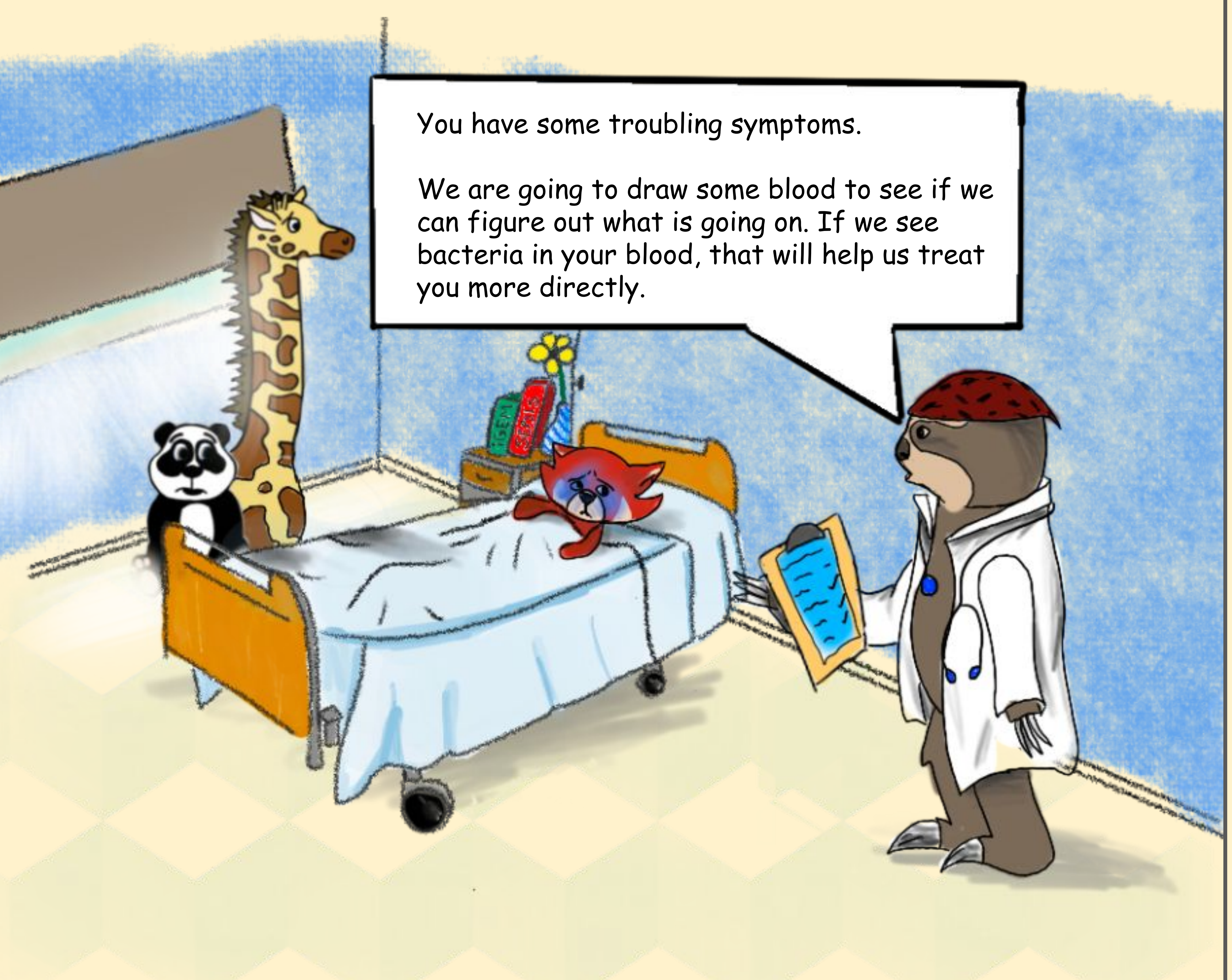

Mom, you have to come look at Randall!

Perri yelled as her mom rushed up the stairs. He did not look good!

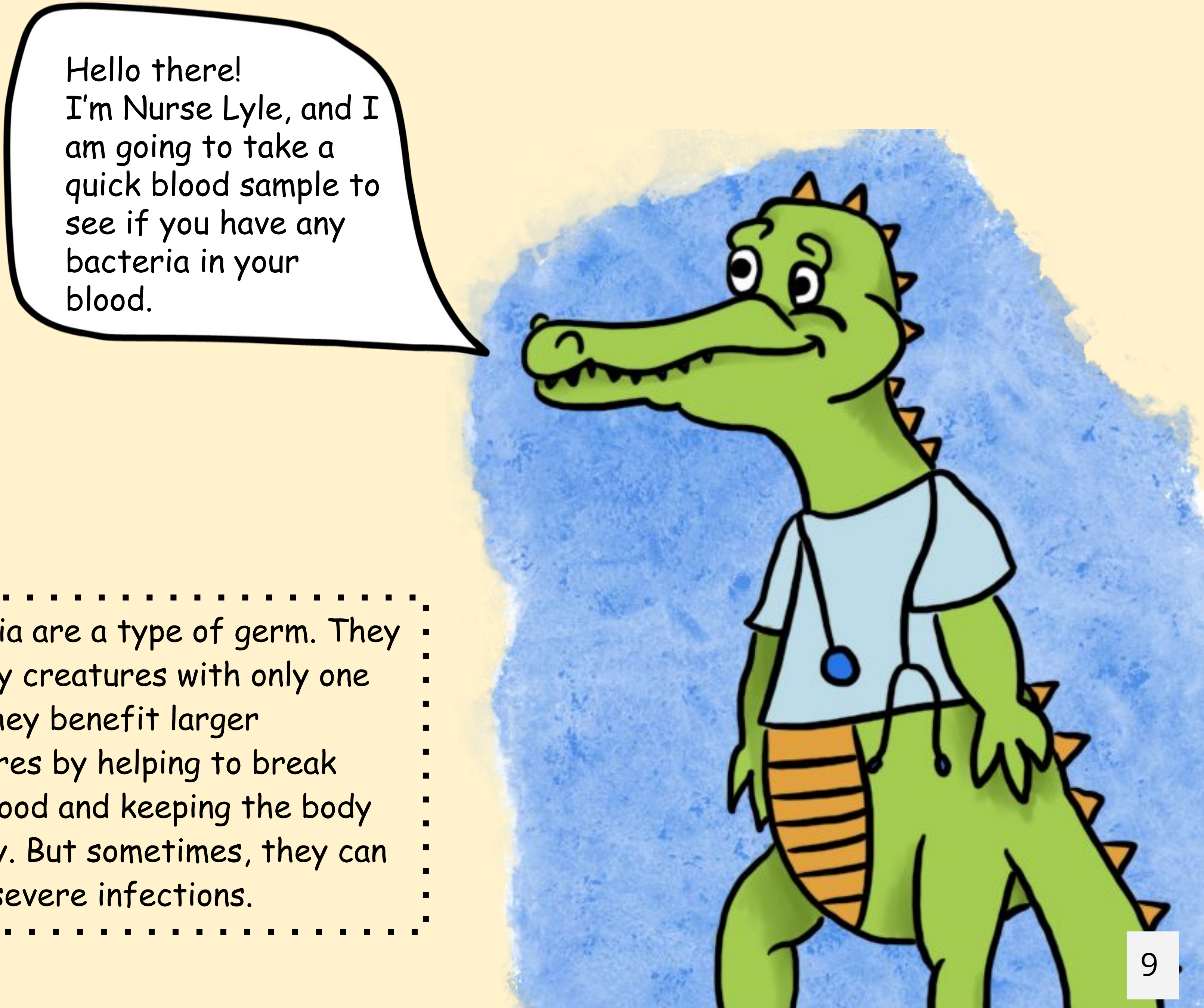

He didn't look this bad when I checked on him earlier! He must be getting worse. We're going to the hospital.
I'mmmm okay, I can go to ssssschoool



Perri and her mom helped Randall get ready and into the car, and off they drove to the hospital. Perri felt scared because her brother didn't look so good.

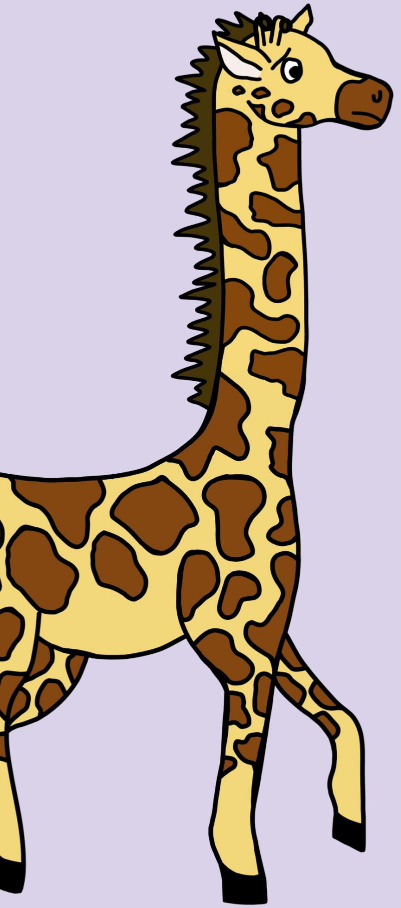

You have some troubling symptoms.

We are going to draw some blood to see if we can figure out what is going on. If we see bacteria in your blood, that will help us treat you more directly.


Hello there!
I'm Nurse Lyle, and I am going to take a quick blood sample to see if you have any bacteria in your blood.

Bacteria are a type of germ. They are tiny creatures with only one cell. They benefit larger creatures by helping to break down food and keeping the body healthy. But sometimes, they can cause severe infections.

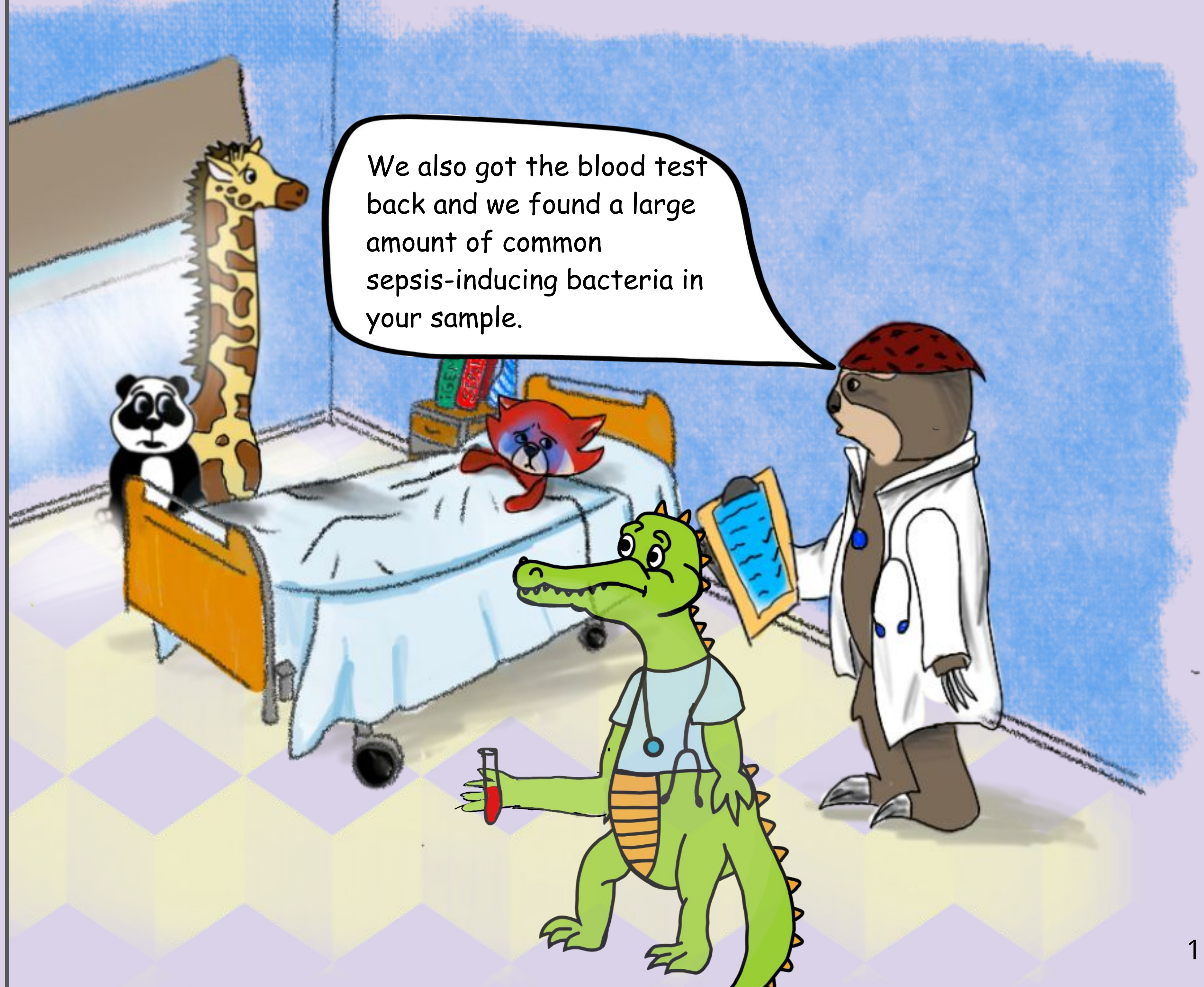
"After observing him for a bit of time, Randall meets most of the physical warning signs of people who have sepsis, which is your body's overreaction to an infection" the doctor announced.

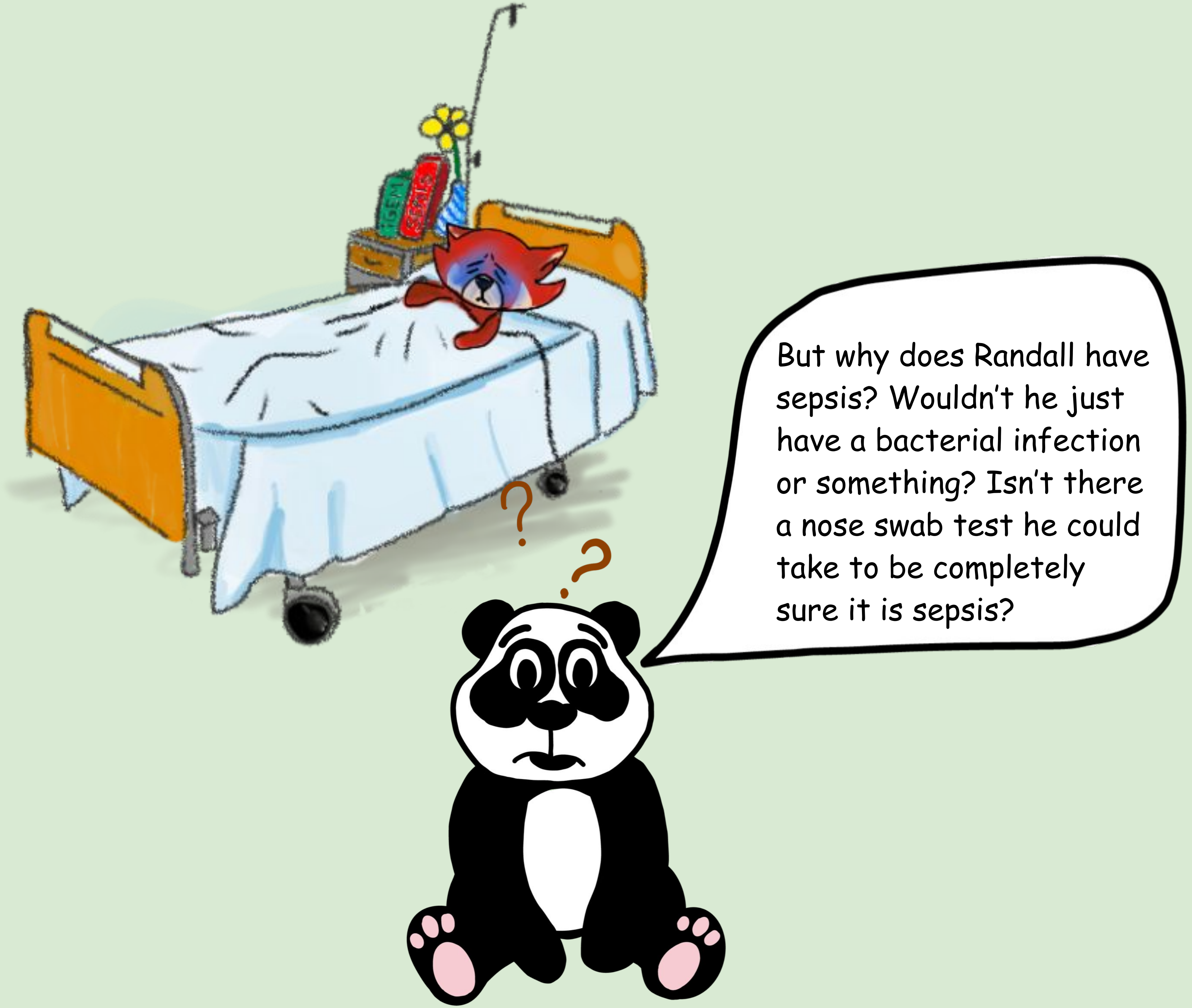

What? Why do you think that?

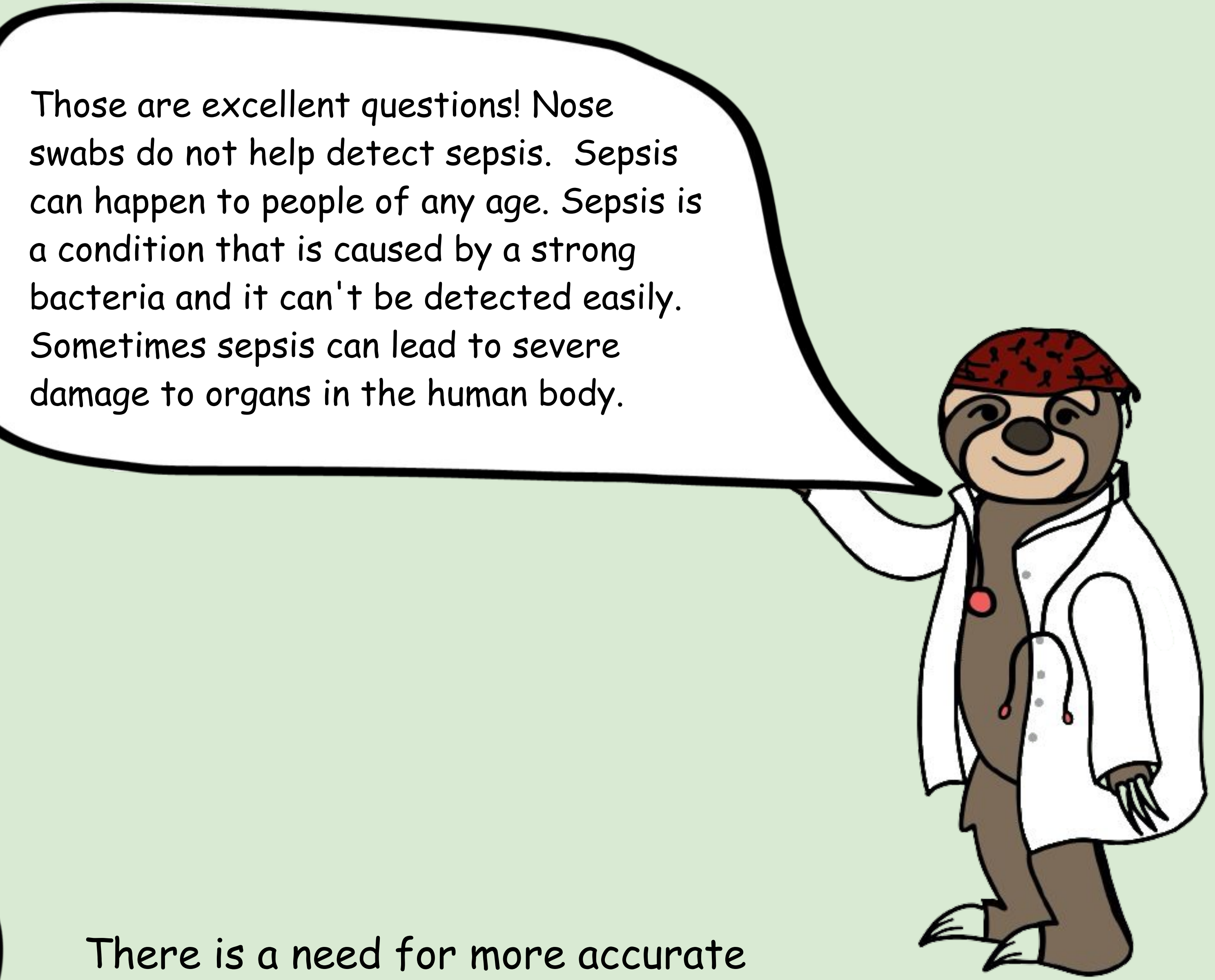
The criteria we look we for include:

- **S**lurred speech,
- **E**xtreme shivering or muscle pain,
- **P**assing no urine in a day,
- **S**evere breathlessness,
- **I**ntense feeling of badness,
- **S**kin mottled or discolored.

-From Sepsis Alliance

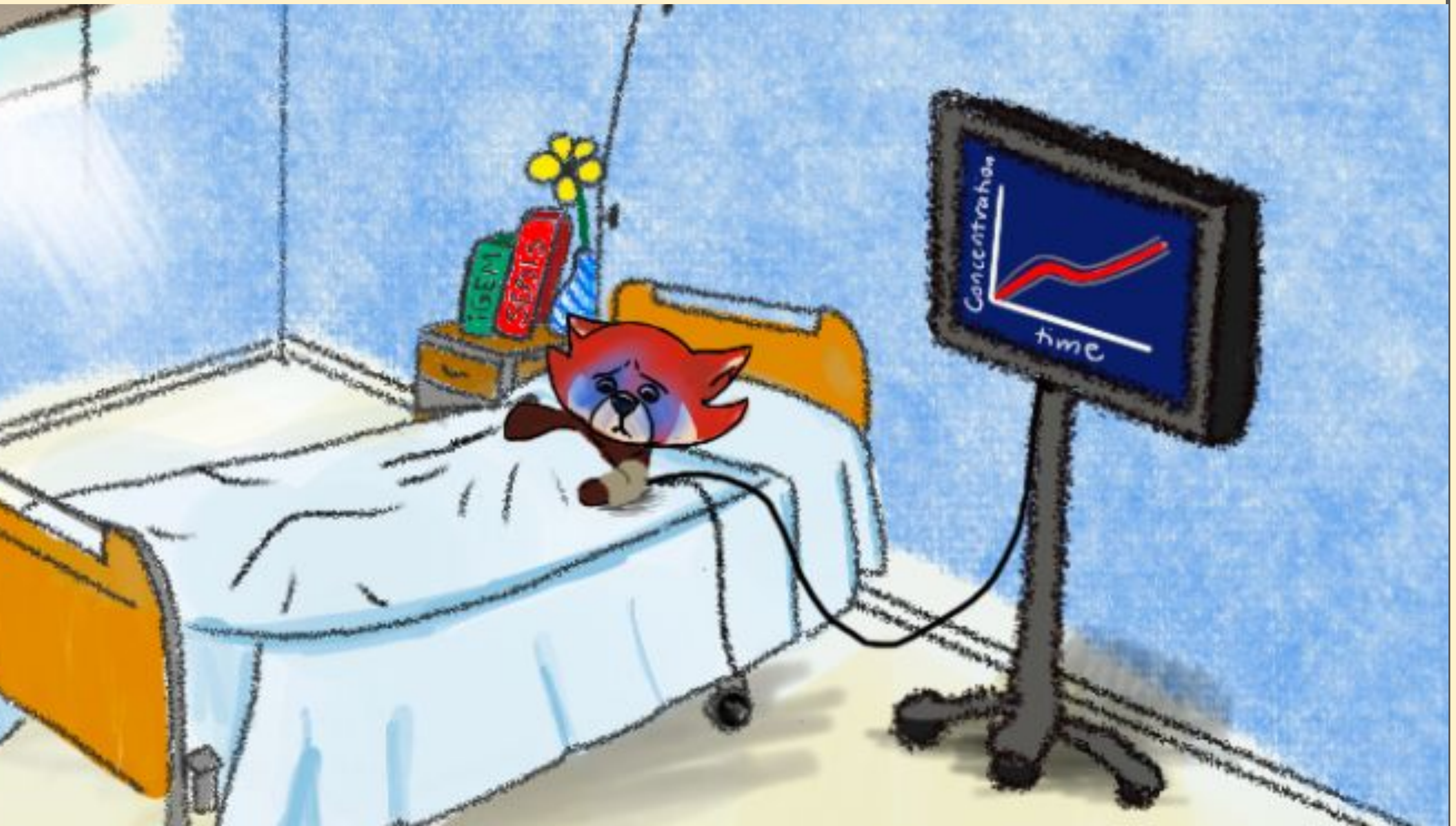

We also got the blood test back and we found a large amount of common sepsis-inducing bacteria in your sample.


But why does Randall have sepsis? Wouldn't he just have a bacterial infection or something? Isn't there a nose swab test he could take to be completely sure it is sepsis?

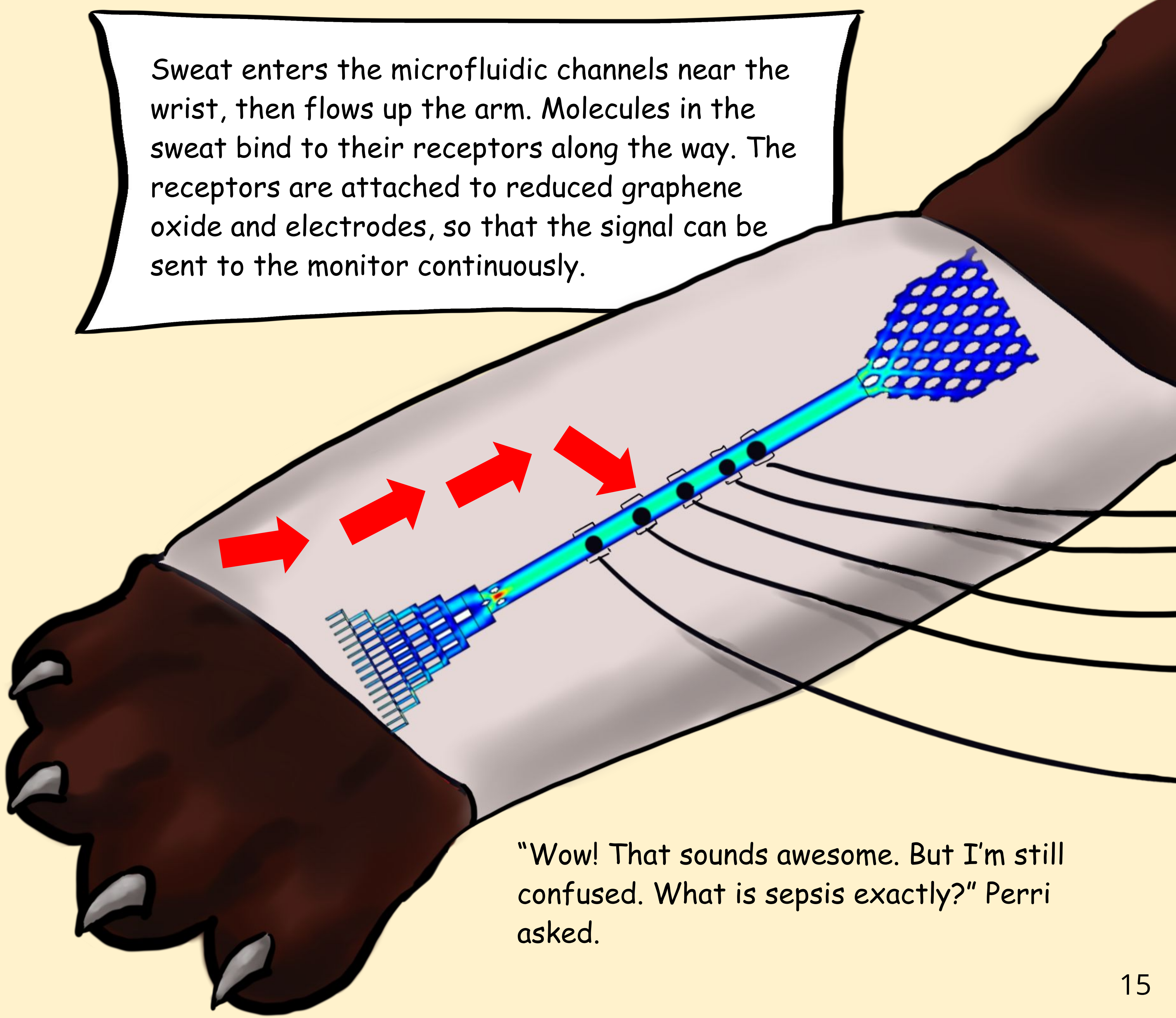

Those are excellent questions! Nose swabs do not help detect sepsis. Sepsis can happen to people of any age. Sepsis is a condition that is caused by a strong bacteria and it can't be detected easily. Sometimes sepsis can lead to severe damage to organs in the human body.

There is a need for more accurate detection to catch sepsis early.

The students on the Rochester 2021 iGEM team are currently working on a sensor that can detect sepsis from a patient's sweat! Doesn't that sound cool? Maybe one day you could be on a team like that to help detect and treat illnesses faster.



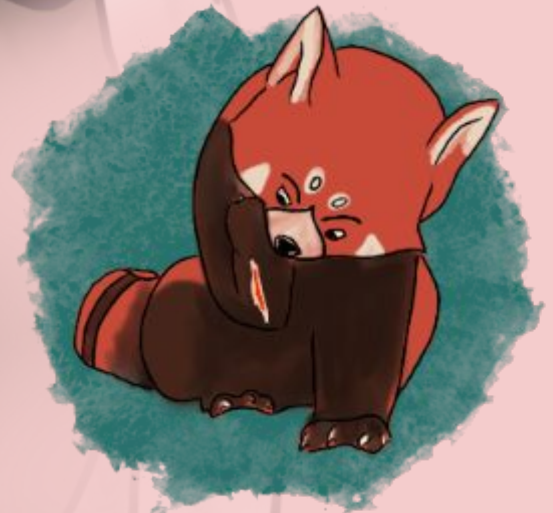
Sweat enters the microfluidic channels near the wrist, then flows up the arm. Molecules in the sweat bind to their receptors along the way. The receptors are attached to reduced graphene oxide and electrodes, so that the signal can be sent to the monitor continuously.

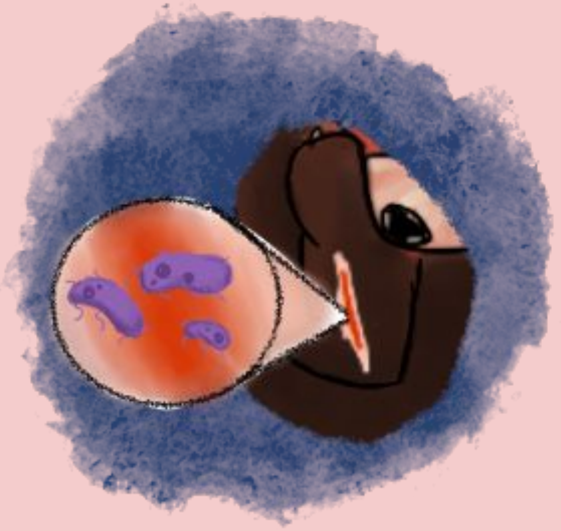


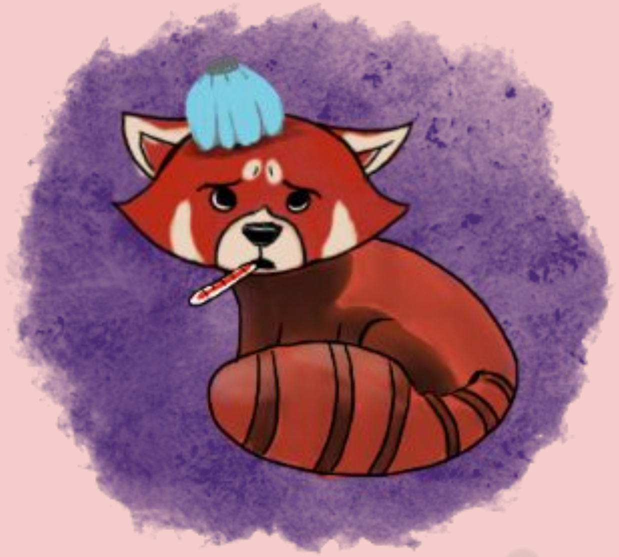
"Wow! That sounds awesome. But I'm still confused. What is sepsis exactly?" Perri asked.

"Good question! Sepsis happens when your body overreacts to an infection.

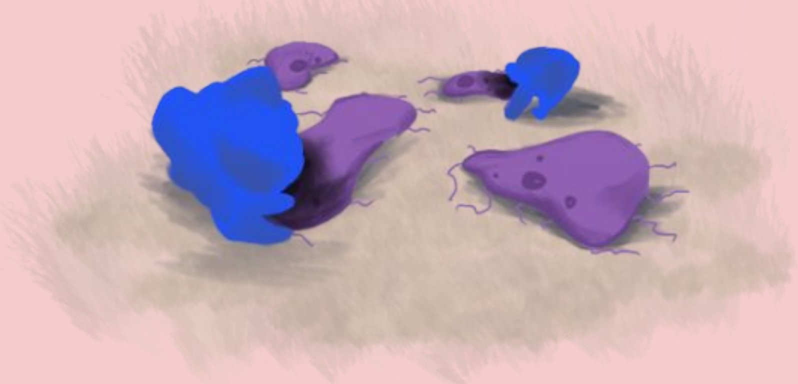
You can get an infection when bacteria enters your body through a cut for example. That bacteria can attack your body and make you very sick."

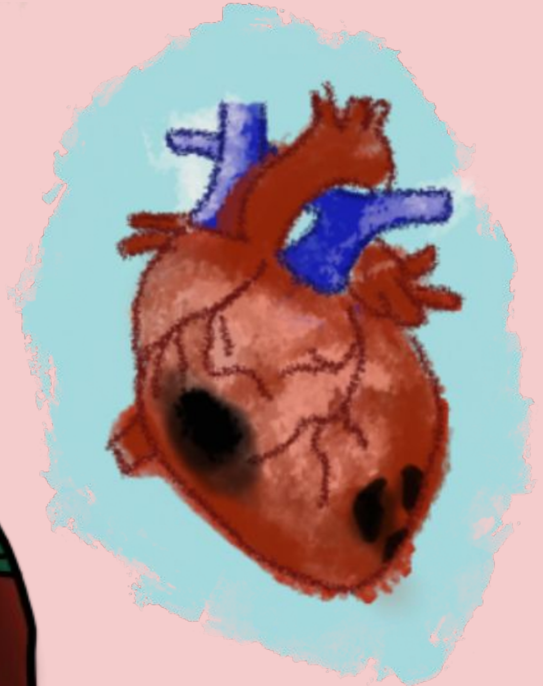






"Your body's immune system fights off the bacteria,

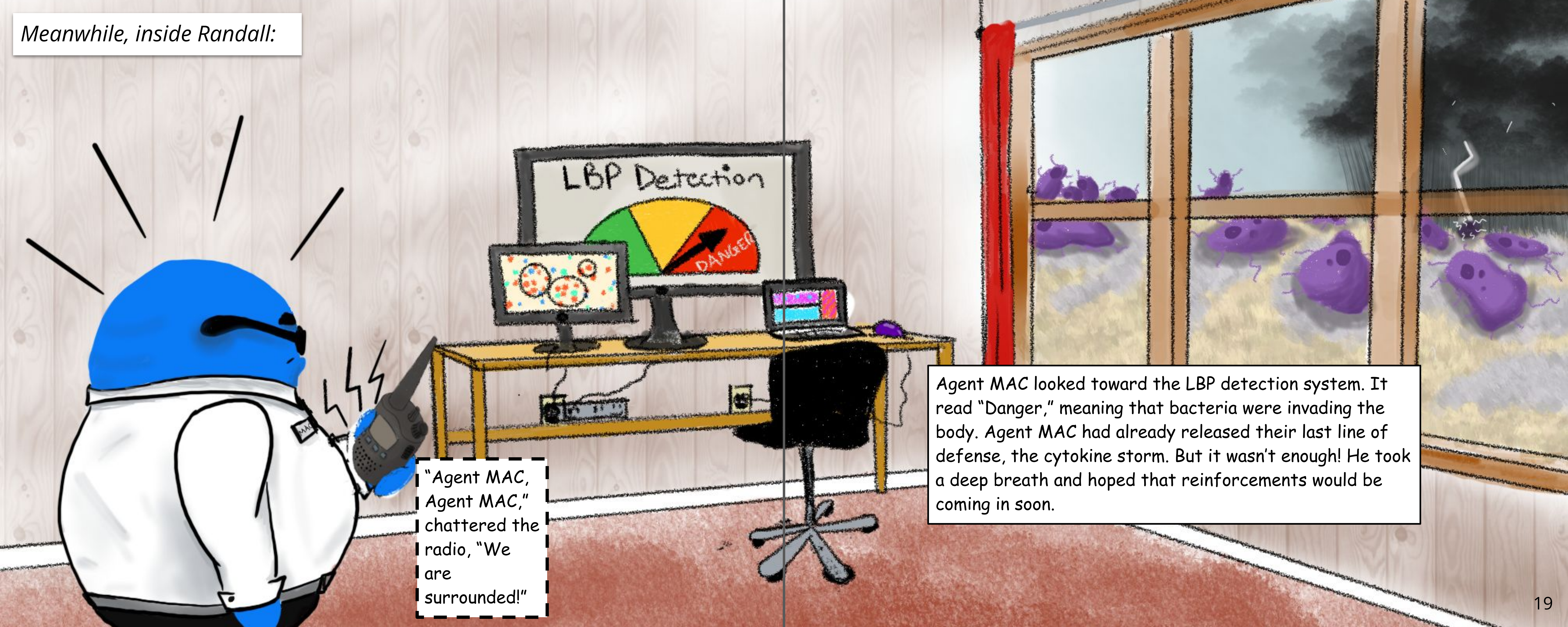




but too much of a response can lead to harmful effects like organ damage. This is what we term sepsis. Does that make sense?"

"Yes it does!" Perri exclaims.

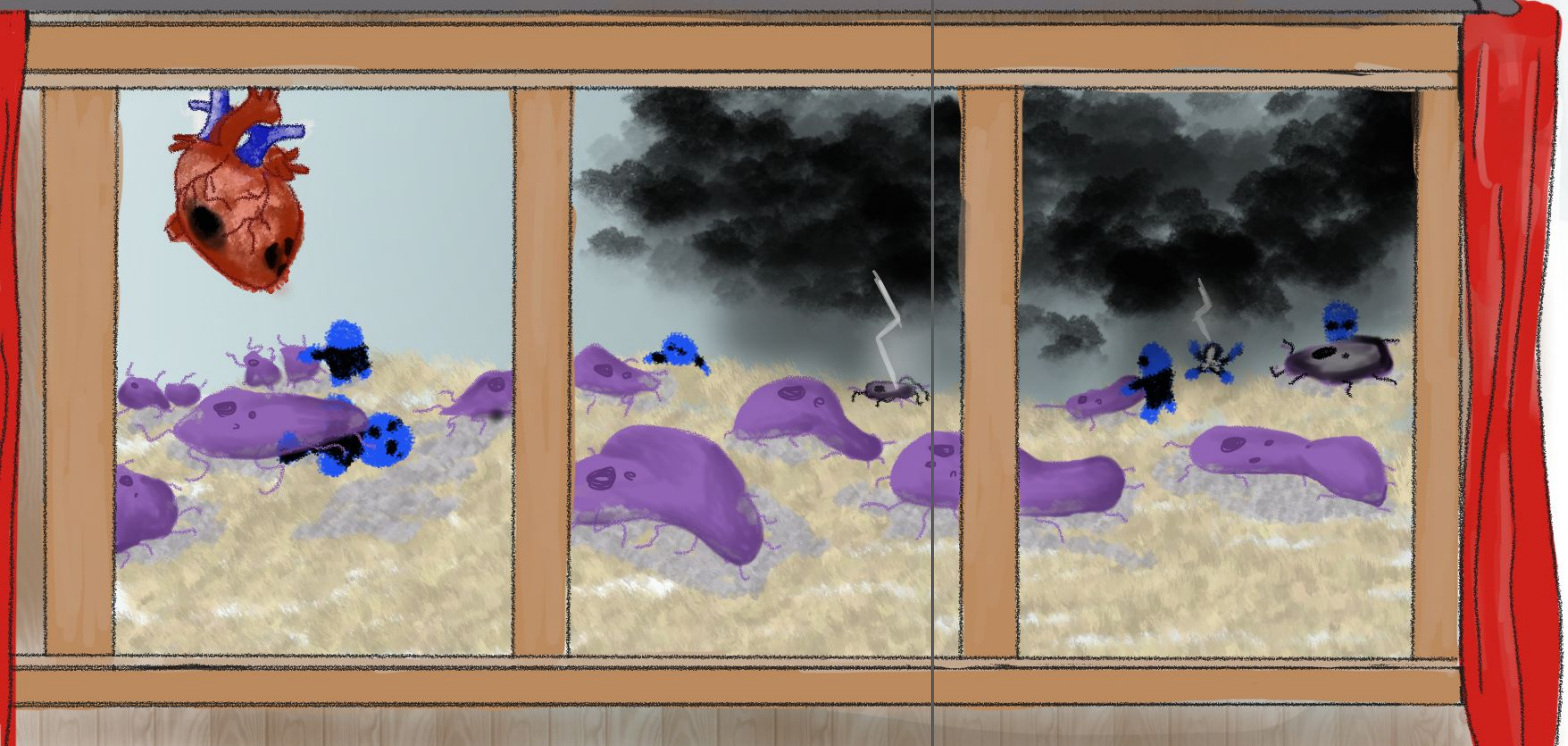
"But wait, what is happening inside me?" Randall croaked.



Meanwhile, inside Randall:

"Agent MAC, Agent MAC," chattered the radio, "We are surrounded!"

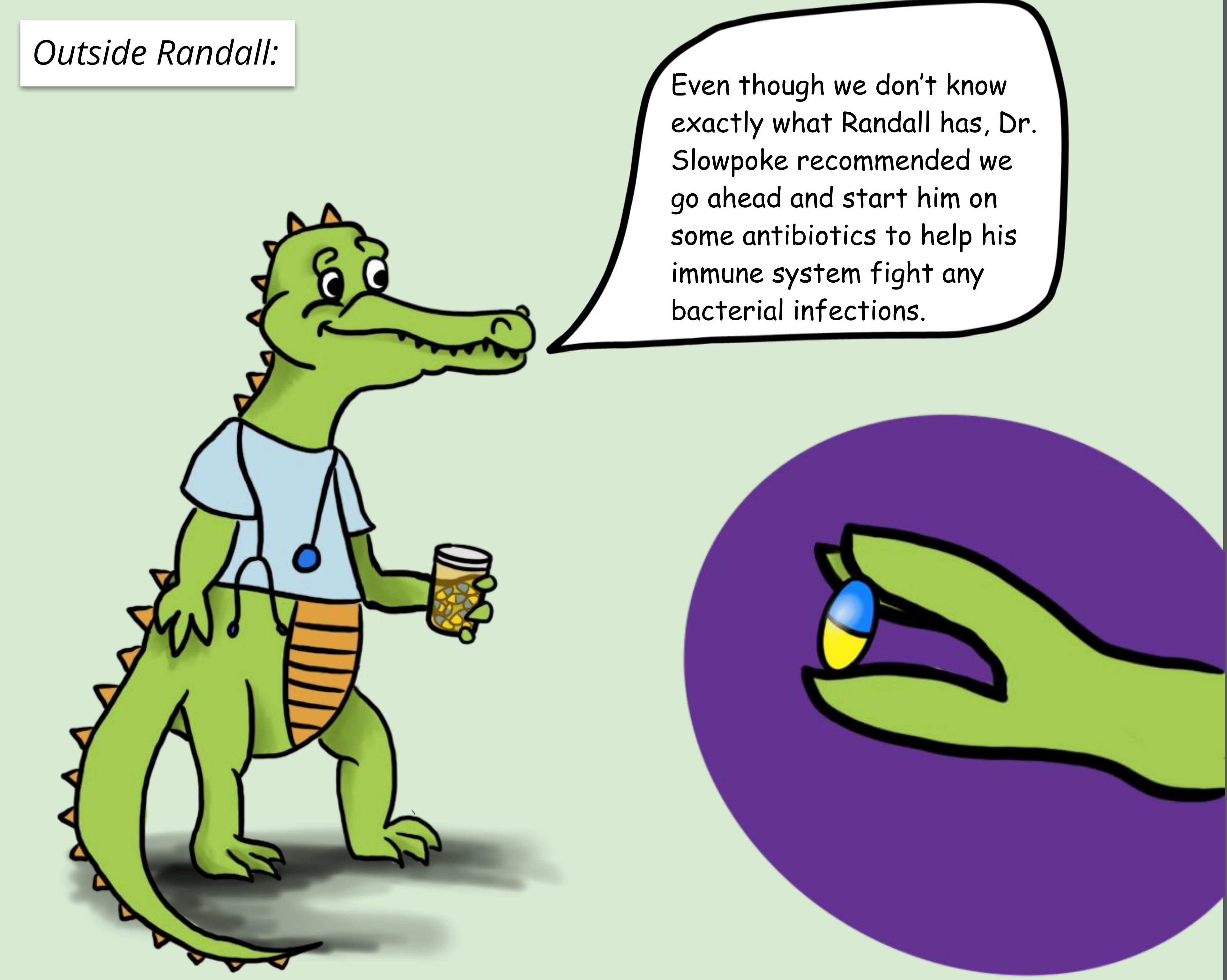
Agent MAC looked toward the LBP detection system. It read "Danger," meaning that bacteria were invading the body. Agent MAC had already released their last line of defense, the cytokine storm. But it wasn't enough! He took a deep breath and hoped that reinforcements would be coming in soon.



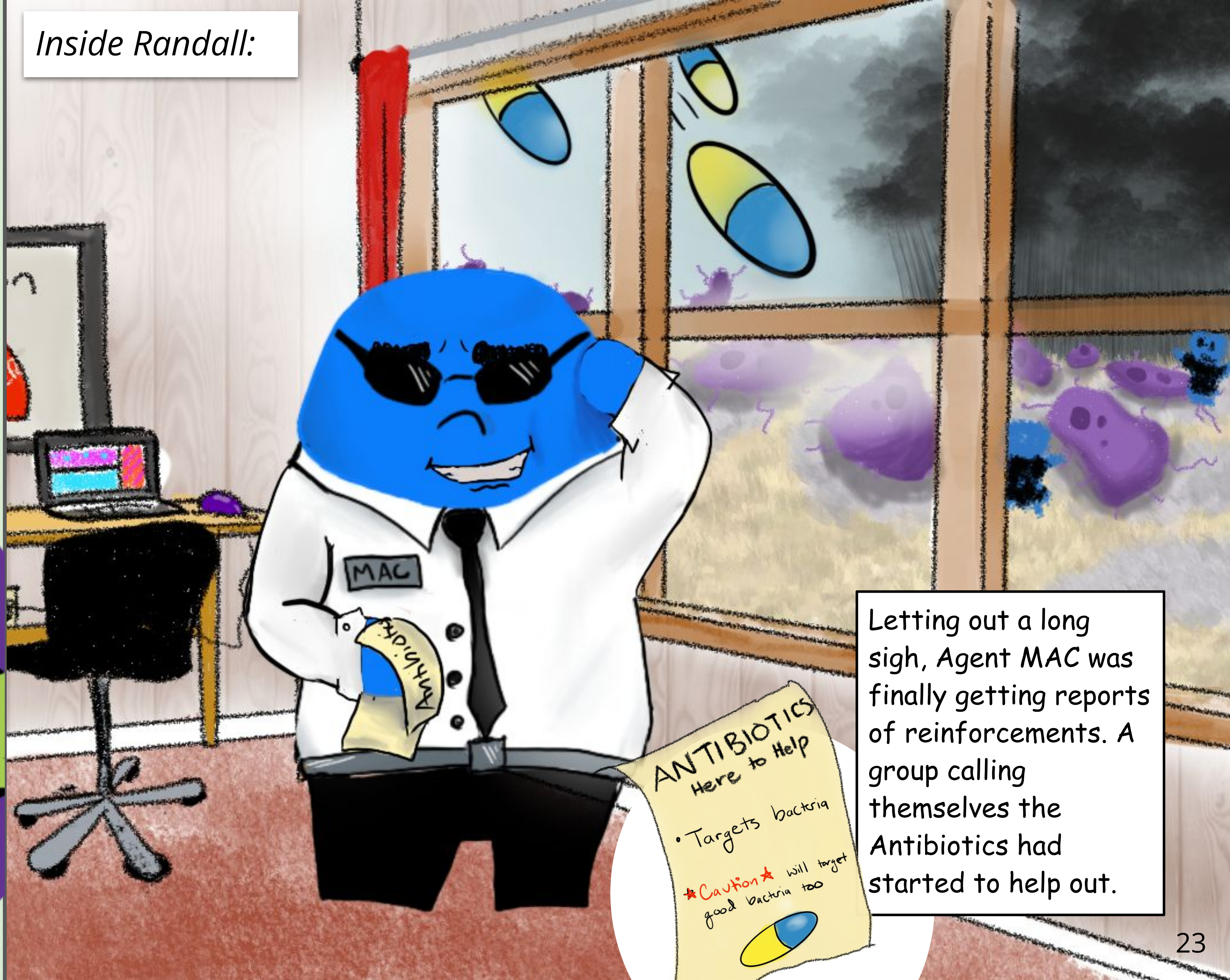
Agent MAC looked out at the raging cytokine storm they had released.

The storm was helping, but it was also hurting. His troops were failing, since the storm was hitting them along with the bacteria. The cytokine storm had also started damaging some of the important organs under Agent MAC's supervision. It might wipe them all out and leave none remaining, which wouldn't turn out so well for Randall.

Outside Randall:


Even though we don't know exactly what Randall has, Dr. Slowpoke recommended we go ahead and start him on some antibiotics to help his immune system fight any bacterial infections.

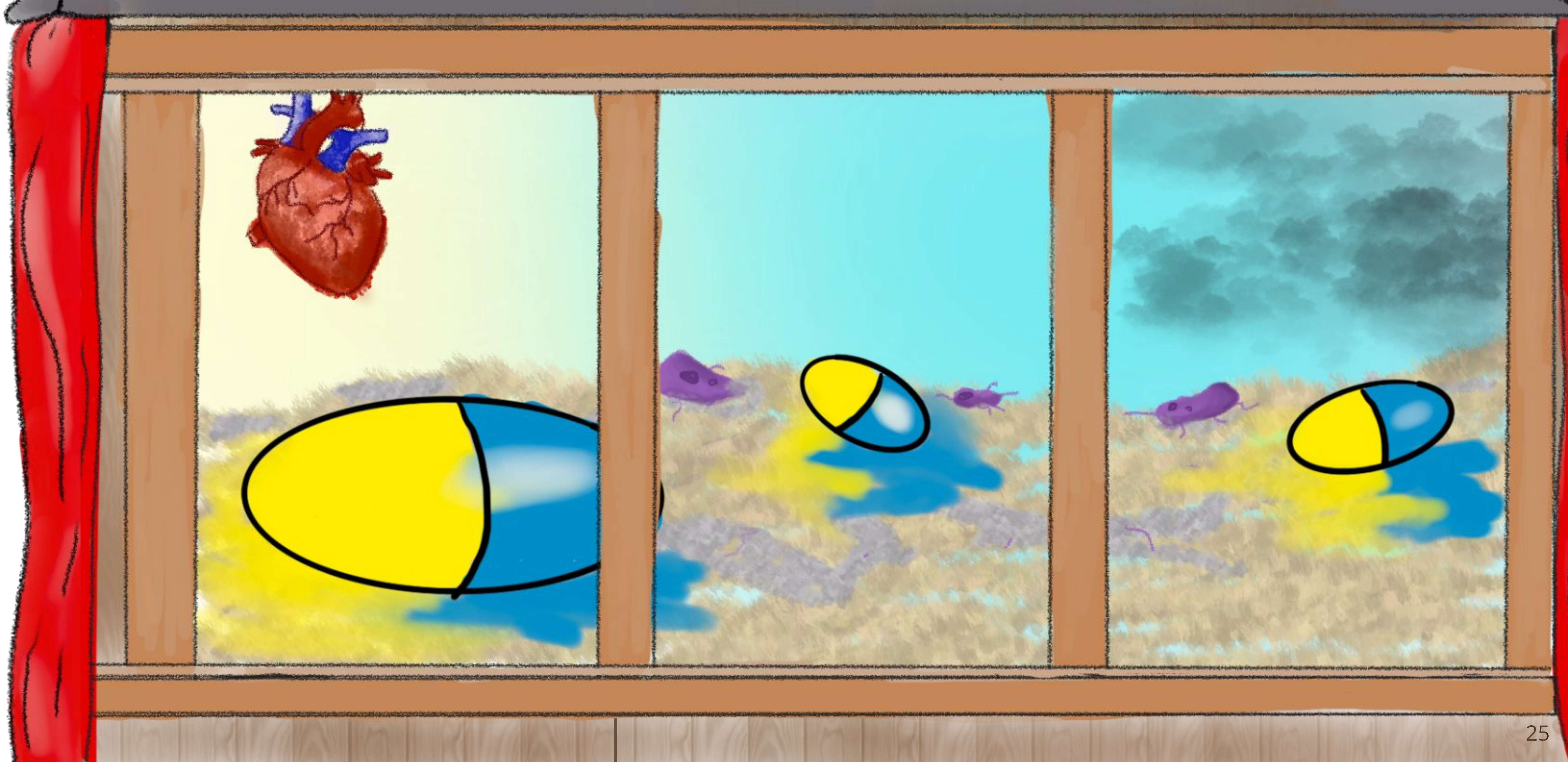
Inside Randall:


MAC
Antibiot
ANTIBIOTICS
Here to Help
• Targets bacteria
★Caution★ will target good bacteria too

Letting out a long sigh, Agent MAC was finally getting reports of reinforcements. A group calling themselves the Antibiotics had started to help out.

Inside Randall:

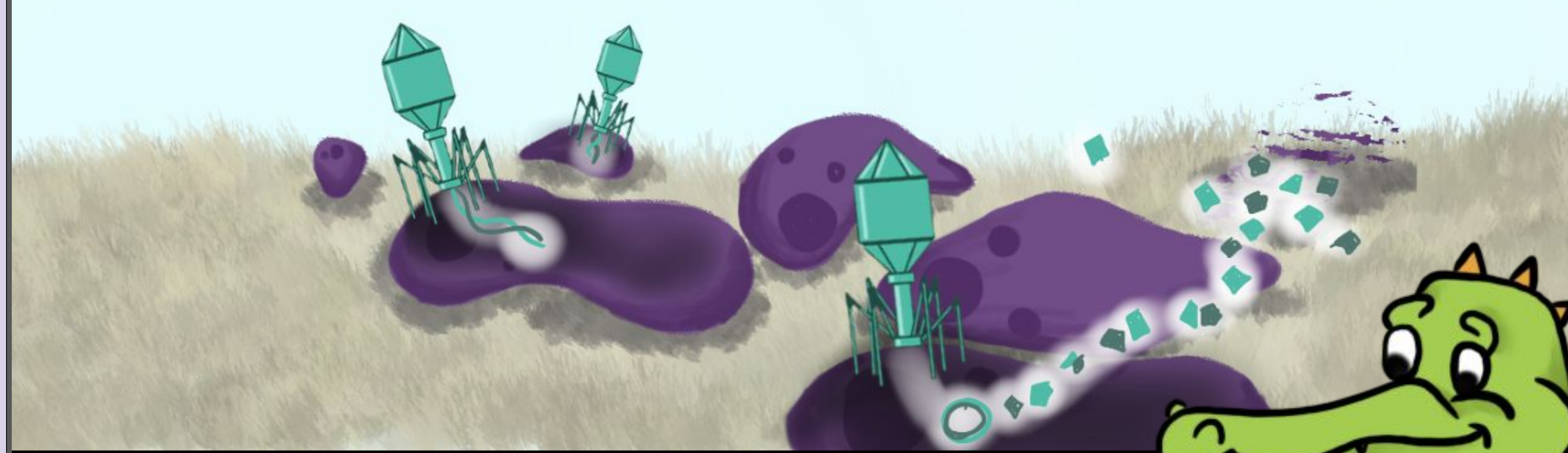
With the new help, the storm had lessened. Hopefully with all the bacteria wiped out soon, the storm will fizzle out, doing no more damage to any organs.



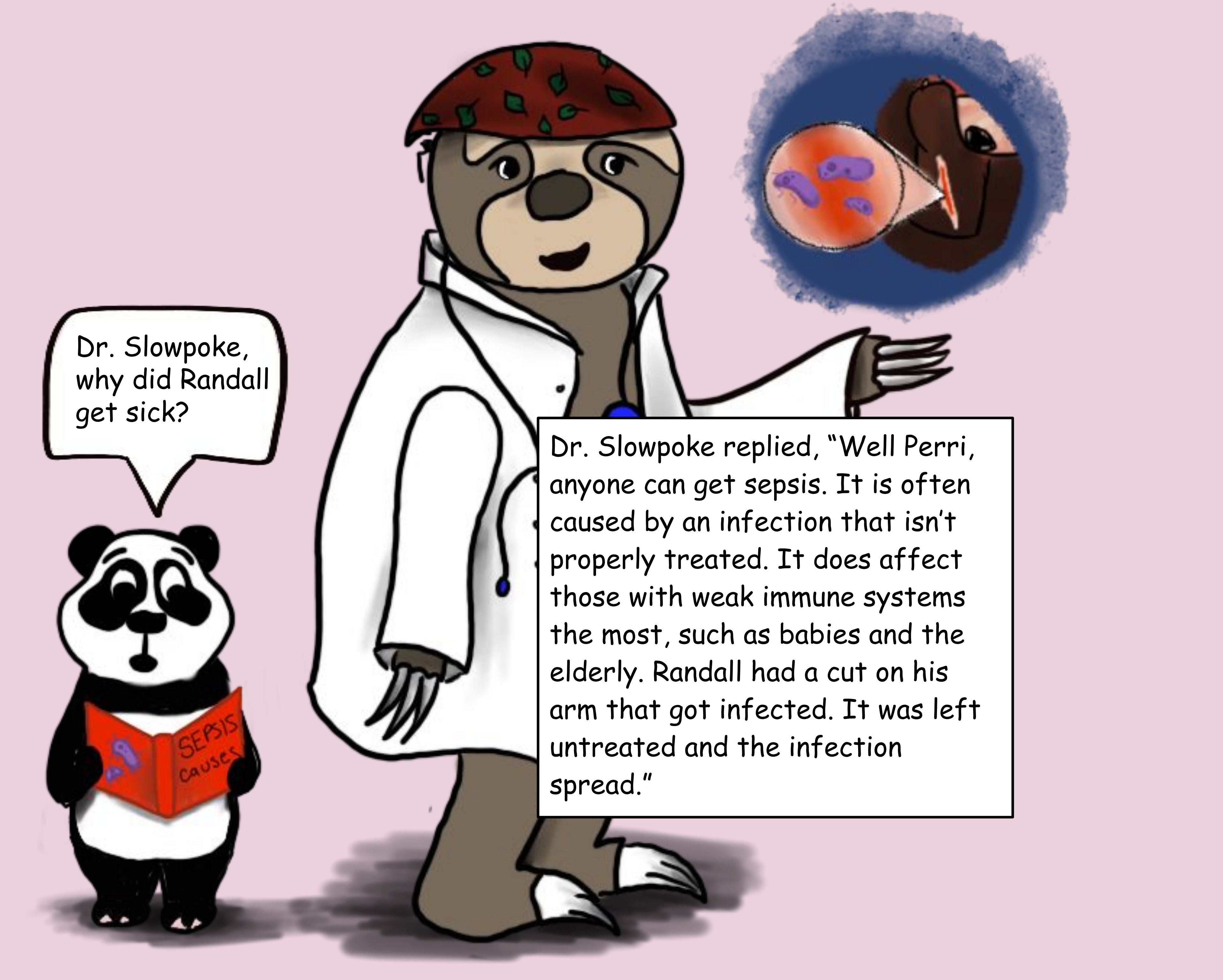
Outside Randall:

Dr. Slowpoke smiled and said, “He seems to be responding positively to the antibiotics. His vital signs are approaching the healthy range.”

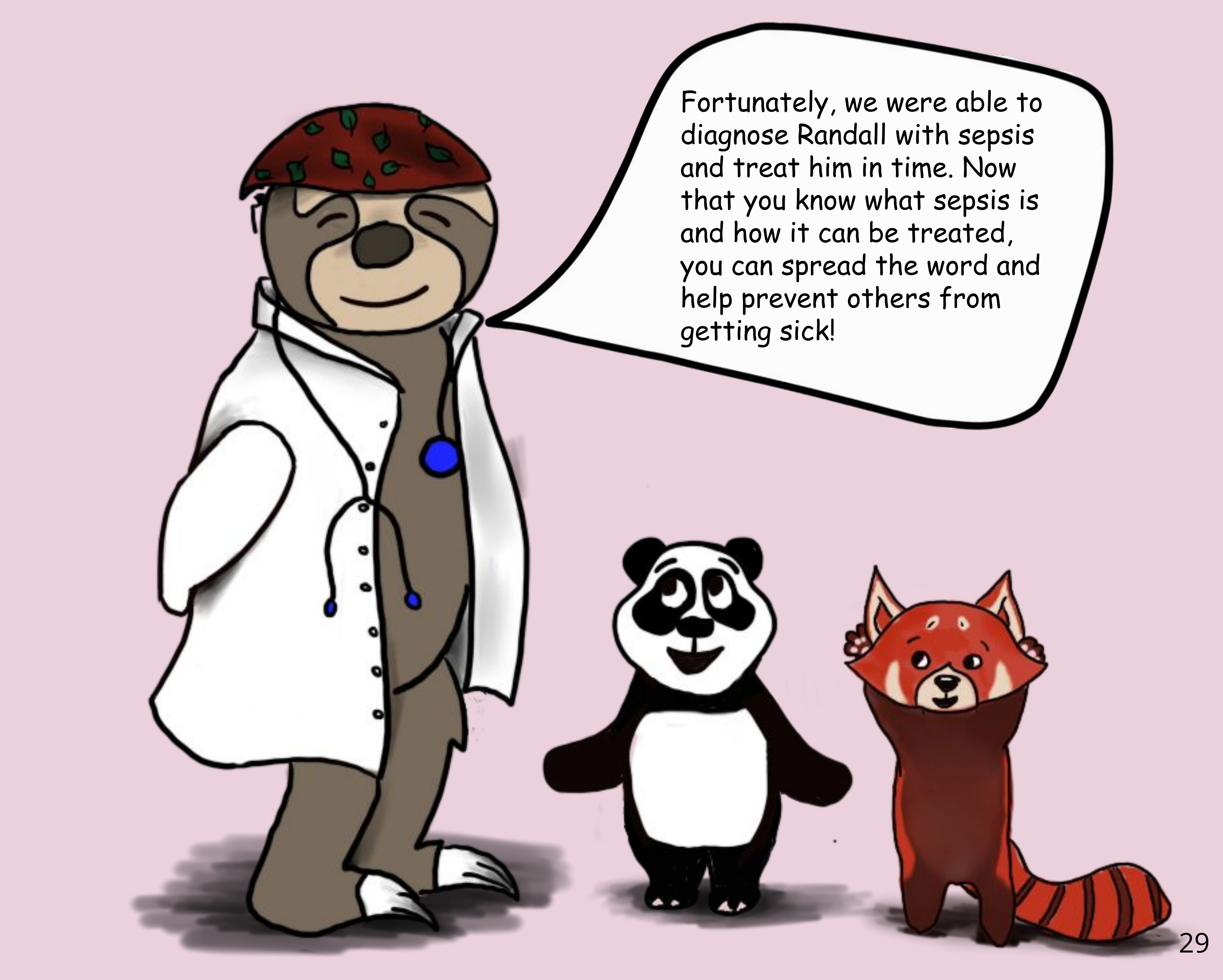
What would have happened if they didn’t work?



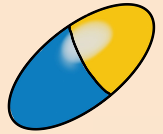
“There are some other treatment options,” Nurse Lyle began. “Antibiotics are usually our first choice, but they can make the sepsis worse. Phage therapy is another option. This uses phages or viruses specific to bacteria. When engineered like the 2021 OhioState iGEM team’s project, phage therapy is capable of not only defeating the infection, but also cleaning up the harmful debris that dead bacteria leave behind.”


Dr. Slowpoke, why did Randall get sick?
SEPSIS CAUSES

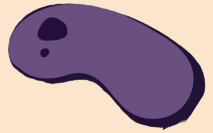
Dr. Slowpoke replied, “Well Perri, anyone can get sepsis. It is often caused by an infection that isn’t properly treated. It does affect those with weak immune systems the most, such as babies and the elderly. Randall had a cut on his arm that got infected. It was left untreated and the infection spread.”


Fortunately, we were able to diagnose Randall with sepsis and treat him in time. Now that you know what sepsis is and how it can be treated, you can spread the word and help prevent others from getting sick!

Glossary



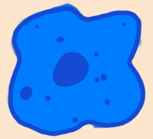
Antibiotics: A type of medicine that kills bacteria or prevents it from growing in the body.



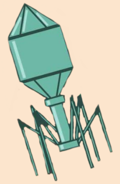
Bacteria: Single-celled organisms found in nature and inside the human body. Some, like the bacteria found in yogurt, are good for our health, while others can cause disease.

Cytokine storm: A severe immune reaction to infection in which too many cytokines are released into the blood too quickly. Cytokines are small proteins in the body that normally help to fight disease.

LBP: An acronym for lipopolysaccharide binding protein. This is the body's molecule for detecting a bacterial infection.



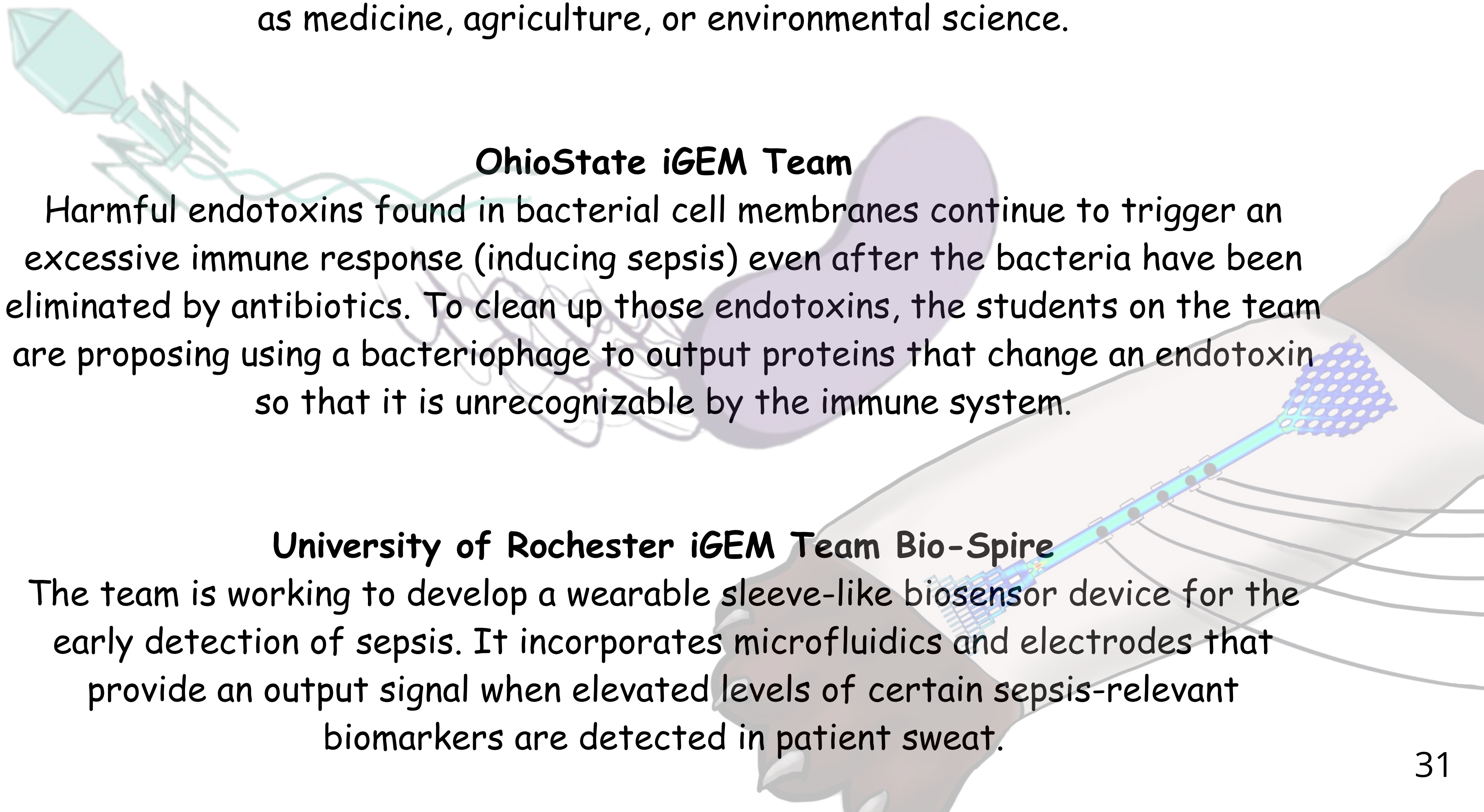
Macrophage: A type of white blood cell that surrounds and kills foreign invaders as part of the body's immune system



Phage therapy: A way to treat disease that uses viruses to fight bacterial infection. The viruses attach to bacterial cells and insert their own DNA into them.

Sepsis: An overwhelming immune response to infection that can lead to inflammation in the body and organ damage.

Dedicated to raising awareness of sepsis to promote earlier detection.



What is iGEM?

The International Genetically Engineered Machines (iGEM) competition is a worldwide competition in which teams of mainly collegiate students compete to create projects that use synthetic biology to tackle important issues in fields such as medicine, agriculture, or environmental science.

OhioState iGEM Team

Harmful endotoxins found in bacterial cell membranes continue to trigger an excessive immune response (inducing sepsis) even after the bacteria have been eliminated by antibiotics. To clean up those endotoxins, the students on the team are proposing using a bacteriophage to output proteins that change an endotoxin so that it is unrecognizable by the immune system.

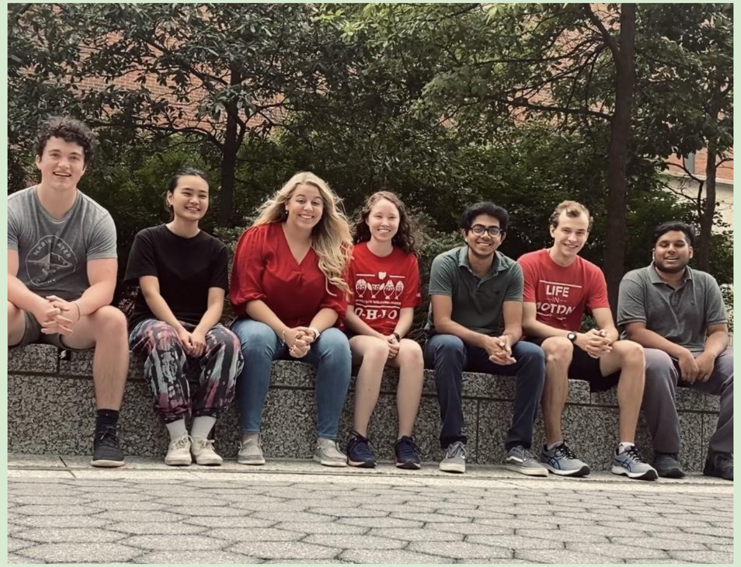
University of Rochester iGEM Team Bio-Spire

The team is working to develop a wearable sleeve-like biosensor device for the early detection of sepsis. It incorporates microfluidics and electrodes that provide an output signal when elevated levels of certain sepsis-relevant biomarkers are detected in patient sweat.

Backmatter

University of Rochester 2021 iGEM Team Bio-Spire

Edited and illustrated by Jingyi (Adela) Yan (back row, third from right), Maria Schapfel (front center), Amanda Adams (front row, second from left), and Muskaan Vasandani (top left).



Ohio State University 2021 iGEM Team

Edited and illustrated by Ryan Burrows (second from right), Lindsay Drumm (third from left), Joey Lo (second from left), and Lindsey Shimoda (fourth from left).

Acknowledgement

We would like to thank everyone who helped with this book, especially the following:

1. **Dr. Anne S. Meyer,** Principal Investigator of Rochester Bio-Spire Team. Dr. Meyer provided constructive feedback for both the content and the target age group of the book.
2. **Beatriz De Las Casas**, LMHC. Mrs. De Las Casas as a mental health counselor and a family friend also provided amazing feedback for the content and organization of the book.
3. **Dr. Ian Barbash** from the University of Pittsburgh. Dr. Barbash is a medical professional who has a clinical focus on sepsis in the ICU. He gave us encouraging feedback and suggested a proper target age group of the book.
4. **Jeffrey and Sheila Burrows**, parents of Ryan Burrows. Gave feedback on reading clarity and consistency.
5. **Angie Chung-Kirby**, Assistant Principal at Elida Elementary School encouraged our efforts in bringing complex topics to young minds.

We wouldn't be able to complete the book without your advice. As a group of university students writing a children's book for the first time, all of your suggestions assisted us immensely on the graphics, texts, and organizations. Thank you again, and we hope you enjoy the book.

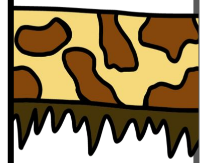
What is sepsis and how can it be treated? When Perri's brother Randall gets sick, she follows him on his trip to the hospital to learn more about the disease. Filled with colorful illustrations and interesting scientific facts, this book will provide you and your child with important knowledge to help raise awareness of an often fatal condition.

"The wording and drawings are fun and interesting for children to learn better and have an understanding of difficult medical concepts."
-Beatriz De Las Casas, LMHC

"Compelling illustrations! Rich vocabulary! Clear explanations! Critical thinking and problem solving skills!" -Elementary School Assistant Principal

"I think it was helpful for teaching about sepsis." -L.S., age 11

See Rochester's and OhioState's wikis for more information on how they designed innovative sepsis diagnosis and treatment options:

https://2021.igem.org/Team:OhioState
https://2021.igem.org/Team:Rochester