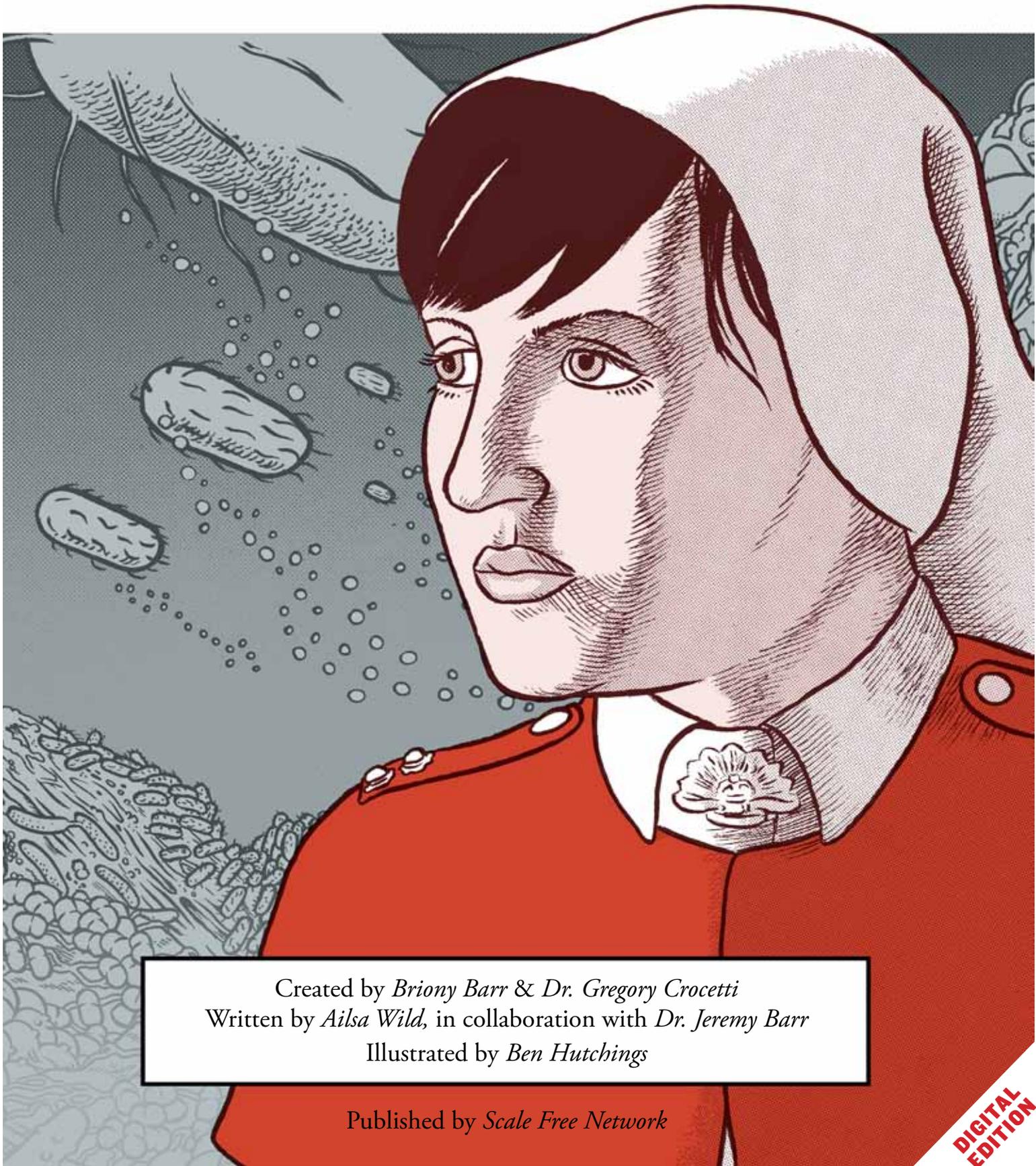


THE INVISIBLE WAR

A Tale on Two Scales



Created by *Briony Barr & Dr. Gregory Crocetti*
Written by *Ailsa Wild*, in collaboration with *Dr. Jeremy Barr*
Illustrated by *Ben Hutchings*

Published by *Scale Free Network*

**DIGITAL
EDITION**

Symbiosis |,simbi'əʊsɪs, -bʌɪ-|

noun (pl. symbioses |-si:z|)

interaction between two or more different organisms living in close physical association, typically to the advantage of each.

**“THE ENEMY OF MY ENEMY
IS MY FRIEND”**

Ancient proverb

HOW TO INTERACT WITH THIS DIGITAL NOVEL



11. WHY IS THE DOCTOR BEING SO MEAN?



see pg 13

Some doctors were reluctant to accept the microscope and the agar plate as new tools to diagnose diseases – and instead preferred to trust their old tools – observation and experience.

of high throughput DNA sequencing, powerful computational analysis – are discovering more and more about the powerful role of different microbes in the world around us.

Diagnosis was a subject of conflict and the doctor in this scene represents the 'old school' who were angry and afraid of the new diagnostic tools. Because of the British army medical establishment's reluctance to accept bacteriology, it was not given much credit within the army at the beginning of WWI. Bacteriologists, the people using microscopes and agar plates – were considered mere technicians – useful for testing water purity but not much else (certainly not for research).



Image: A laboratory in the field.
Source: Wellcome Library, London.

Our story is set at a British run Casualty Clearing Station. Australian medical culture supported bacteriology as a diagnostic tool slightly earlier and Annie would have been trained to respect it. By the end of the war, Bacteriology had become firmly established as a respected tool of medicine.

Today, bacteriologists are usually referred to as microbiologists – who, with the aid

82

If you click on the *numbered circles* that appear throughout the story, they will take you to another page with additional information about what is going on.

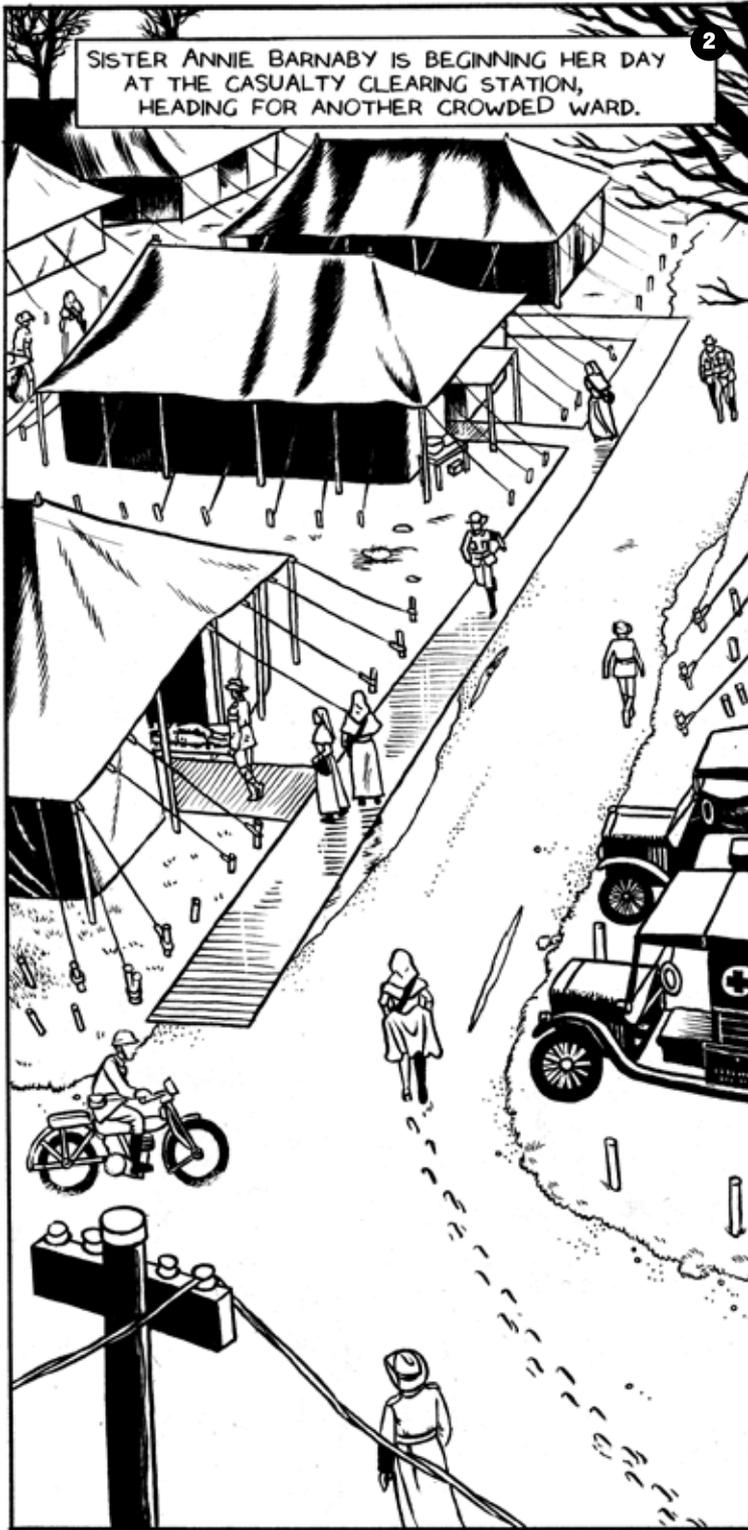
When you have finished reading, another link will take you back to the story.



The WESTERN FRONT



23rd AUGUST 1916, FRANCE, WORLD WAR 1. THE BATTLE OF POZIÈRES HAS BEEN DRAGGING ON FOR EXACTLY ONE MONTH. THOUSANDS ARE DEAD AND MORE ARE WOUNDED. SOLDIERS WITH SERIOUS ILLNESS OR INJURY ARE TAKEN TO THE CASUALTY CLEARING STATION.



SISTER ANNIE BARNABY IS BEGINNING HER DAY AT THE CASUALTY CLEARING STATION, HEADING FOR ANOTHER CROWDED WARD.

2



FIVE GUNSHOT WOUNDS ON THE WAY!

TRENCH FEVER CASE HERE! NEEDS IMMEDIATE CARE!

ORDERLY, OVER HERE NOW!

UGHHHH...



ANOTHER LOAD... ALREADY? WE BARELY HAVE ANY BEDS!





DOCTOR! DYSENTERY CASE HERE!



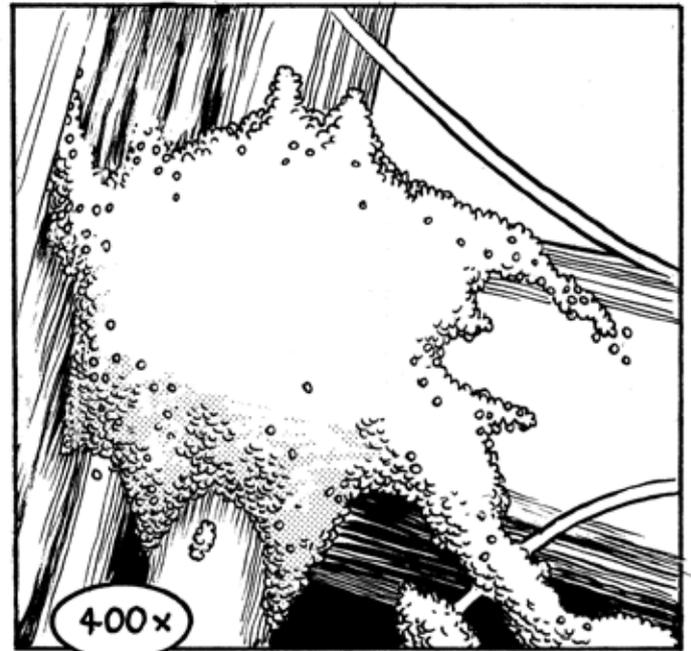
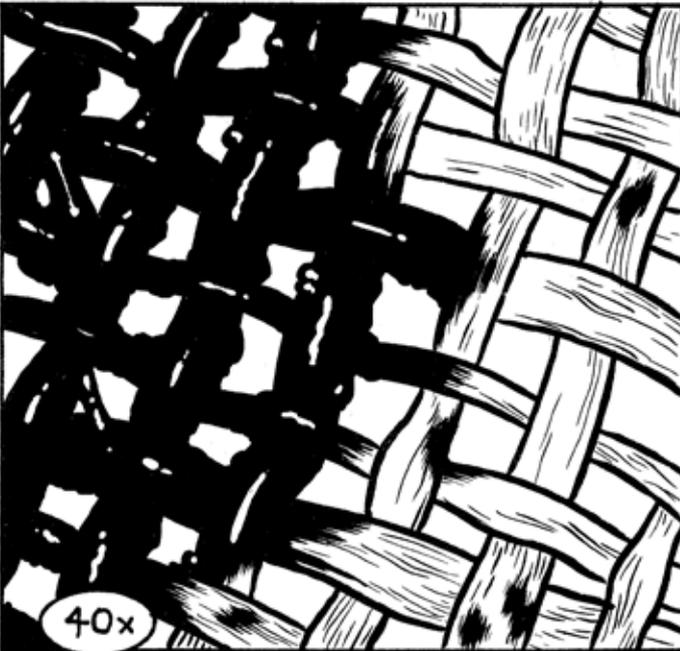
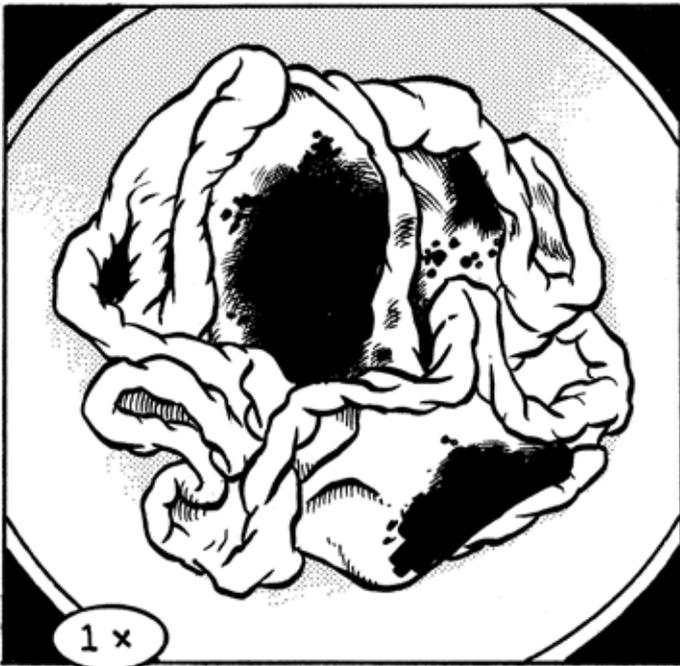
ISOLATE HIM QUICKLY SISTER. I'LL MAKE SURE WE SEND A TELEGRAM TO HEADQUARTERS. THEY REQUIRE NOTIFICATION, EVEN IF IT'S JUST A SUSPECTED CASE OF DYSENTERY.

6

ONCE HE'S IN A BED MAKE SURE YOU TAKE STOOL SAMPLES AND GET THEM TO THE MOBILE LABORATORY.

7





MEET THE SHIGA GANG (SHIGELLA FLEXNERI)... FRESH FROM CAUSING WRETCHED DEVASTATION IN PRIVATE ROBBINS' GUT. ...AND LOOKING FOR SOMEWHERE NEW TO BREED!

8

9

WHAT IS THIS GARBAGE DUMP?

HOW COME WE EVACUATED?

MUCUS STRANDS

RED BLOOD CELL

DUNNO, BUT THAT WAS AN AWESOME POPULATION EXPLOSION BACK THERE!

YEAH, SICK AS. SO MUCH SLIME!

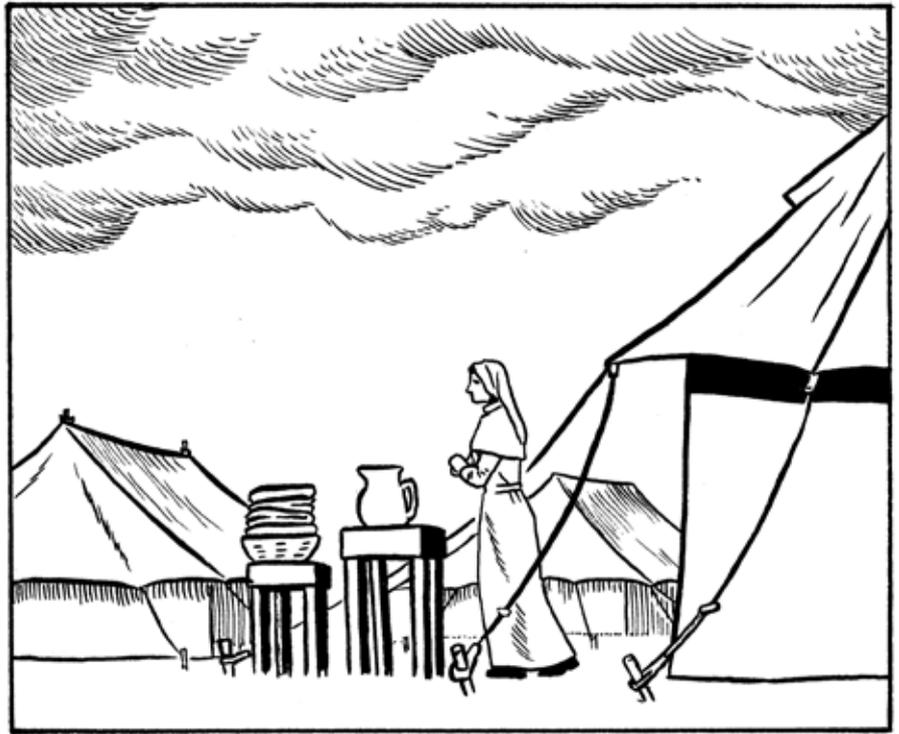
SHIGELLA FLEXNERI

WE SHOULD DO IT AGAIN REAL SOON.

CAN'T DO ANYTHING WITH NO SLIME TO RIDE...

YEAH...

I'M HUNGRY.



AFTER WASHING HER HANDS CAREFULLY, ANNIE IS STRAIGHT BACK ON THE WARD.



"I'M A FITZROY GIRL. FITZROY, MELBOURNE."





IT SURE IS GOOD TO BE OUT OF THAT DEATHTRAP, SISTER.

...AND TO SEE A FACE FROM HOME.

MEANWHILE IN THE BIN, THE SHIGA GANG AREN'T VERY HAPPY.



THIS PLACE IS A DEATH TRAP!



IT'S TOTALLY FREEZING.

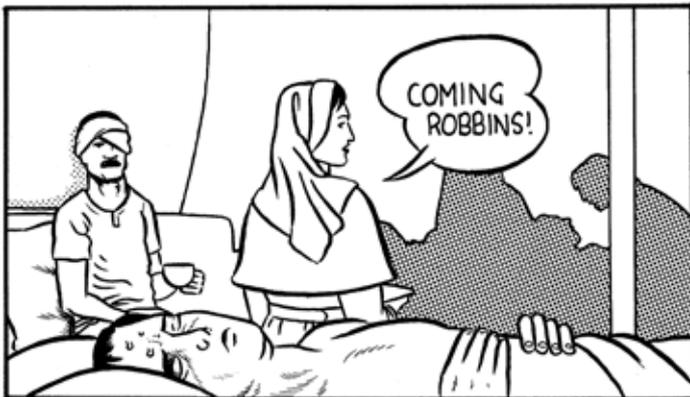


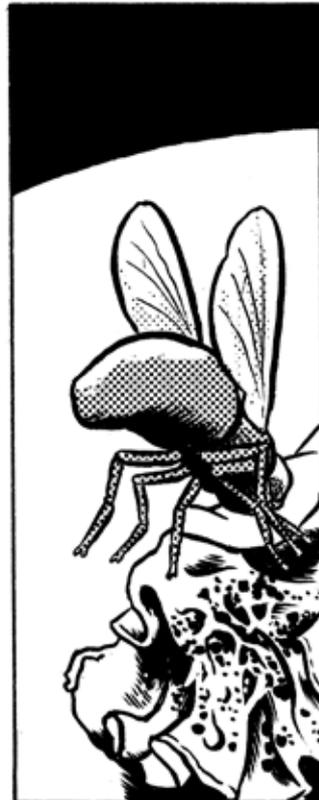
AND THIS BLOODY MUCUS AIN'T GONNA LAST.

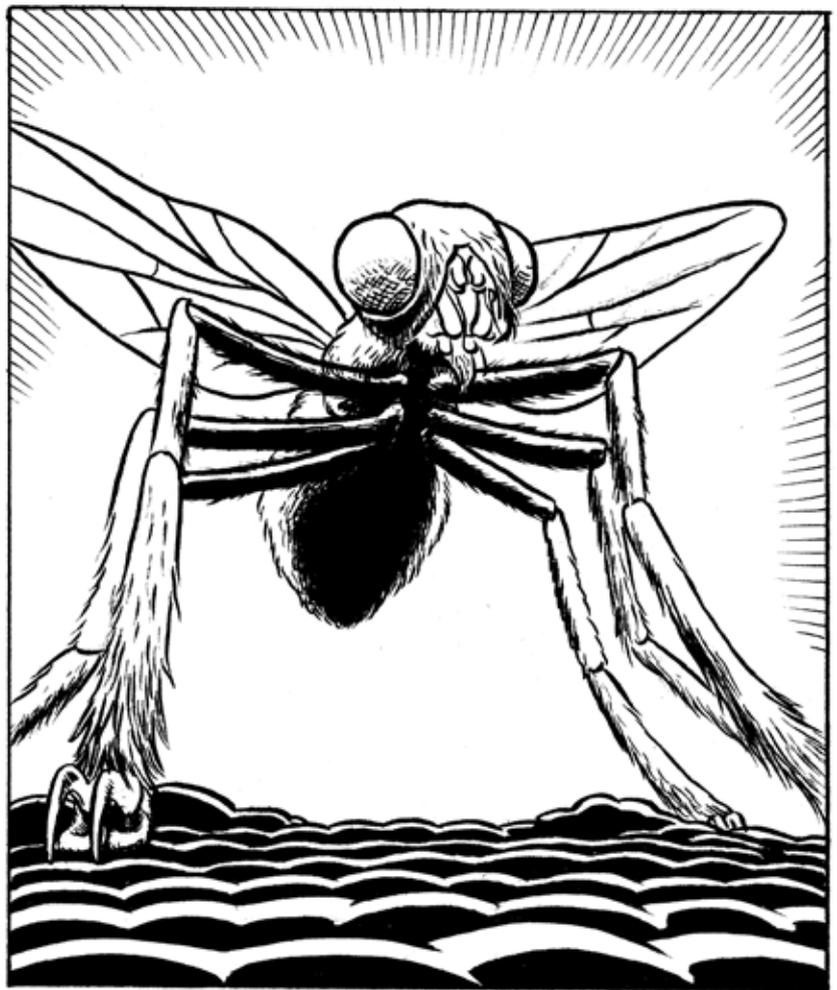
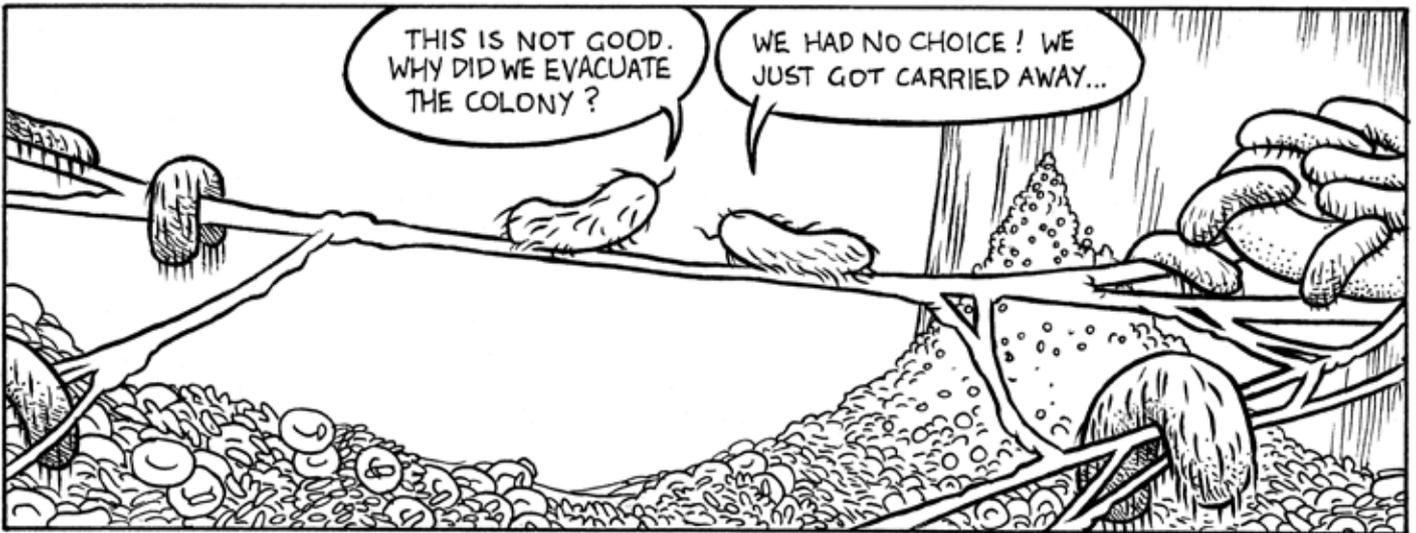
SERIOUSLY GANG, THIS STINKS. WE GOTTA GET OUT!

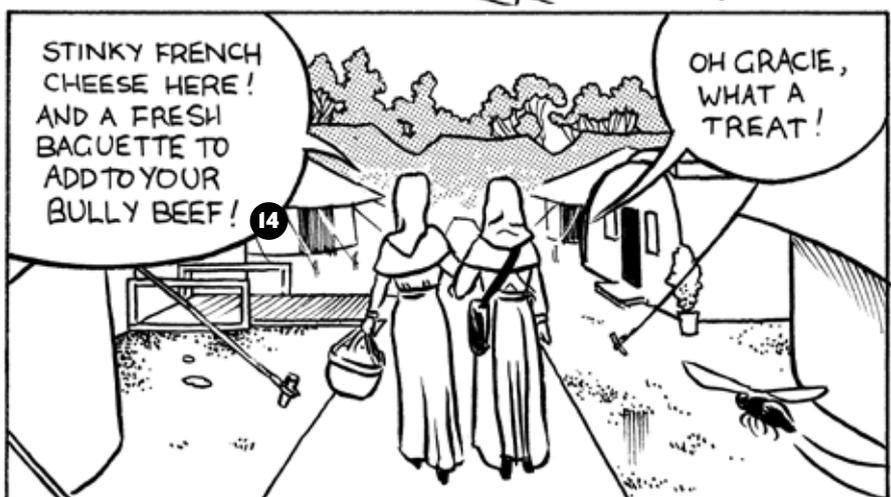
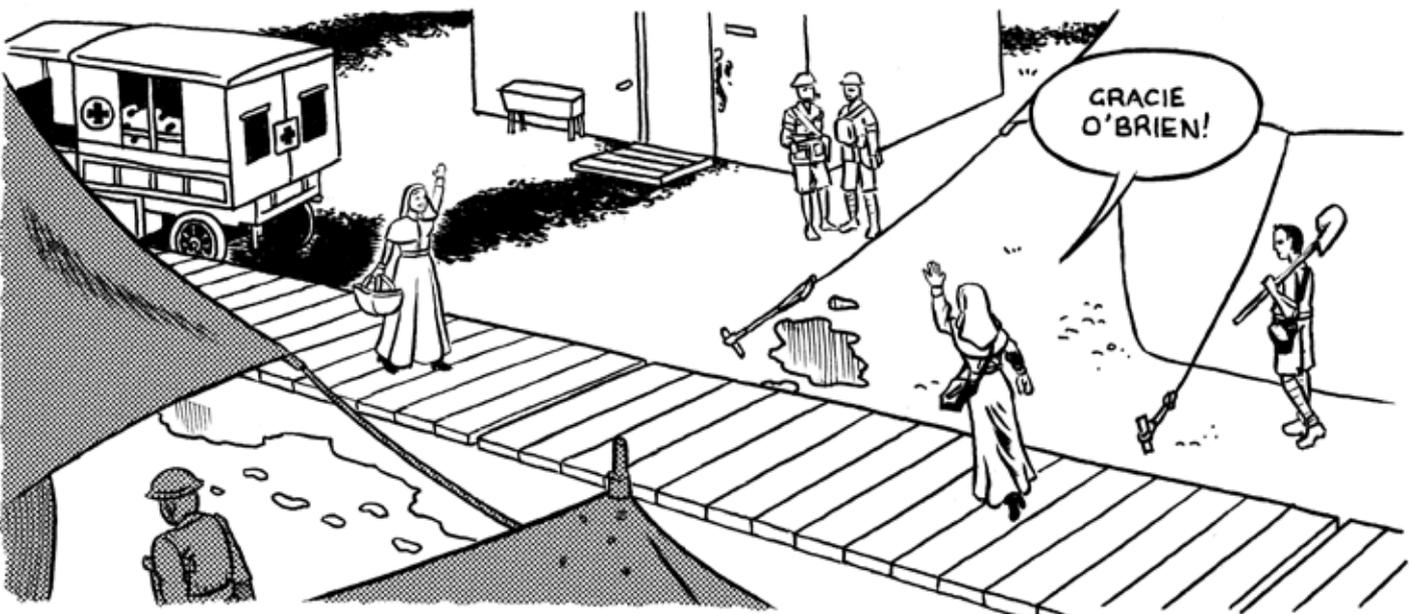


BUT HOW?









HOW WAS YOUR
BARGE TRIP ?

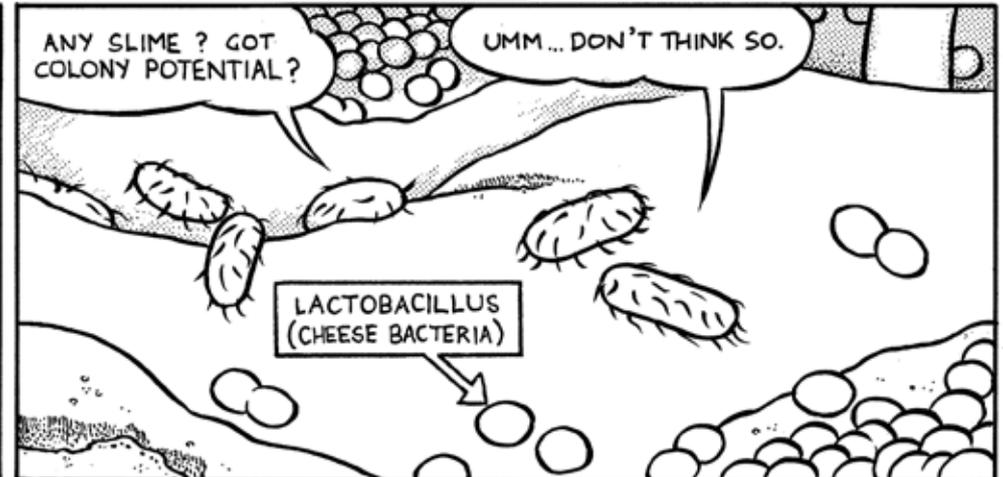
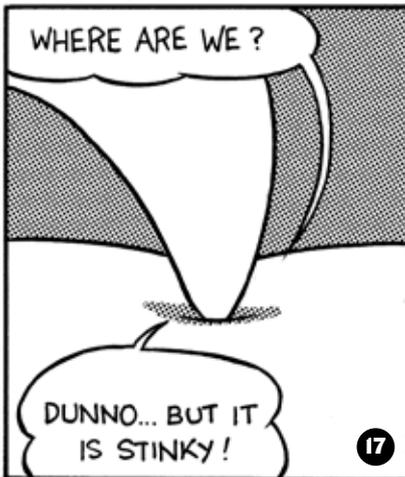
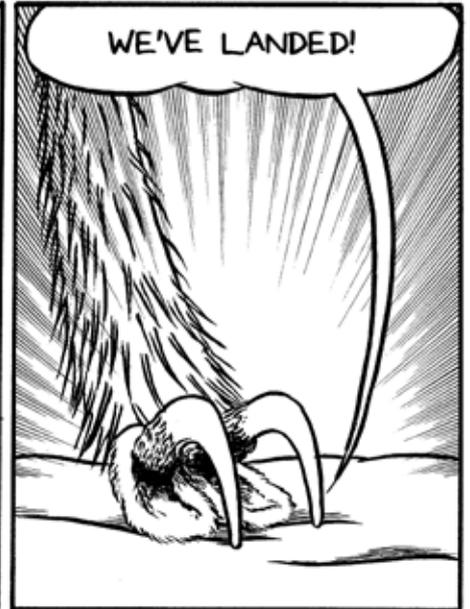
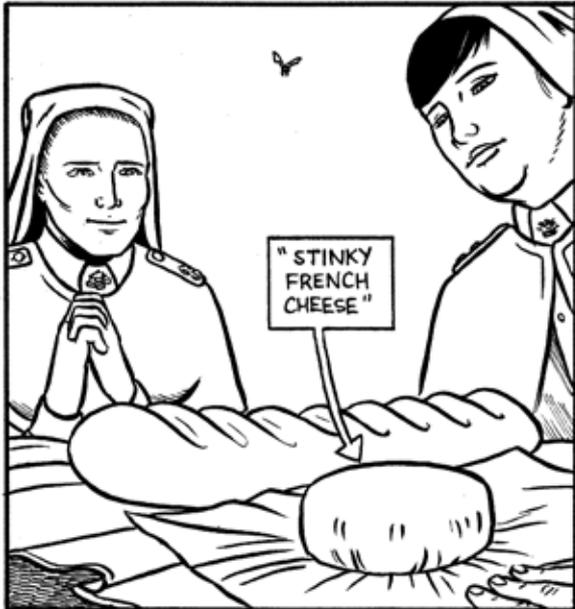
COMING BACK UP ON AN EMPTY BARGE?
LOVELY. I CAUGHT UP ON ALL MY MELBOURNE
LETTERS AND WENT SHOPPING ON THE WAY.

BUT
BEFORE THAT ?
ON YOUR WAY DOWN
WITH THE
INJURED ?

AWFUL. STIFLING. THE WINDOWS WERE
CLOSED ALL NIGHT BECAUSE OF THE LIGHT.
EVEN A CRACK COULD GIVE AWAY OUR POSITION
TO FRITZ.

"HALF THE
BOYS HAD BEEN
GASSED AND THE
REST WERE
BASICALLY
ROTTING."

"I COULD
BARELY BREATHE.
SO MANY DEATHS,
ANNIE."



THEY SAY THERE'S HUNDREDS MORE INJURED EXPECTED TOMORROW.



I DON'T KNOW IF I CAN BEAR IT.



YOU WILL. AS SOON AS THE NEXT POOR INJURED BOY IS IN FRONT OF YOU.



ANY WORD FROM YOUR BROTHER, EDITH?



HE WROTE A WEEK AGO. FROM THE FRONT. I SUPPOSE IF HE'S STILL ALIVE THAT'S WHERE HE IS.



I WISH AUSTRALIA WOULD HURRY UP AND CALL THAT REFERENDUM, CONSCRIPT MORE SOLDIERS, AND WIN THIS THING SO WE CAN ALL GO HOME.



REALLY EDITH? YOU WANT CONSCRIPTION?



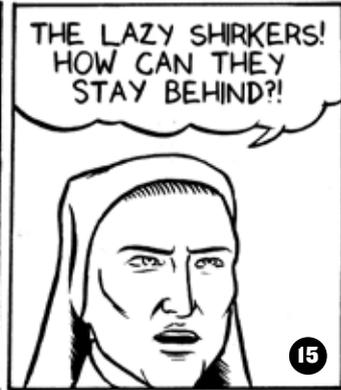
AFTER GALLIPOLI AND ALL THE DEATH AND SUFFERING WE'RE SEEING OUT OF POZIÈRES?



COULD YOU FORCE MORE BOYS TO GO THROUGH IT?



THE LAZY SHIRKERS! HOW CAN THEY STAY BEHIND?!



HIDING AT HOME BEHIND THE SKIRTS OF THEIR WOMENFOLK, LEAVING MY BROTHER TO FIGHT FOR THEIR FREEDOM.



BUT WHOSE FREEDOM?



ALL OF OURS. AUSTRALIA. THE EMPIRE.



EDITH... THE BRITISH EMPIRE DOESN'T PROVIDE FREEDOM FOR EVERYONE...



YOU SAW WHAT HAPPENED IN IRELAND AFTER EASTER! THEY AREN'T EXACTLY FREE!



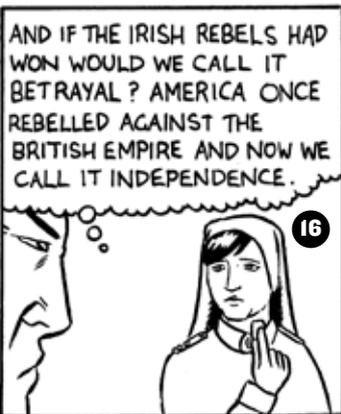
THE IRISH ARE BACKSTABBING COWARDS... WHO BETRAYED US IN OUR TIME OF NEED!

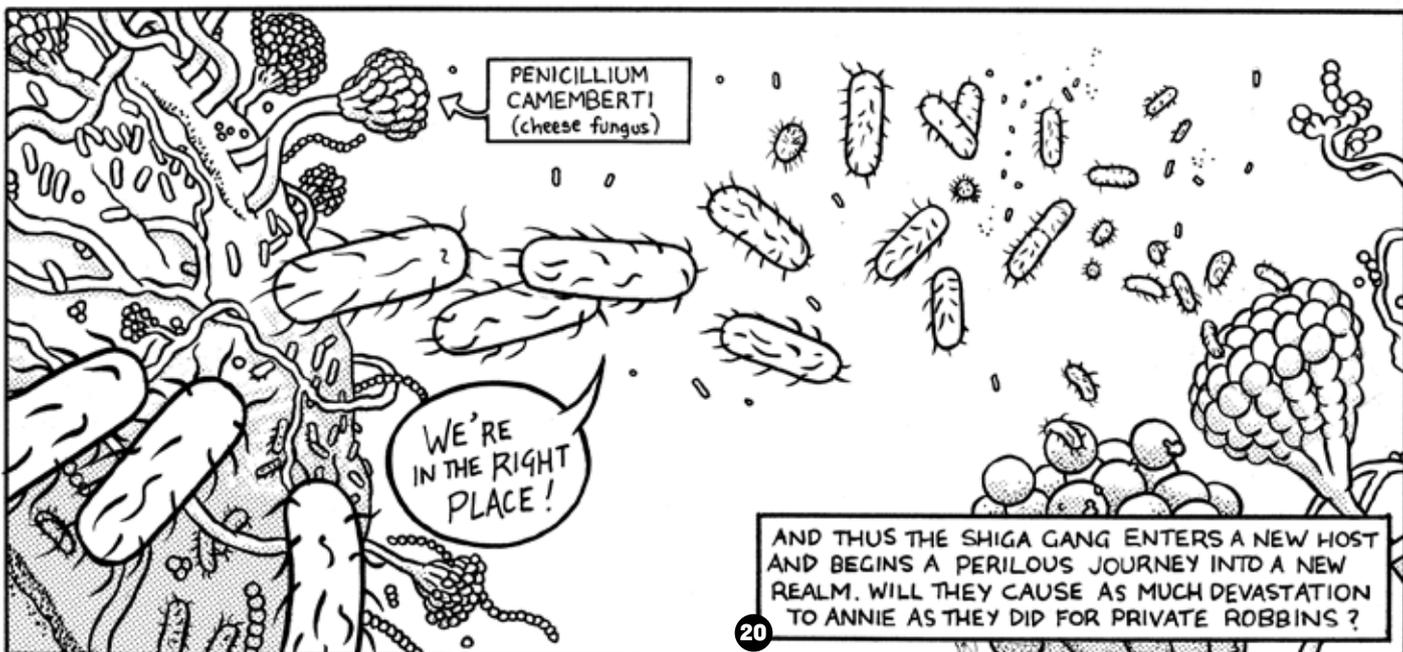
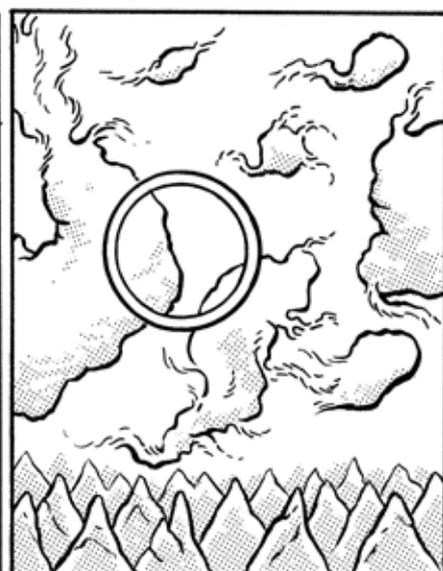
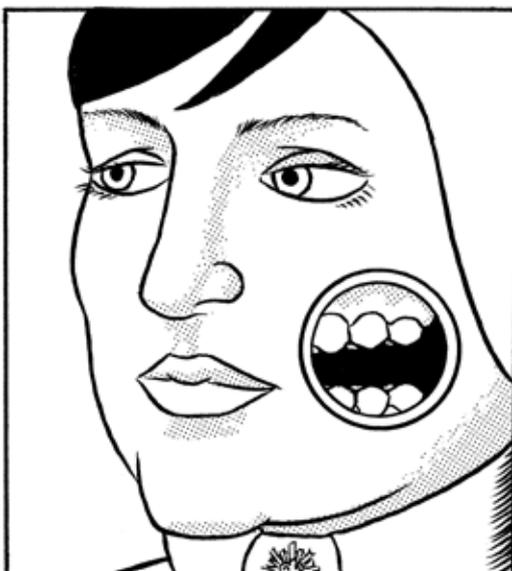


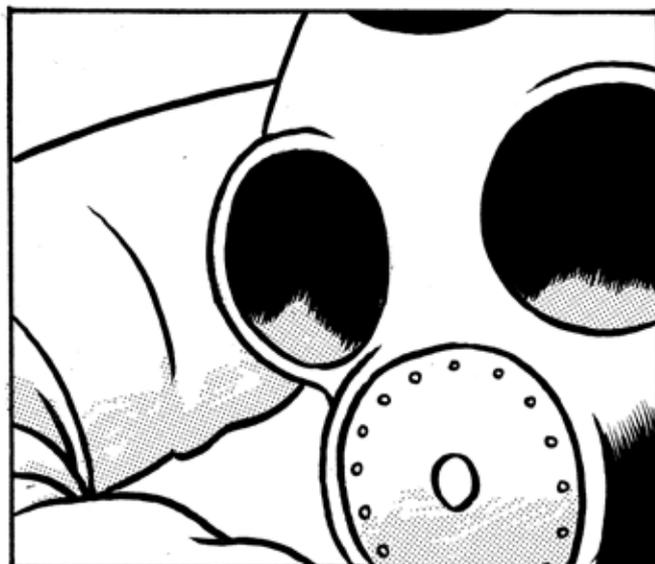
CAREFUL, EDITH. PLENTY OF US IRISH IN MELBOURNE. MY GRANNIE REMEMBERS THE FAMINE YOU KNOW.



AND IF THE IRISH REBELS HAD WON WOULD WE CALL IT BETRAYAL? AMERICA ONCE REBELLED AGAINST THE BRITISH EMPIRE AND NOW WE CALL IT INDEPENDENCE.

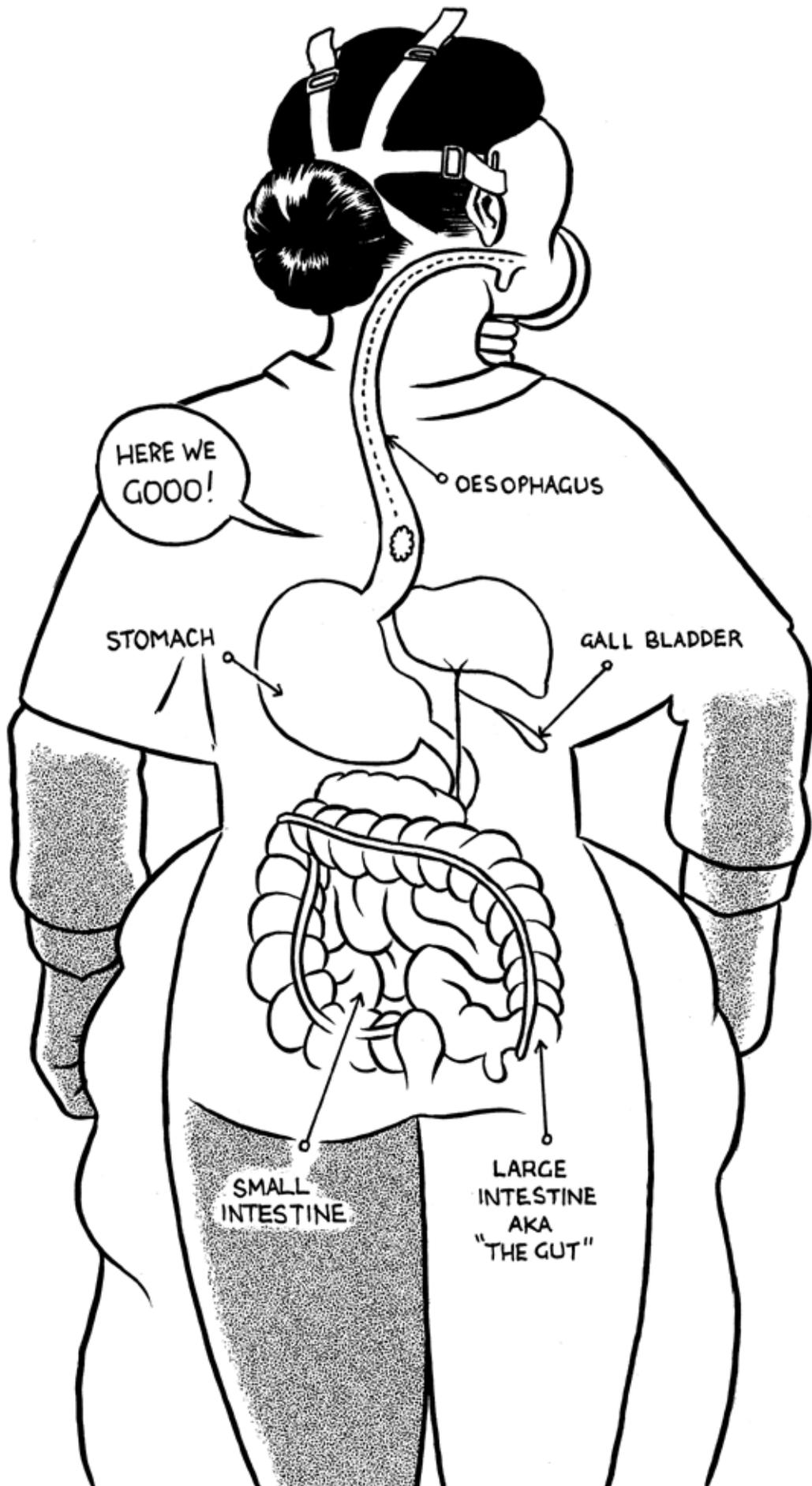


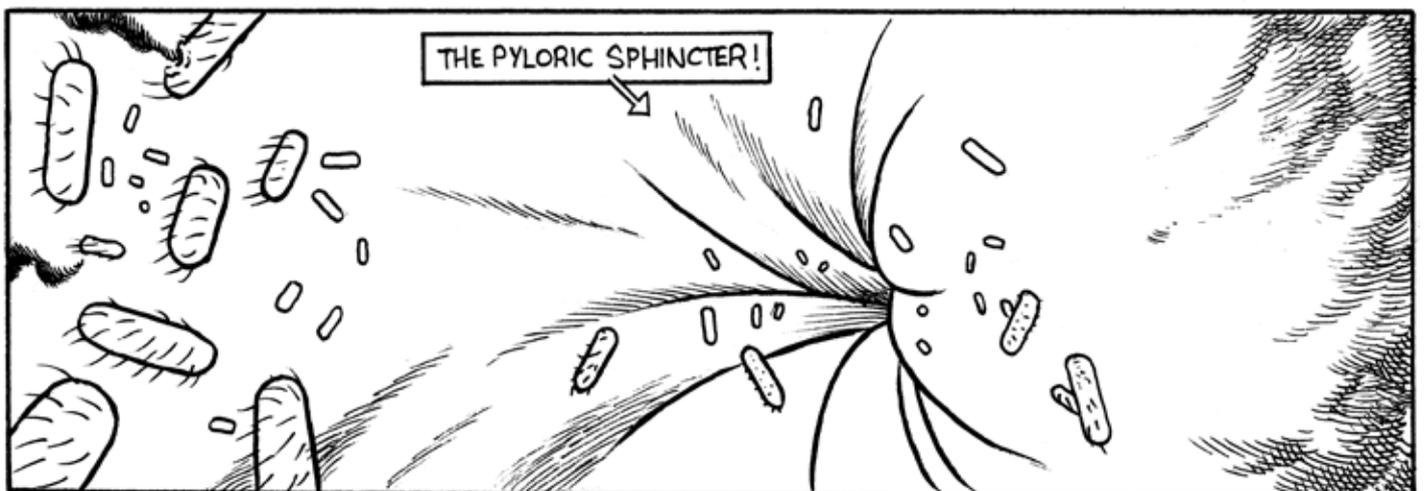
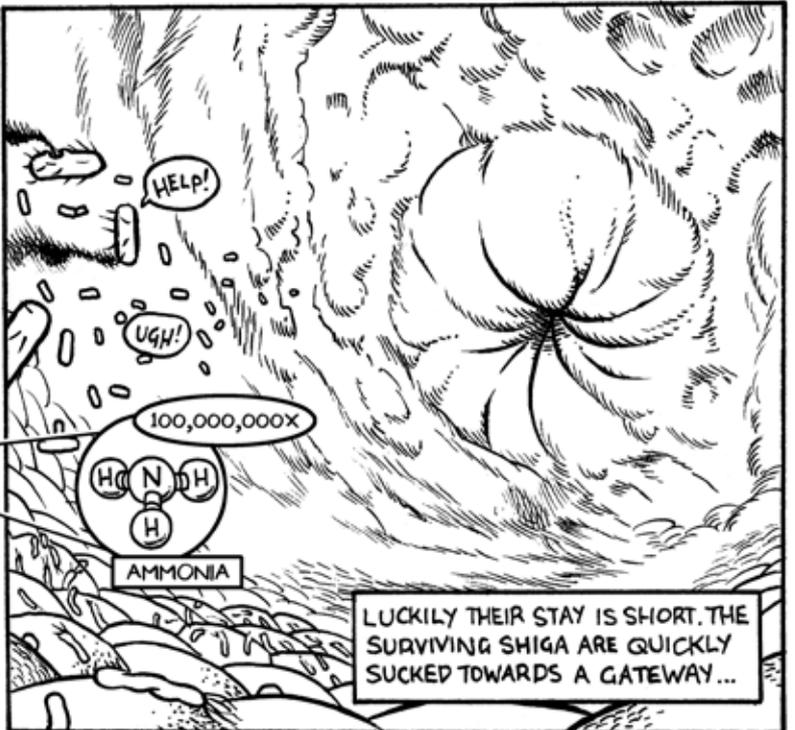
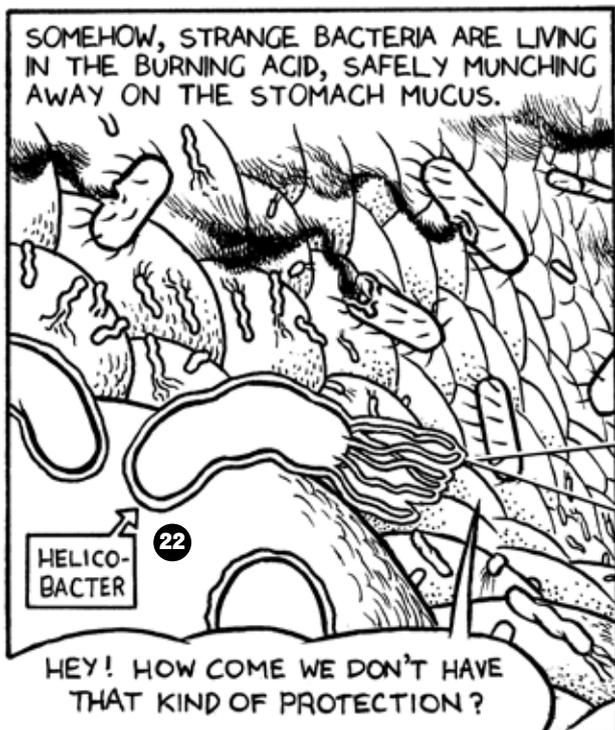
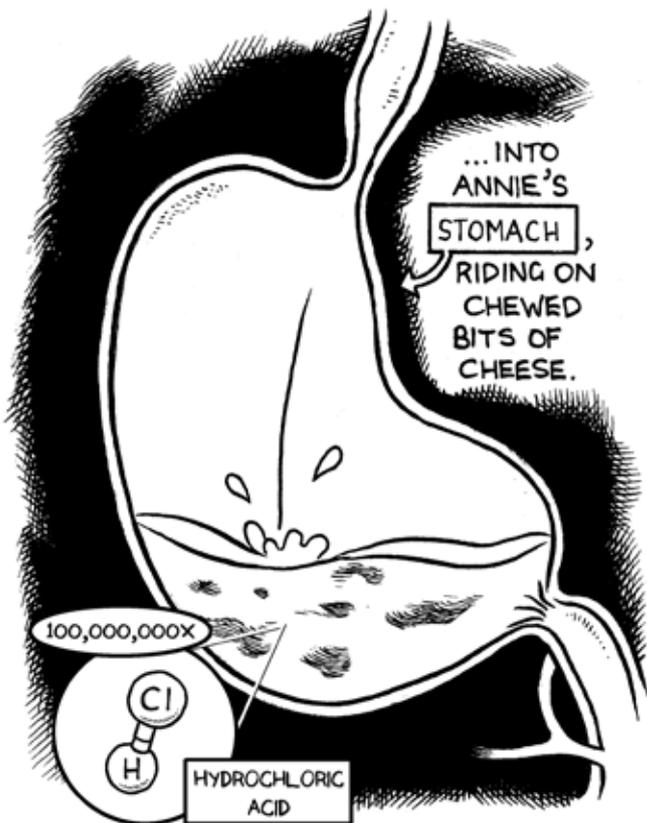


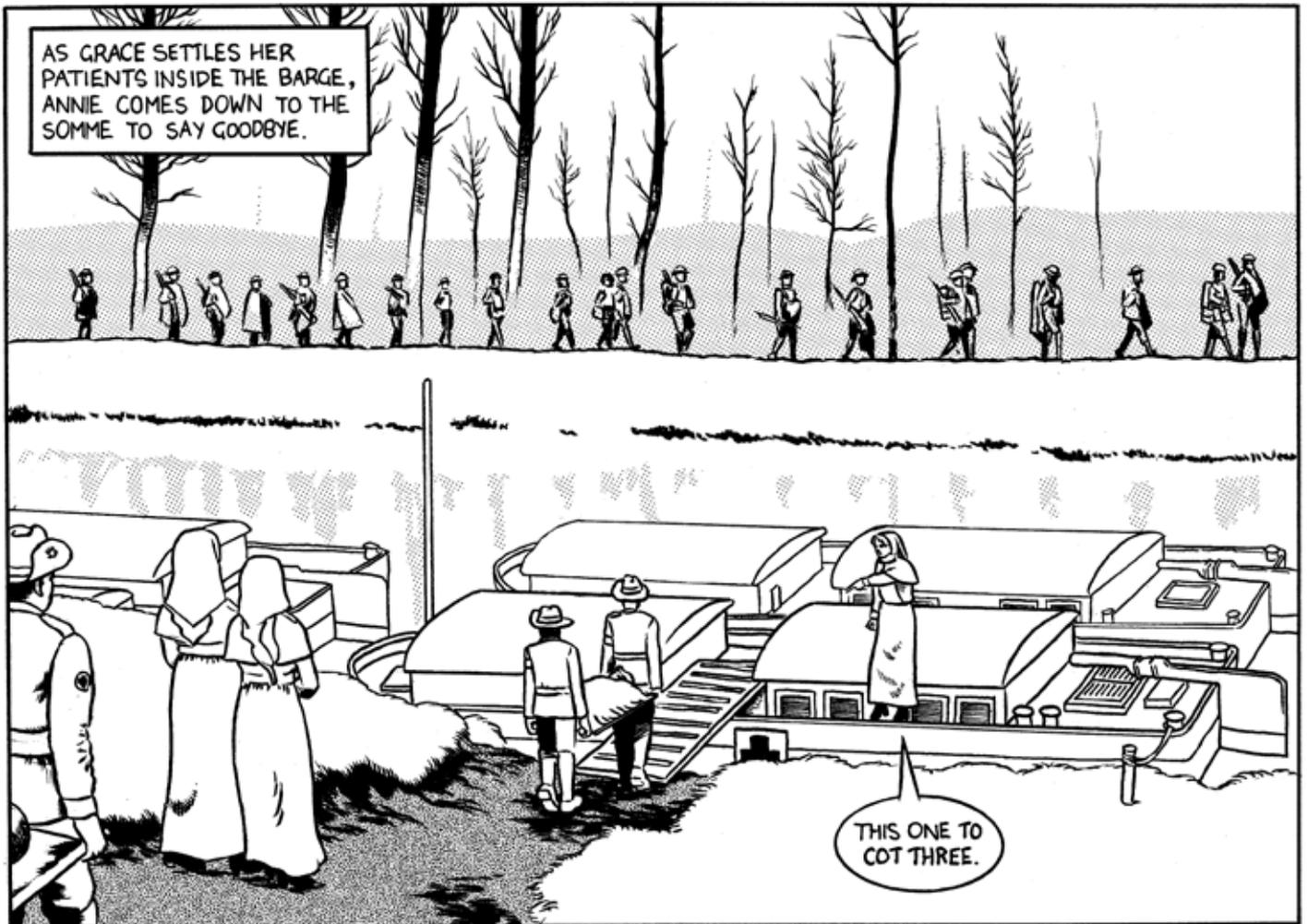
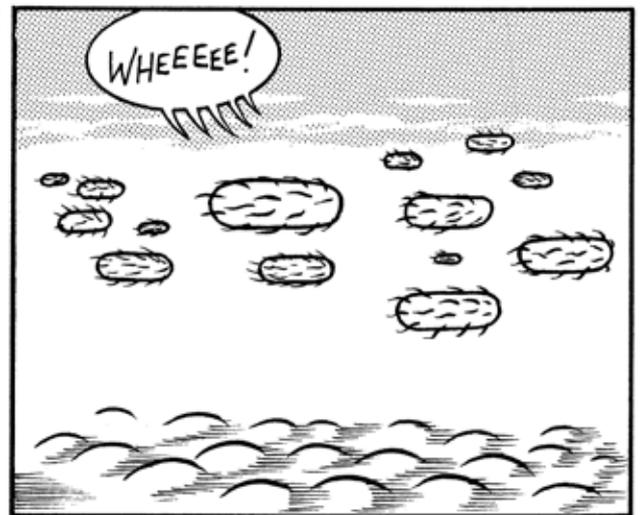
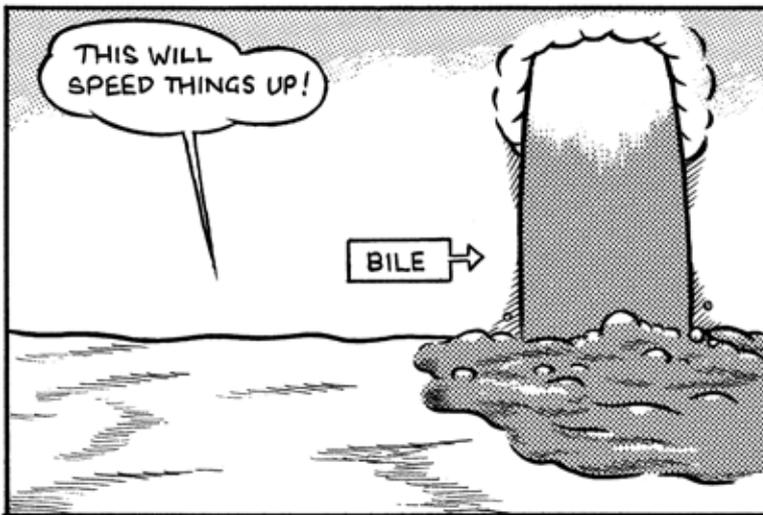


AS ANNIE BREATHES ANXIOUSLY THROUGH HER GAS MASK, THE SHIGA GANG SLIDE DOWN...

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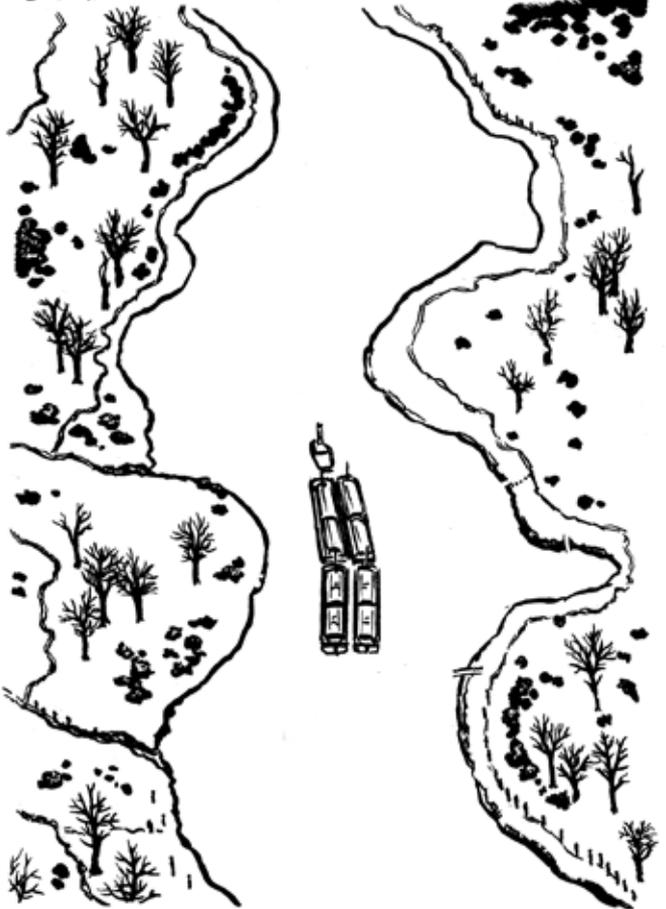




HAVE YOU GOT EVERYTHING?

YES, THANKS DUCKIE!

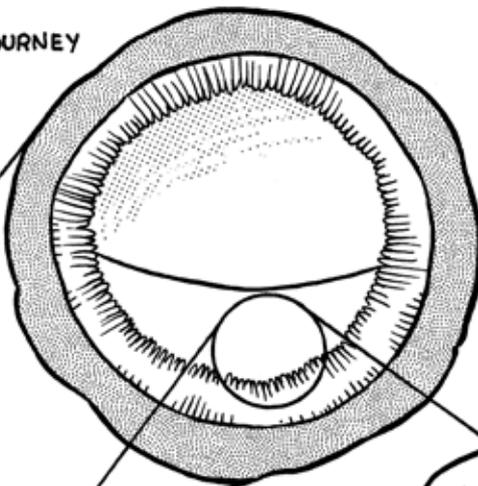
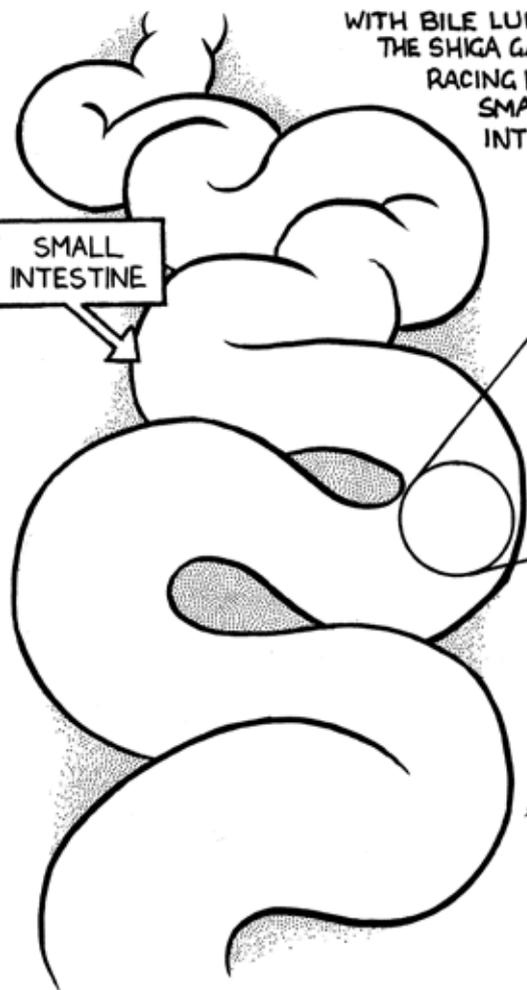
THE BARGES MOVE OFF, BUDGING THE SLUGGARD RIPPLES OF THE SOMME.



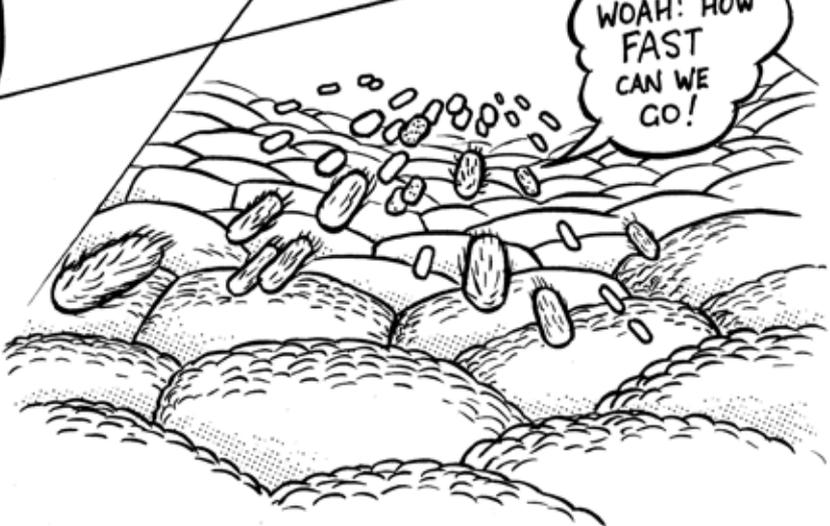
WITH BILE LUBING THE JOURNEY THE SHIGA GANG GO RACING DOWN THE SMALL INTESTINE!

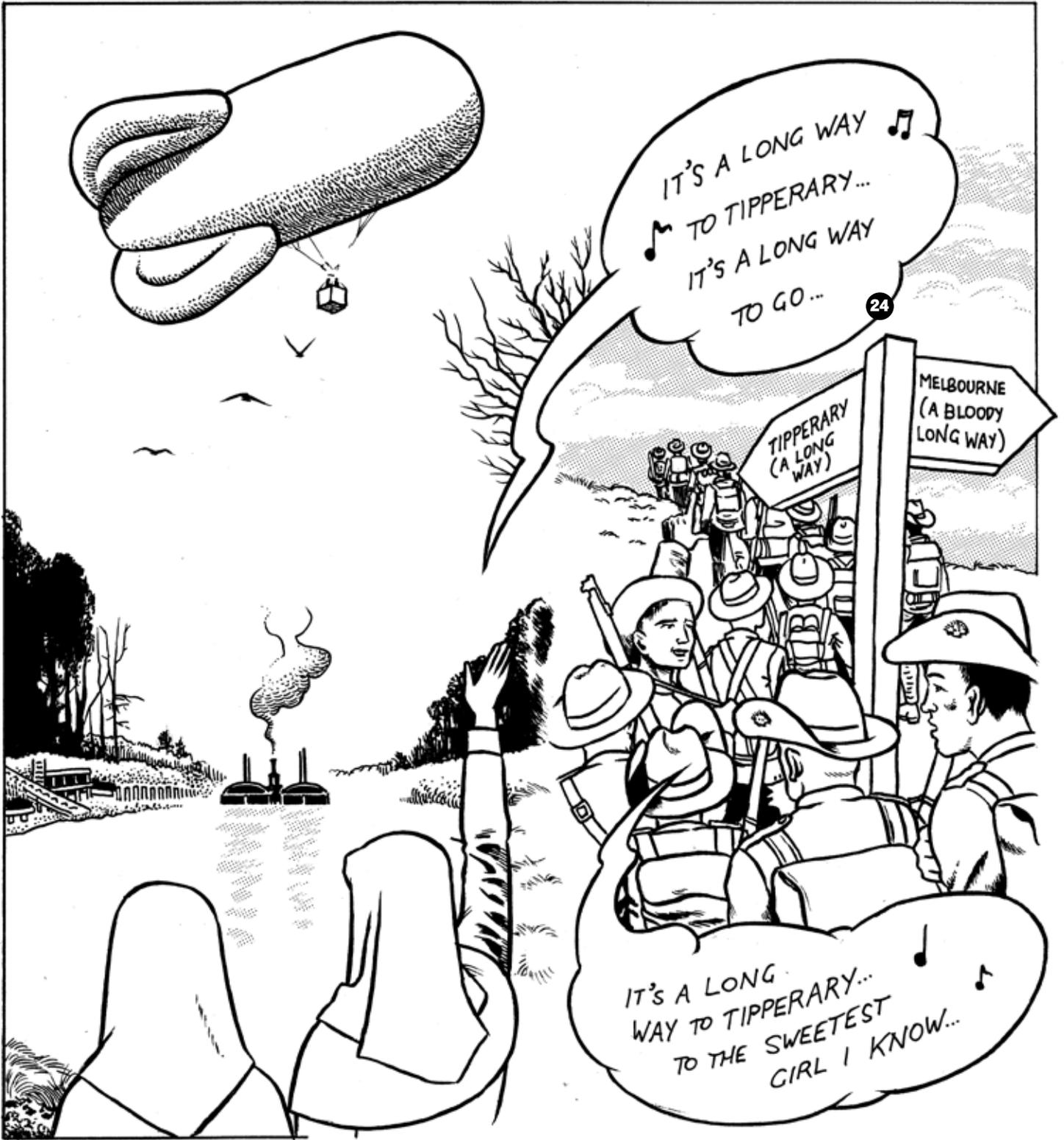
23

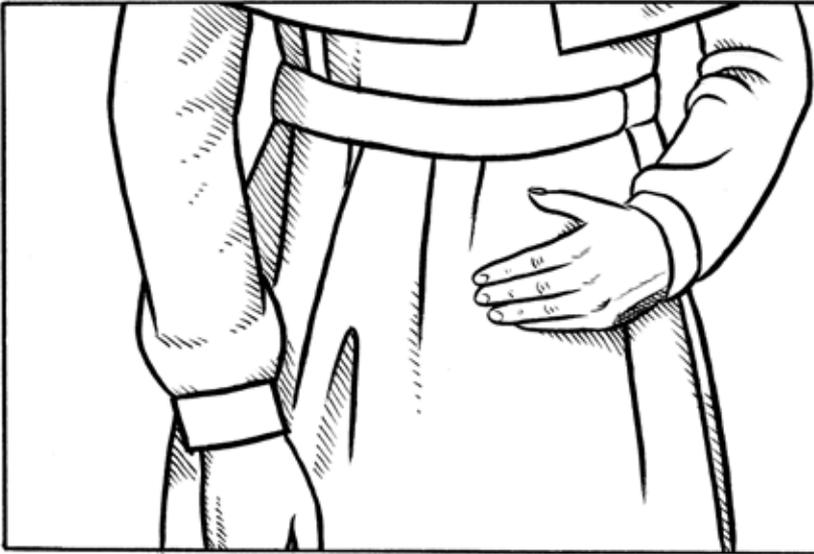
SMALL INTESTINE



WOAH! HOW FAST CAN WE GO!







MEANWHILE, IN ANNIE'S GUT (LARGE INTESTINE), ALL IS AS IT SHOULD BE... SO FAR...



WELCOME TO THE GUT.

A THRIVING, TEEMING WILDERNESS OF TINY CREATURES IS BUSY WORKING WITH FRIENDS, COMPETING WITH OTHERS, FIGHTING AND BREEDING, EATING AND SHARING FOOD. MILLIONS, BILLIONS AND TRILLIONS OF THEM, LIVING IN AND AROUND THE GREAT RIVER OF CHYME THAT FLUSHES DOWN THE GUT.

25

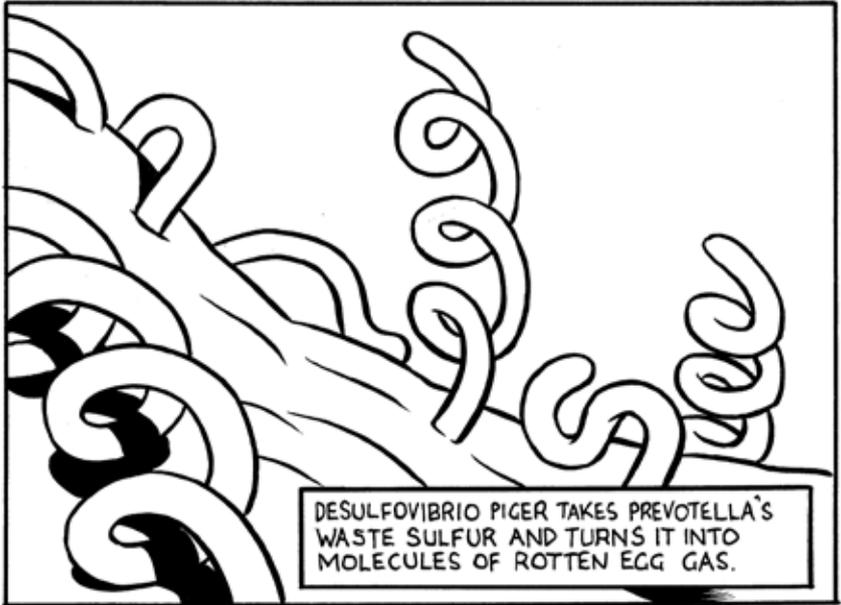
27



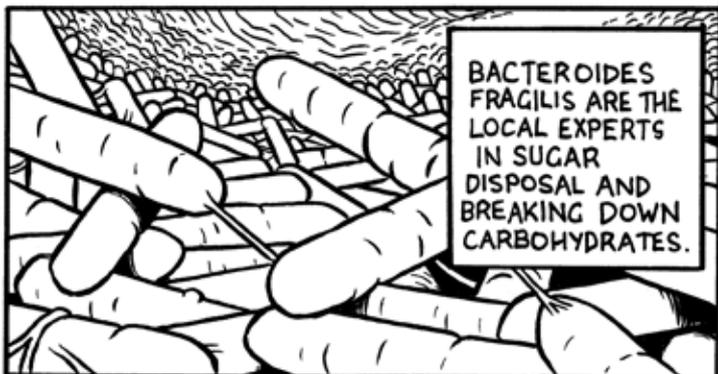
THICK CLUMPS OF BACTERIA STICK TOGETHER TO STOP THEMSELVES BEING WASHED DOWNSTREAM IN THE RELENTLESS GUT CURRENT.



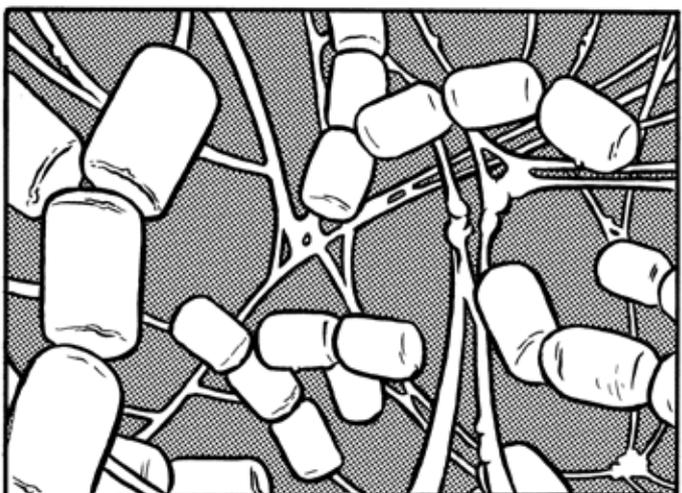
PREVOTELLA IS WORKING TO CREATE VITAMIN B1, WHICH WILL INSULATE ANNIE'S NERVES.



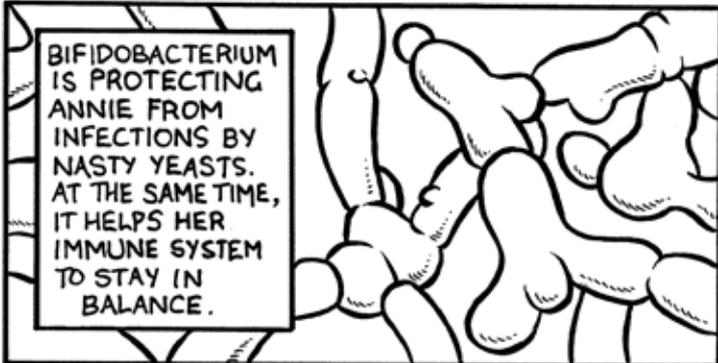
DESULFOVIBRIO PIGER TAKES PREVOTELLA'S WASTE SULFUR AND TURNS IT INTO MOLECULES OF ROTTEN EGG GAS.



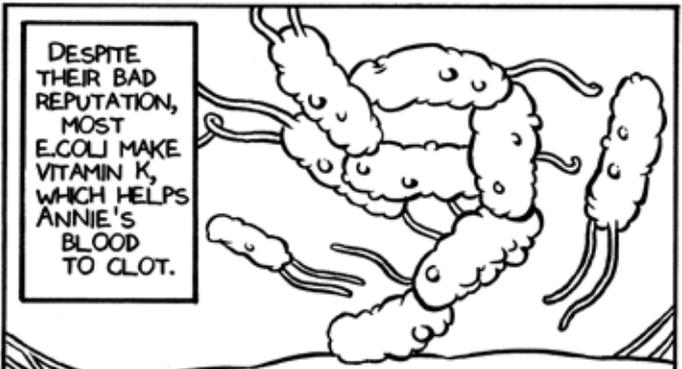
BACTEROIDES FRAGILIS ARE THE LOCAL EXPERTS IN SUGAR DISPOSAL AND BREAKING DOWN CARBOHYDRATES.



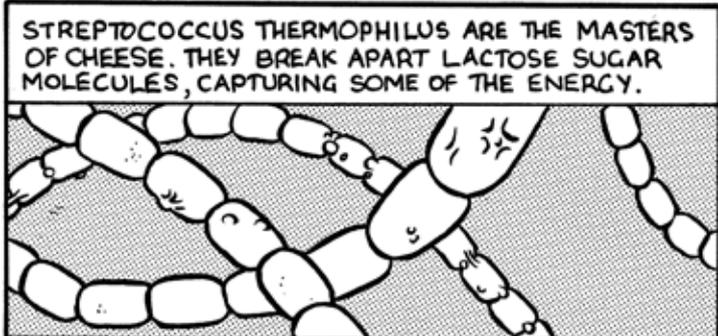
THE ARCHAEANS METHANOBREVIBACTER SMITHII ARE RECYCLERS, TAKING WASTES FROM OTHER MICROBES TO CREATE AN ODOURLESS METHANE GAS WHICH FEED OTHER GOOD BACTERIA.



BIFIDOBACTERIUM IS PROTECTING ANNIE FROM INFECTIONS BY NASTY YEASTS. AT THE SAME TIME, IT HELPS HER IMMUNE SYSTEM TO STAY IN BALANCE.



DESPITE THEIR BAD REPUTATION, MOST E.COLI MAKE VITAMIN K, WHICH HELPS ANNIE'S BLOOD TO CLOT.

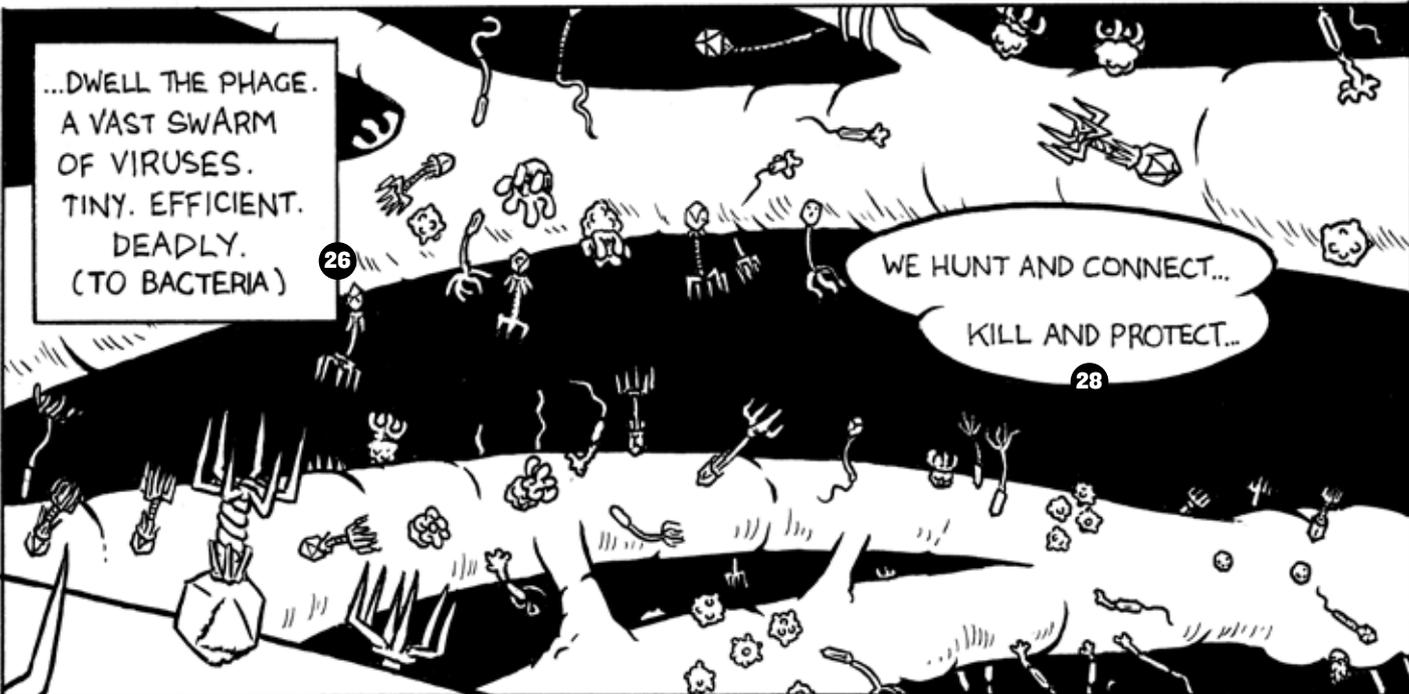


STREPTOCOCCUS THERMOPHILUS ARE THE MASTERS OF CHEESE. THEY BREAK APART LACTOSE SUGAR MOLECULES, CAPTURING SOME OF THE ENERGY.

ALL OF THEM LIVING IN AND ON THE GREAT MATRIX OF MUCUS WHICH LINES THE GUT.



BUT EVEN DEEPER
WITHIN THE
MUCUS...

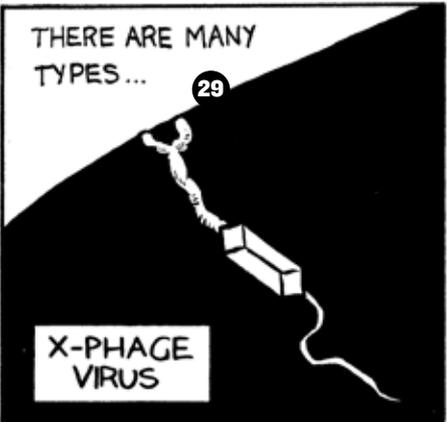


...DWELL THE PHAGE.
A VAST SWARM
OF VIRUSES.
TINY. EFFICIENT.
DEADLY.
(TO BACTERIA)

26

WE HUNT AND CONNECT...
KILL AND PROTECT...

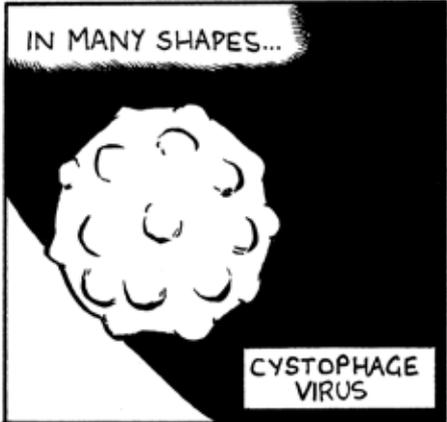
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THERE ARE MANY
TYPES ...

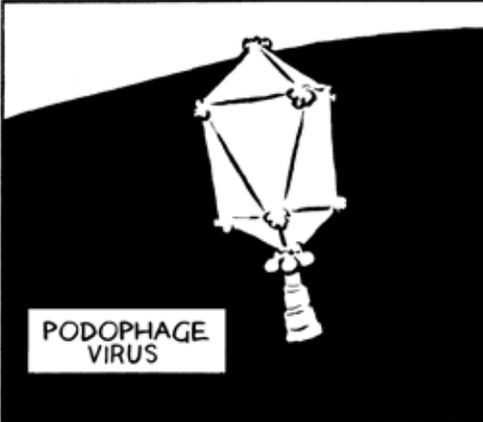
29

X-PHAGE
VIRUS



IN MANY SHAPES...

CYSTOPHAGE
VIRUS



PODOPHAGE
VIRUS

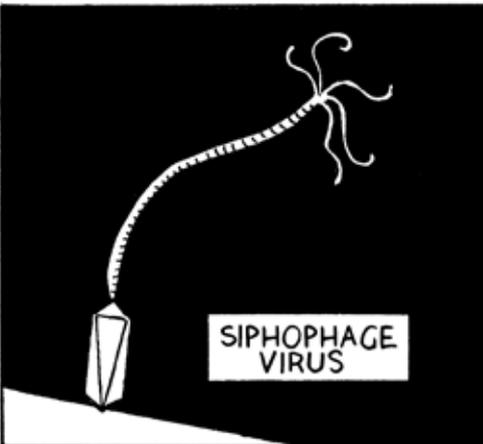


SIPHOPHAGE
VIRUS

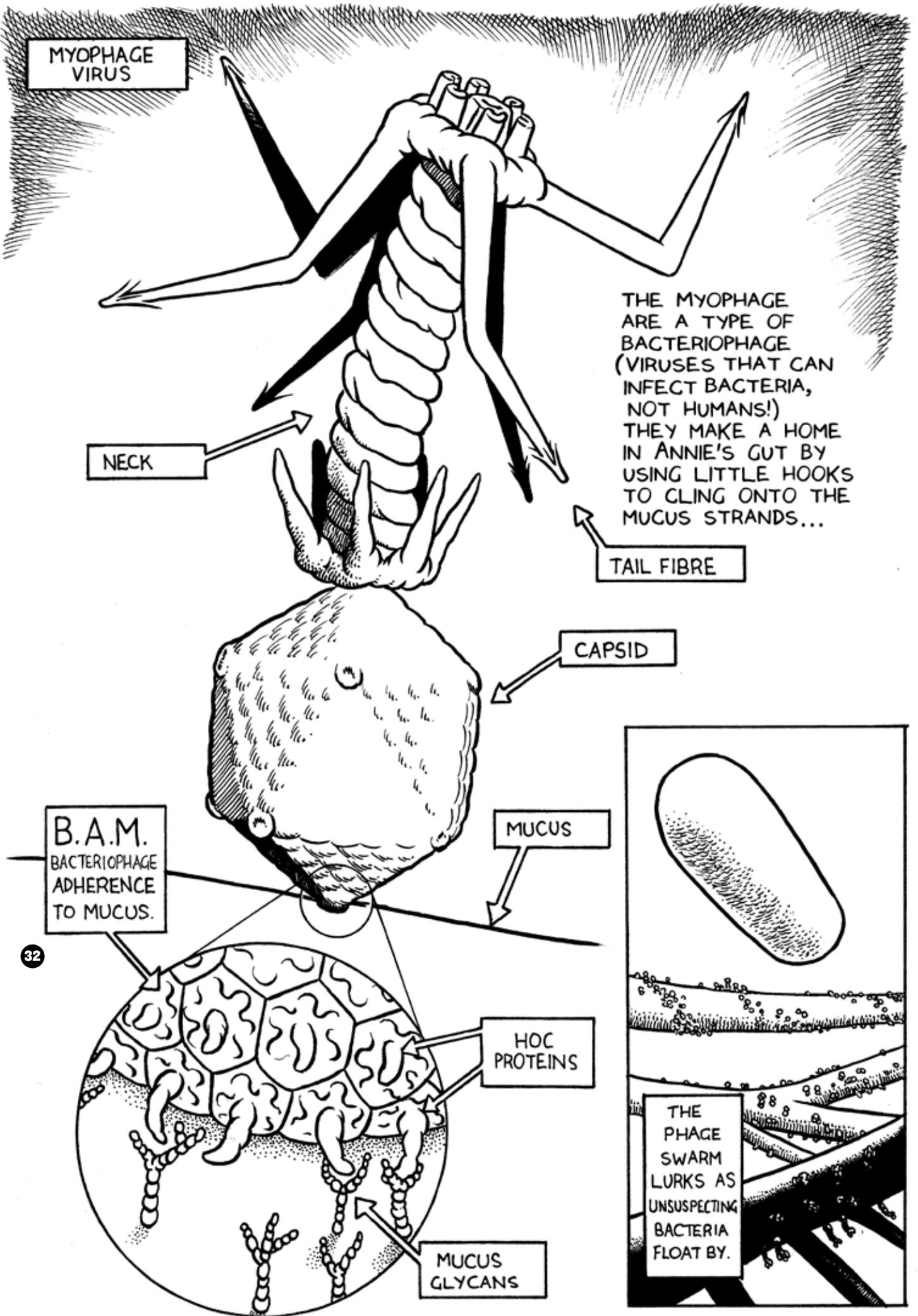


BUT THEY ALL DO A SIMILAR JOB.

PODOPHAGE
VIRUS



SIPHOPHAGE
VIRUS



MYOPHAGE VIRUS

THE MYOPHAGE ARE A TYPE OF BACTERIOPHAGE (VIRUSES THAT CAN INFECT BACTERIA, NOT HUMANS!) THEY MAKE A HOME IN ANNIE'S GUT BY USING LITTLE HOOKS TO CLING ONTO THE MUCUS STRANDS...

NECK

TAIL FIBRE

CAPSID

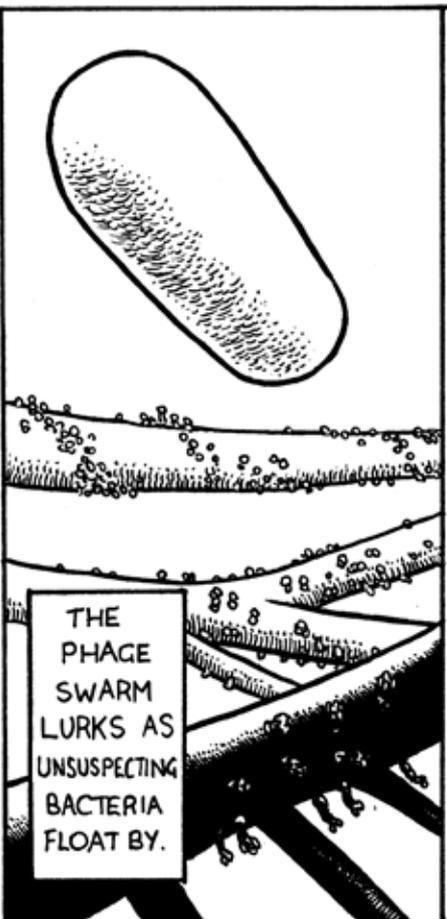
MUCUS

B.A.M. BACTERIOPHAGE ADHERENCE TO MUCUS.

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HOC PROTEINS

MUCUS GLYCANS



THE PHAGE SWARM LURKS AS UNSUSPECTING BACTERIA FLOAT BY.

THE SENSITIVE TAIL FIBRES OF THE PHAGE HUNT FOR BACTERIA TO INFECT... TESTING AND TASTING... AS THEY JUMP BETWEEN MUCUS STRANDS.

SALMONELLA

WE BIND THE MUCUS.

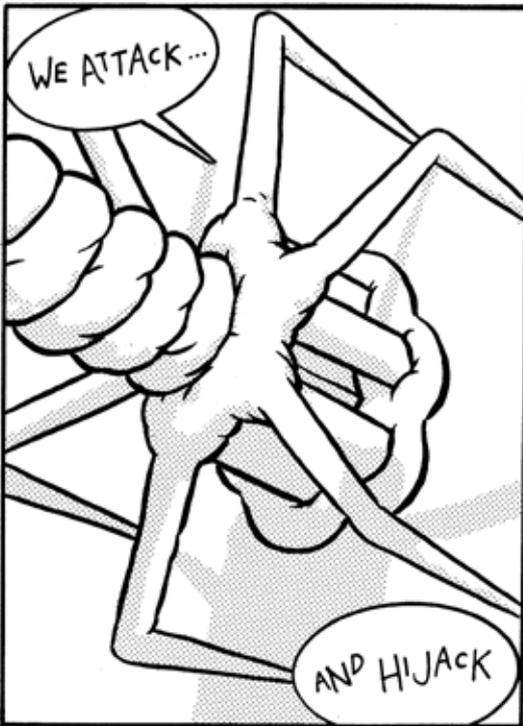
OUR SEARCH IS RUTHLESS...

HIDING IS USELESS!

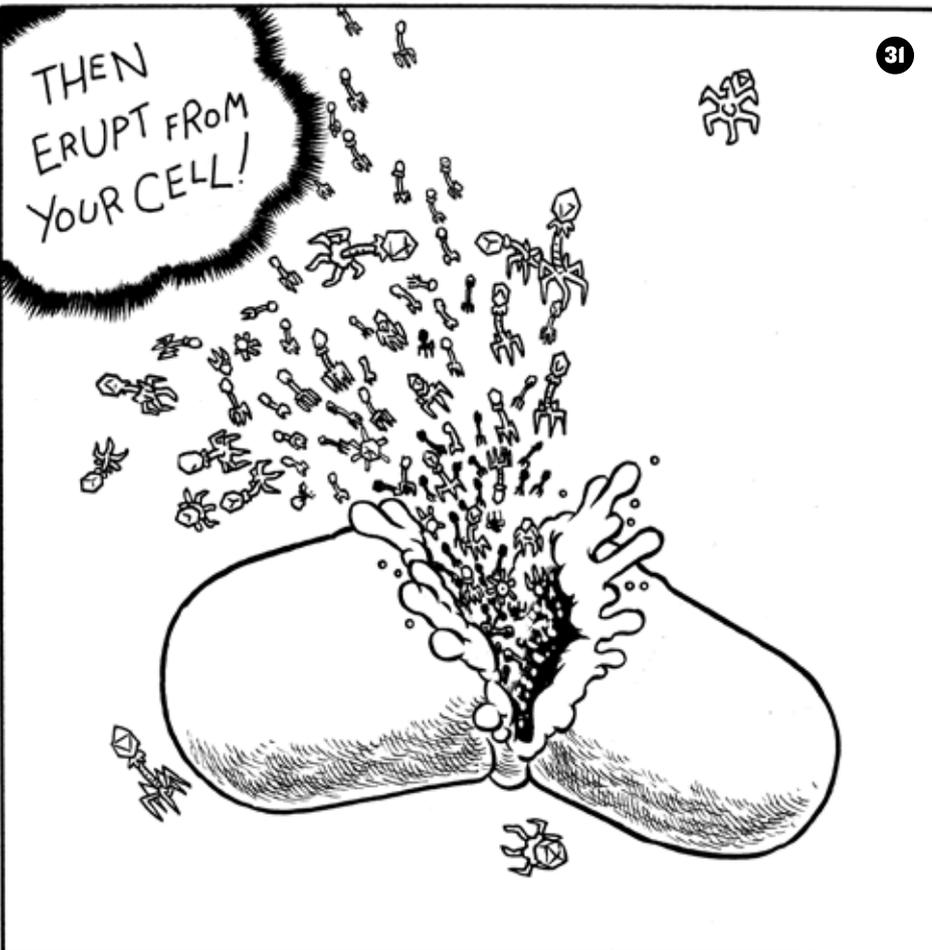
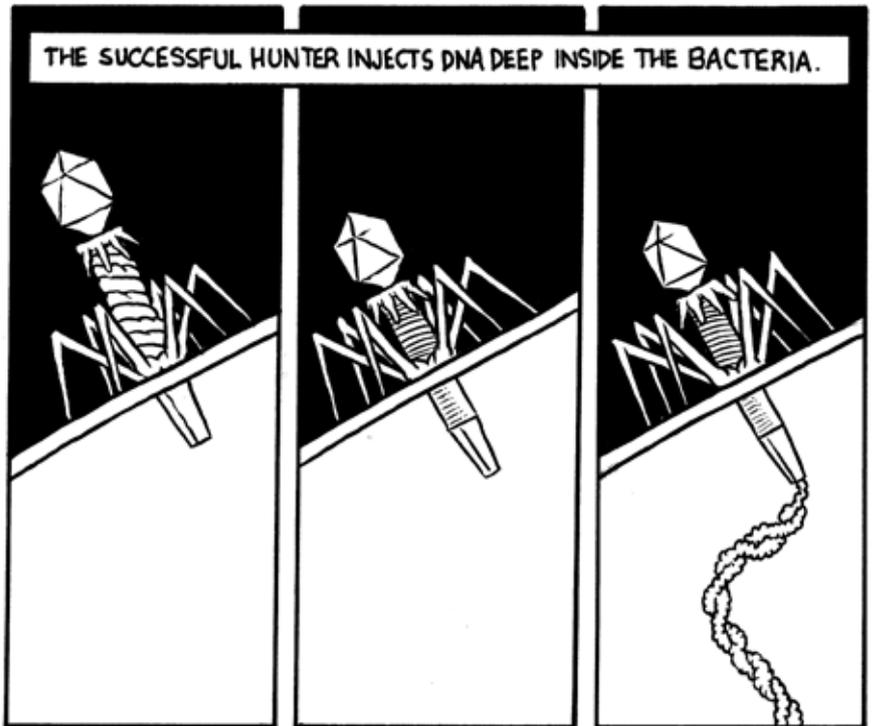
A PHAGE LANDS ON ITS PREY- WHICH IS COVERED IN UNIQUE RECEPTORS.

THE RECEPTORS ARE A KIND OF LOCK... 30

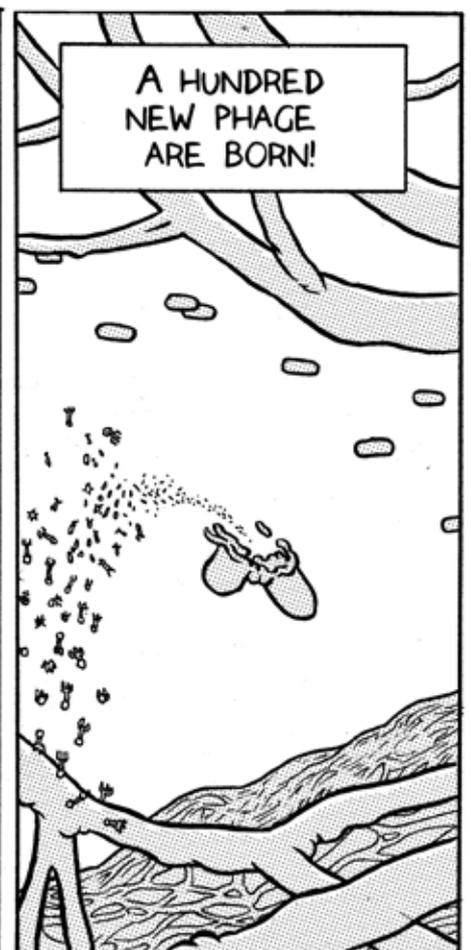
... TO WHICH THIS PHAGE HAS THE KEY.

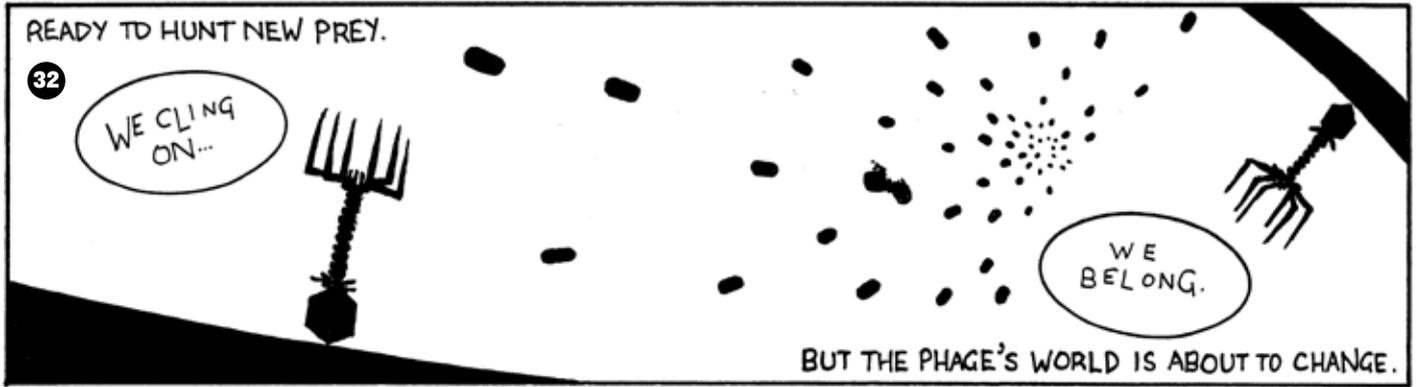


THE SUCCESSFUL HUNTER INJECTS DNA DEEP INSIDE THE BACTERIA.



31





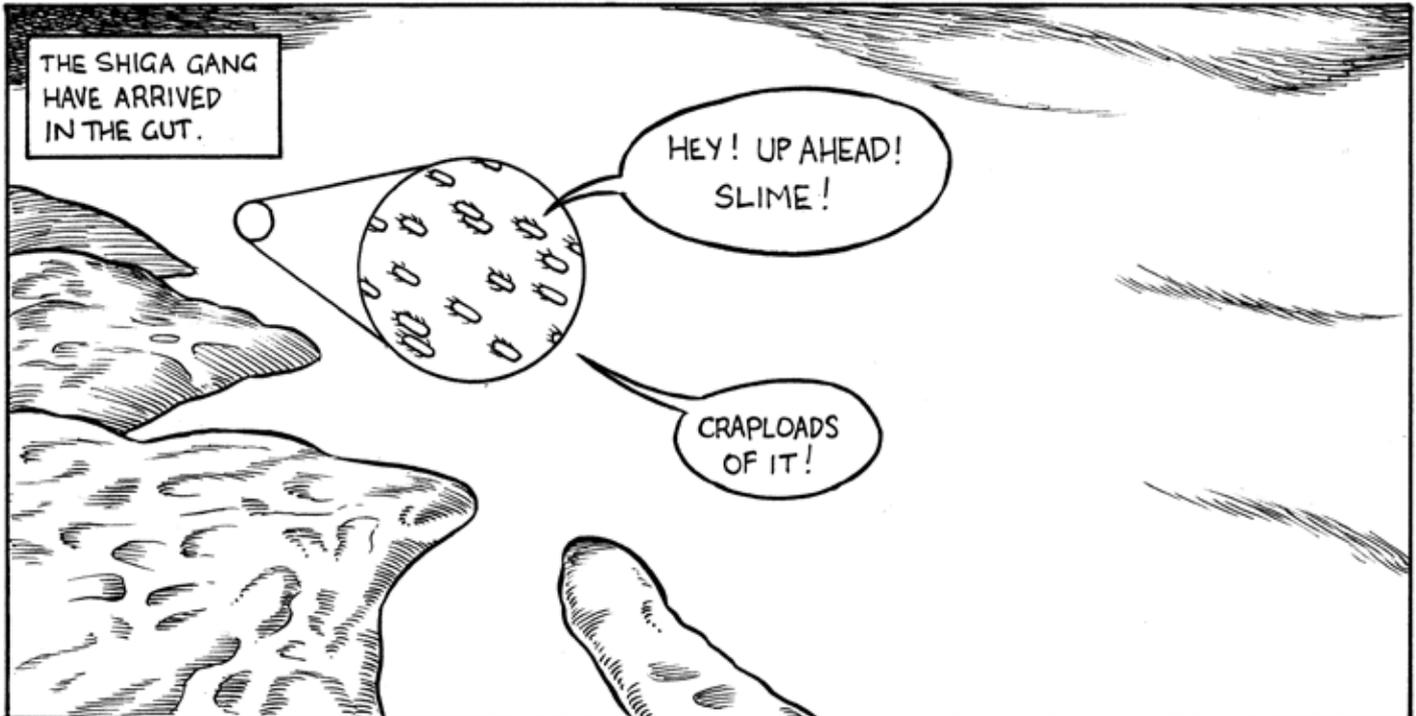
READY TO HUNT NEW PREY.

32

WE CLING ON...

WE BELONG.

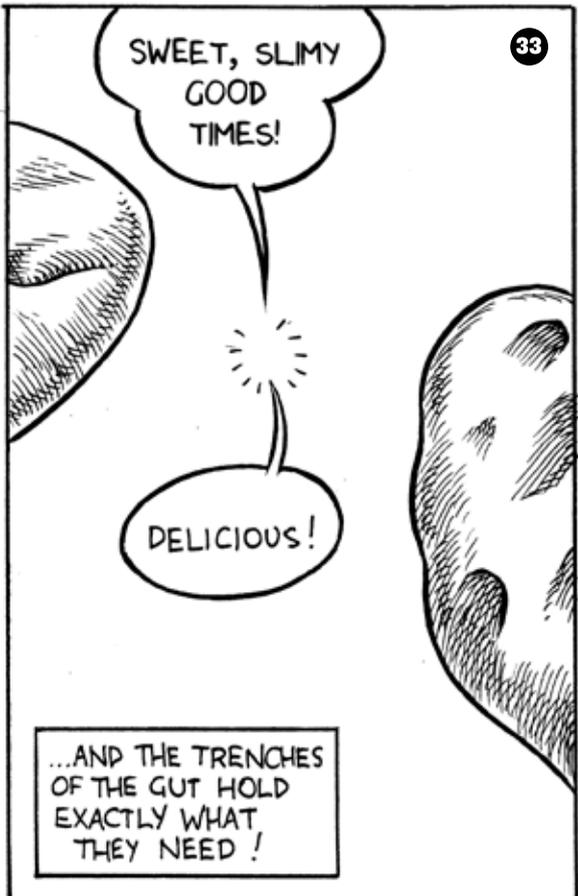
BUT THE PHAGE'S WORLD IS ABOUT TO CHANGE.



THE SHIGA GANG HAVE ARRIVED IN THE GUT.

HEY! UP AHEAD! SLIME!

CRAPLOADS OF IT!



SWEET, SLIMY GOOD TIMES!

DELICIOUS!

...AND THE TRENCHES OF THE GUT HOLD EXACTLY WHAT THEY NEED!

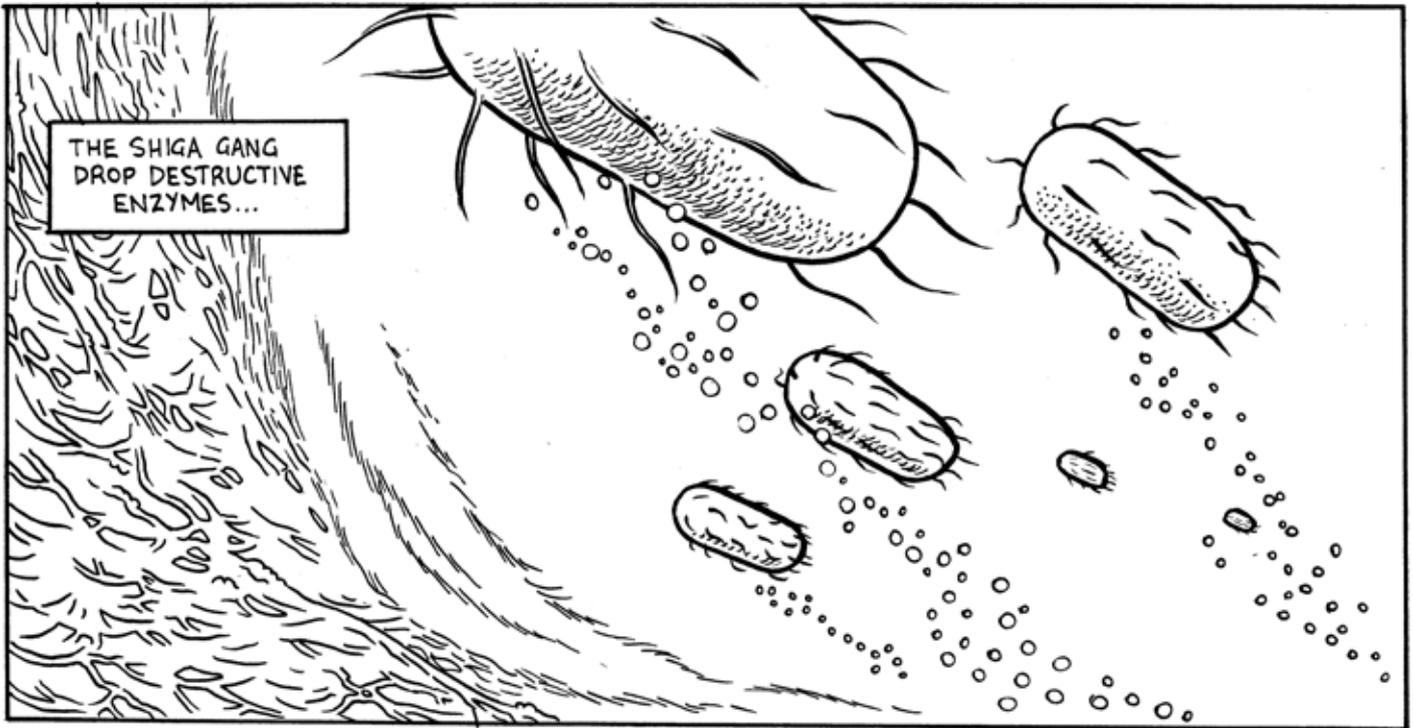
33



I'M GONNA DIG ME INTO A TRENCH RIGHT NOW!

34

LET'S FIND OURSELVES SOMEWHERE TO BREED!



THE SHIGA GANG
DROP DESTRUCTIVE
ENZYMES...



DISSOLVING THE PROTECTIVE
MUCUS...

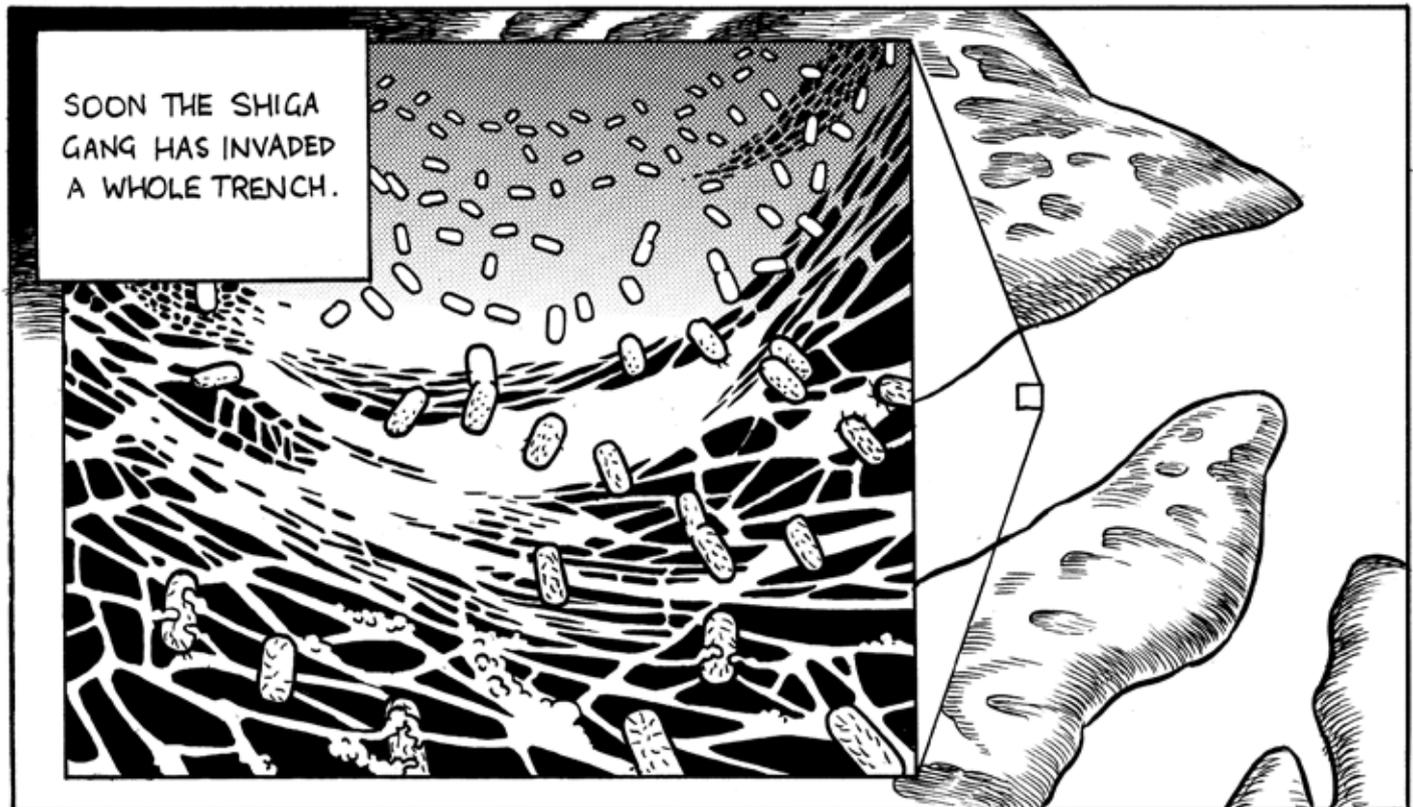


SEEKING A WAY THROUGH...

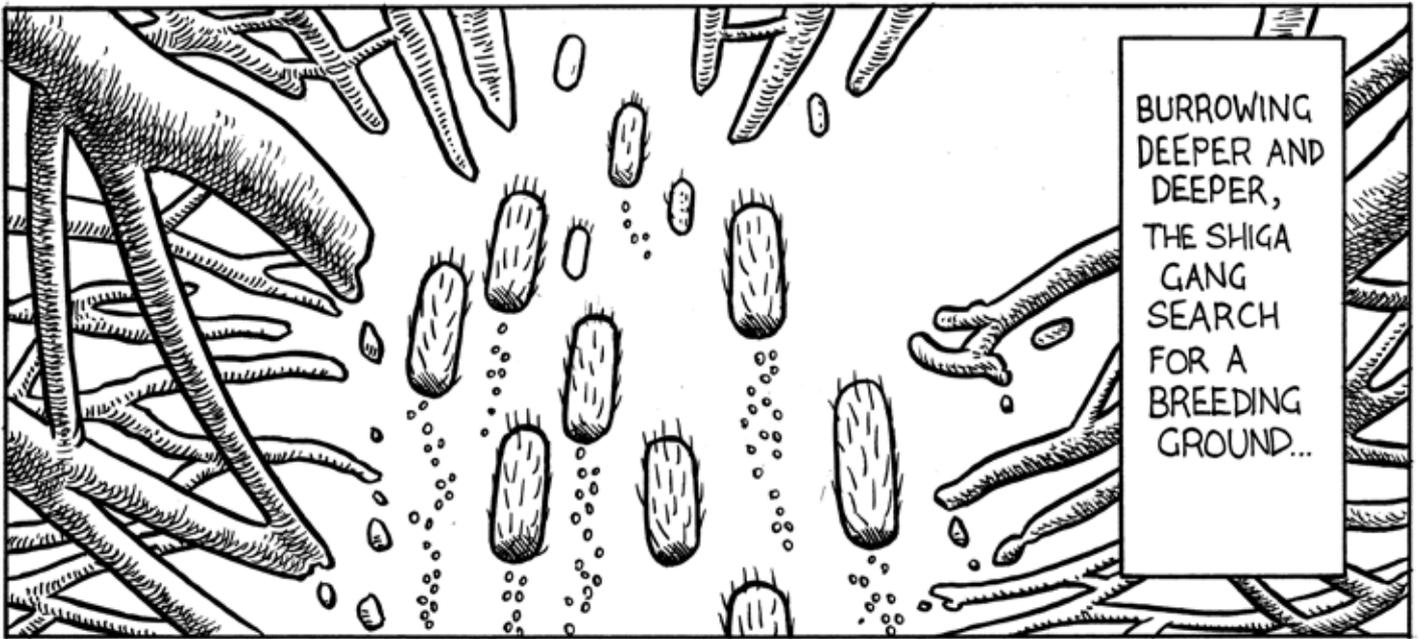


TO THE SKIN OF ANNIE'S
GUT.

35



SOON THE SHIGA
GANG HAS INVADDED
A WHOLE TRENCH.



BURROWING DEEPER AND DEEPER, THE SHIGA GANG SEARCH FOR A BREEDING GROUND...



WE HUNT...

BUT THE PHAGE ARE READY.

WE BIND...



WE SENSE...

WE FIND...



YOU INFECT, WE PROTECT!

A SINGLE, TINY
PODOPHAGE
VENTURES OUT
TO INFECT AN
INVADING
SHIGELLA.

ARE YOU SERIOUS!?
GOOD LUCK
PUNY DUDE!
YOU DON'T EVEN
KNOW ME!
HOW'RE YOU GONNA
ATTACK ME!

WE HUNT
FOR THE
LOCK - THE
WAY TO
UNBLOCK!

WE ROLL
WE SEEK...
WE ARE
STRONG,
YOU ARE
WEAK!

INCORRECT
KEY...
OUR PREY
GOES
FREE!

HA HA!
YOU PUNY
DUDES!

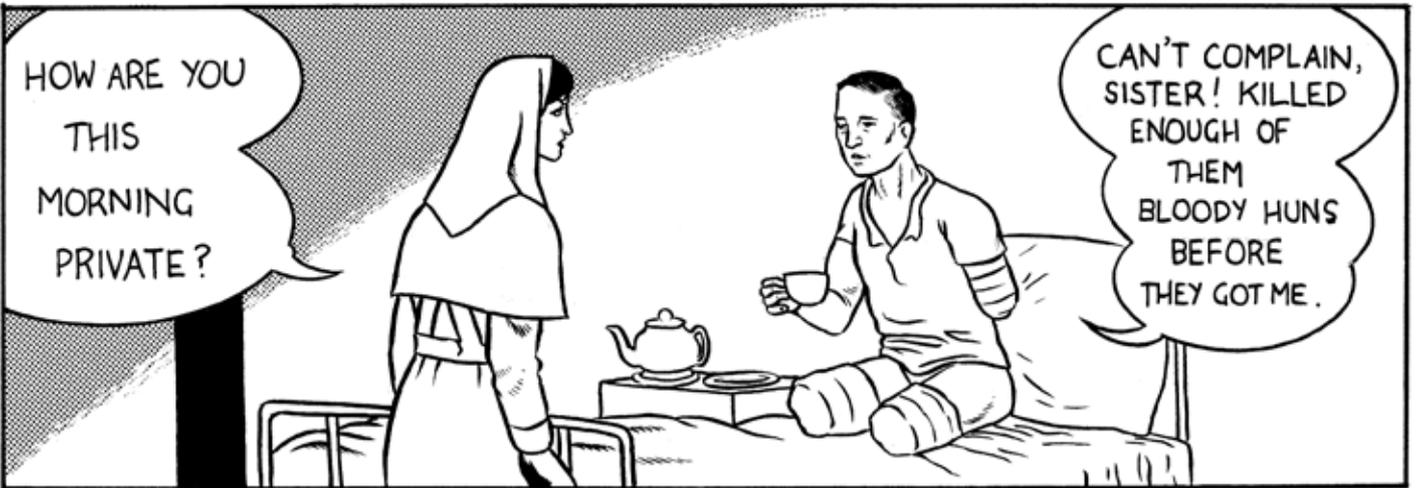
WE UPDATED
OUR LOCKS
MONTHS
AGO!

WRONG SHAPE!
OUR PREY
ESCAPES!

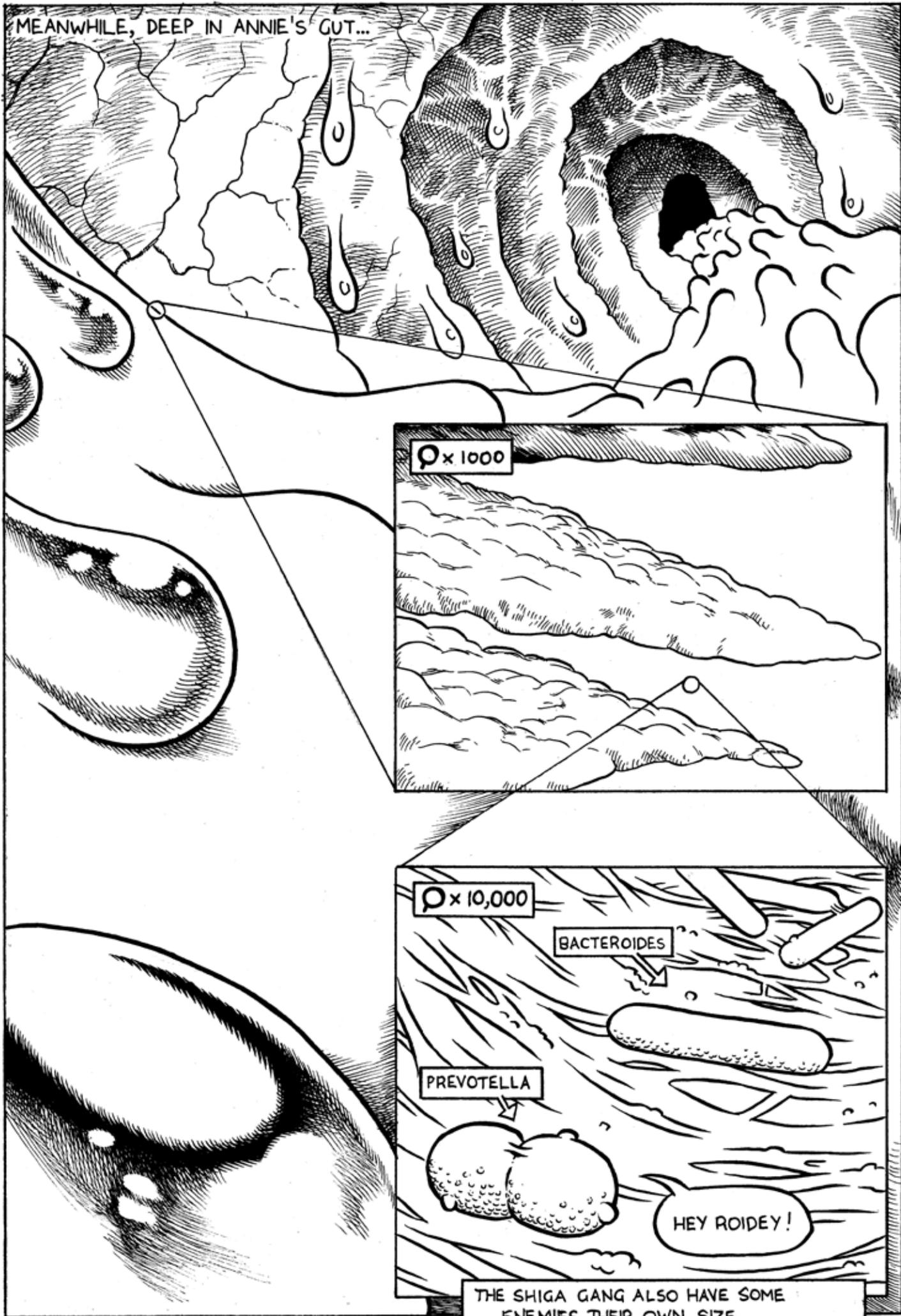
BUT NONE OF
THE PHAGE
HAVE A KEY TO
FIT THE SHIGA
LOCK. THEY ARE
HELPLESS.

MEANWHILE...





MEANWHILE, DEEP IN ANNIE'S GUT...



x 1000

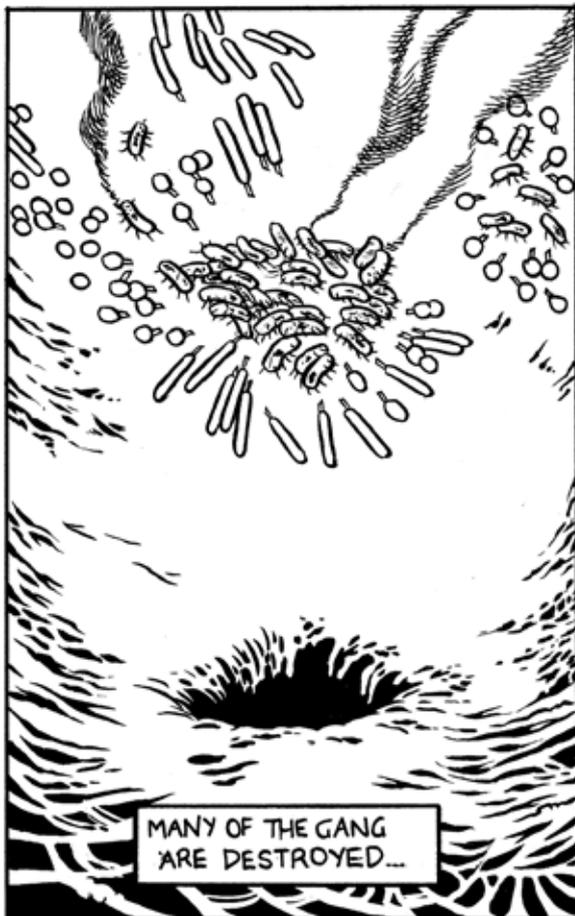
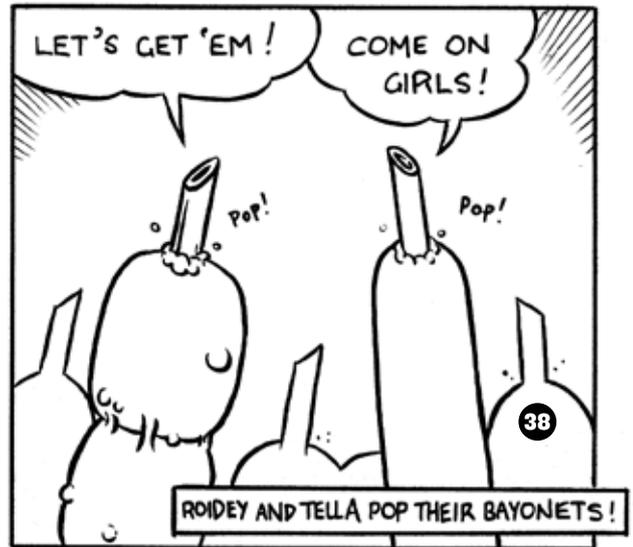
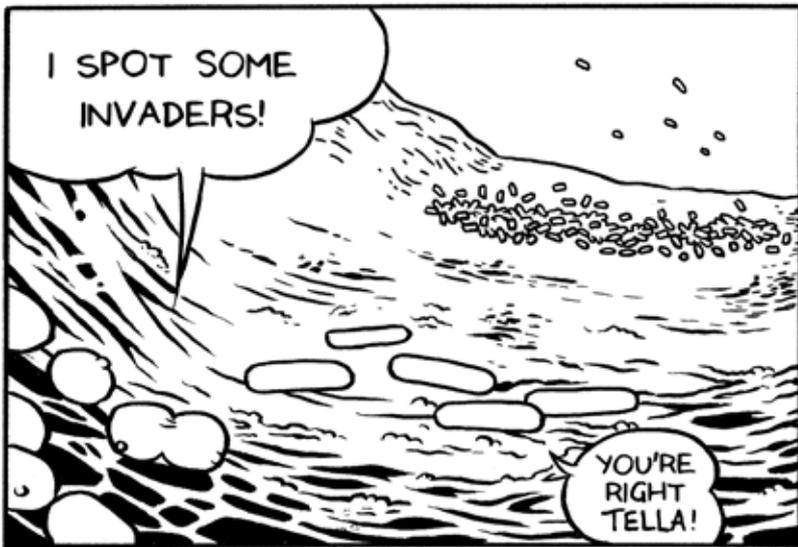
x 10,000

BACTEROIDES

PREVOTELLA

HEY ROIDEY!

THE SHIGA GANG ALSO HAVE SOME ENEMIES THEIR OWN SIZE...



IN FACT, ONE SHIGA HAS FINALLY REACHED THE SKIN OF THE GUT.

TOUCH DOWN!

EPITHELIAL CELL LINING ANNIE'S GUT

AND TRICKS THE CELL INTO OPENING UP!

39

OOH! NOW I KNOW WHAT THIS INJECTOR IS FOR!

OK WOW... DÉJÀ VU.

I SUDDENLY FEEL LIKE I KNOW EXACTLY WHAT TO DO...

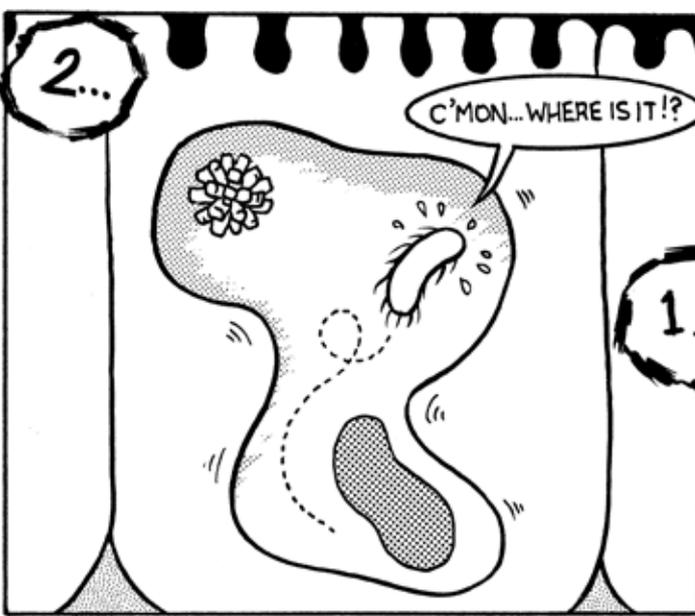
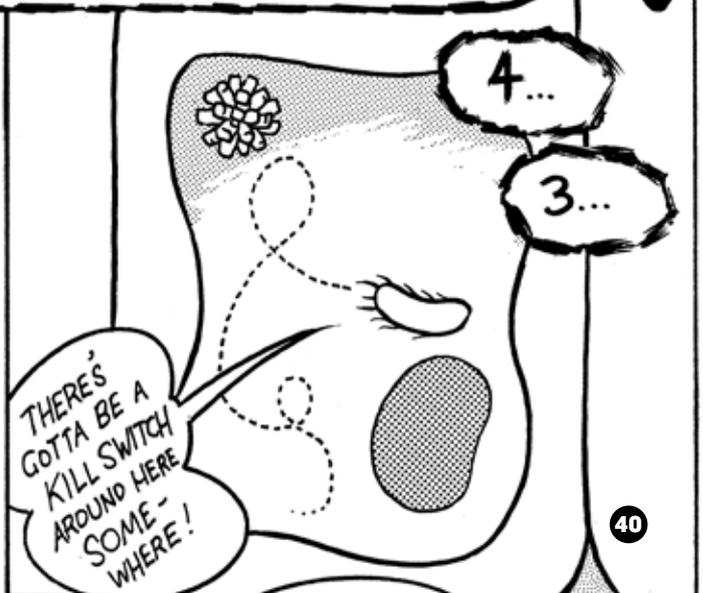
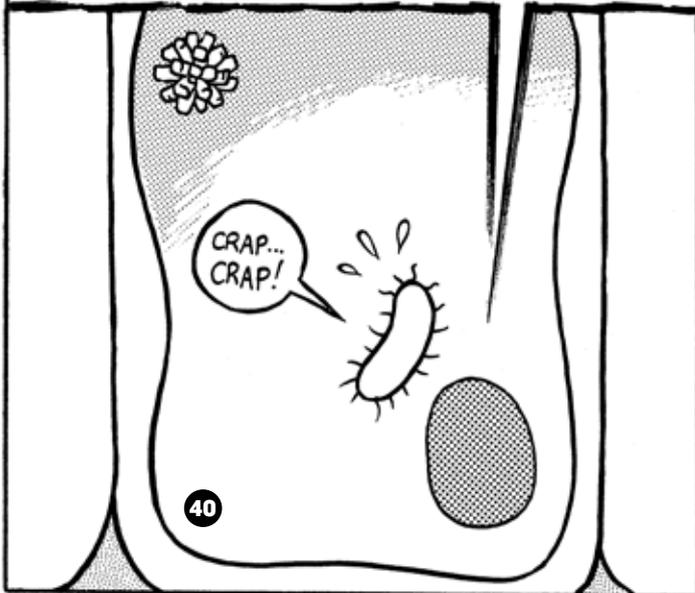
HERE I COME!

HA..I'VE TOTALLY GOT THIS.

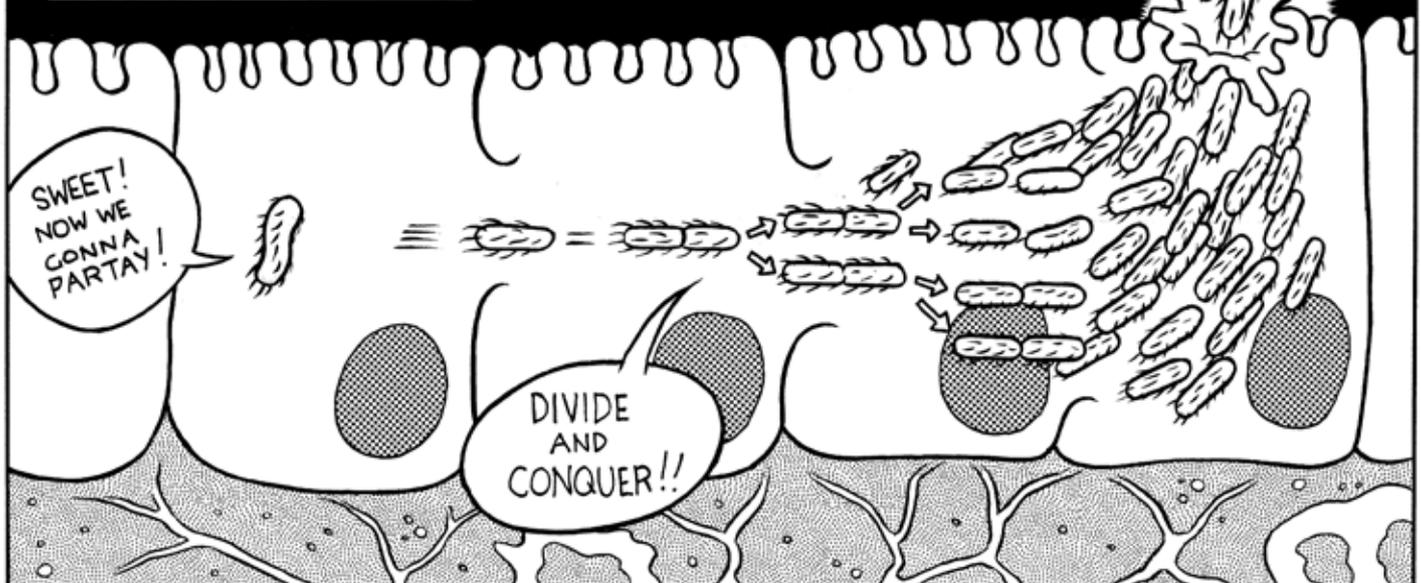
HERE WE GO.

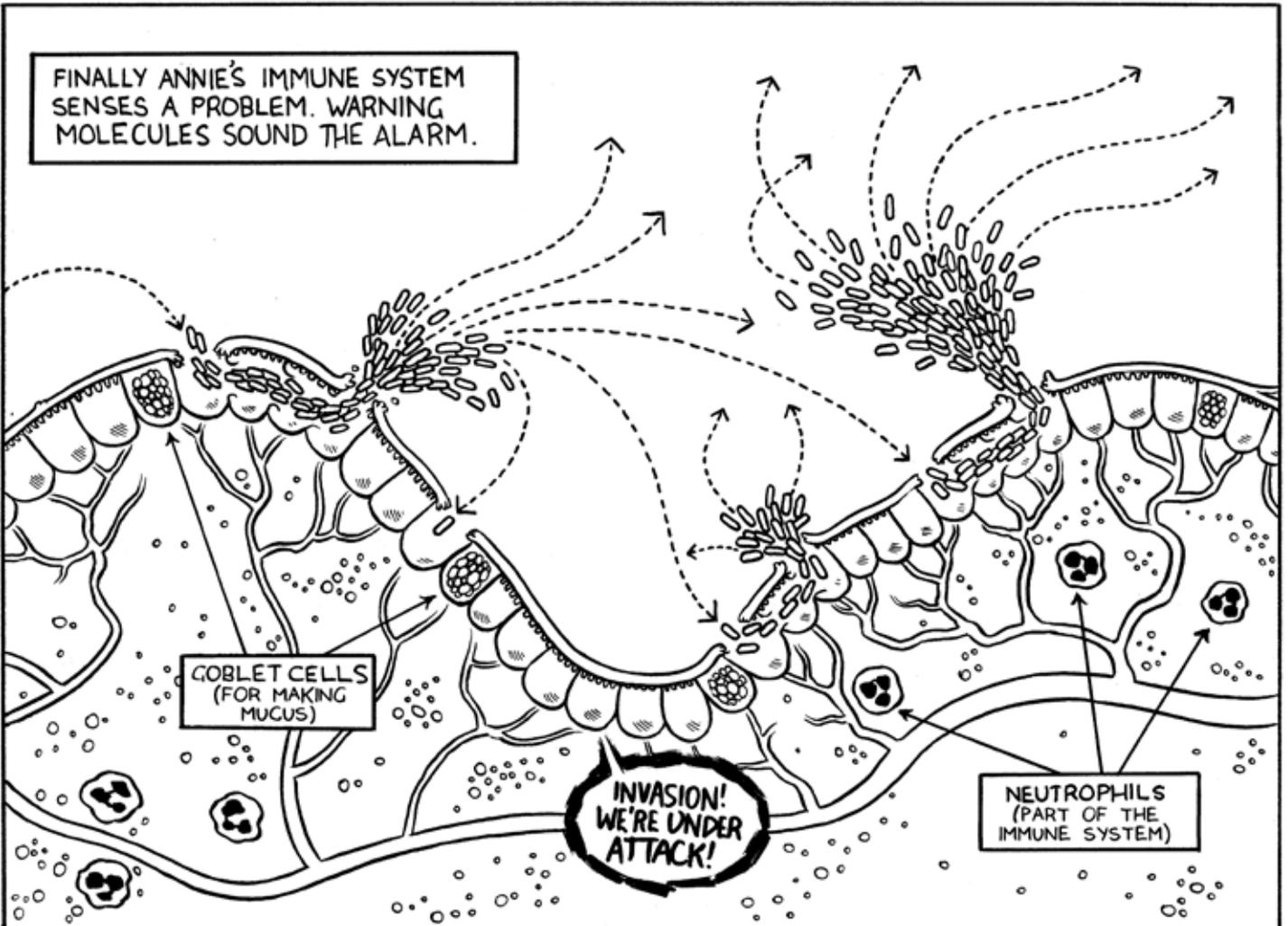
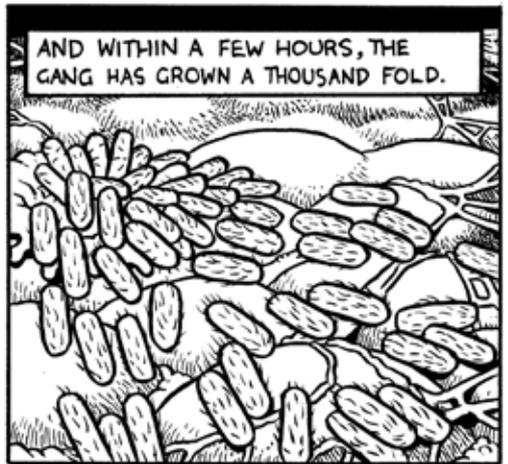
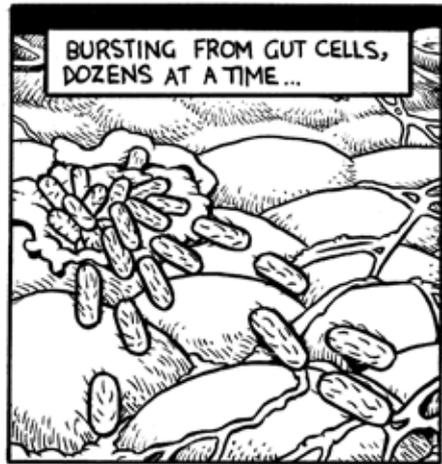
DOWN DOWN...

INVADER DETECTED! THIS CELL WILL SELF DESTRUCT IN 5...



AFTER THEIR ARDUOUS JOURNEY, THE SHIGA BEGIN TO BREED MORE GANG MEMBERS.







NEUTROPHILS

PROTECTIVE NEUTROPHILS SQUEEZE UP FROM UNDER THE CELLS RESPONDING TO THE ALARM MOLECULES.

REINFORCEMENTS REPORTING FOR DUTY!

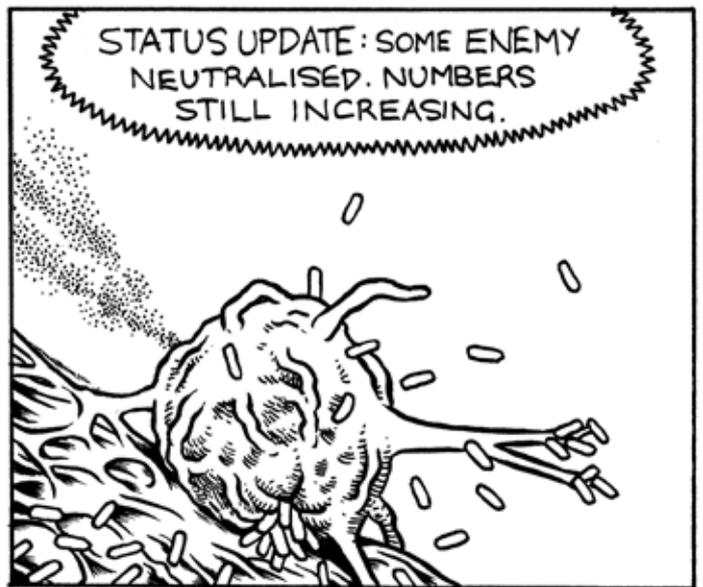
41



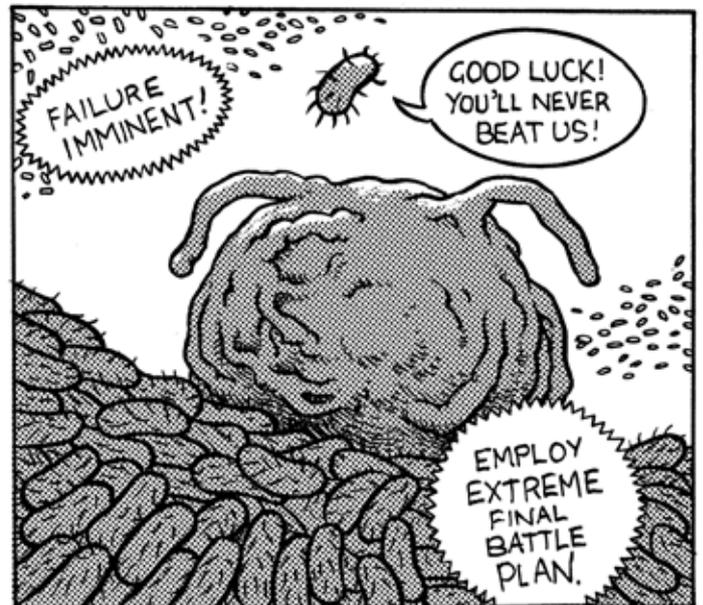
EMPLOYING PHAGOCYTOSIS DEFENCES.

YOU CAN KILL SOME OF US BUT WE'LL GET YOU IN THE END AAAARRGH!!

NEUTROPHILS ENGLUF THE SHIGA, DESTROYING THEM ONE BY ONE.



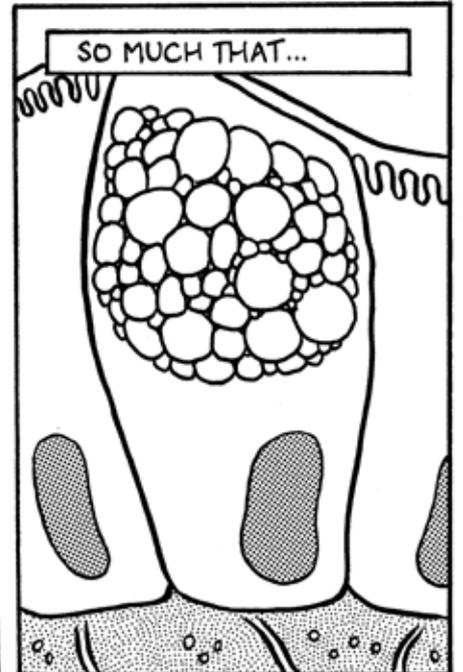
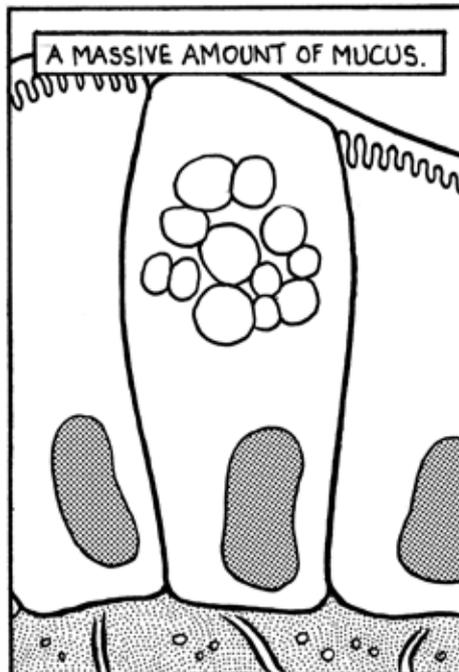
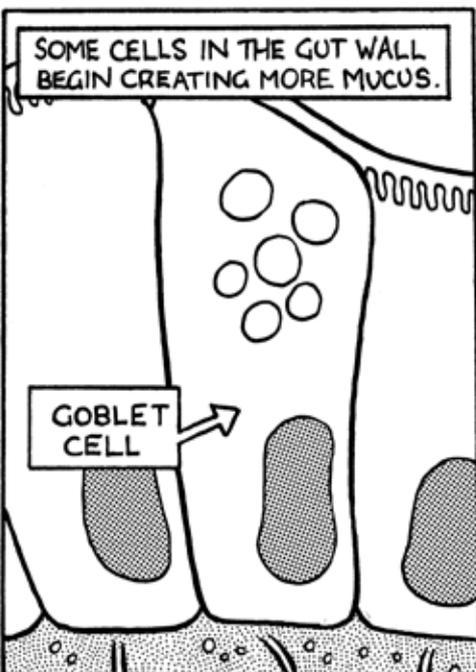
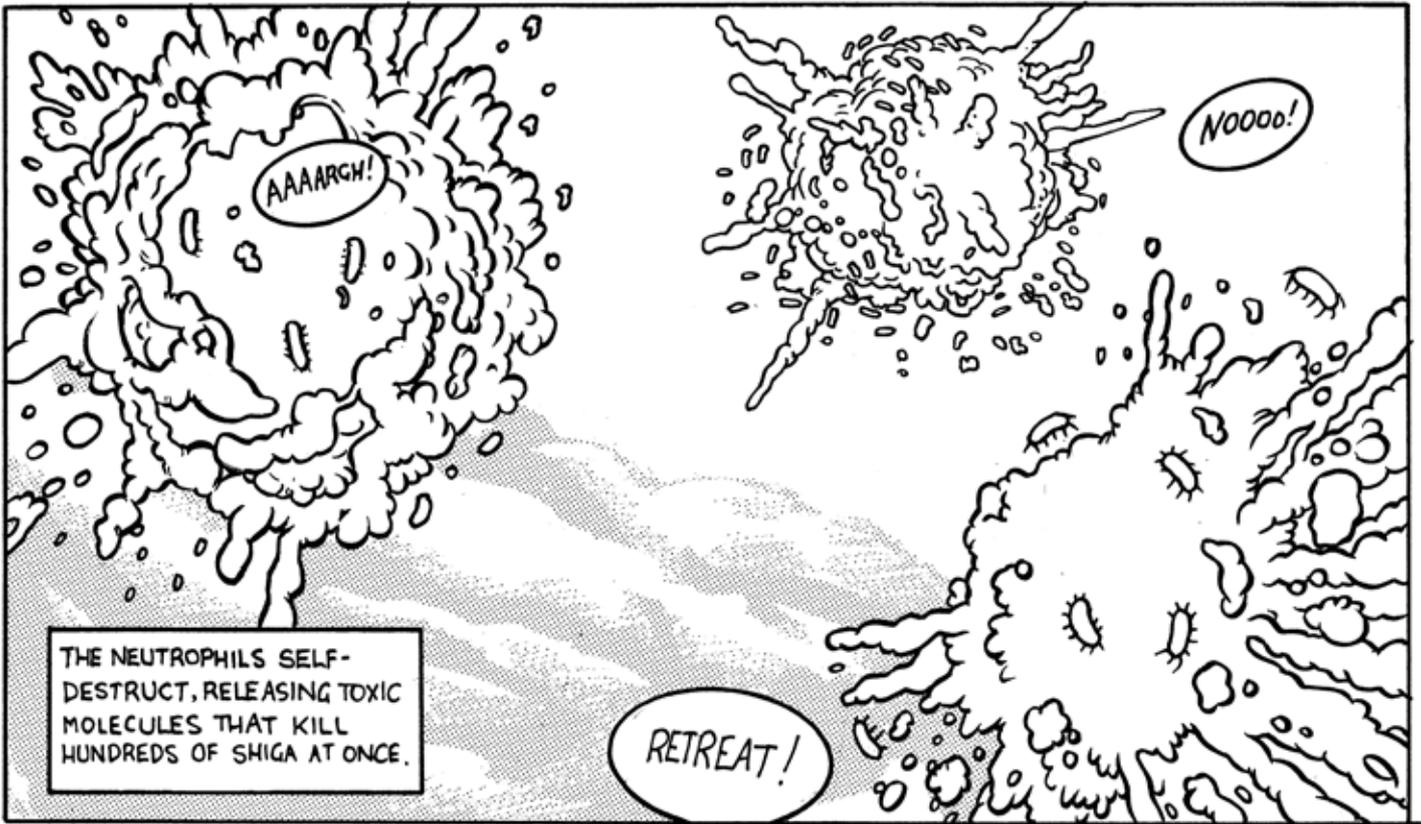
STATUS UPDATE: SOME ENEMY NEUTRALISED. NUMBERS STILL INCREASING.

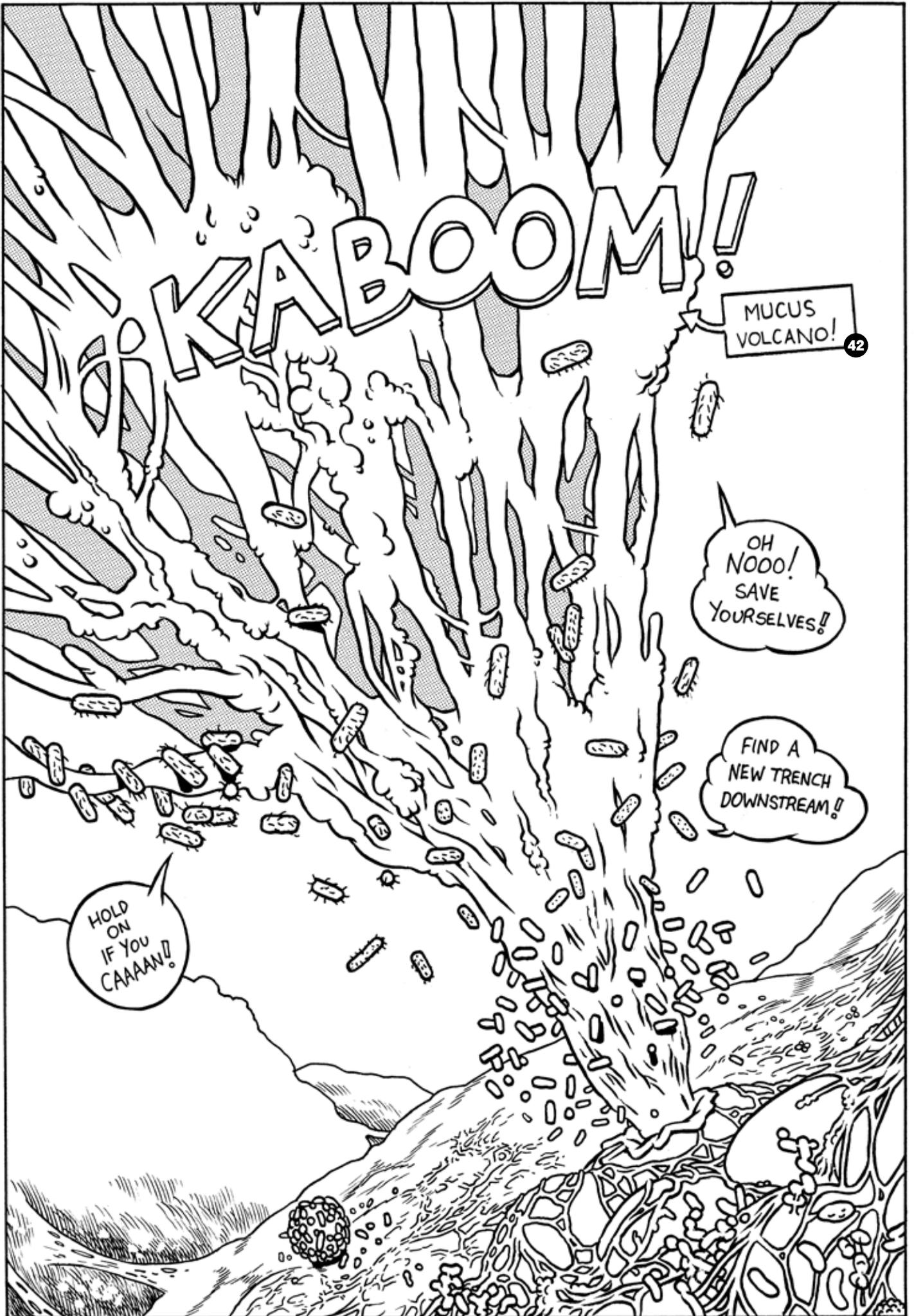


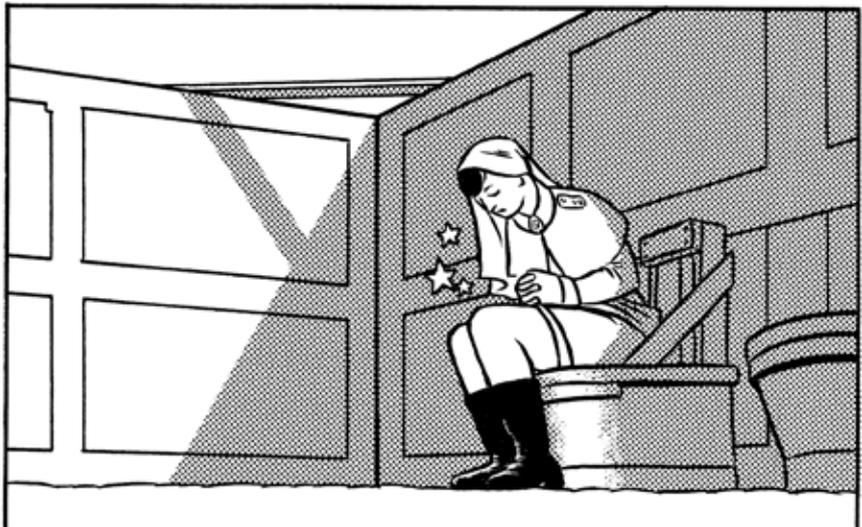
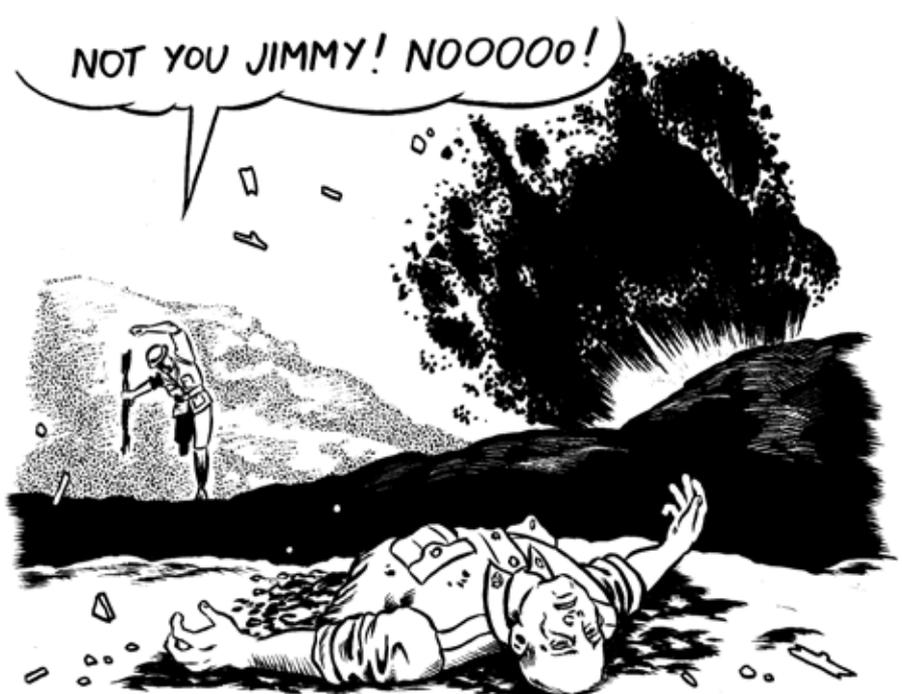
FAILURE IMMINENT!

GOOD LUCK! YOU'LL NEVER BEAT US!

EMPLOY EXTREME FINAL BATTLE PLAN.

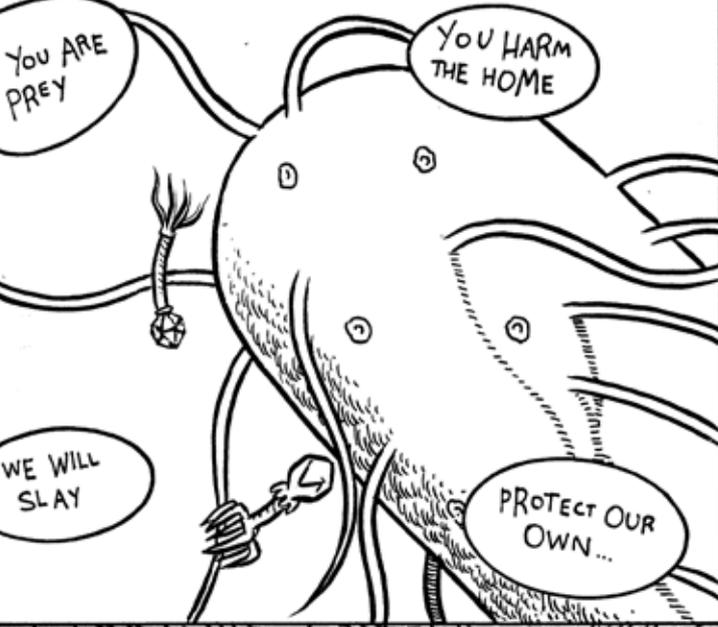






THROUGHOUT ANNIE'S GUT,
CONDITIONS ARE WORSENING.
VOLCANOES OF MUCUS
CONTINUALLY ERUPT,
DESPERATELY TRYING TO
ERADICATE THE SHIGA GANG.

OUR TINY HEROES CONTINUE TO ATTACK THE SHIGA...



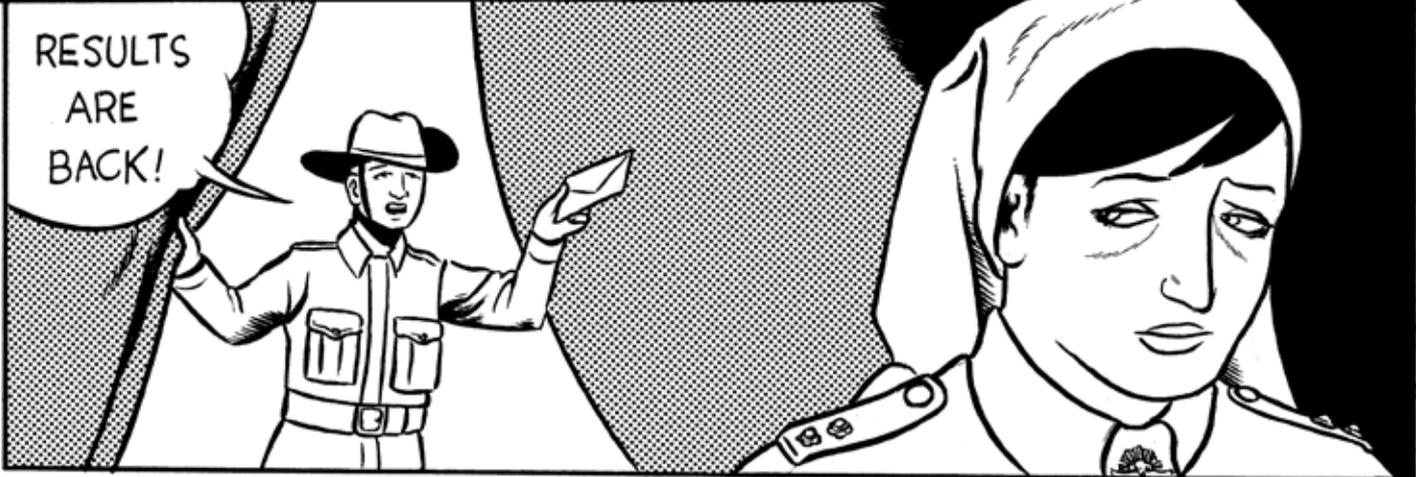
I REGRET NOTHING!

AAAH!

KA-BOOM!



DESPITE HER WRETCHED DISCOMFORT, ANNIE KEEPS ON WORKING.



RESULTS ARE BACK!

PRIVATE ROBBINS
DIAGNOSIS CONFIRMED.
DYSENTERY FLEXNER.
HIGH COMMAND HAS
BEEN NOTIFIED.



ANNIE SEEKS PRIVATE ROBBINS,
ONLY TO FIND...

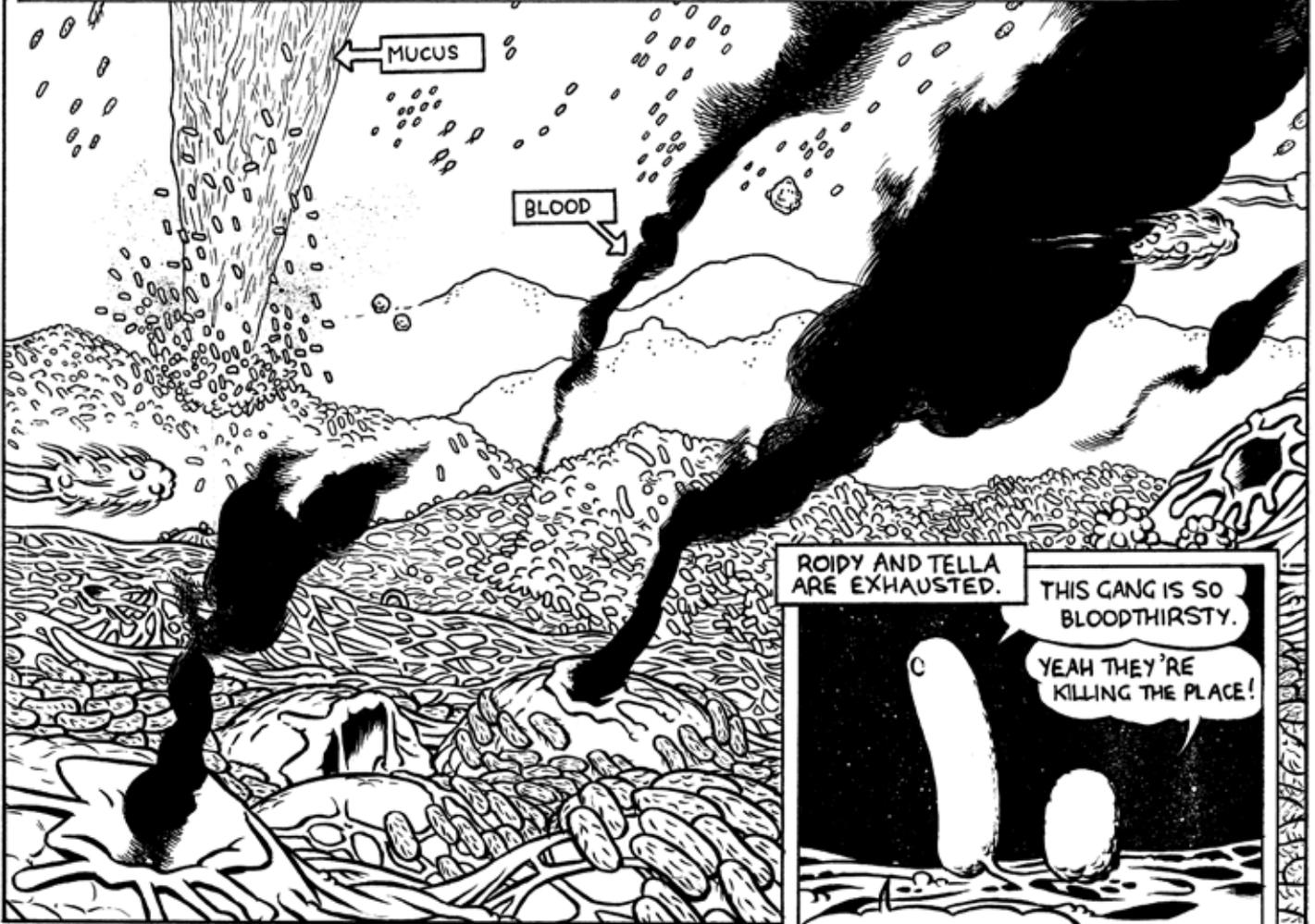


WE LOST YOU.
GOODBYE PRIVATE.
I PROMISE I'LL WRITE TO YOUR MOTHER.



PLEASE NO BLOOD...
PLEASE NO BLOOD...

AS ANNIE PRAYS FOR HEALTH, HER GUT IS BEING REDUCED TO AN EXPLODING WASTELAND.



ROIDY AND TELLA ARE EXHAUSTED.

THIS GANG IS SO BLOODTHIRSTY.

YEAH THEY'RE KILLING THE PLACE!

BUT I'M TOO TIRED TO KEEP AFTER THEM.

THE PHAGE FEEL HOPELESS, BUT TOGETHER THEY COME UP WITH A PLAN...

THEY NEED TO FIND A NEW KEY TO FIT THE SHIGA LOCKS. BUT HOW...?

THIS LOCK IS NEW. WE NEED A KEY THAT BREAKS INTO THIS ENEMY.

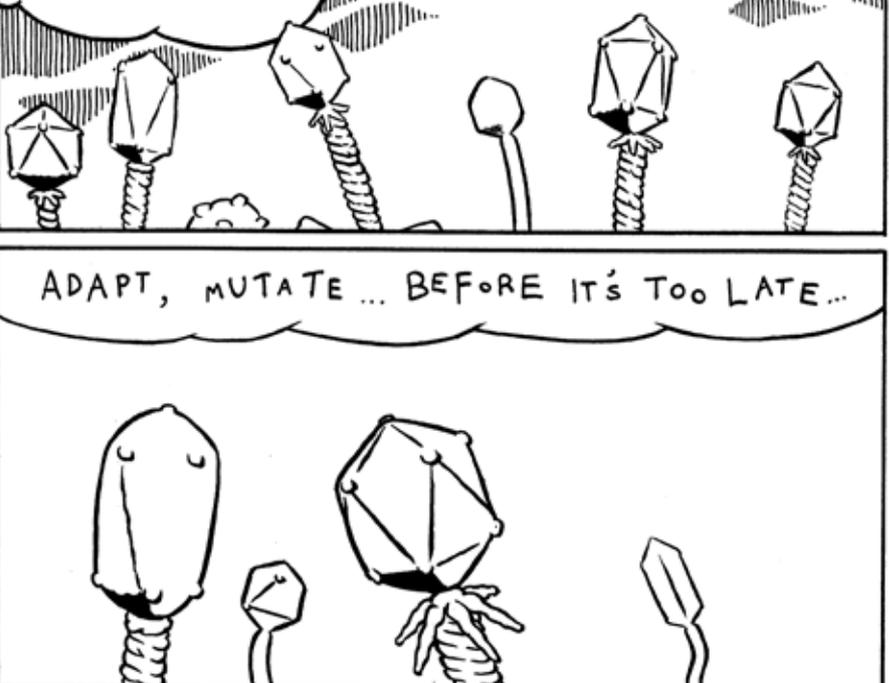
WE MUST BE CLEVER. WE MUST BE WARY. WE HAVE TO CHANGE. WE HAVE TO VARY.

HUNTING FAILS... FEAR PREVAILS.

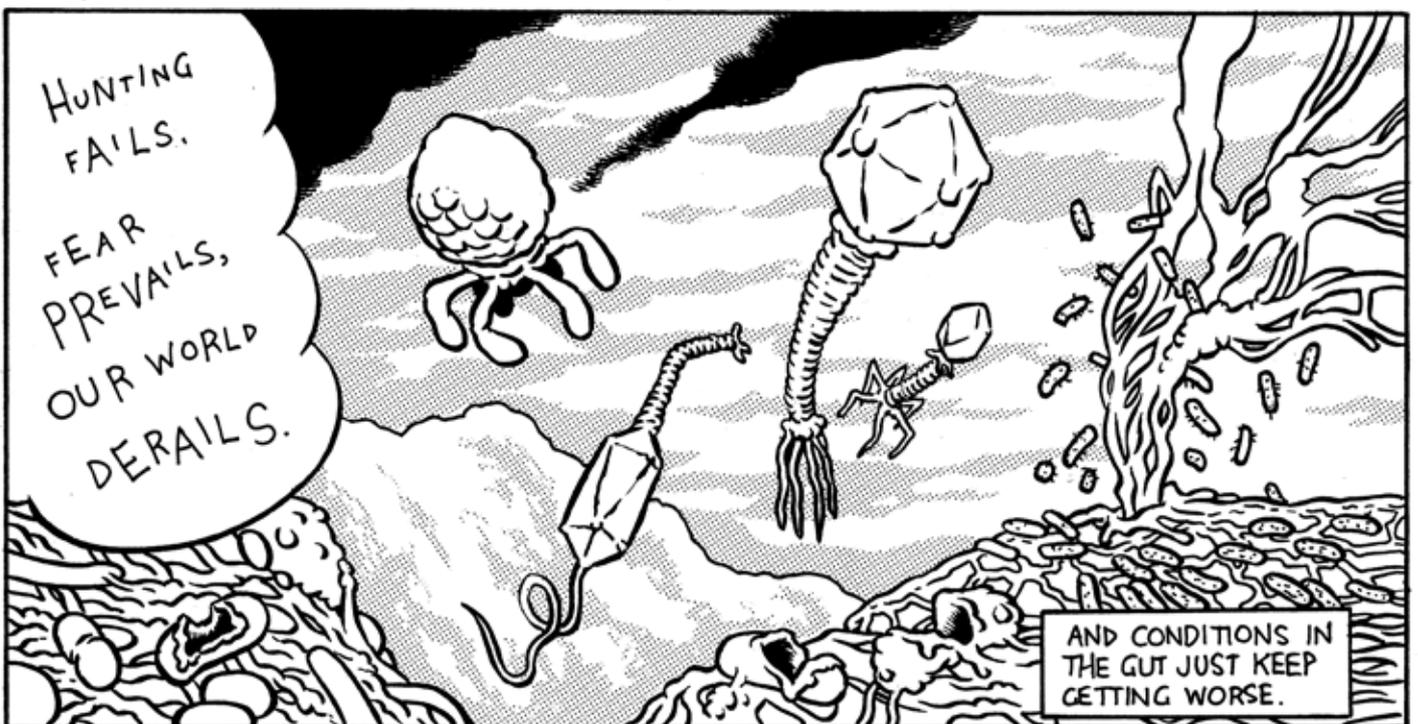
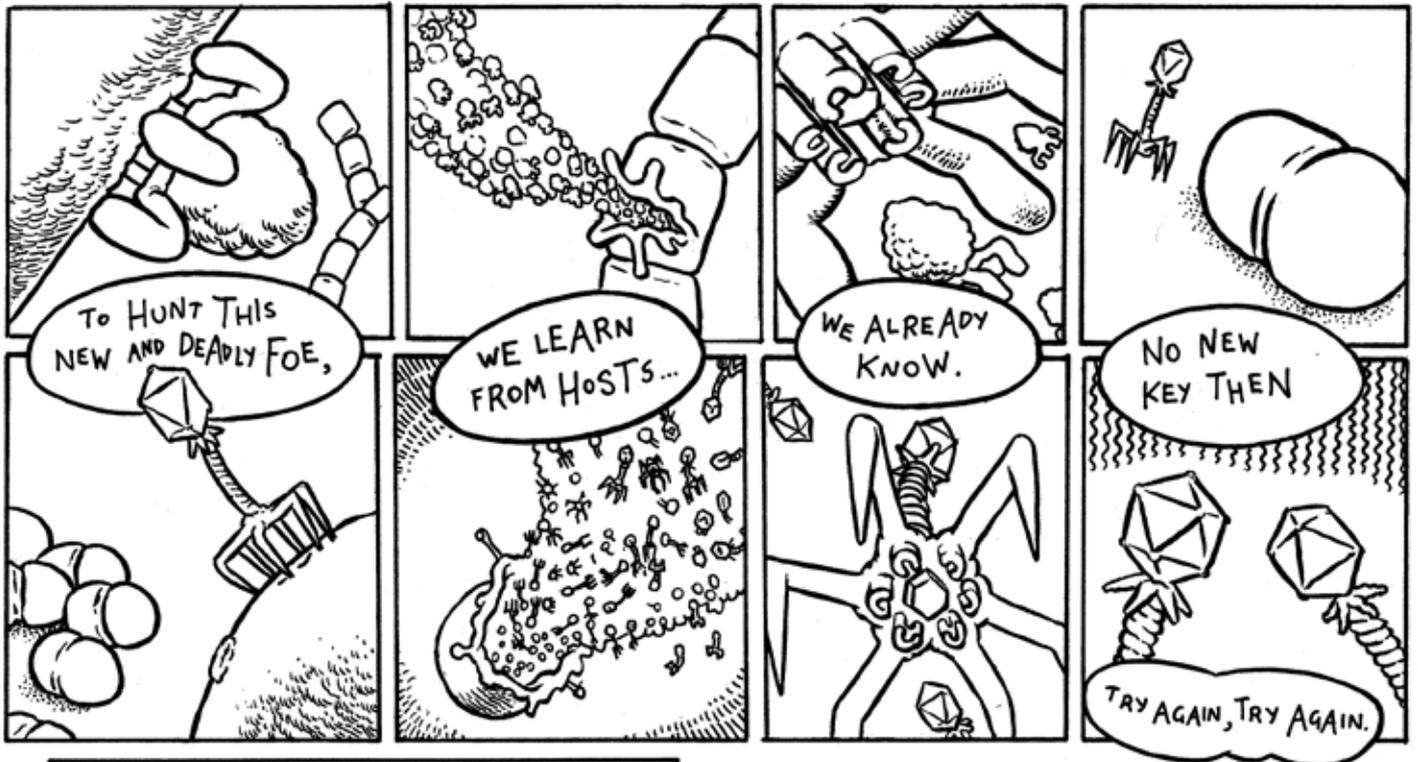
THEY TIP THE SCALES.

OUR WORLD DERAILS.

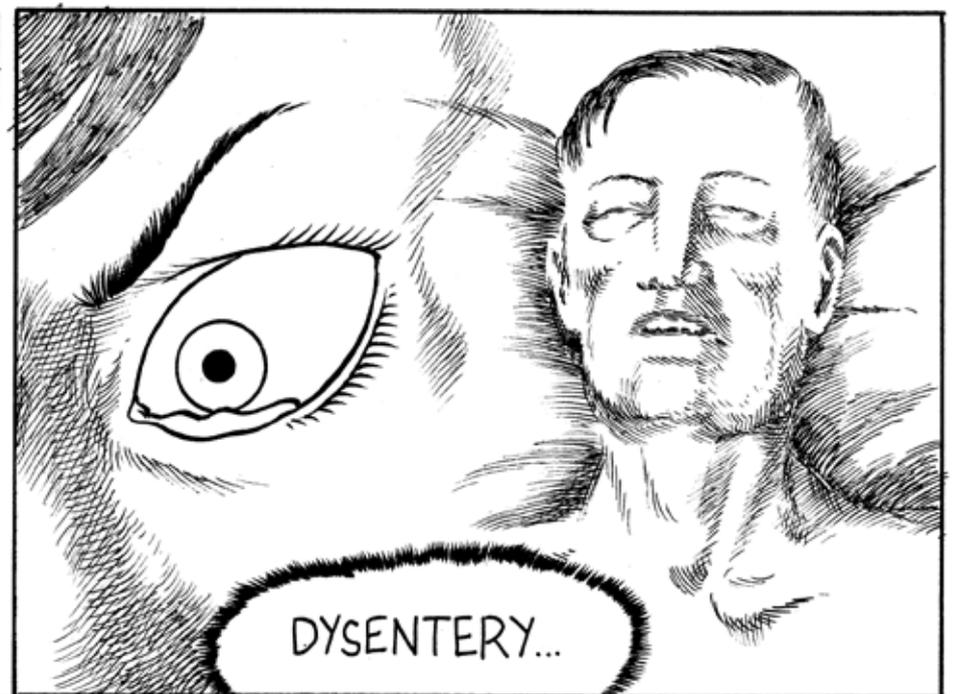
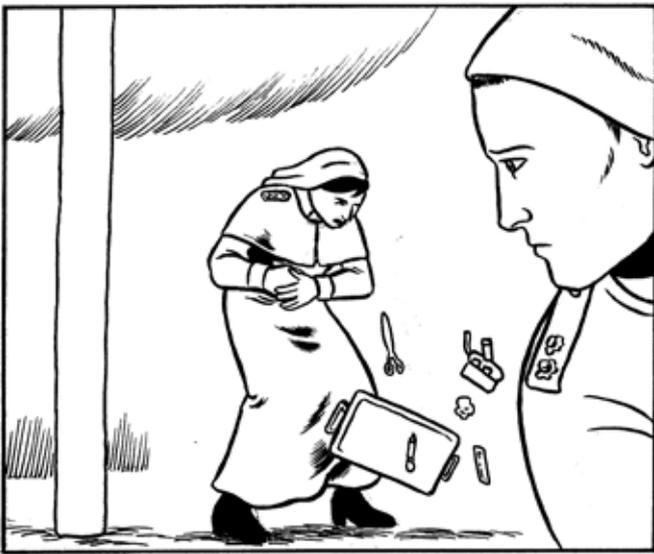
ADAPT, MUTATE ... BEFORE IT'S TOO LATE...

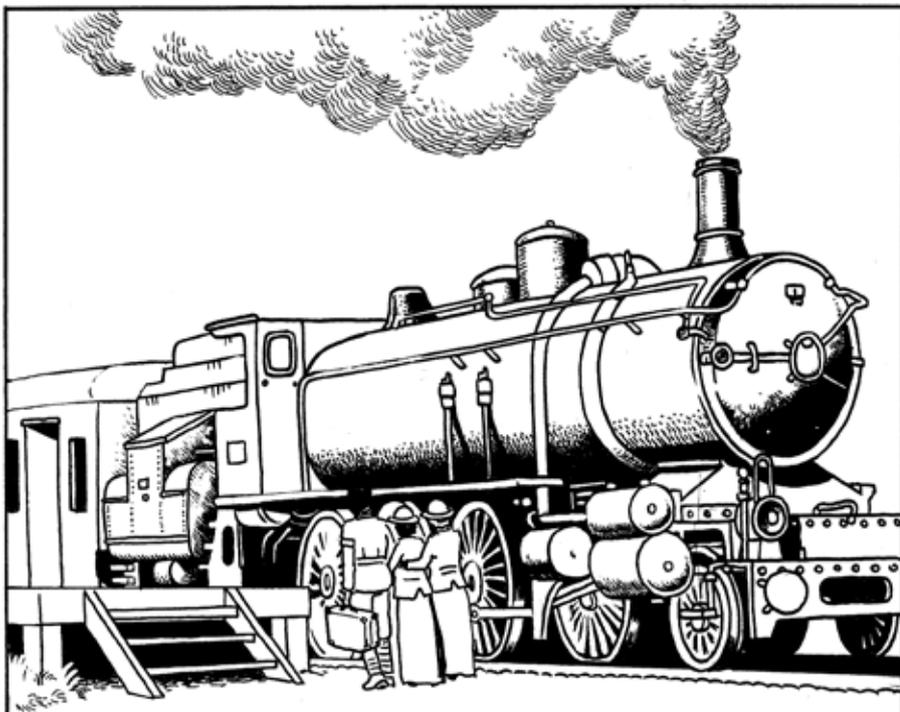
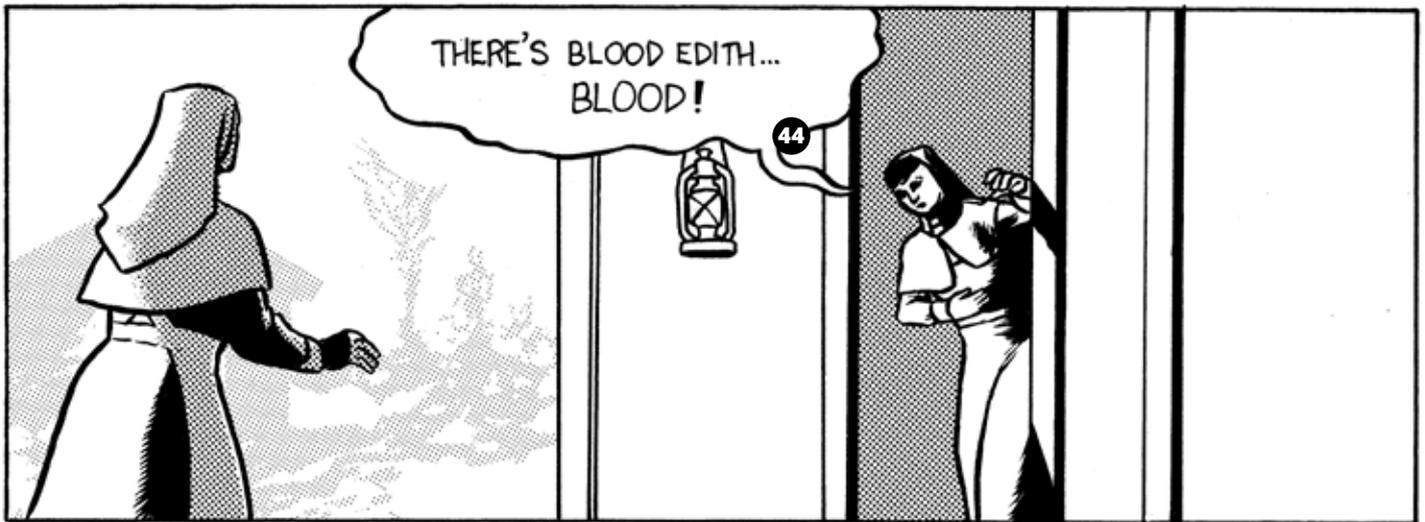


THE PHAGE REPLICATE QUICKLY, HOPING FOR A MUTANT KEY. THEY HUNT FAMILIAR PREY, INFECTING AND BREEDING OVER AND OVER AGAIN... BUT THEY FAIL.



AND CONDITIONS IN THE GUT JUST KEEP GETTING WORSE.









GRACE ? WHY ARE YOU HERE ? WHAT ABOUT THE BARGE ?



I'M ON DISCIPLINE FOR FLIRTING WITH LT. PERKINS. HE DIDN'T TELL ME HE WAS MARRIED...

BUT I'M ALLOWED TO LOOK AFTER YOU GIRLS.



I'M A MESS GRACE , SORRY.



DON'T WORRY DUCK, WE'VE BOTH DEALT WITH WORSE.



SO GRACE DOES ALL SHE CAN TO HELP HER FRIEND.



SLOW DOWN, DUCKIE.



SO THIRSTY...



SORRY, I NEED CHANGING AGAIN.



I TOLD YOU TO GO SLOW WITH THAT WATER.



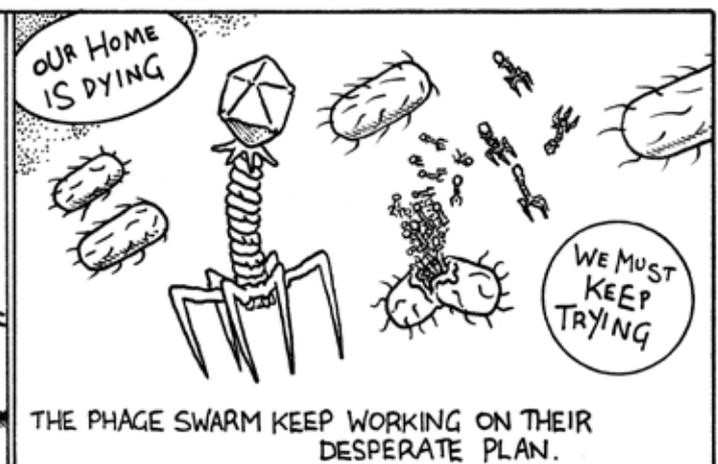
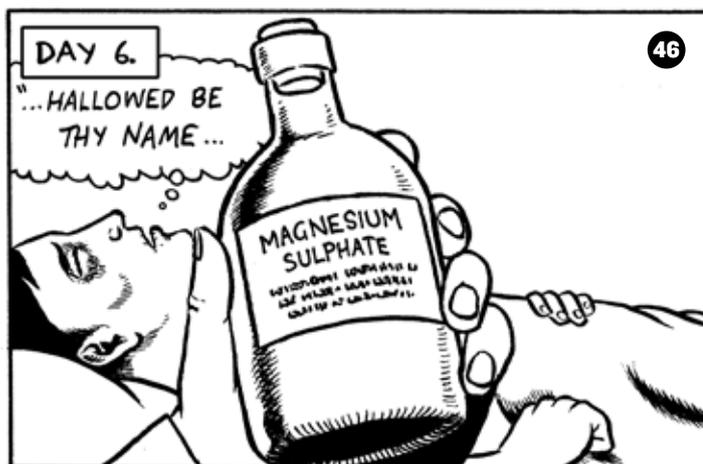
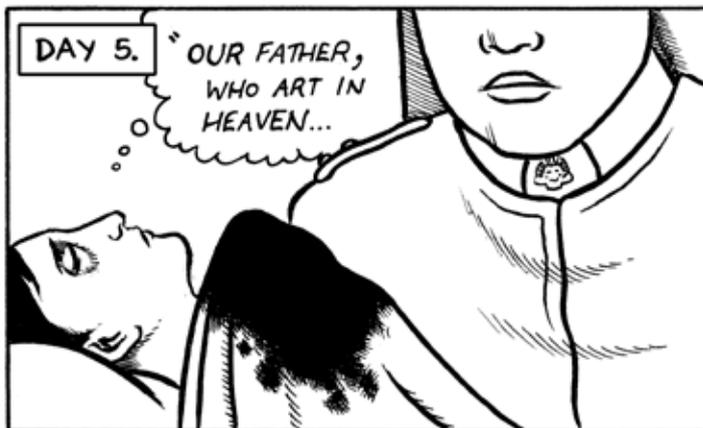
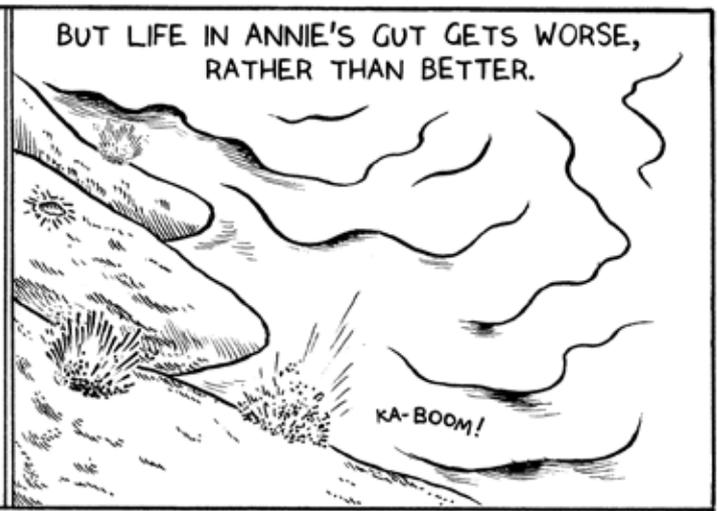
...THOUGH IT IS A SAD AND DISGUSTING JOB.

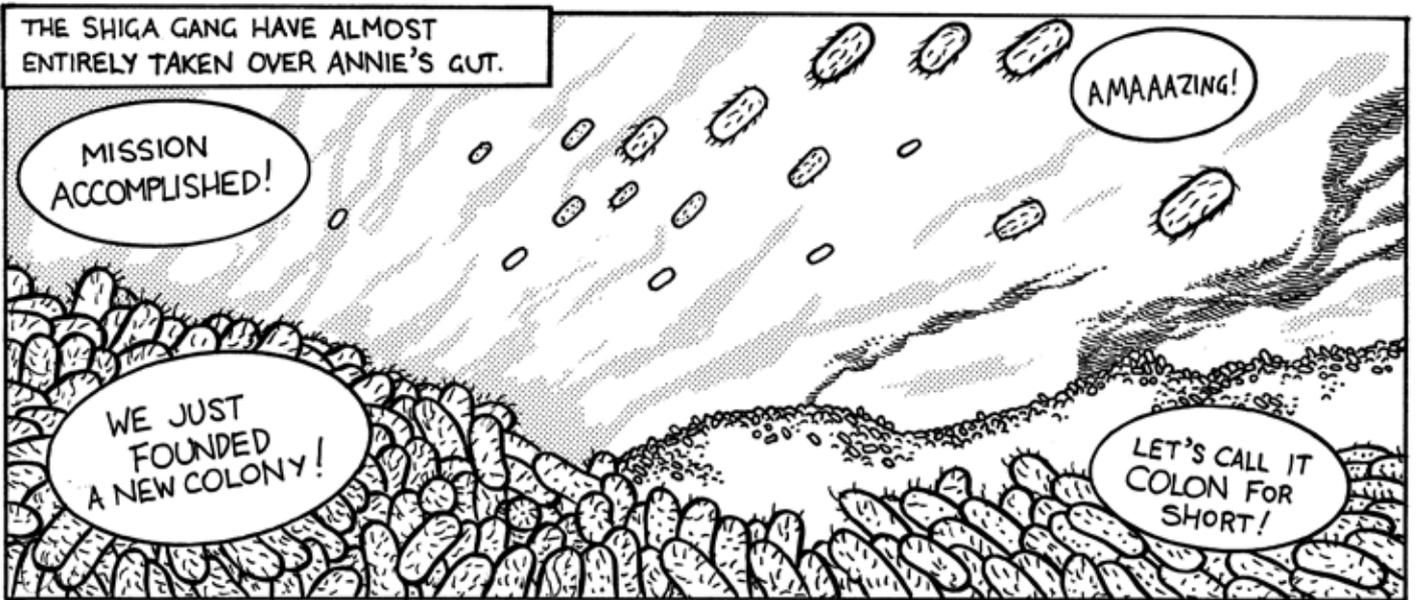
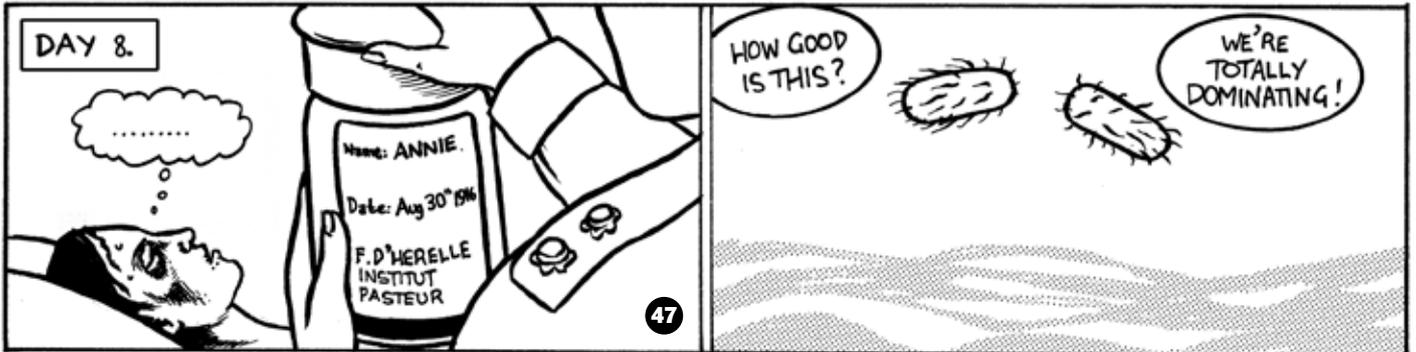


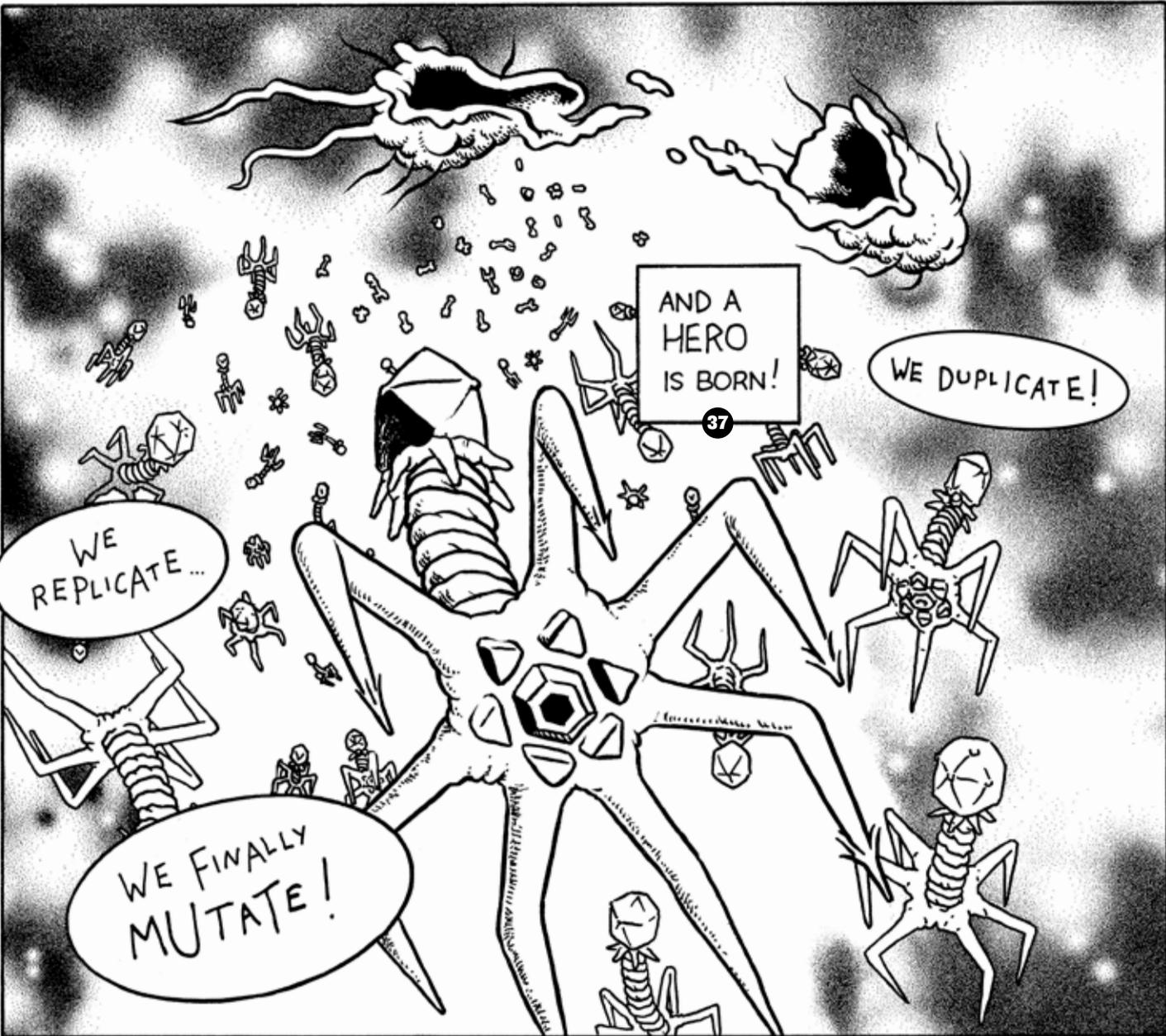
JUST A SIP.

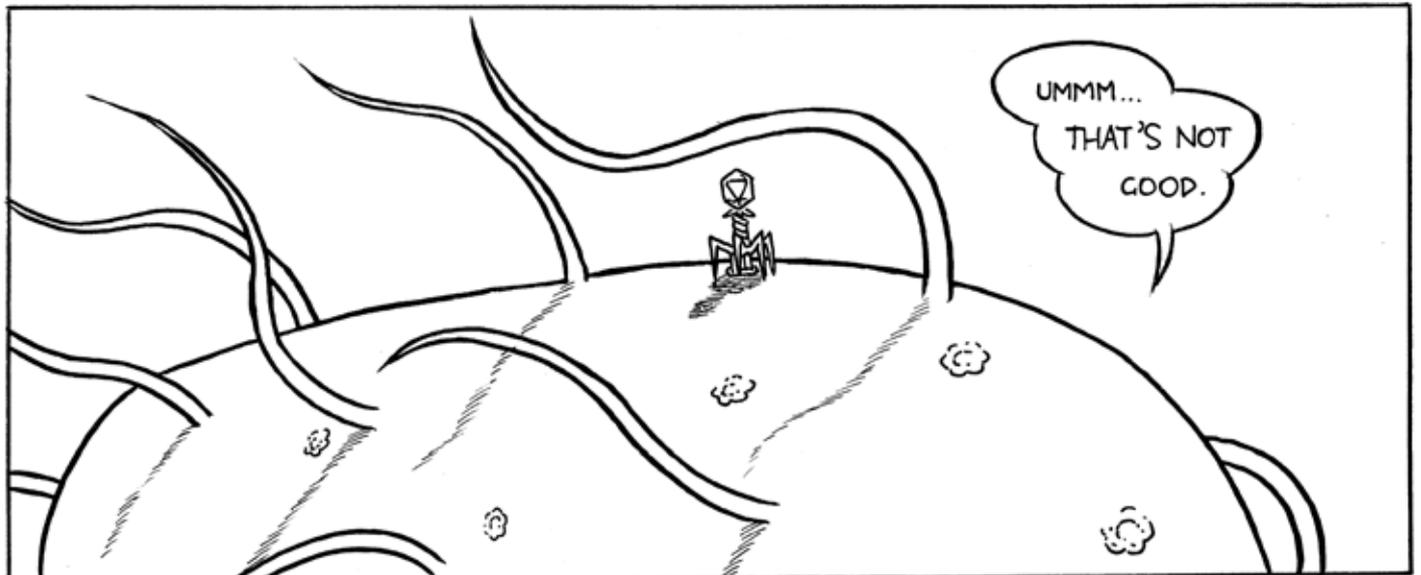
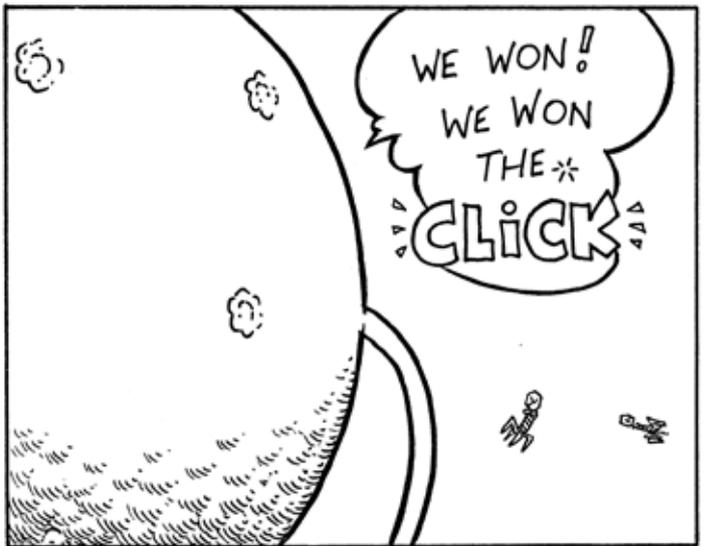
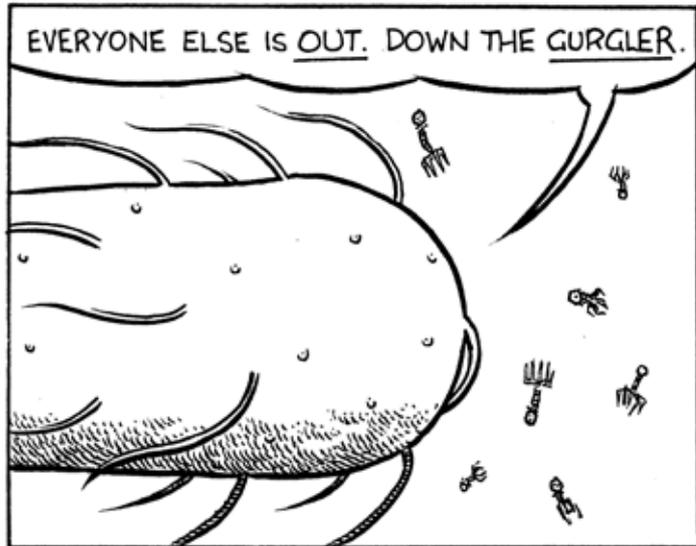
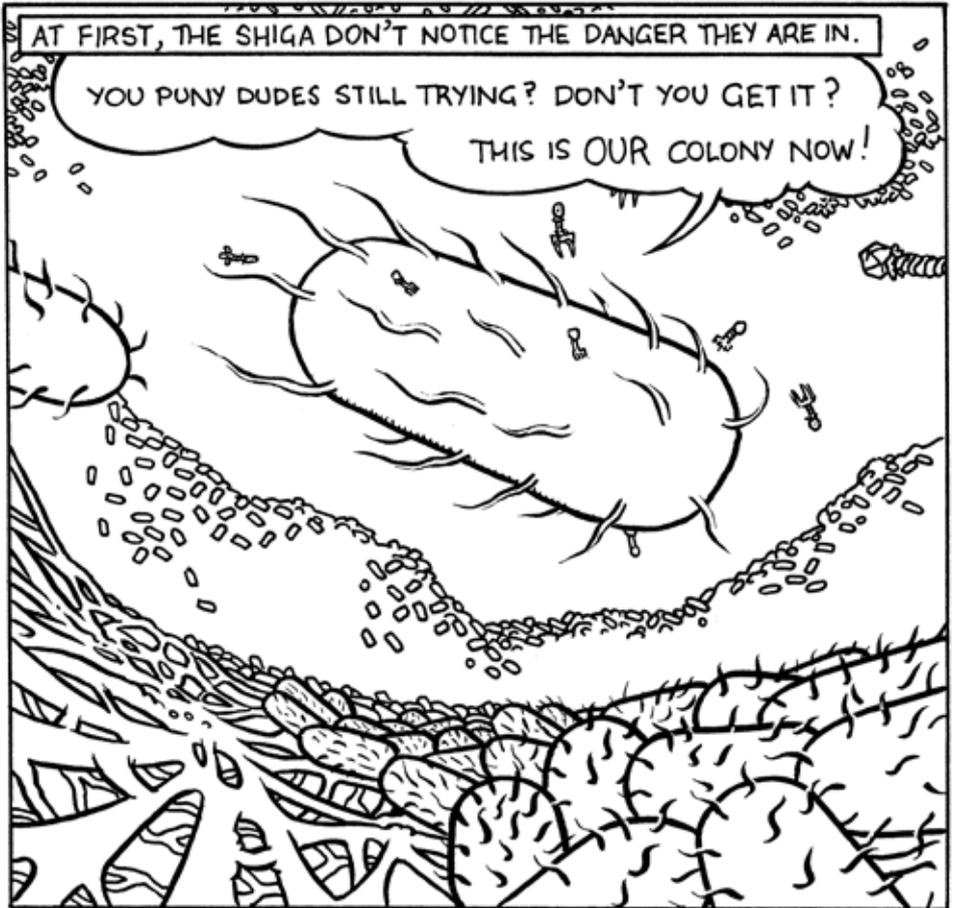
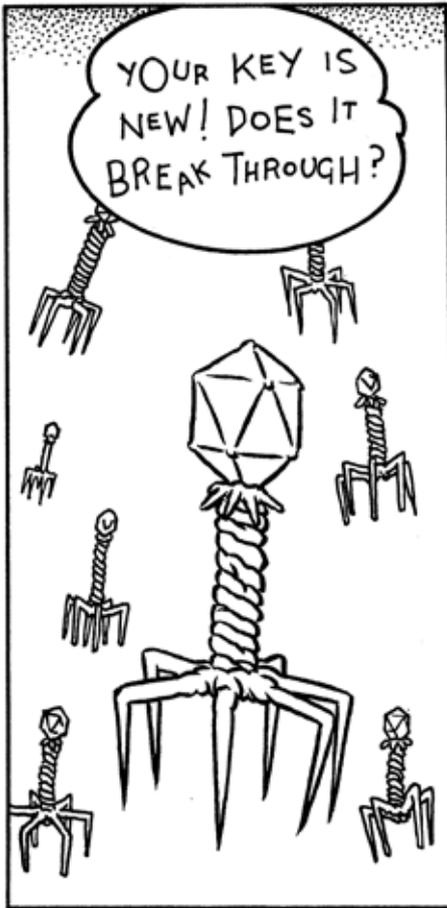


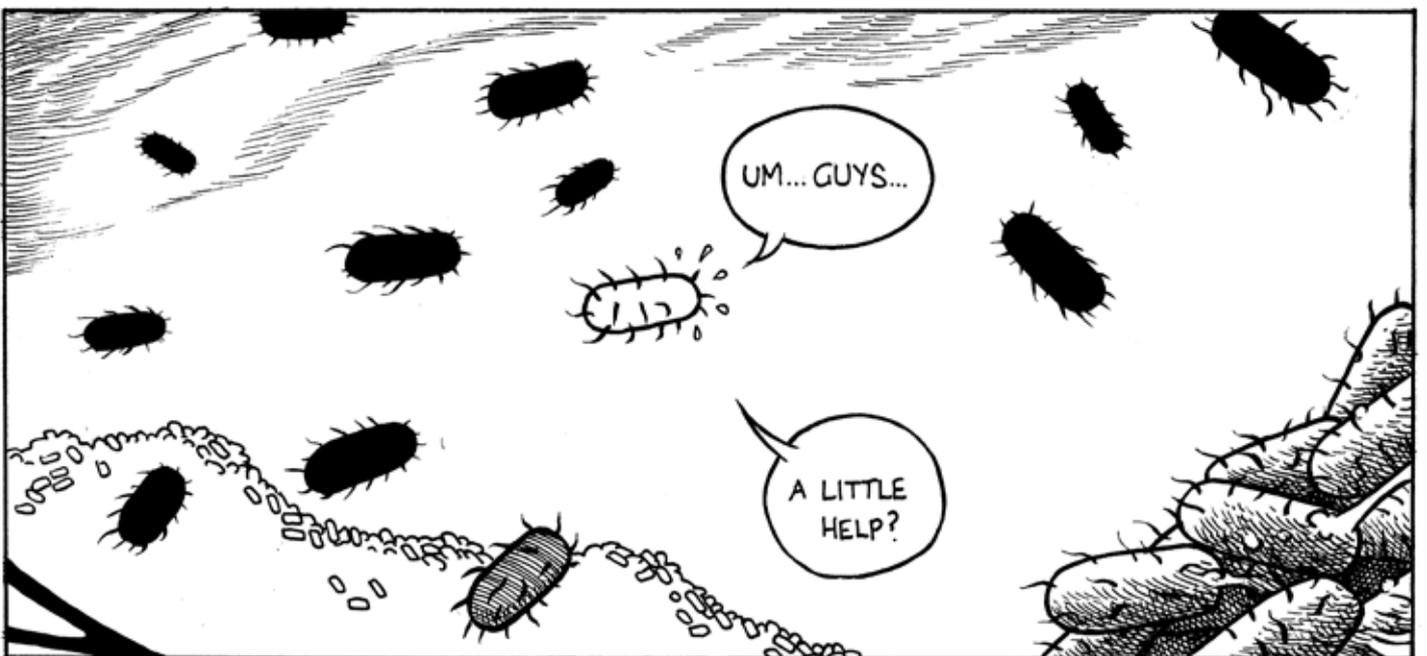
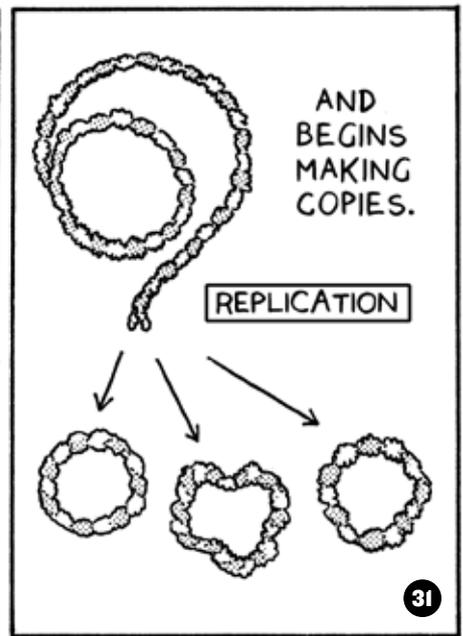
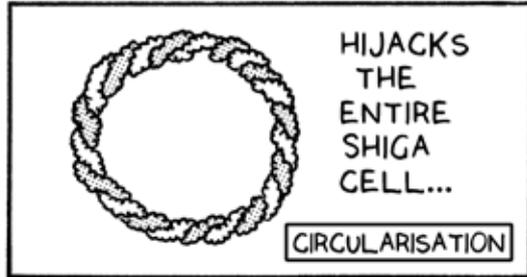
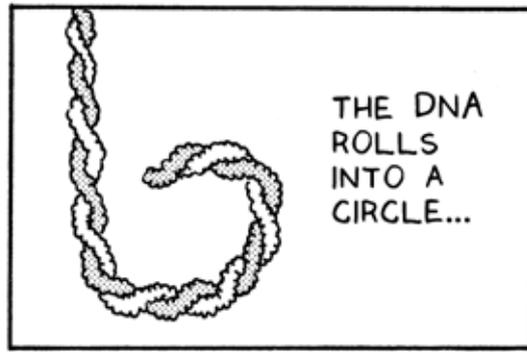
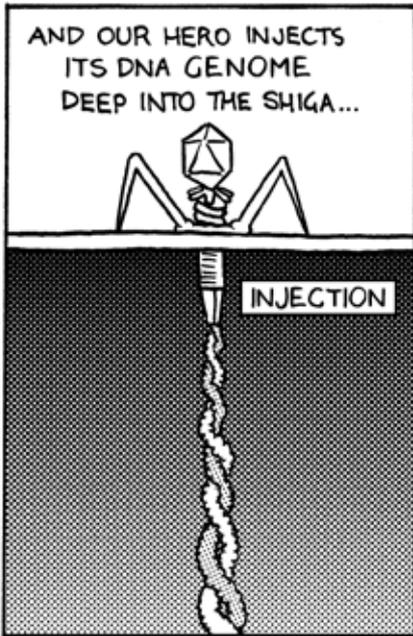
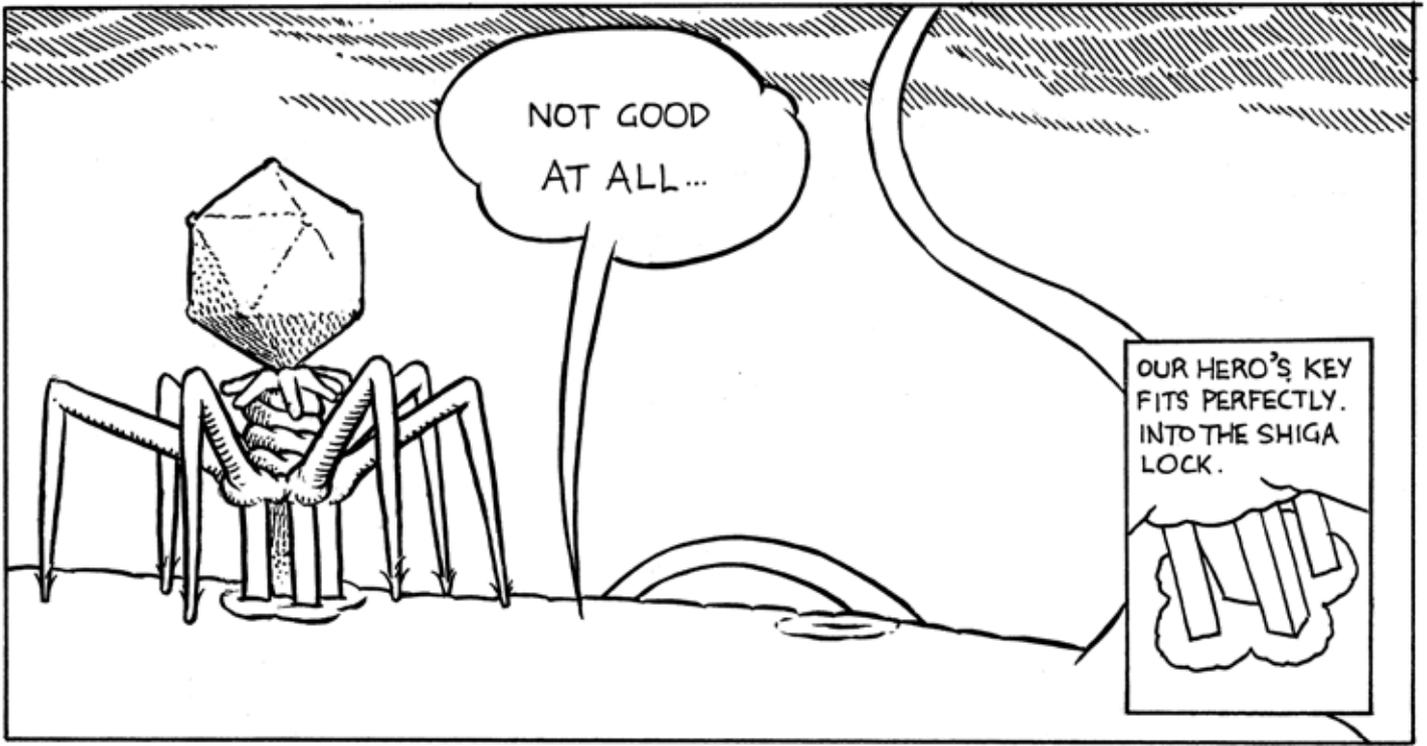
BRANDY. DO YOU GOOD.

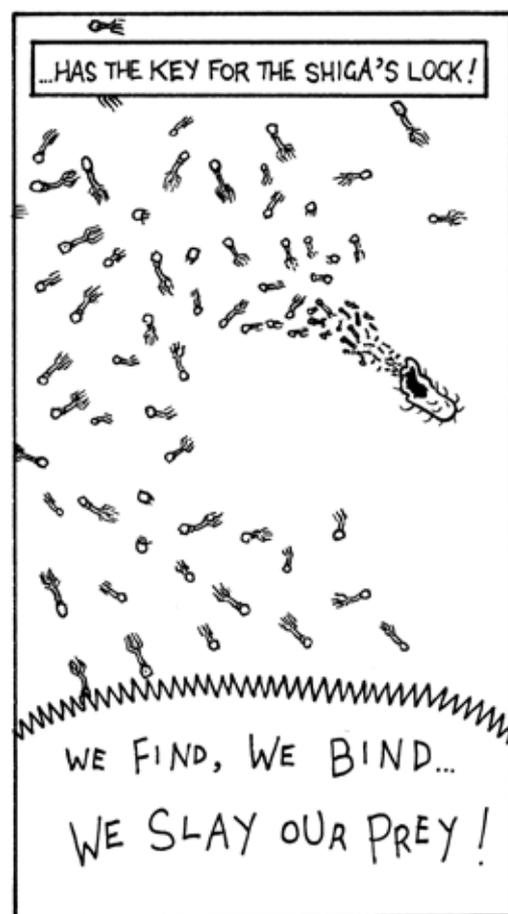
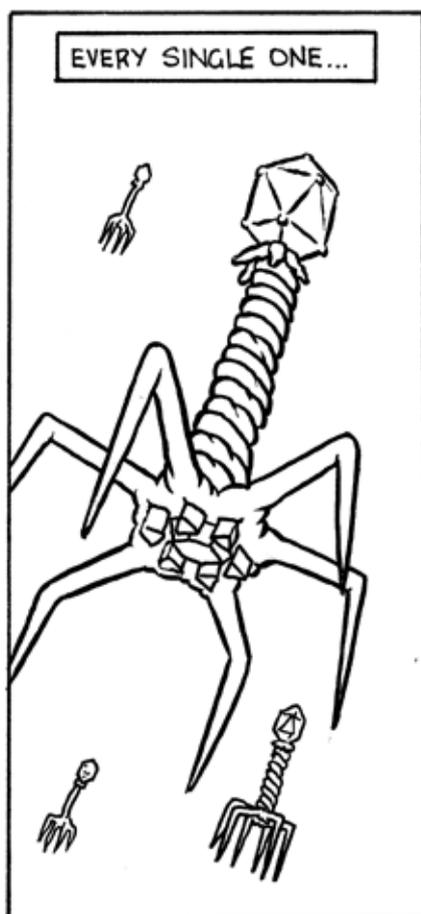
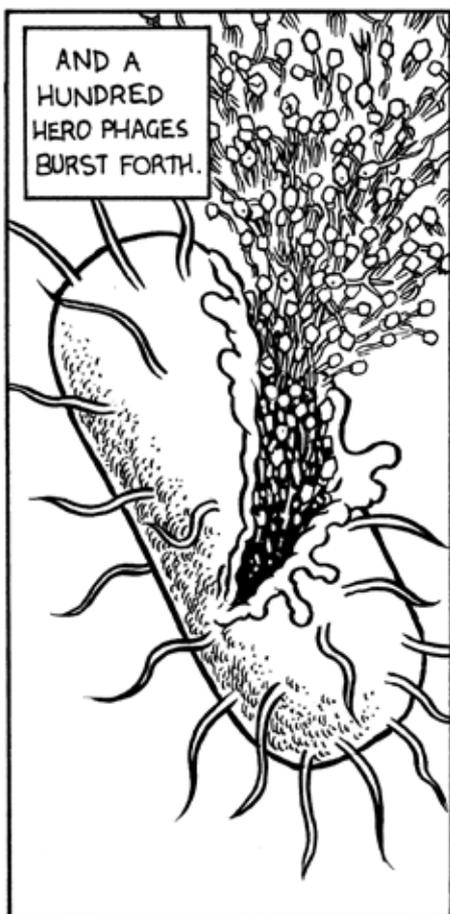
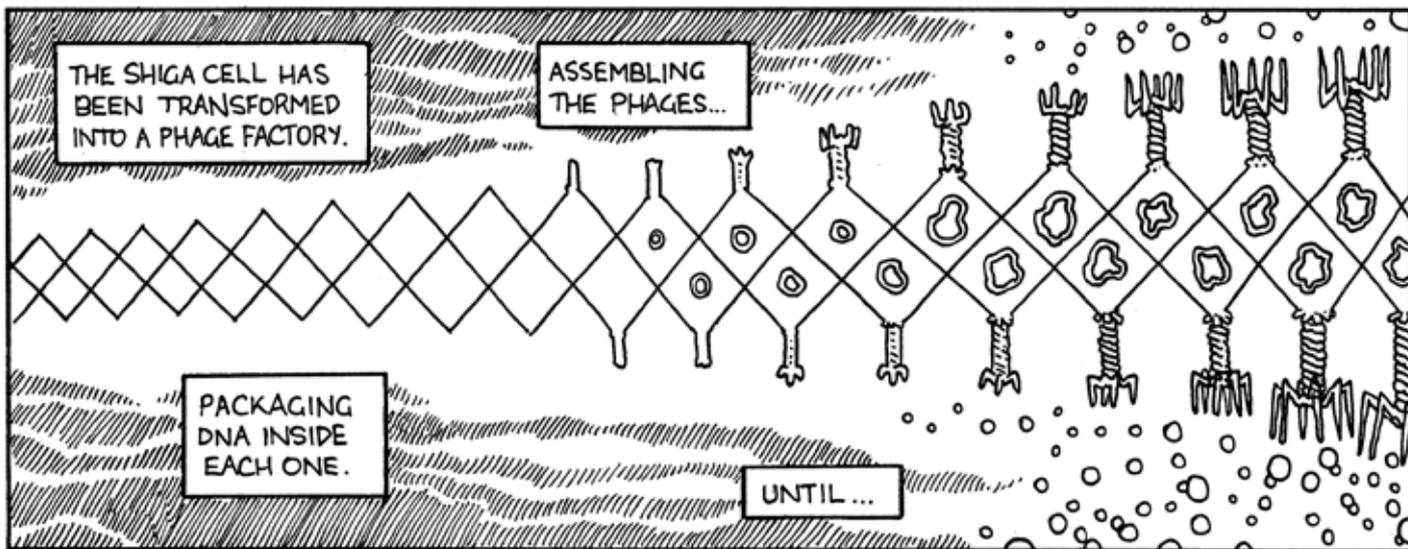












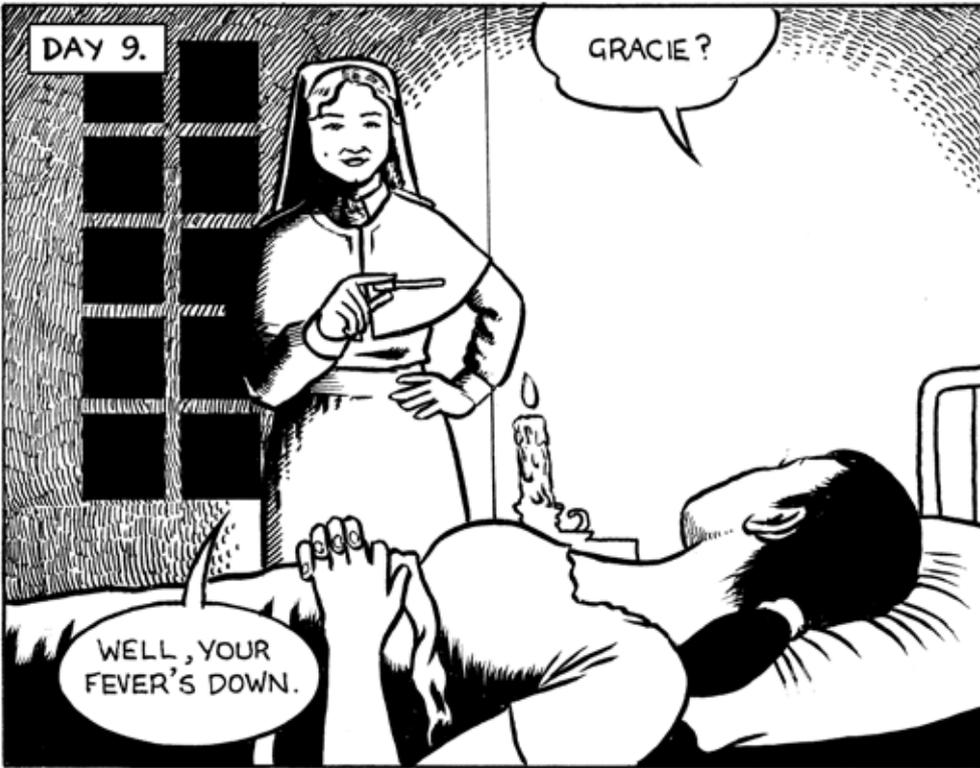


AAAUGH!

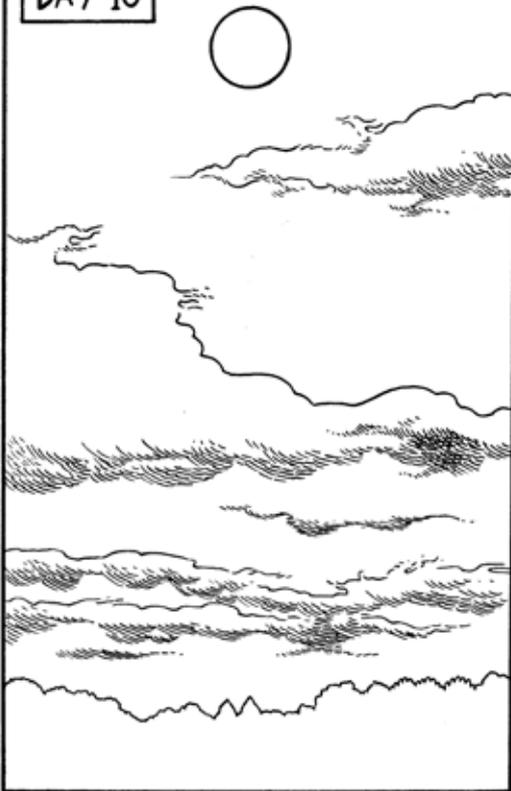
AAAAH!

WE HUNT IN THE HOME PROTECTING OUR OWN.

YOU INFECT WE PROTECT.



DAY 10



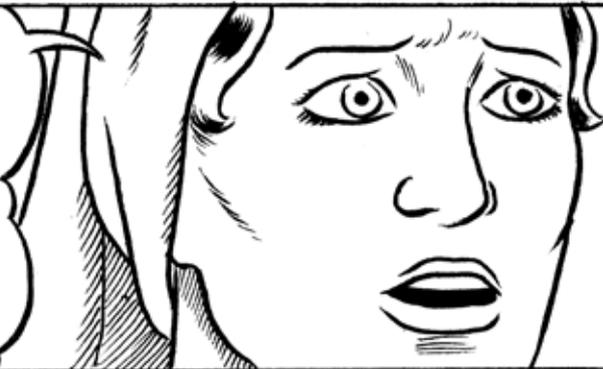
HOW ARE YOU FEELING ?

A BIT BETTER...
I MISS EVERYONE.
IS THERE ANY NEWS
FROM EDITH ?



WHAT !?
WHAT IS IT ?

OH ANNIE, HER BROTHER'S
GONE. HIS LEGS WERE BLOWN
OFF. HE SPENT TWELVE HOURS
IN A SHELL HOLE AND DIED OF
SEPTICAEMIA TWO DAYS LATER.
WHEN SHE GOT THE NEWS
SHE HAD A CUP OF TEA THEN
KEPT ON WORKING.



I CAN'T BEAR IT...
HOW DOES SHE
BEAR IT ?

HOW DO WE
KEEP GOING ?



I'M SO GLAD
YOU'RE PAST
THE WORST.



THANK-YOU FOR
LOOKING AFTER
ME.





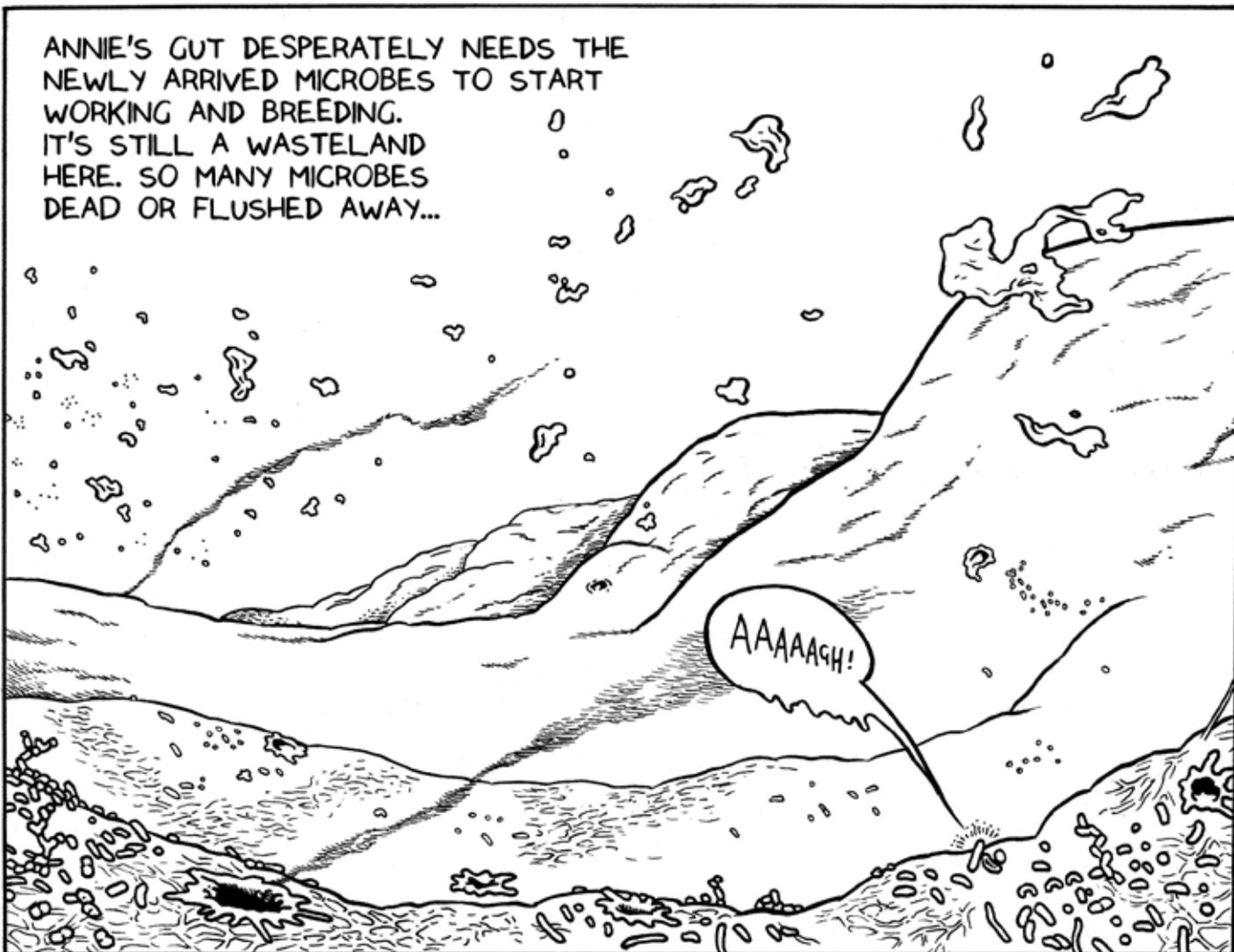
RIDING ON FOOD PARTICLES OR EMERGING FROM THE APPENDIX, NEW BACTERIA ARRIVE IN THE GUT.



HEY TELLA D'YOU RECKON THESE ARE THE LAST SHIGELLA?

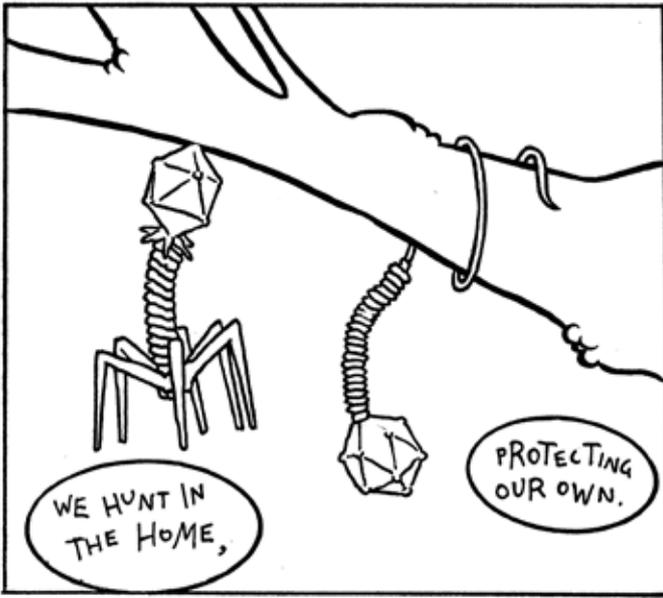
NOT QUITE! I SAY KILL 'EM AND KEEP HUNTING.

NO... PLEASE! HAVE MERCY!



ANNIE'S GUT DESPERATELY NEEDS THE NEWLY ARRIVED MICROBES TO START WORKING AND BREEDING. IT'S STILL A WASTELAND HERE. SO MANY MICROBES DEAD OR FLUSHED AWAY...

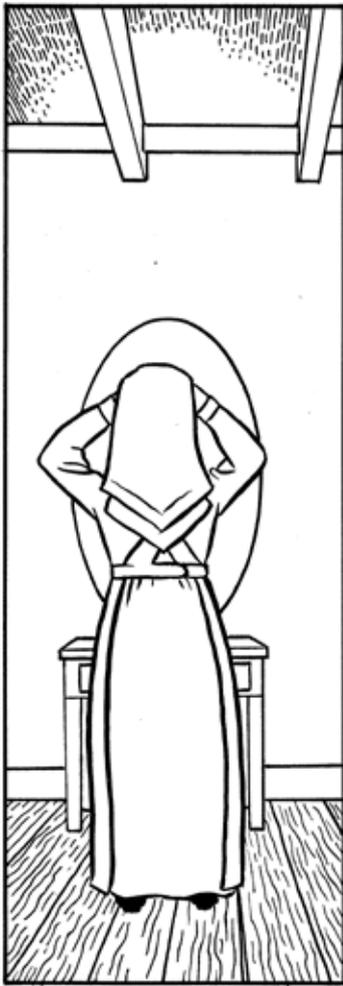
AAAAAGH!



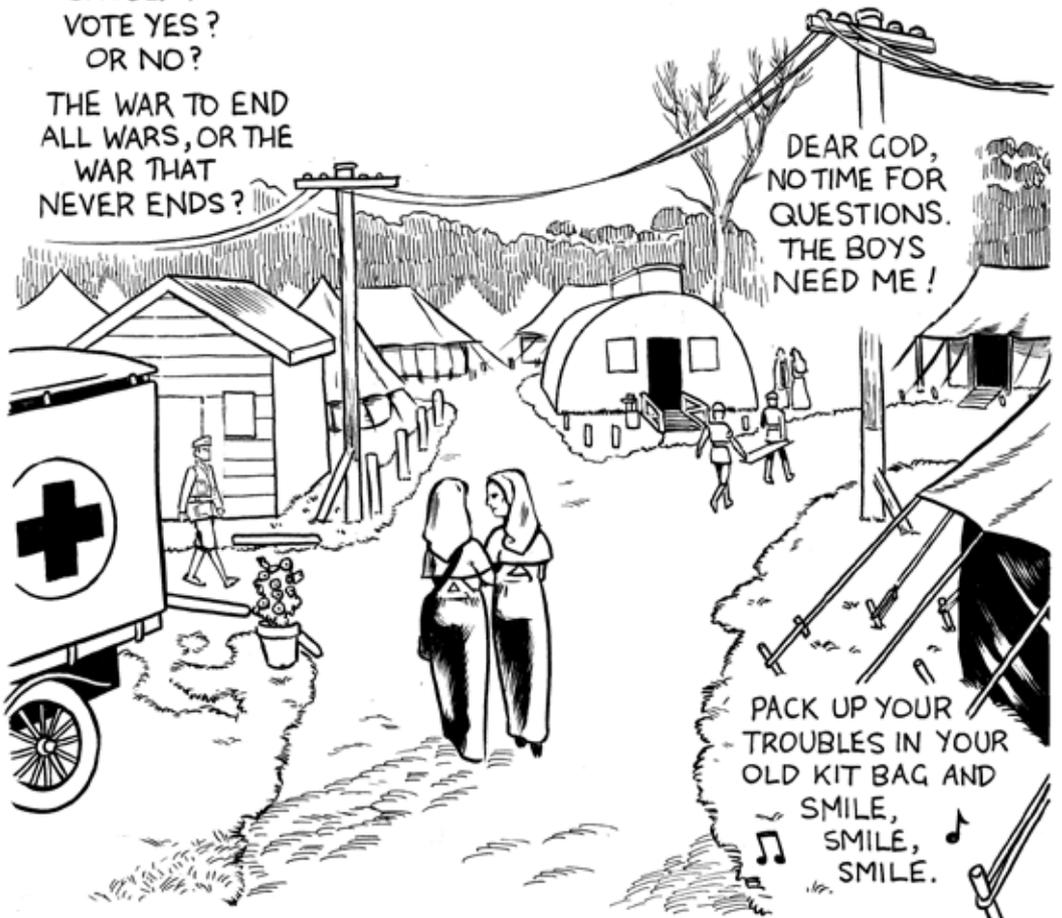


GRACIE SAYS I CAME SO CLOSE TO DYING. I CAN'T REMEMBER. JUST A FEVERISH MIND... AND THE PAIN! OH, I DON'T WANT TO THINK ABOUT IT. I SHOULD FOCUS ON THE PAPER... THIS MATTER OF CONSCRIPTION.

COULD I FORCE BOYS TO FACE DEATH? TO TURN THEM INTO KILLERS? BUT WHAT ABOUT SUPPORTING THE POOR MEN ALREADY FIGHTING? EDITH'S BROTHER? IF AUSTRALIA SENT MORE SOLDIERS, MIGHT HE HAVE SURVIVED? I NEARLY DIED. BUT AT LEAST IT WAS MY CHOICE TO BE HERE.



SHOULD I VOTE YES? OR NO? THE WAR TO END ALL WARS, OR THE WAR THAT NEVER ENDS?



DEAR GOD, NO TIME FOR QUESTIONS. THE BOYS NEED ME!

PACK UP YOUR TROUBLES IN YOUR OLD KIT BAG AND SMILE, SMILE, SMILE.

WANT TO KNOW MORE?

**CONTINUE READING TO LEARN MORE ABOUT THE SCIENCE,
THE HISTORY AND THE TEAM BEHIND THE STORY.**

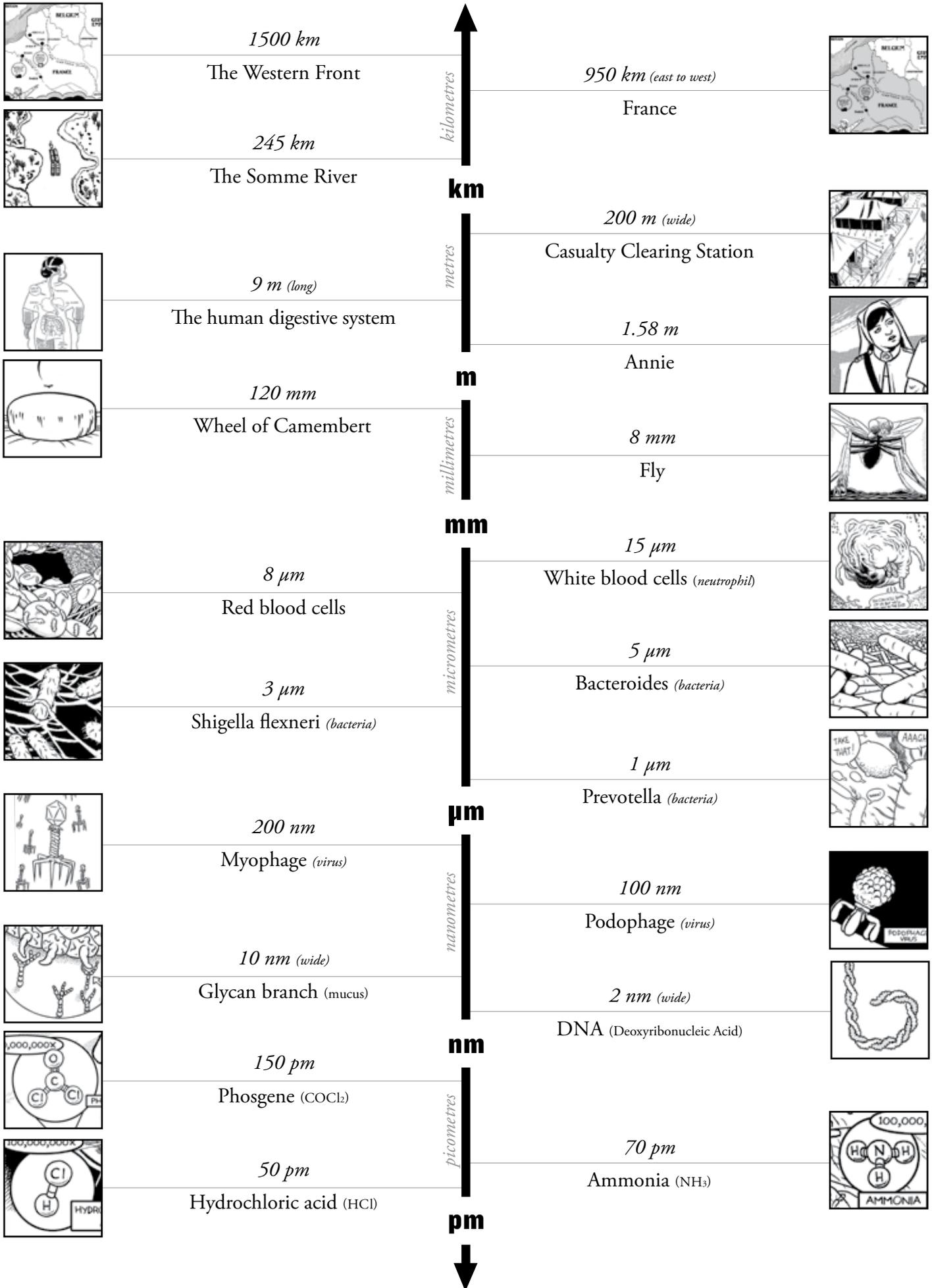
And visit

www.theinvisiblewar.com.au

to:

- download teaching resources,
- order print copies of *The Invisible War*,
- and more...

THE INVISIBLE WAR: BIG TO SMALL



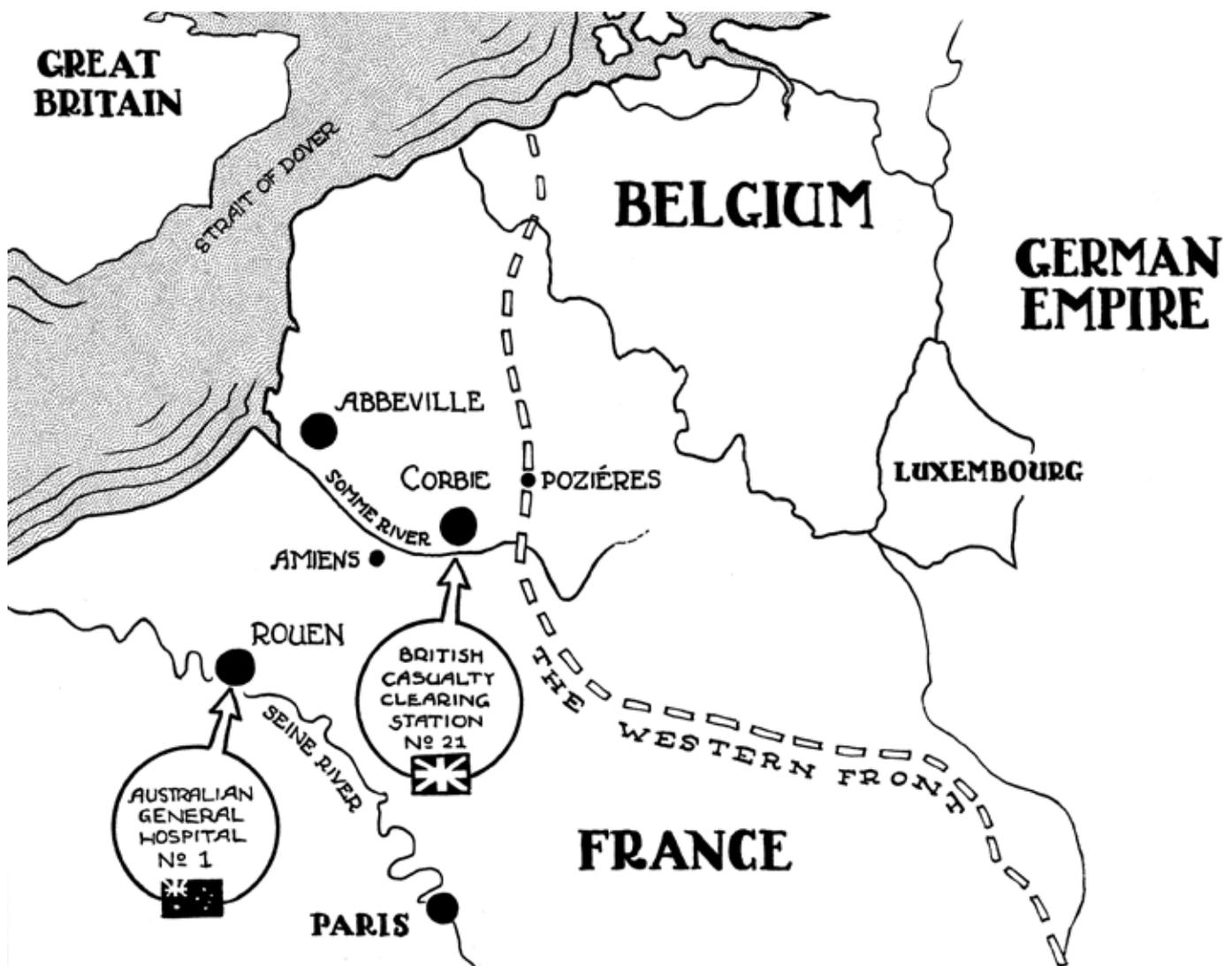
**BUT HOW,
AND WHY,
AND ARE YOU
SERIOUS?**

I. WHERE WAS THE WESTERN FRONT?



see pg 4 >

The Western Front was the main theatre of war during World War I (WWI). Essentially it was a series of trenches across 1500 km of Europe, from the North Sea across Belgium and France to the border of Switzerland.



2. WHAT IS A CASUALTY CLEARING STATION?



see pg 5 >

A Casualty Clearing Station (CCS) is a military medical facility behind (but close to) the front line. They were usually out of reach of artillery fire, but not always! They were sometimes in range of gas attacks – depending on the way the wind blew, and they were often bombed from the air.

These stations were not for long-term patients. They were for initial medical treatment that couldn't be handled closer to the front, or a stop on the way to larger hospitals. Nurses from the Australian Army Nursing Service and New Zealand Army Nursing Service worked in Australian and New Zealand CCSs but both also served in the British ones as necessary.

The Clearing Station in the story is British Casualty Clearing Station 21. We chose it because it was a busy place in August 1916. It was also next to a canal, which was part of the transportation system we wanted to show.



Image: Duckboards and tents at a Casualty Clearing Station.
Source: Australian War Memorial.

3. WHO ARE THE NURSES?



see pg 6 >



see pg 11 >

Australian nurses joined the war effort for similar reasons men did – adventure, patriotism, and a desire to see the world. They also went to be closer to their brothers, friends and to the men enlisted to fight. Their work was hard and dirty. It included lifting heavy patients and dealing with blood, pus and excrement.

Nurses lived under strict military discipline. Women were only allowed to serve as nurses in the Australian military if they were not married or were widowed. They were required to have a high standard of moral behavior. There were 2286 members of the Australian Army Nursing Service who served during WWI and more than 500 in the New Zealand Army Nursing Service.

SCIENTIFIC CLASSIFICATION OF HUMANS

Domain:	<i>Eukarya</i>
Kingdom:	<i>Animalia</i>
Phylum:	<i>Chordata</i>
Class:	<i>Mammalia</i>
Subclass:	<i>Theria</i>
Infraclass:	<i>Placentalia</i>
Order:	<i>Primates</i>
Family:	<i>Hominidae</i>
Subfamily:	<i>Homininae</i>
Tribe:	<i>Hominini</i>
Subtribe:	<i>Hominina</i>
Genus:	<i>Homo</i>
Species:	<i>sapiens</i>

WHY DOES PRIVATE ROBBINS SAY 'HELLO AUSTRALIA' WHEN HE SEES ANNIE?

Australian soldiers recognised the uniforms of Australian nurses and would often greet them with the friendly, 'hello Australia!' which signified comradeship without requiring names. Australian soldiers might just have easily been treated by nurses of another nationality, but many said it was good to see a face from home.



Image: No.2 Australian CCS at Trois Arbres 1917.
Source: Australian War Memorial.

4. WHO ARE THE PATIENTS?



see pg 6 >

The soldiers at the Casualty Clearing Station came via the field ambulance, where battles led to awful wounds. Shells, bullets and hand-to-hand bayonet fighting blew holes in men, ruptured their skin, destroyed organs, and tore off limbs. Nurses' caseloads included many surgical patients treated for shrapnel removal and amputations. Poison gas and gangrene were also common. Stress, lack of nutrition and poor hygiene meant nurses were also working with a large numbers of sick and diseased soldiers, not just the battle-injured. Rations for soldiers were poor, lacking in fresh food or any diversity. Sleep was continuously interrupted, causing huge stresses on the body.

Drinking water was not always clean. The British forces knew about the importance of clean drinking water and used ceramic filters and later chlorine to make water potable. But, there were still times when clean water was inaccessible and the only available drinking water was rainwater collected from shell-holes. These holes might have had blown-apart human or animal corpses in them. Shell-hole water, polluted by a corpse, was commonly known as ANZAC soup.



Image: An injured soldier being treated in a trench.
Source: Wellcome Library, London.



Image: Pools of water in shell holes.
Source: Wellcome Library, London.

5. WHAT IS DYSENTERY?



see pg 7 >

Dysentery is a disease of the human intestine that causes bloody diarrhoea. Widespread infection of the intestinal wall typically leads to ulceration, loss of blood and the production of massive amounts of mucus – resulting in catastrophic loss of fluid from the human body – and often death.

A few different types of dysentery have been described by doctors and scientists, but the two most important types during WWI were amoebic dysentery and bacillary dysentery. The amoeba parasite that causes amoebic dysentery prefers warmer weather, and so this disease was more of a problem in the trenches of Gallipoli.

Bacillary dysentery (or Shigellosis) is named after the bacillus (or rod-shaped) bacteria from the genus *Shigella*. There are four different species of *Shigella* – *dysenteriae*, *flexneri*, *sonnei*, *boydii*. These all call human intestines home but cause slightly different forms of dysentery.

Dysentery is tragically still a common disease among many poor communities around the world, particularly in Asia and Africa, where more than two billion people live without

regular access to clean drinking water and toilets ([WaterAid](#)).

Antibiotic-resistant *Shigella* are also making a comeback around the world ([Institut Pasteur](#)), including outbreaks in wealthy countries, such as the USA ([USNews](#)).

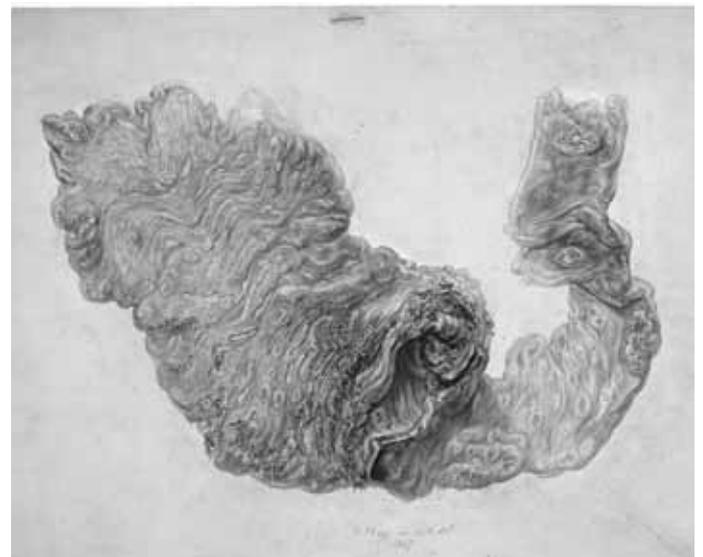


Image: Medical drawing of a portion of large intestine from 1848, illustrating the devastating ulceration of dysentery. Source: St Bartholomew's Hospital Archives & Museum, Wellcome Images.

6. WHY ARE THE DOCTORS AND NURSES SO WORRIED ABOUT DYSENTERY?



see pg 8 >

Dysentery was on the list of highly infectious diseases. Along with cholera, typhoid, and scarlet fever, it required an immediate telegram to the Director General of Medical Services at General Headquarters. Dysentery was the only disease for which even a *suspected case* required a telegram. Perhaps this is because Australian troops had suffered so horribly from dysentery during the Gallipoli campaign in Turkey. In August 1915, more than 80 per cent of soldiers at ANZAC Cove were suffering from dysentery. Of the 5000 men a week evacuated for illness, more than 30 per cent of these were due to dysentery.

There were several reasons for this: lack of water for washing and drinking; a large fly problem; and an inability to manage sanitation due to the small land area inhabited. The trenches of WWI were commonly wet and always cramped, making it hard to maintain reasonable levels of hygiene, such as serving food and water in clean mugs. Even worse, it was hard keeping flies off food and human faeces.

During and after Gallipoli, bacteriologists working in army laboratories did important

research into diagnosing dysentery. By the time Australians were fighting on the Western Front, diagnosis and water sanitation had significantly improved. On the Western Front, less than two per cent of the soldiers incapacitated by an infectious disease were suffering from dysentery.

Dysentery is no longer common in regions such as Australia, Europe and North America. However, it still infects over 100 million people and causes over half a million deaths in the *Global South* each year – especially in the most crowded parts of Asia and Africa. Health experts suggest that access to clean water and basic sanitation would likely reduce this problem.



Image: Drawing of sickly dysentery patient from WWI. Source: Wellcome Library, London.

7. WHAT WAS THE MOBILE LABORATORY?



see pg 8 >

Mobile laboratories were first developed during WWI. They consisted of a truck outfitted with all the necessary tools of the bacteriologist, including microscopes, centrifuges and incubators. The first of these was built in 1915, and by the end of the war there were about 15 operating near the front. Each had a cycle car attached for gathering specimens, as a single mobile laboratory might have serviced several Casualty Clearing Stations.



Image: Mobile laboratory, outside.
Source: Wellcome Library, London.



Image: Mobile laboratory, inside.
Source: Wellcome Library, London.

8. WHO THE HECK ARE THE SHIGA GANG?



see pg 10 >

The genus *Shigella* originates from the name *Shiga*, after its discoverer – Lord Kiyoshi Shiga of Japan.

Shigella flexneri and *S. dysenteriae* were the most problematic of these in the trenches of WWI, with *S. flexneri* being more common on the Western Front. We set our story on the Western Front to avoid the chaotic conditions of Gallipoli, where the more toxic *S. dysenteriae* was spread extensively throughout water supplies and between the soldiers.

In the early 1900s (including during WWI), the name ‘Shiga’ was used to describe the bacterium *Shigella dysenteriae*, while *Shigella flexneri* were referred to as ‘Flexner’. It wasn’t until the 1950s that the different species were united within the same genus, given the name *Shigella*.

ARE SHIGELLA BACTERIA REALLY THAT HAIRY?

The hairs illustrated on the *Shigella* in the story are called fimbriae. These hairs are also called attachment pili. They can range from a few nanometres to a few micrometres long. These hairs help bacteria attach to other

bacteria and surfaces, such as mucus.

More information [here](#).

SCIENTIFIC CLASSIFICATION OF SHIGELLA BACTERIA

Domain:	<i>Bacteria</i>
Kingdom:	<i>Bacteria</i>
Phylum:	<i>Proteobacteria</i>
Class:	<i>Gammaproteobacteria</i>
Order:	<i>Enterobacteriales</i>
Family:	<i>Enterobacteriaceae</i>
Genus:	<i>Shigella</i>
Species:	<i>flexneri</i>



Image: Digital illustration of *Shigella* bacteria.
Source: James Archer, U.S. Centers for Disease Control and Prevention.

9. WHY DO THE SHIGA LEAVE PRIVATE ROBBINS' GUT?



see pg 10 >

Once the *Shigella* began to infect the epithelial cells lining the human intestine, their numbers explode exponentially – from tens to thousands to millions to billions within 24–48 hours! In response, the human intestine makes several litres of mucus in an attempt to flush out as many *Shigella* as possible. This means that most *Shigella* bacteria don't really leave their host intestine by choice. Rather, they are forced out. But it doesn't have to end there, because there is always a small chance the *Shigella* might find their way onto food or into drinking water, to colonise new human hosts.

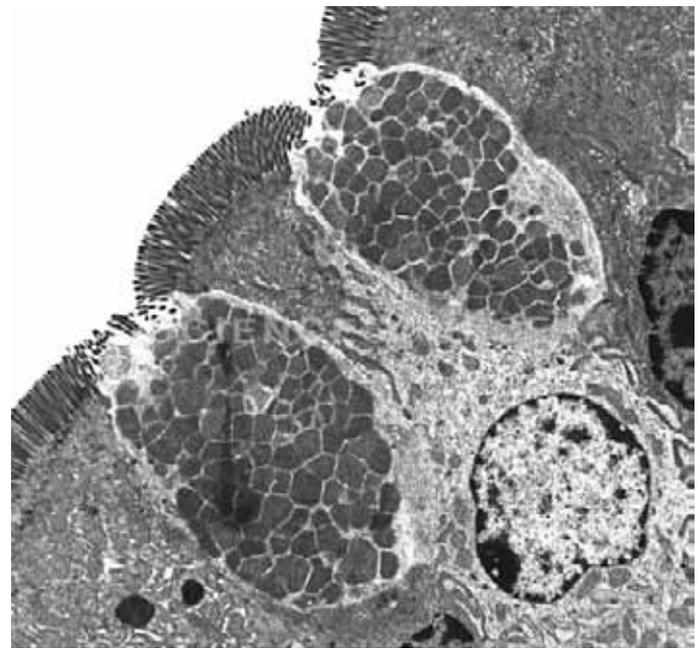


Image: Electron microscope image of goblet cells, showing mucin granules with the classic goblet shape.
Source: OpenStax College.

WHAT IS THE SLIME?

The slime referred to by the *Shigella* is the mucus made by specialised human epithelial cells in the large intestine (called goblet cells).

WHY ARE THEY COLD IN THE BIN?

The optimum growing temperature for *Shigella* bacteria is 37°C, which is the human body temperature. The hospital bin is much cooler than the warm intestine from which they had just been squirted.

10. WHAT'S SO INTERESTING ABOUT ANNIE TAKING A STOOL SAMPLE?



see pg 13 >

Some tools for diagnosing dysentery were developed during the war by Australian medical staff: Lieutenant Colonel C. J. Martin and Sister F. E. Williams. A combination of tests would have been used to diagnose a suspected case of dysentery:

- Direct observation of the size and shape of the bacteria under a microscope.
- Spreading bacteria from the stool sample on an agar plate designed to only allow *Shigella* bacteria to grow.
- A serum analysis that involved exposing a patient's stool sample to a mixture of different antibodies. If the stool contained *Shigella flexneri*, the antibodies would recognise and bind to the bacteria, forming visible clumps in the test tube. That patient was then considered positive for Flexner (*Shigella flexneri*). The serum analysis was the most accurate test available to doctors at the time.

These were very new diagnostic tools at the time. In the early 1900s, the scientific understanding of microbes and microbiology was still limited. Antibiotics, such as penicillin, were not developed until the 1940s – becoming available during World War II

(WWII). This means WWI was fought *without antibiotics* and many soldiers died from bacterial infections resulting from small wounds and scratches.

THE CHANCE OF RECOVERING DYSENTERY BACILLI FROM THE STOOLS ACCORDING TO THE TIME ELAPSING SINCE THE ONSET OF THE DISEASE.
EXPERIENCE AT A BASE HOSPITAL IN FRANCE.
BY
LIEUT.-COLONEL C. J. MARTIN, F.R.S., A.A.M.C.,
AND
SISTER F. E. WILLIAMS, A.A.N.S.

Prior to the war the notion seems to have been widespread that the bacteriological diagnosis of dysentery was as satisfactory as, say, that of diphtheria, and measures for the control of epidemics have been founded to some extent on this assumption. Our experience of laboratory work in the Eastern Mediterranean and Egypt in 1915 and 1916, however, led us to the conclusion that the chance of recovering dysentery bacilli from the stools was, after the first few days of the disease, a small one.

Similar experience seems to have been gathered elsewhere. Kolle and his co-workers¹ give an account of the bacteriology of an epidemic on the Russo-German front with which they dealt. They isolated *B. dysenteriae* Shiga from such a minute fraction of the samples examined that they came to the conclusion that, notwithstanding the general clinical resemblance to dysentery of this type, they must have had to deal with an outbreak from some other cause. Seligmann and Cossmann² also obtained very unsatisfactory results when working at a base hospital in Austria. They state that "they nearly always failed to recover dysentery bacilli" in undoubted clinical cases of dysentery. During eight months' work they recovered a dysentery bacillus but fifteen times out of "hundreds of attempts."

Later Seligmann was removed to a laboratory nearer the front, where he had opportunity to examine material from the recently evacuated sick. Under these conditions the results were entirely different, *B. dysenteriae* Shiga being

Image: Article by C. J. Martin and F. E. Williams published in 1918.
Source: The British Medical Journal 1.2990 (1918): 447-448.



see pg 13 >

SISTER WILLIAMS – HOW THE INTERSECTION OF BACTERIOLOGY AND WAR MADE A WOMAN’S CAREER POSSIBLE.

One bacteriologist studying dysentery was Sister Fannie Eleanor Williams – a rare role for a woman at that time. She trained as a nurse, but became a research attendant in the bacteriology laboratory in Adelaide Hospital before deciding to join the war effort. During WWI, the only capacity in which a woman was allowed to join the armed forces was as a nurse, so Sister Williams was titled and ranked accordingly. However her role was far more specialised than regular nurses. She spent the war years working in laboratories attached to various military hospitals, as well as the Lister Institute diagnosing and researching infectious diseases and their treatments. She worked in Lemnos (the closest hospital base for the Gallipoli campaign), Cairo, London and Rouen.

Her work with Charles Martin on the dysentery outbreaks in Gallipoli, and later developing treatment serums, was published in prestigious journals and she was considered an expert in the field. When she returned to Australia, Sister Williams was

appointed second assistant at Australia’s newest research institute – the Walter and Eliza Hall Institute of Medical Research – based in Melbourne. She was the first bacteriologist and serologist to be appointed there. She was also the first woman.



Image: Sister Williams.
Source: Australian War Memorial.

II. WHY IS THE DOCTOR BEING SO MEAN?



see pg 13 >

Some doctors were reluctant to accept the microscope and the agar plate as new tools to diagnose diseases – and instead preferred to trust their old tools – observation and experience.

Diagnosis was a subject of conflict and the doctor in this scene represents the ‘old school’ who were angry and afraid of the new diagnostic tools. Because of the British army medical establishment’s reluctance to accept bacteriology, it was not given much credit within the army at the beginning of WWI. Bacteriologists, the people using microscopes and agar plates, were considered mere technicians – useful for testing water purity – but not much else (certainly not for research).

Our story is set at a British-run Casualty Clearing Station. Australian medical culture supported bacteriology as a diagnostic tool slightly earlier and Annie would have been trained to respect it. By the end of the war, bacteriology had become firmly established as a respected tool of medicine.

Today, bacteriologists are usually referred to as microbiologists – who, with the aid

of high throughput DNA sequencing and powerful computational analysis – are discovering more and more about the powerful role of different microbes in the world inside us and around us.



Image: A laboratory in the field.
Source: Wellcome Library, London.

12. ARE FLIES REALLY THAT DIRTY?



see pg 16 >

Flies are great at spreading bacteria between food, water, animals, people and faeces, especially because of the way they vomit up digestive juices onto food, before sucking it back up again. It is thought that flies carried much of the *Shigella*-caused dysentery around during WWI, mostly between uncovered human faeces and drinking water.

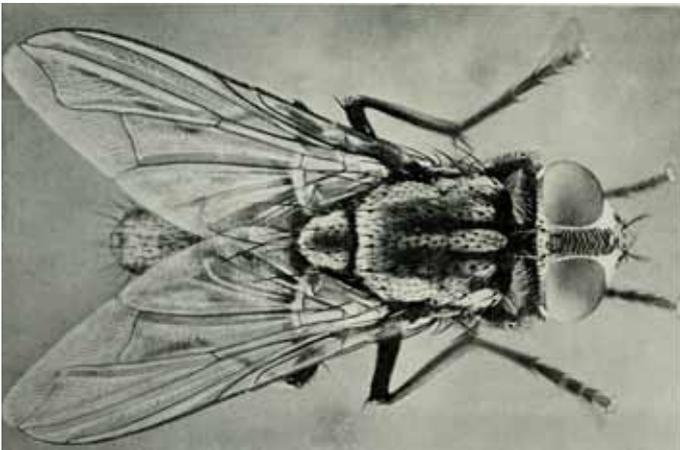


Image: The common house-fly (or Typhoid fly).
Source: The American Museum of Natural History (ca. 1900 – 1918)

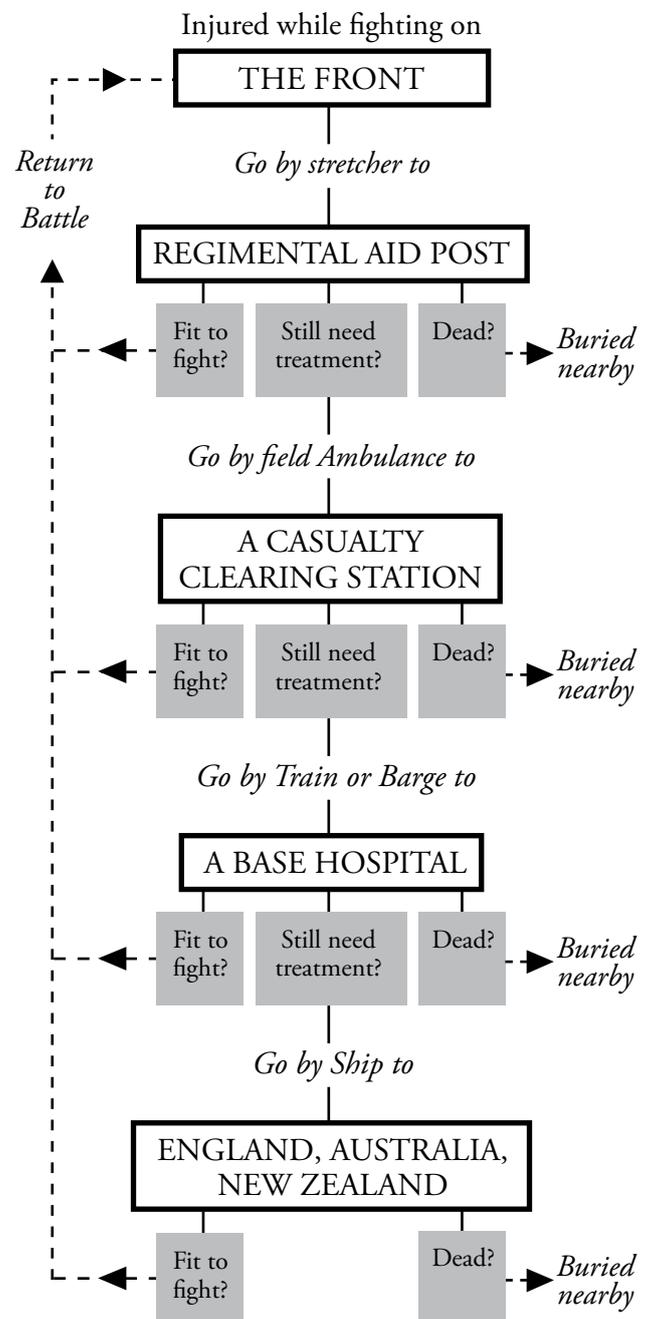
13. WHAT DOES ANNIE MEAN BY 'DOWN THE LINE'?



see pg 16 >

'Down the line' means away from the front, through military channels (and 'up the line' means towards the front).

The flow chart opposite shows how the sick and injured were transported 'down the line' and what the various stops along the way were.



14. WHAT THE HECK IS BULLY BEEF?



see pg 16 >

‘Bully beef’ was the nickname for canned corned beef – the standard daily ration of Australian soldiers. Nurses were fed similar rations. ‘Corned’ means preserved in salt, and bully beef was infamous for being salty, greasy and a bit disgusting. It has become a symbol of the ANZAC’s daily hardships. This means food rations for soldiers and nurses contained little fibre and resistant starches, which are important for maintaining a healthy diversity of gut microbes (called microbiota). If Private Robbins’ diet had been better, his gut microbes may have more easily repelled the invasion by *Shigella flexneri*.



Image: Soldiers eating their rations.
Source: Australian War Memorial.



Image: Corned beef packaging.
Source: Australian War Memorial.

15. WHAT'S THE ISSUE WITH CONSCRIPTION AND WHAT IS A SHIRKER?



see pg 19 >

During WWI, Australia was bitterly divided by the conscription debate. People on both sides felt very strongly and communities and families were split down the middle. Both nurses and soldiers serving at the front were permitted to vote in the two referendums deciding whether Australia should have conscription in 1916 and 1917. The conversation in our story is very similar to discussions from real nurses' diaries and letters home. One of the reasons some Australians voted no to conscription is the impact of the terrible losses the ANZAC troops suffered during the battle of Pozières (when our story is set).



Image: The Prime Minister, Mr William Morris Hughes, speaking to a large crowd during the conscription referendum campaign. Brisbane, 1916. Source: Australian War Memorial.

Men who refused to fight were despised by many as shirkers – cowards refusing their duty to Australia. They were often ostracised by their communities. Men chose not to fight for many reasons, including religious or ethical objections to killing, or to this particular war. For some, it took bravery to *refuse* to fight.



Image: Propaganda poster against conscription. Source: Australian War Memorial.

Both conscription referenda ultimately delivered a narrow 'no' result – with three states voting 'yes' and three 'no'.

16. WHAT'S THE DEAL WITH THE IRISH?



see pg 19 >

Another event that had an impact on the conscription debate in Australia was the Irish Easter Rising. In April 1916 (four months before our story is set), a group of armed Irish rebels seized key locations, mostly in Dublin. They fought the British military and declared an Irish Republic. The rebellion was unsuccessful and 90 people were sentenced to death under British law and 15 executions were carried out. The executions were seen as brutal and there was a groundswell of reaction against British rule. Many of the Irish population in Australia, lead by Archbishop Mannix, were swayed by these events. They were against conscripting Australians to fight for what they saw as an unjust British Empire. In the story, Gracie reflects this point of view.

17. CAN THE SHIGELLA BACTERIA REALLY SMELL?



see pg 18 >

Shigella bacteria don't have noses like humans and other animals. But many different types of cells, including bacteria, are able to use chemoreceptors to detect different molecules in their surrounding environment, which is much like the sense of smell.

18. WHY IS THERE A GAS ATTACK?



see pg 21 >

Prior to WWI, Britain, France and Germany were all signatories to a treaty agreeing not to use poison gas (Hague Conventions of 1899 and 1907).

When the Germans first attacked with gas, it was seen by their enemies as deeply dishonourable. The British and Australian public were outraged. However, soon both sides were using and developing new methods of chemical warfare. Initially chlorine gas was used, and then later phosgene and mustard gas. Symptoms of exposure to gas included coughing, vomiting and irritation to the eyes and throat. In high doses it was fatal. Those at and near the front relied on a small box respirator (pictured) for protection from phosgene.

Gas attacks were unpredictable because gas was affected by the wind and it crept along the ground. This meant that Casualty Clearing Stations were sometimes vulnerable to these attacks.

More information about poison gases used in WWI [here](#).



Image: Soldiers wearing small box respirators.
Source: Musee Somme.



Image: Phosgene gas attack at Fromelles.
Source: Hermann Rex.

19. WHERE ARE THE SHIGELLA GOING INSIDE OF ANNIE?



see pg 22 >

The *Shigella* bacteria enter Annie's digestive system through her mouth. The job of the human digestive system is to break down the food we eat into smaller and smaller bits that can be absorbed to make energy and new cells for our bodies. The gastrointestinal tract runs from our mouth, through the stomach, small intestine and large intestine, ending at the anus. Much like our external skin cells, the gastrointestinal tract is lined with an internal type of skin, called an epithelium, which creates a protective layer of mucus.

The gastrointestinal tract is comprised of the small intestine and large intestine (colon), and is about 7 – 10 metres long in an adult human.

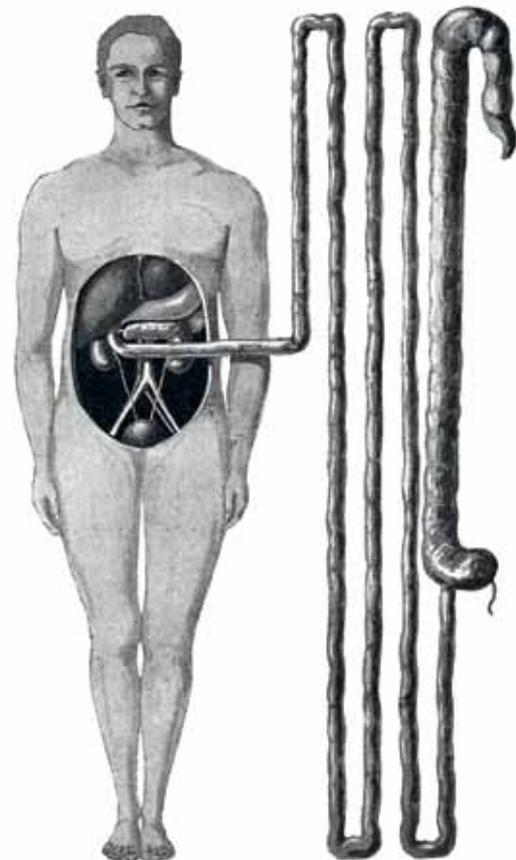
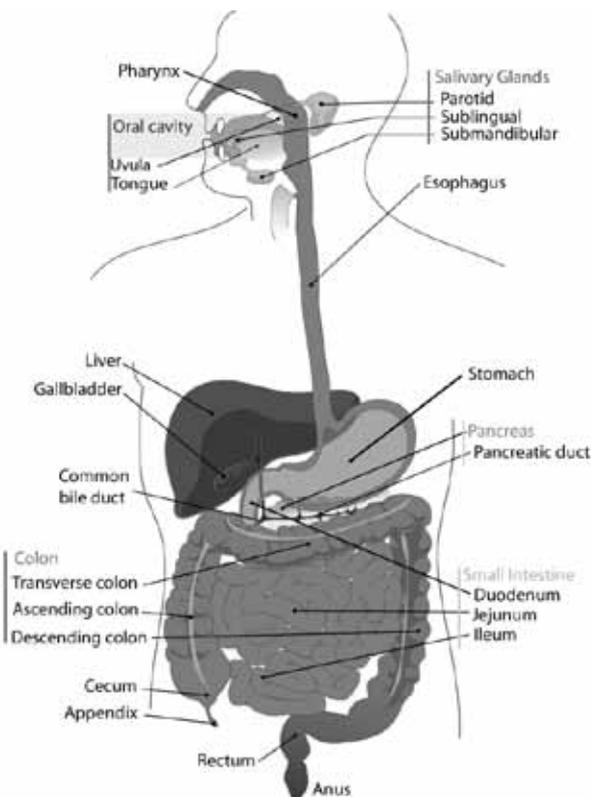


Image: © Fritz Kahn in: Das Leben des Menschen, Vol. III (1928), Kosmos, www.fritz-kahn.com



20. WHAT'S HAPPENING IN ANNIE'S MOUTH?



see pg 20 >

When the *Shigella* bacteria enter Annie's mouth, they encounter a mix of the food and drink consumed by Annie, combined with freshly secreted saliva, and the resident bacteria and viruses that live in her mouth. Our mouth makes about one litre of saliva each day, mostly to help lubricate chewing, but also to begin the process of breaking apart the chemical bonds holding the food molecules together.

Human saliva also contains the enzyme lysozyme. This enzyme is antimicrobial and kills many pathogenic (disease-causing) bacteria threatening to invade our bodies. Luckily for the invading *Shigella* bacteria, lysozyme can't kill them!

21. WHY ARE BACTERIA DYING IN THE STOMACH?



see pg 23 >

The stomach uses both physical and chemical processes to break food into smaller and smaller particles – allowing the body to absorb many of the tiny molecules, such as glucose, through the stomach wall and into our bloodstream. Simple foods like bananas can be broken down in minutes, while red meat can take several hours to break down.

The physical action of the stomach's smooth muscles create a mixing and churning motion, much like a washing machine. Even so, the most dangerous thing bacteria encounter within the stomach are the highly acidic conditions. The regular release of hydrochloric acid (HCl) into the digestive juices of the stomach creates a pH of between 1–2. This helps to break apart many of the food molecules for easier absorption, and kills many bacteria hitching a ride on any swallowed pieces of food.

22. WHAT ARE *HELICOBACTER* AND HOW DO THEY PROTECT THEMSELVES FROM THE STOMACH ACID?



see pg 23 >

Some bacteria are able to resist the highly acidic conditions of the stomach.

Shigella bacteria can survive for a short period in this harsh environment – however, other bacteria called *Helicobacter pylori* can protect themselves by creating a bubble of alkaline ammonia (NH₃) around each cell, that neutralises the strong hydrochloric acid in the stomach. *Helicobacter* bacteria can also burrow deep into the stomach mucus where the pH is less acidic, sticking there, and keeping them from being swept away down the gut.

In the 1980s, Australian scientists Barry Marshall and Robin Warren hypothesised that *Helicobacter pylori* bacteria can survive the harsh acidic conditions of the stomach, and that they might be a cause of stomach ulcers. To help prove this hypothesis, Marshall drank a concoction made from cultured *Helicobacter pylori* and in a few days, he came down with gastritis – the inflammation of the stomach (which causes stomach ulcers). In 2005, Marshall and Warren were awarded the Nobel Prize in Physiology/Medicine for their discovery.

Some scientists now believe that *Helicobacter*

pylori might play an important beneficial role in the human stomach – by regulating acid production and influencing the amount of the hormones ghrelin and leptin, which help signal to our brain that we feel hungry and when we feel full.

More information [here](#).

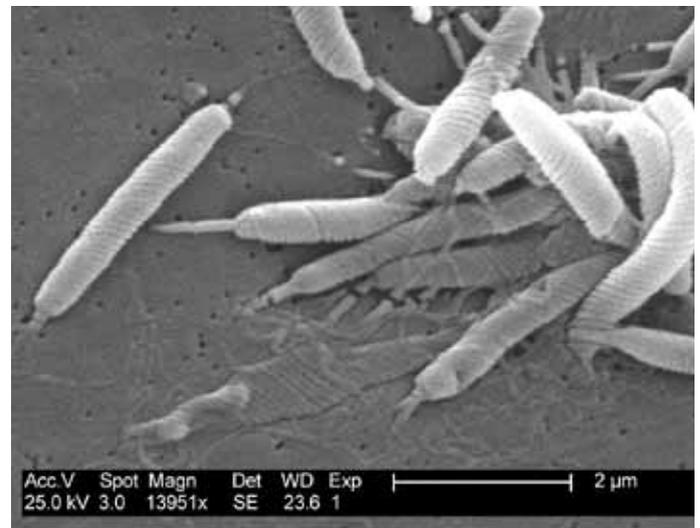
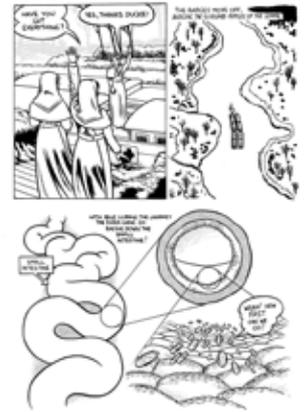


Image: *Helicobacter* bacteria embedded in mucus.
Source: Dr. Patricia Fields and Dr. Collette Fitzgerald.

23. WHY ARE THE SHIGA GANG GOING SO FAST DOWN THE SMALL INTESTINE? AND WHAT IS THE BILE WATERFALL?



see pg 25 >

The entry of food into the small intestine triggers the release of a digestive juice called bile, which flows from the gall bladder.

Bile contains enzymes to help break down food and salts that help mop up healthy fat particles (cholesterol) for absorption into the body. Together with the mucus lining the small intestine, bile also helps to further lubricate the continuous movement of all food particles, along with any bacteria, further downstream.

The 4–5 metres of small intestine is coated in tiny finger-like clusters of cells called microvilli that help absorb food particles. If flattened out, the surface area of the microvilli would add up to about 30 square metres – the size of a large room.

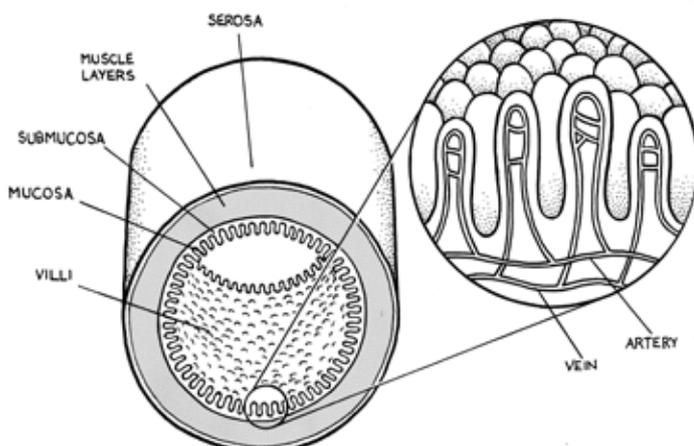


Image: Cross-section of the small intestine, showing finger-like microvilli.

24. WHERE ARE THESE QUOTES FROM?



see pg 25 >



see pg 26 >

BUDGING THE SLUGGARD RIPPLES OF THE SOMME

The poetry quoted on page 25 comes from the poem *The Hospital Barge* by Wilfred Owen.

Owen was a Welsh officer and a war poet who fought on the Western Front. He suffered shellshock and was treated at the Craiglockhart War Hospital in Edinburgh, where he met Siegfried Sassoon, a war poet whom Owen hero-worshipped. Later Owen returned to the front, tragically died in battle one week before Armistice day. *The Hospital Barge* is different from most of his other war poems because it focuses on a moment of peace and beauty. He is known as a bleak realist and poems like his famous *Dulce Et Decorum Est* are much more graphic and gruesome.

When he was first inspired to write the poem, Owen was at a Casualty Clearing Station at Gailly, about 10 kilometres away from the Casualty Clearing Station in our story. It wasn't written or published until 1918 so it's slightly out of our story's timeline!

The Hospital Barge

Budging the sluggard ripples of the Somme,
A barge round old C erisy slowly slewed.
Softly her engines down the current screwed,
And chuckled softly with contented hum,
Till fairy tinklings struck their croonings dumb.
The waters rumpling at the stern subdued;
The lock-gate took her bulging amplitude;
Gently from out the gurgling lock she swum.

One reading by that calm bank shaded eyes
To watch her lessening westward quietly.
Then, as she neared the bend, her funnel screamed.
And that long lamentation made him wise
How unto Avalon, in agony,
Kings passed in the dark barge, which Merlin dreamed.

by Wilfred Owen.

IT'S A LONG WAY TO TIPPERARY...

Tipperary is a town and a county in the south of Ireland. *A Long Way to Tipperary* was one of the most popular songs at this time. It is full of nostalgia for home. Songs were often used this way, evoking a sense of love and patriotism in the soldiers for their home countries. For those at home, such songs summoned up a sense of love and support for the soldiers fighting. Generating these feelings through propaganda was one way to ensure the public continued to support the war effort.

25. WHY ARE THERE SO MANY BACTERIA IN THE GUT?



see pg 27 >

It is estimated that 10–100 trillion bacteria live in and on the human body, making up much of the ‘human microbiota’. Most of these live inside the large intestine – often referred to as our ‘gut’. It is estimated that most of the trillions of bacteria in the human body can be found living inside the large intestine (often called the gut, or colon). These bacteria are responsible for breaking down anything that hasn’t been previously broken down by the actions of the human digestive system in the mouth, stomach or small intestine. The two most common types of bacteria in the gut are from the genus *Prevotella* and genus *Bacteroides* (called Tella and Roidey in our story). In return for a home and a somewhat regular supply of food, these and other resident bacteria create and release nutrients for their human host, such as calcium, vitamins B1/B2/B12/K and hormones such as serotonin.

Many scientists now believe that the appendix, which is attached to the large intestine, acts as a storeroom of our most beneficial bacteria, used to restock our microbiota after heavy bouts of diarrhoea. *Spoiler alert!* Luckily for Annie, there are reinforcements of good bacteria waiting in

her appendix to repopulate the gut as she recovers from dysentery.

NOT JUST BACTERIA! ANNIE’S GUT MICROBES IN NUMBERS:

- Fungi and Protists by the millions;
- Archaea by the billions;
- Bacteria and viruses by the trillions.

There are greater numbers of viruses on Earth than all other life forms put together. Viruses are now considered the ‘dark matter’ of biology – because we know they are out there (or in there), but yet know so little about them! Scientists are now turning their attention to viruses – especially bacteriophage – so we should discover a lot more about them in years to come.

HUMAN MICROBIOTA: BASIC FACTS

- The human microbiota is dominated by approximately 10–100 trillion bacteria across the different niches of the human body. Bacterial species can vary widely depending on where they live in the body. Most types of underarm bacteria would be different from



see pg 27 >

belly button bacteria, which would be very different from bacteria in the vagina, mouth, teeth, hair, stomach, gut and so on.

- To put this in context, a single tiny grain of salt would take up the same space as about five million bacteria. One gram of human faeces contains more bacteria than people on Earth.
- Most of our microbiota is found in our gut, which alone is thought to contain approximately 1000 different species of bacteria.
- These gut bacteria contain about 150 times more genetic diversity than their human host!
- These bacteria have co-evolved with their human hosts for million of years.
- We swallow billions of new living bacteria every day on our food, but they usually have little, if any, negative effect on our resident gut microbes. Some new ones might even help create a beneficial new niche!
- The community of microbes in our gut reaches maturity by the time we are three years old. It can be difficult to disrupt,

although a course of antibiotics can often wreak havoc, usually taking weeks or months to recover.

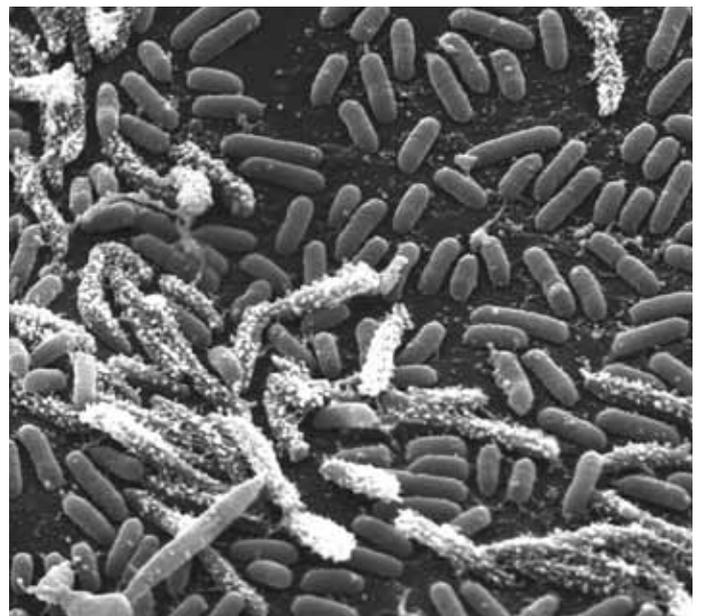


Image: Populations of different bacteria within the human gut.
Source: Tina Carvalho, University of Hawaii.

BUT AREN'T BACTERIA BAD?

While some bacteria such as *Shigella* and *Salmonella* are considered to be parasites – causing harm to their host – most microbes in the gut are considered beneficial because they create valuable vitamins, nutrients, and hormones. Even harmful or parasitic microbes can help to better train our immune system, leading to a lower level of auto-immune diseases.



see pg 27 >

The type of food and how much we eat can be a matter of life and death for many of the microbes in our gut. Not being able to digest any food or water during a bout of dysentery could ultimately mean death for both microbes and their host.

The microbes in the gut mostly cooperate, much like they would in a compost heap – recycling everything. The waste product of one type of bacteria is the foodstuff of another type of bacteria, and so on, creating a sea of possible ingredients to swap and share with other.

But it's not all happy times and cooperation, because many microbes compete for food and space. In fact, one major role of our resident gut bacteria is to take up space in and on the mucus, preventing harmful bacteria from gaining a foothold and causing disease.

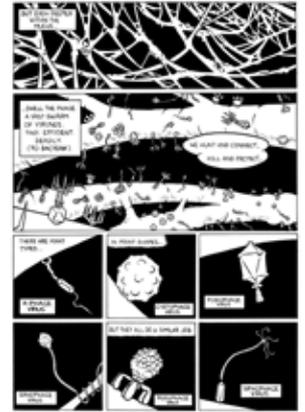
Sometimes competition can turn nasty, involving chemical warfare. The age-old battle of antibiotics has been waged between bacteria and fungi in soil and water for millions of years, and localised skirmishes can also occur in the human gut.

More information [here](#).



Image: Populations of different bacteria within the human gut.
Source: Tina Carvalho, University of Hawaii.

26. WHO ARE THE PHAGE SWARM?



see pg 29 >

Bacteriophage (or phage) are the types of viruses that infect bacteria. The name comes from two parts, *bacteria*, and the Greek word *phagein* – to eat. Taken together it literally means bacterial eaters.

Bacteriophage are the most numerous biological entity on the planet! There are an estimated 10^{31} phage on Earth. That is a one with 31 zeroes after it. That is more than the number of stars in the observed universe. If you stacked all the phage on Earth end to end, the stack would go about 100 million light years!

WHAT IS A VIRUS?

Viruses are small DNA- or RNA-based life forms, typically ranging in size from 20 to 300 nanometres. Viruses need to infect a host cell in order to replicate and have been found to infect all types of cellular life forms on Earth. This makes viruses the most successful predators on the planet.

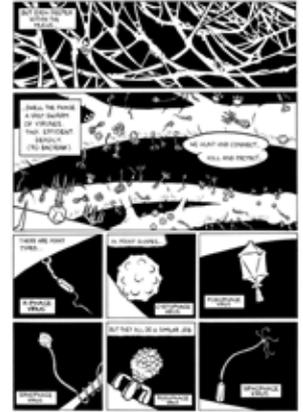
Common viruses of humans include influenza, cold sores (herpes), norovirus/rotavirus (gastroenteritis), HIV, chicken pox, the hepatitis viruses, and the common cold. They also cause more rare infections,

such as Rabies, Ebola, SARS and Polio.

However, not all viruses are bad. Given that bacteriophage are nature's most successful predators of bacteria, many scientists now consider them to be beneficial to their hosts, including humans.

Other viruses have been described to bring new genetic tools (abilities) to their hosts, including:

- a virus that infects a fungus provides the fungus new genes, which in turn allow their host 'Panic Grass' to grow in much hotter weather conditions;
- a virus that infects a parasitic wasp, which helps protect the wasp's eggs after they are laid inside a caterpillar host;
- a type of Herpesvirus, which provides their human hosts with resistance to infection by the bacterium *Yersina pestis* (that is, resistance to Plague or Black Death).



see pg 29 >

SCIENTIFIC CLASSIFICATION OF THE MYOPHAGE

Kingdom:	<i>Unclassified</i>
Phylum:	<i>Unclassified</i>
Class:	<i>Unclassified</i>
Group:	<i>Group I (dsDNA)</i>
Order:	<i>Caudovirales</i>
Family:	<i>Myoviridae</i>
Subfamily:	<i>Tevenvirinae</i>
Genus:	<i>T4likevirus</i>

SPANISH FLU

The most lethal virus ever documented, ‘Spanish flu’ or ‘La Grippe’, spread widely throughout the trenches during the last year of WWI – with infected troops returning to their various homes in different countries, leading to the death of over 50 million people worldwide between 1918 and 1919.

More information from: the [University of Oxford](#) and [Stanford University](#).

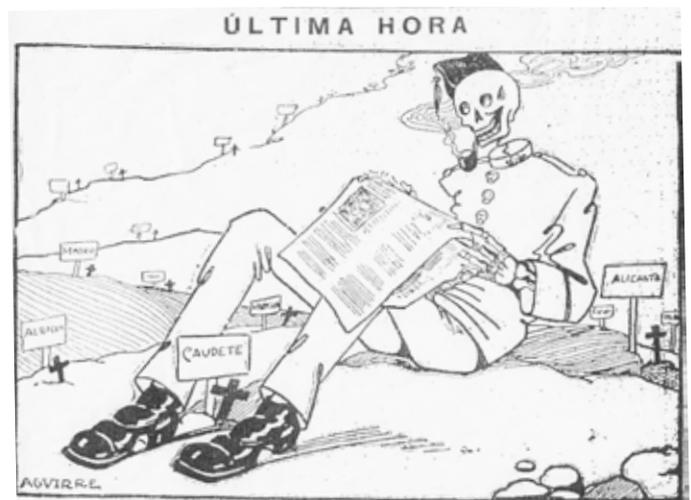


Image: The Naples Soldier (metaphor for the Spanish Flu in Spain).
Source: El Fígaro, Sept. 25, 1918

Image: Digital illustration of a T4 (myophage) bacteriophage by Mike Smith.

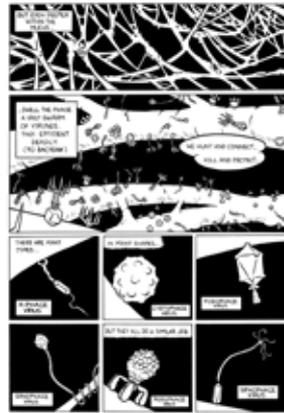
27 . WHAT IS THE RIVER?



see pg 27 >

The river in the story is also referred to as chyme. It is a mixture of food and liquids swallowed by Annie, mixed together with saliva from the mouth, hydrochloric acid from the stomach and bile from the small intestine.

28. ARE VIRUSES ALIVE?

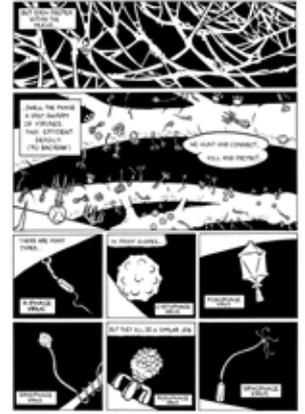


see pg 29 >

Unlike almost all other forms of life, viruses do not breathe or respire. Nor do they carry many of the genes or machinery to perform the chemical reactions typically associated with being alive.

While some scientists describe viruses ‘at the edge of life’, many now do consider viruses to be alive, due to their ability to replicate and evolve their DNA- or RNA-based genome. Viruses also possess a creative ability to make decisions and adapt to changing situations like cellular life forms.

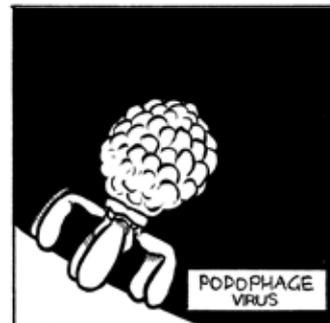
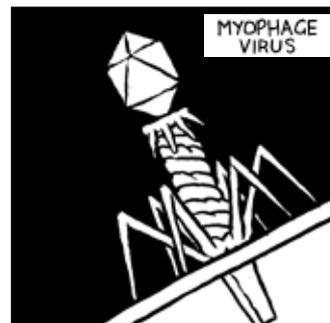
29. WHAT ARE THE DIFFERENT TYPES OF BACTERIOPHAGE?



see pg 29 >

Virologists usually group different types of bacteriophage based on their physical appearance, such as size or shape. The large group *Caudovirales* are bacteriophage that contain tails, including:

- Myophage, with the classic space lander shape;
- Siphophage, with a long siphon or cylinder shaped tail; and
- Podophage, with a very short or foot-like tail.



Other phage types, such as the Cystophage, don't have tails.

HOW CAN BACTERIOPHAGE HAVE SUCH ROBOTIC SHAPES AND PATTERNS?

Most of the viruses found in nature are assembled by the repeated connection of a few types of proteins. These repeated connections typically create viruses with the symmetrical form of a helix or an icosahedron (20-sided shape). Bacteriophage are remarkable, because many of them carry both an icosahedron head and a helix tail.

30. WHAT IS THIS LOCK THING?

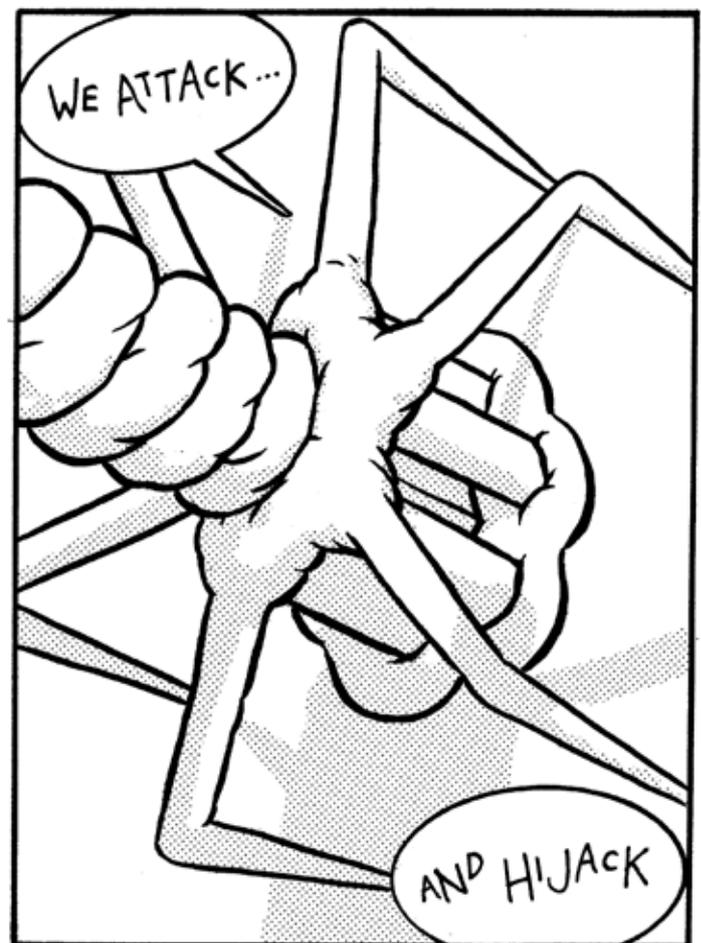


see pg 31 >

Like all viruses, bacteriophage need to get inside their specific host cell before they can replicate. To do this, they must first attach to specific receptors on the surface of the cell. The receptors on the surface of bacteria (such as proteins or lipopolysaccharides) are usually specific to that type of bacteria, so bacteriophage have to create their own attachment proteins to fit the precise shape of these surface receptors, much like fitting a key into a lock.

Once the bacteriophage key successfully locks onto the surface protein of a bacterium, the infection process begins. Some viruses will trick their host into swallowing them through their cell wall and membrane, disguised as a food molecule.

But most bacteriophage will instead puncture a hole in the bacterial cell wall and cell membrane, then deliver their DNA or RNA genome through their tail and into the cell – leaving an empty phage shell behind on the surface of the cell.



31. HOW DO PHAGE KILL BACTERIA?



see pg 32 >



see pg 60 >

Once a virus or viral genome enters a cell, it will try to quickly take control of the host machinery. Sometimes the bacterial host defences succeed in critically damaging or destroying the invading virus genome, by using DNA-cutting enzymes (called restriction endonucleases). But viruses are small and fast, adapting quickly to new challenges.

VIRUS REPLICATION: 1 TO 100 IN 20 MINUTES.

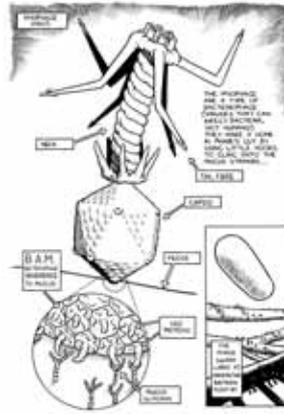
1. Within a matter of seconds after injection, the virus genes initiate their own counter-attack to silence host bacterial defences.
2. Next the virus genome forms into a circle (Circularisation) to begin the process of making new copies using host DNA (Replication).
3. Structural proteins are made next, using amino acids from the host to build new bacteriophage 'shells'.
4. New virus components (both proteins and the genome) are assembled together into dozens of new complete bacteriophage.
5. Finally, the phage produce a mixture of two killer enzymes – called a holin and a

lysins. Holins first form a hole in the bacterial membrane, which then let the lysin enzymes chew through the bacterial cell wall. Both enzymes combined cause the bacteria to burst, releasing dozens of new bacteriophage into the surrounding liquid.

Instead of killing their host bacterium, sometimes a bacteriophage will choose to insert their DNA into the host bacterial genome – called the lysogenic cycle. There, the phage can sit and wait while their genome is automatically copied, each time the host bacterial cell divides in half to create two new daughter cells. But amazingly, the phage DNA can often sense when the host bacterium is under stress (e.g. starvation) and withdraw from the the host genome – triggering the lytic cycle – where dozens of new copies of the phage are quickly assembled and burst from their host.

AREN'T ALL VIRUSES BAD?

There is an ancient proverb which says "*the enemy of my enemy is my friend*". By killing bacteria that might otherwise cause deadly infections, such as the *Shigella* bacteria in our story, many resident human bacteriophage can be considered our friends.



see pg 30 >



see pg 33 >

The BAM model can be considered a beneficial symbiosis – the animal producing the mucus benefits from an added protection of bacteriophage, while the bacteriophage benefit from extra opportunities to infect more bacteria, thereby reproducing more often and producing more copies of themselves. Some scientists have gone so far as to describe this as a new type of immune system within our bodies, protecting our bodies from being invaded and overrun by any potentially nasty bacteria.

More information from [*National Geographic*](#) or the original scientific article in [*PNAS*](#).

33. WHY ARE THE SHIGA GANG SO HAPPY THEY FOUND SOME SLIME?



see pg 33 >

The slime referred to in the story by the Shiga gang (*Shigella* bacteria) is the mucus created by the small and large intestine. The mucus is a source of food for microbes and its presence suggests the *Shigella* are near their ideal habitat.

WHAT IS MUCUS ANYWAY?

Mucus is a matrix of microbes and molecules, which is mostly made of water (90–95 per cent). Mucus gets its slimy structure from the long bottle-brush like molecule called mucins. Made by goblet cells, mucins cover the epithelium and line the intestine. This molecule has a protein backbone surrounded by carbohydrate (sugar) branches. The mucus matrix is the perfect place for good bacteria to live in your body. It also acts as a barrier against bad bacteria.

More information [here](#).

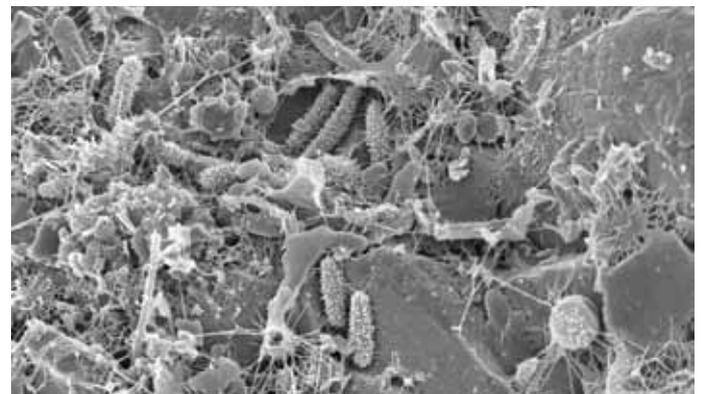
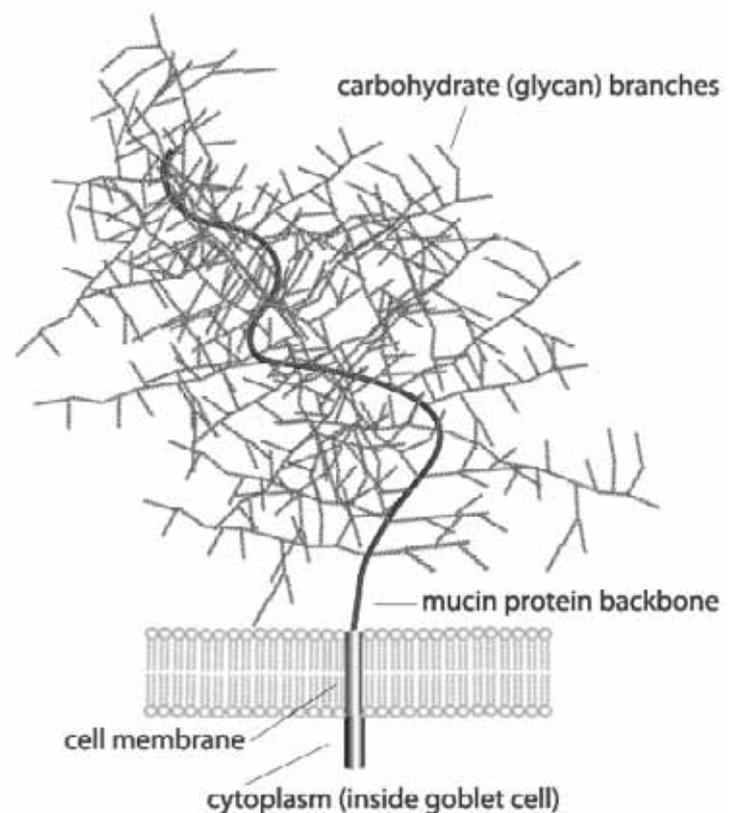


Image: Mucus under the microscope.
Source: Image courtesy of the Lewis Lab at Northeastern University.
Image created by Anthony D'Onofrio, William H. Fowle, Eric J. Stewart and Kim Lewis.

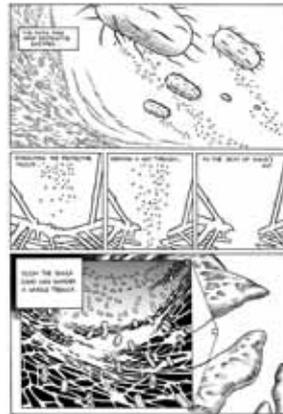


34. WHAT ARE THE TRENCHES THE SHIGA GANG ARE TALKING ABOUT?

35. HOW DO THE SHIGA GANG DISSOLVE THE MUCUS?



see pg 33 >

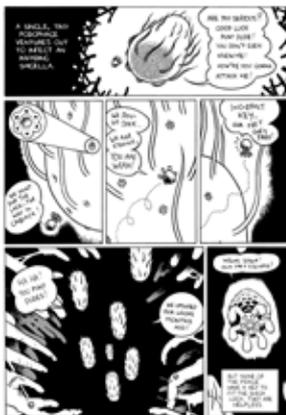


see pg 34 >

The twists and turns of the large intestine contain many folds and creases. From the perspective of bacteria, some of these folds and creases would appear as large canyons, all the way down to tiny trenches. In a sense, the battle between the *Shigella* bacteria and bacteriophage (viruses) in the trenches of Annie's intestine isn't so different from the human trench warfare on the Western Front!

Many bacteria release enzymes into the surrounding soup of food, drink and intestinal juices to help them in some way. *Shigella* bacteria can release an enzyme called a glycohydrolase that cuts away at the carbohydrate (sugar) molecules attached to the mucus. When released, the carbohydrate molecules can act as an energy source for the *Shigella*. And once the protective layer of mucus lining the walls of the intestine has been dissolved, the *Shigella* bacteria can potentially achieve their major goal – to infect the underlying human epithelium cells and reproduce.

36. HOW AND WHY DO SHIGELLA UPDATE THEIR LOCKS?



see pg 36 >

37. SPOILER ALERT! HOW DID THE HERO PHAGE FINALLY HAVE THE RIGHT KEY?



see pg 58 >

It is thought that bacteria and their viruses have been constantly engaged in an evolutionary arms race for billions of years. Because bacteria and viruses reproduce rapidly, they are able to evolve rapidly too – much faster than plants or animals. Each time a virus attacks a population of bacteria there are usually a handful of bacterial survivors who are able to resist infection thanks to a mutation or adaptation. These survivors then reproduce to share or spread their protective trait... until the bacteriophage eventually adapts to find a new way to infect. And so on.

One evolutionary strategy bacteria use to survive bacteriophage infection is to occasionally change their surface receptors. Even a subtle change to this 'lock' can block the virus 'key' from attaching and infecting.

It's a mutant!

In order to adapt to new surface receptors ('locks'), bacteriophage allow for regular mutations when copying their genes during replication. Even tiny mutations to the bacteriophage genes can cause significant changes to the binding proteins ('keys') in their tail, creating the possibility of binding to new bacterial surface receptors. This ability to adapt and continue being effective hunters can mean the difference between life and death for the bacteriophage and for their human host.

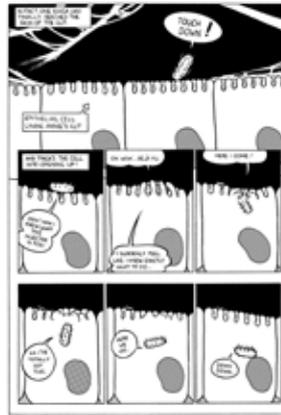
38. DO BACTEROIDES AND PREVOTELLA REALLY HAVE BAYONETS?



see pg 40 >

Some types of bacteria – including *Prevotella* and *Bacteroides* (called Tella and Roidey in our story) – have bayonet or syringe-like structures called Type 6 Secretion Systems (T6SS) that they use to attack other bacteria. The main strategy is to puncture the membrane of the opponent bacteria, either to rupture their cell or to inject a lethal chemical inside.

39. WHY DOES THE GUT EPITHELIUM CELL LET A SHIGELLA BACTERIUM INSIDE?



see pg 41 >

The *Shigella* tricks the epithelial cell into swallowing it by injecting a signal molecule that hijacks the cell's machinery, causing it to open. The epithelial cell then contracts, engulfing the *Shigella*. Once inside, the *Shigella* is able to multiply rapidly and travel sideways into neighbouring epithelial cells.

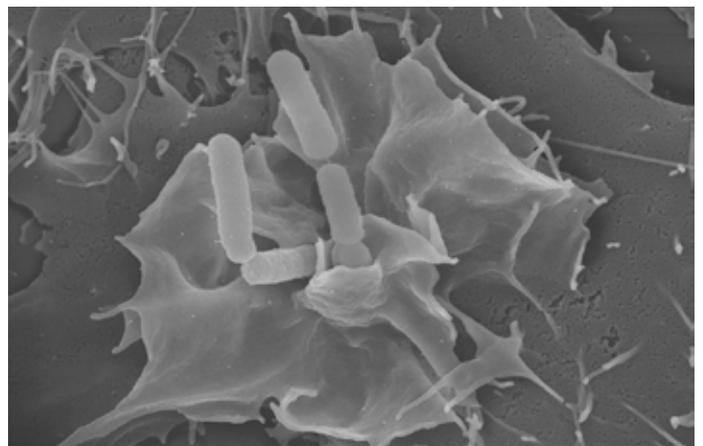
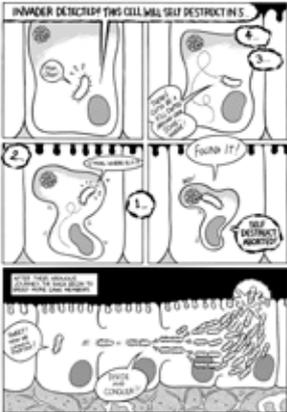


Image: Human epithelium cell engulfing *Shigella* bacteria.
Source: P. Sansonetti, Pathogénie Microbienne Moléculaire, Institut Pasteur.

40. WHY IS THE EPITHELIUM CELL SELF-DESTRUCTING?



see pg 42 >

The epithelial cell recognises the *Shigella* as a foreign invader. In an attempt to save the surrounding cells and the body, it activates a programmed cell death sequence that attempts to kill itself and everything inside it.

HOW DOES THE SHIGELLA BACTERIUM USE THE KILL SWITCH?

Shigella bacteria can release a molecule to deactivate the programmed cell death sequence. We chose to introduce a kill switch molecule to simplify this very complex process.

41. WHAT ARE NEUTROPHILS?



see pg 44 >

The infection of the gut epithelium by *Shigella* bacteria triggers the release of alarm molecules – which then activates a response from the immune system. The first line of defense against *Shigella* is the release of a type of white blood cells, called neutrophils. Neutrophils migrate from the bloodstream across the epithelium to the site of infection, where they can directly phagocytose (that means to engulf and degrade) the bacteria. In an extreme situation, the neutrophils can create Neutrophil Extracellular Traps (NETs) – a form of self-destruction where the release of massive amounts of deadly chemicals kill themselves – and many surrounding bacteria.

42. WHAT ARE THESE VOLCANOES?



see pg 46 >

When under attack from an invasion of pathogenic (disease-causing) microbes such as *Shigella* bacteria, the mucosal cells (called goblet cells) in the human intestinal wall will regularly erupt with volcanoes of mucus to flush out the pathogen.

But this flushing response requires several litres of water each day. If the flushing action of the gut doesn't quickly succeed in removing the invading cells, its host will eventually risk death from dehydration (loss of water).

43. WHAT IS WRONG WITH THIS GUY?



see pg 47 >

This soldier has what we would now call Post Traumatic Stress Disorder (PTSD) – a set of ongoing reactions to a trauma that includes mental and emotional stress and re-living the event (flashbacks). For many soldiers serving in WWI, this created family trauma and upheaval upon their return home... often lasting a lifetime.

During WWI, the condition began to be recognised as a medical condition. During this early stage of our understanding it was called 'shell shock', or later 'neurasthaenia'. It wasn't until after the Vietnam War that we began to use the term PTSD.

44. WHAT DOES THE BLOOD IN ANNIE'S DIARRHOEA MEAN?



see pg 53 >

The presence of blood in Annie's poo means she has an infection in her gut. Based on Annie's experience treating Private Robbins, she (correctly) suspects that she also has dysentery.

The epithelium lining of the gut is only one cell thick, with blood capillaries sitting directly underneath. Each time clusters of *Shigella* burst through the epithelium they break capillaries and blood flows into the gut and downstream into the poo.

45. WHAT WAS THE SICK SISTERS HOSPITAL?



see pg 54 >

Nurses who became ill during service were treated in their own wards because it was not thought appropriate that they be treated alongside soldiers or civilians. There was a Sick Sister's Ward attached to the 8th British General Hospital in Rouen, France, for this purpose. There were also convalescent homes further from the front if nurses required a longer recovery time.

46. DID THEY REALLY USE ALL THESE AS CURES, AND WHY?



see pg 56 >

- Brandy was thought to warm you up, calm nerves, and ease pain. It would have had negative effects on the body, but nothing too major.
- Lister's Antidysenteric Serum, was created by the Lister Institute, a British research institute working on preventative medicine with a strong focus on microbiology. The serum was prepared in a horse by injecting the horse with both *Shigella dysenteriae* and *S. flexneri*. The antibodies created by the horse's immune system were thought to help the human immune system mount an attack against infecting *Shigella*, and were injected into patients.
- Magnesium Sulphate and Sodium Sulphate were both used to induce vomit, but this wouldn't effectively remove the required numbers of *Shigella* bacteria from the gut. It may in fact be harmful, as dysentery patients already lose too much fluid and become fatally dehydrated. Losing more fluid through vomit would just add to this problem.



Image: WWI propaganda poster.
Source: David Henry Souter.

47. WHO IS FELIX D'HERELLE AND WHY IS GRACE SENDING HIM A SAMPLE?



see pg 57 >

Felix d'Herelle was a French-Canadian microbiologist who discovered and named bacteriophage whilst working at the Institut Pasteur (Pasteur Institute) in France during WWI. In his famous 1917 scientific article, d'Herelle described “an invisible, antagonistic microbe of the dysentery bacillus... a filterable virus, but a virus parasitic on bacteria”. We chose to include the reference of Grace sending this sample, because at the time of our story (August 1916), d'Herelle had requested for as many samples of dysentery stools to be sent to him as possible from around France!

After his original discovery, Felix d'Herelle also pioneered much of the early research into the use of bacteriophage as a medical tool for overcoming bacterial diseases such as dysentery, cholera, and typhoid. There is now a renewed interest in this medical approach – commonly referred to as ‘phage therapy’ – due to the current crisis caused by the growing resistance of bacteria to antibiotics.



Image: Photograph of Felix d'Herelle (ca. 1926).

More information [*here*](#).

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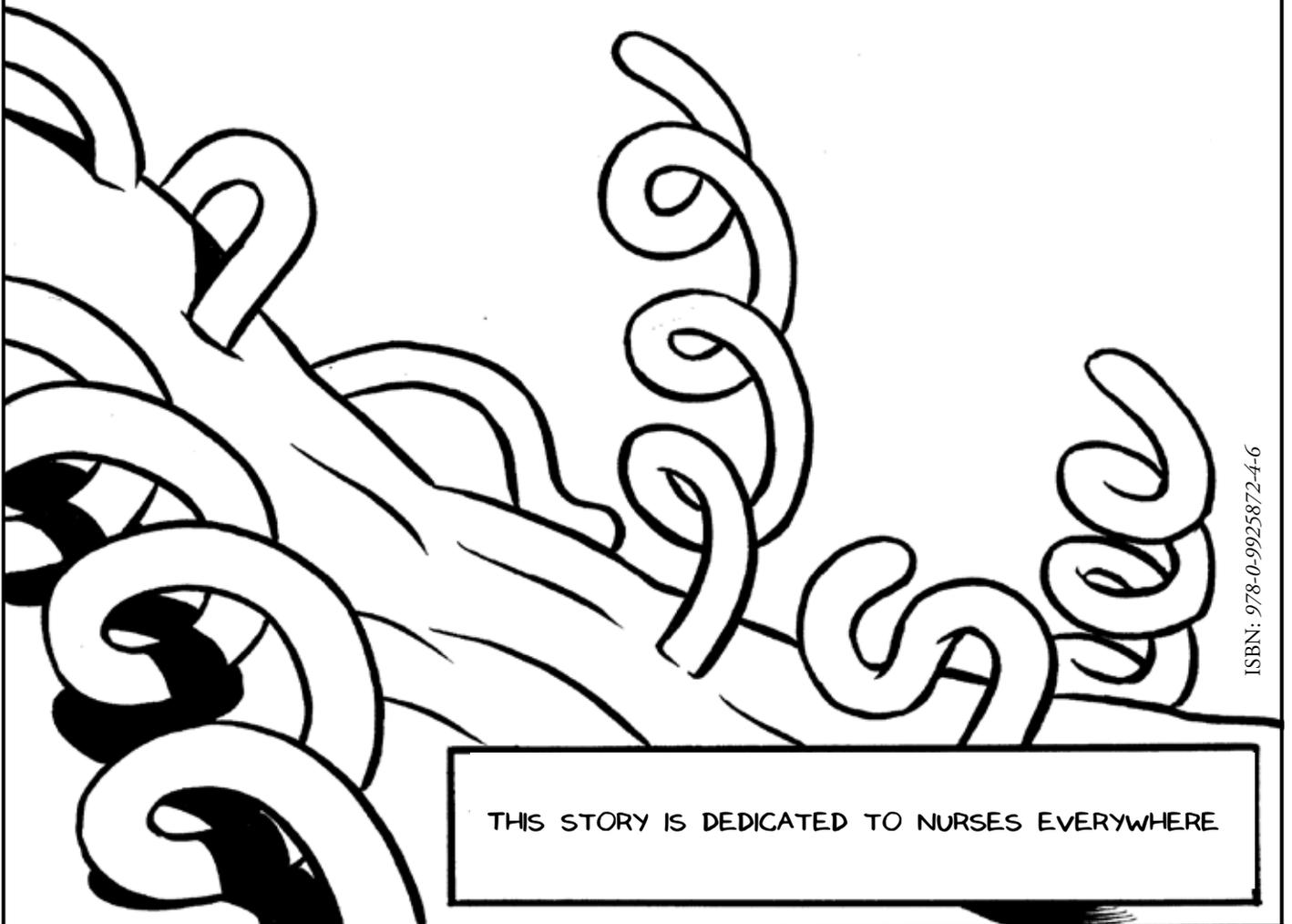
ONE NURSE TRILLIONS OF MICROBES A DEADLY WORLD WAR ONE BATTLE...

While treating a patient with dysentery, Sister Annie Barnaby encounters a strain of lethal bacteria. As the invaders journey deep into her gut, the resident microbes must fight to survive. Annie's life hangs in the balance. Enter the phage, a deadly predator, ready to wage war to protect their host.

Created by an expert team of scientists, artists, educators, writers and historians, *The Invisible War* is a story like no other.

"It shows and tells" *Hamish*, 14

"This book is a brilliant example of what the human mind can produce" *Harry*, 14



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THIS STORY IS DEDICATED TO NURSES EVERYWHERE