A gathering of disease-causing bacteria waits on a sharp splinter on a fence post. These single-celled pirates are eager to raid the multicellular community of a human body.

Once we've infected a human, we'll have it made! All those human cells will do all the work of getting food, and we'll just mooch off them.

I hear it can be hard for germs like us to get past a human's outer defenses.

It's true, it's tough to get inside.
IF YOU GET INTO THE NOSE AND AIRWAYS, THERE ARE CELLS THAT MAKE MUCUS TO TRAP YOU.

IF YOU GET IN WITH THE FOOD THEY SWALLOW, THEY'VE GOT CELLS IN THEIR STOMACHS THAT GUSH HYDROCHLORIC ACID!

IF YOU GET IN THERE ARE OTHER CELLS THAT USE LONG, THIN CILIA TO PUSH YOU BACK OUT THE WAY YOU CAME.

SKIN CELLS PROTECT MOST OF THE HUMAN BODY. THE OUTER LAYER IS MADE OF TOUGH, DEAD CELLS.

KNock, KNOck... LET ME IN!

NO WAY!

BUT LOOK! NOW'S OUR CHANCE! THERE'S A HUMAN COMING, AND HE'S ABOUT TO SCRATCH HIS HAND ON THIS FENCE WE'RE SITTING ON. WITH ANY LUCK, THE SKIN WILL BREAK AND WE'LL GET IN!
A sharp splinter of wood scrapes across the skin, breaking connections between skin cells. Red blood cells and plasma (the clear liquid part of blood) exit the wound... and germs enter.

Wood splinter, made of dead plant cells.

SCRATCH!!!

Red blood cells

WE'RE COMIN' IN!

HOLD ON!

I'M TRYING!

I'M GETTING WASHED AWAY BY THE BLOOD PLASMA!

AAAAAGH!

COMING THROUGH, SUCKERS!
Inside the wound...

STOP THE BLEEDING!

SAVED BY THE PLATELETS!

AAAAAGH!

HELP!

WHHEW, I MADE IT!

IT WAS HARDER TO GET IN THAN I EXPECTED!

YEAH, BUT NOW WE'RE IN THE LAND OF MILK AND HONEY, BABY!

WE NEED MORE SKIN CELLS TO REPAIR THIS WOUND!

YUM...

Short-term repair: Small cell fragments called platelets circulate in the blood. When they reach a wound, they change shape and join together to form a sort of net. This helps form a blood clot, preventing more red blood cells from pouring out of damaged blood vessels while other cells make repairs.

WE NEED MORE SKIN CELLS TO REPAIR THIS WOUND!

GROW!

PLLLLLLL!

DIVIDE! DIVIDE!

Hey, you dumb human cells can go ahead and patch up the scratch if you want. We're already in, and we're happy to stay, losers!

Hey, you dumb human cells can go ahead and patch up the scratch if you want. We're already in, and we're happy to stay, losers!

Rude.

DID SOMEBODY CALL MAINTENANCE?

Long-term repair: Over the next few days, fibroblast cells will arrive to lay down fibers that help with permanent repairs.
THERE ARE A LOT OF DELICIOUS MOLECULES FLOATING AROUND HERE!

MOLLY-WHO?

MOLECULES: LITTLE PARTICLES THAT EVERYTHING'S MADE OF.

HEY, THAT FOOD IS MEANT FOR US! YOU'RE STEALING!

UGH... AND POLLUTING!

TIME TO GROW AND DIVIDE.

POP!

GASP!

ENJOY THE PARTY WHILE YOU CAN. THIS WHOLE BODY IS PATROLLED BY WHITE BLOOD CELLS LIKE NEUTROPHILS AND MACROPHAGES THAT ARE ON THE LOOKOUT FOR GERMS LIKE YOU.

MACROPHAGE? WHAT THE HECK DOES THAT MEAN?

IT MEANS "BIG EATER."

WHY ARE THEY CALLED THAT?

YOU'RE ABOUT TO FIND OUT.

HEY YOU... ?!
The non-specific immune response begins. It's called non-specific because it doesn't depend on the immune system being familiar with the particular germ involved.

WHO ARE YOU?
UM... THAT'S FOR ME TO KNOW AND YOU TO FIND OUT. LET GO OF ME AND MIND YOUR OWN BUSINESS!

HI MAC! ARE WE GLAD TO SEE YOU!

I'M A MACROPHAGE, AND RIGHT NOW, MY BUSINESS IS FINDING OUT WHAT YOU ARE.

HEY, THAT TICKLES...

I'M CHECKING TO SEE IF YOUR MEMBRANE HAS ANY SUSPICIOUS MOLECULES THAT WOULD IDENTIFY YOU AS A DISEASE-CAUSING GERM.

CLOSE-UP:
The macrophage has special receptor molecules embedded in its membrane.

The macrophage uses its receptors to examine other cells. They fit like a lock and key with molecules that many germs have on their membranes. Human cells don't have these same tell-tale molecules, so the macrophage leaves them alone.

(Neutrophils often spot germs first, and identify them the same way. We'll meet them soon...)

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When a macrophage recognizes an invader, it becomes a crazed germ-eating machine.

**Phagocytosis** (meaning cell-devouring process):
1. Macrophage takes in germ, enclosing it in a membrane pouch.
2. Packets of chemicals merge with the pouch and destroy the germ.
3. Macrophage spits out whatever parts of the germ it can't use as food.

But macrophages are more than just germ eaters. They also use chemical signals to help organize defense with other human cells.

This macrophage is broadcasting a signal for other cells to help fight this bacterial infection. Things are about to heat up.
Not far from where the macrophage is fighting the germs, the cells of a capillary—a small blood vessel—go about their usual business.

Epithelial cells form the wall of the capillary. Nerve cells relax nearby.

Cutaway view:

Inside the capillary, red blood cells deliver oxygen and take away carbon dioxide. And neutrophils, the most common kind of white blood cell, tumble lazily along in the blood stream.

Suddenly, the chemical signal from the macrophage pours in. These other human cells read the signal using receptors on their membranes (the same way the macrophage used receptors to identify molecules on the germs).

**RED ALERT!**
**RELEASE THE NEUTROPHILS!**

**ZAP!**
**OUCH! PASS IT ON TO THE BRAIN.**

**OUCH!**
**(PASS IT ON.)**

**ROAR!!!**
What the immune system is doing now is called inflammation. Blood vessels widen, increasing blood flow and causing redness and heat. The heat can help kill germs. More fluid leaks from the vessels into infected tissue, giving white blood cells more room to maneuver. The extra fluid causes swelling, and the pressure causes pain.

Ouch...

The neutrophils eat fast, but also die fast. Dead neutrophils make up most of the pus that forms at an infection site.

Ew...

More neutrophils and macrophages join the fight.

So many germs!

But these germs aren't giving up easily. They keep multiplying as fast as the white blood cells can eat them.

Another kind of white blood cell arrives on the scene: a dendritic cell.

Denny! Am I glad to see you!

Hi Mac! We need more expertise. We need a specialist who understands this particular kind of bacteria.

We've got a real mess here.

And I know just who can help: my friends in the lymph nodes!
While the battle rages back at the site of infection, Denny slips through the wall of lymph vessel and travels to a distant lymph node.

Denny's mission is to activate a specific immune response, especially tailored to this specific infection.

Coming into a lymph node, home of the lymphocytes.

HMMMM... WHERE DO I EVEN START?
There are millions of lymphocytes, and each one carries a different kind of receptor on its membrane. The dendritic cells is trying to find a match for its germ sample molecule (called an antigen). This search can take a while!

Later...

COME ON. ANYBODY?

NOT EVEN CLOSE.

NO.

NO.

HEY! THAT'S MY SHAPE! THAT'S MY ANTIGEN!
The activated lymphocyte starts dividing. All of its daughter cells have the same receptor. Some of them become memory cells. Memory cells will remain on the lookout for future infections by the same germ.

The other branch of daughter cells turn into plasma cells. These cells generate antibody molecules that match the germ’s antigen. Each plasma cell can crank out about 2000 antibody molecules per second! All this antibody is released into the bloodstream and floods the entire body.
Back at the infection site...

HEEY, DENNY MUST HAVE FOUND THE CORRECT LYMPHOCYTE. HERE COMES SOME ANTIBODY!

And now the antibody starts to do its thing.

Each antibody molecule has a basic Y shape. The arms of the Y have parts that fit perfectly onto the antigen structures of the germs for which they were generated.

=CLICK=

HEY, WHAT’S THAT?

GET IT OFF ME! GET IT OFF ME!

Antibody can interfere with the functioning of germs, and can make them clump together.

And while the arms of the Y are different for each kind of germ the immune system fights, the base of the Y always sends the same strong signal to the cells of the immune system...

I CAN’T MOVE RIGHT! I CAN’T EAT RIGHT! THIS STINKS!

Eat Me! Eat Me! Eat Me!

Eat Me!

Uh-oh...
Antibody molecules tag germs for faster, more efficient destruction. They send germ-eating white blood cells into a feeding frenzy, and give them a better grip on their prey.

Oh well, it was fun while it lasted.

Just gotta mop up these dead neutrophils, now.

Pretty soon, it's all over.

I'm so full...

Whew! I'm glad that's over!

Good job, everyone!

(Yes, macrophages eat pus. You're welcome.)
Every time a new kind of germ infects the body, the immune system starts this process from the beginning. First responders like macrophages and neutrophils launch an inflammatory response, doing their best to control the infection until the lymphocytes can help the body adapt to fight the specific kind of germs involved.

But if the same kind of germ tries to reinfect the body, the immune system is several steps ahead.

HAHA! I'M IN! I'M GOING TO--

HMM...

The memory cells generated during the earlier infection make it easier to launch a fast, overwhelming response.

HEY, I KNOW YOU! YOU'RE NOT ALLOWED IN HERE!

I SMELL ANTIBODY. IS THERE ANYBODY TO EAT?

NO, IT'S ALL TAKEN CARE OF.

So the immune system learns from experience, and adapts to fight familiar enemies more effectively. This process is called immunological memory.
For many diseases, a process called **vaccination** can give immunological memory a headstart.

Vaccinating someone against a germ usually involves injecting them with antigen from that germ.

The antigen gets the lymphocytes to prepare memory cells that will be on the lookout for that kind of germ.

That way, the immune system can "remember" a disease that the person has never actually had before!

Have I seen your ugly mug somewhere before?

In addition to fighting off germs from outside the body, the immune system is on the lookout for **cancer**, the out-of-control reproduction of the body's own cells. Cancerous cells have been damaged in a way that makes them forget how to cooperate with the rest of the multicellular community. They often spread aggressively, hogging space and resources.

*These cells are human, but I'm detecting cancer antigens on their membranes!*

*They're no longer part of the team.*

*Attack!*

Bacteria, viruses, cancer... If it's not one thing, it's another! But the cells of the immune system are on guard 24/7, working to keep the whole body healthy.

Keep a sharp lookout, everyone.