2010

World of Viruses: the Frozen Horror

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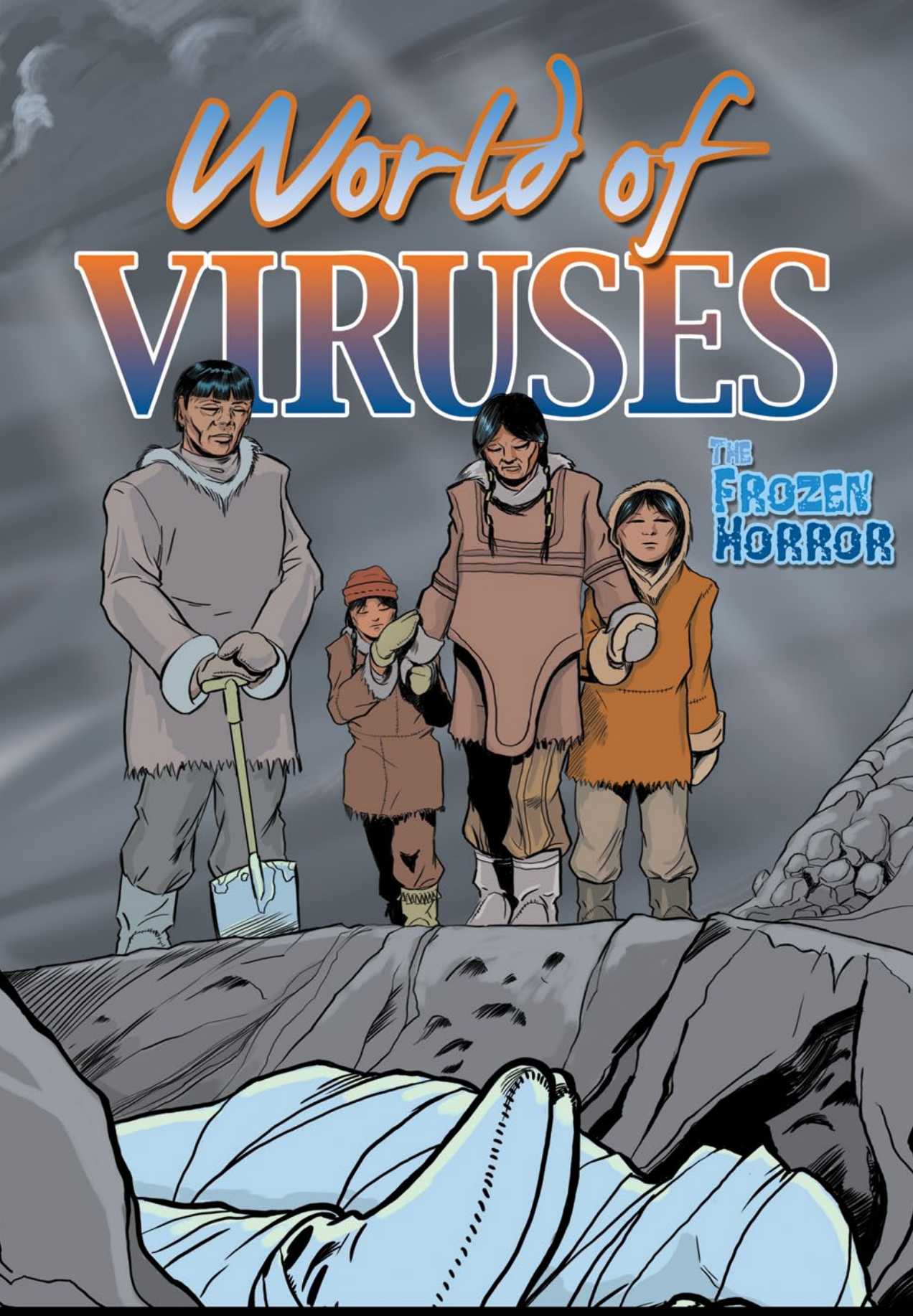

SEPA SCIENCE EDUCATION PARTNERSHIP AWARD
Supported by the National Center for Research Resources, a part of the National Institutes of Health

University of Nebraska Lincoln

World of VIRUSES

Graphic Novel
THE FROZEN HORROR

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art and letters by **TOM FLOYD**
produced by **ANGIE FOX**

Essay
INFLUENZA: LOOKING DOWN FROM THE STARS

written by **CARL ZIMMER**

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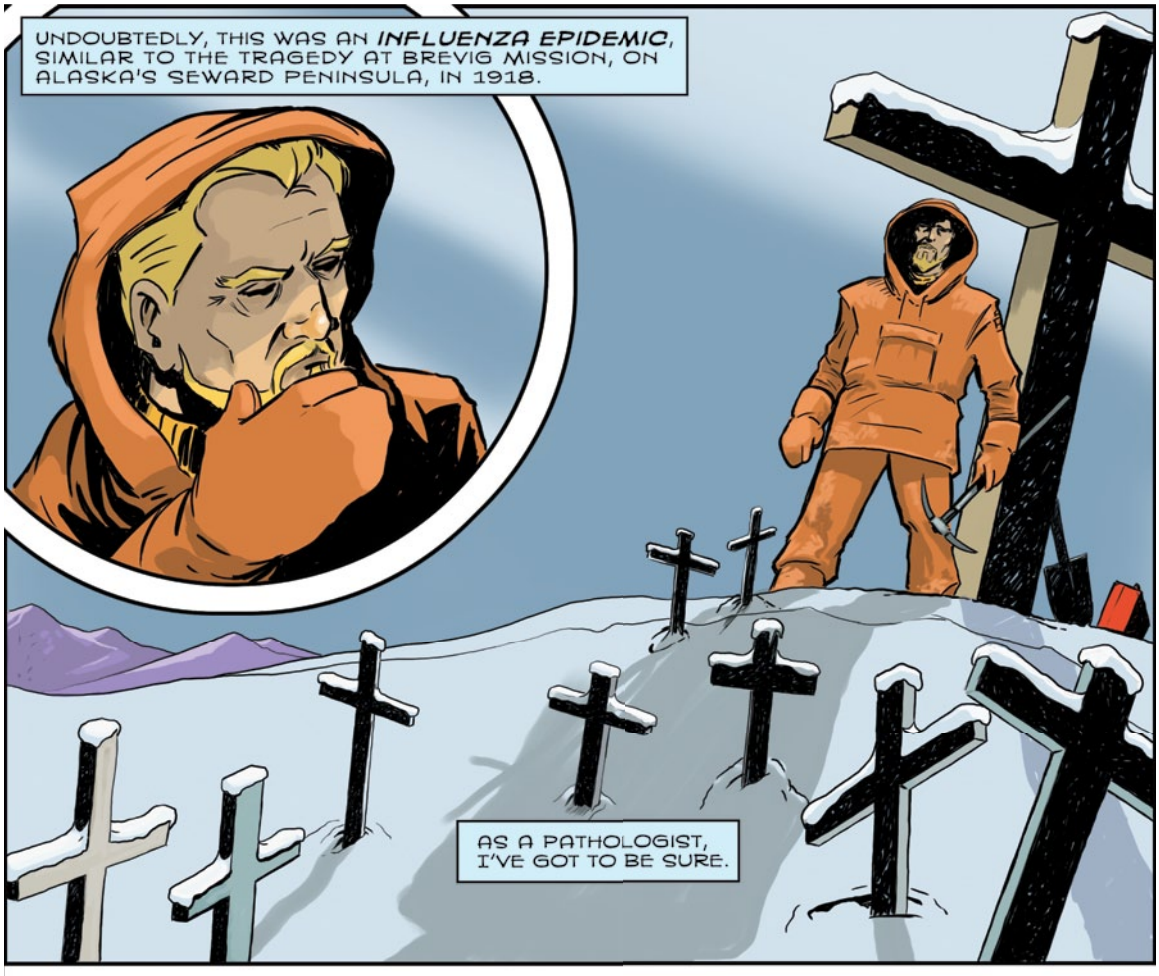
THE FROZEN HORROR
THIS IS THE PLACE. TRANSLATED BY THE NATIVES AS "THE LAND OF HAUNTED SHADOWS."
I CAN SEE WHY.
NOT FOUND ON ANY ALASKAN MAP, THE LOCATION IS KNOWN ONLY THROUGH WORD-OF-MOUTH, PASSED DOWN THROUGH COUNTLESS GENERATIONS.
TOOK ME THE BETTER PART OF A YEAR TO LOCATE IT.
SO, THIS IS WHAT IT LOOKS LIKE.
SO QUIET AND SERENE. NO ONE WOULD EVER THINK THIS WAS ONCE THE SITE OF A MASSACRE...
...AND ONE OF THE GREATEST BIOLOGICAL MYSTERIES ON THE PLANET.
103 Native Villagers Lie in Rest Here, Losing Their Lives in the Short Span of Six Days, October 1918


UNDOUBTEDLY, THIS WAS AN *INFLUENZA EPIDEMIC*, SIMILAR TO THE TRAGEDY AT BREVIG MISSION, ON ALASKA'S SEWARD PENINSULA, IN 1918.
AS A PATHOLOGIST, I'VE GOT TO BE SURE.


BEWARE...


WHY DO YOU WAKE THE DEAD?
YOU STARTLED ME!
I APOLOGIZE, THIS MUST LOOK VERY STRANGE TO YOU. MY NAME IS DR. JOSEPH ERICKSON. I'M A SCIENTIST, SENT HERE TO INVESTIGATE THE PLAGUE THAT SEIZED THIS VILLAGE NINETY YEARS AGO.
UH, I HAVE THE PROPER PERMITS FOR THIS EXCAVATION. YOU SEE, WE NEED TO EXTRACT SOME TISSUE FROM ONE OF THE DECEASED, PRESERVED HERE IN THE PERMAFROST.
LATER, IN THE LABORATORY, WE'LL HOPEFULLY BE ABLE TO IDENTIFY THE VIRUS AND POSSIBLY CREATE A VACCINE AGAINST THE EVENT OF A FUTURE OUTBREAK—
YOU SHOULD LEAVE. NOW. THIS VERY MOMENT.
THERE IS STILL DEADLY DANGER HERE.


I... I'M AFRAID I DON'T UNDERSTAND.
YOU SHOULD BE AFRAID.
MY NAME IS HINSHLAI. THE PLACE WHERE WE ARE STANDING WAS ONCE THE HOME OF THE GREAT DYING.
I AM HERE TO TELL YOU THE TALE.
NINETY YEARS AGO THIS WAS A NORMAL, HAPPY FISHING VILLAGE.
ONE WHO LIVED THERE WAS A LITTLE CHILD, FIVE YEARS OLD.


ONE BRIGHT BUSY DAY, AS THE OTHERS HURRIED ABOUT WITH THEIR BASKETS AND NETS, SHE WANDERED OFF IN HER LONELINESS...
...AND SHE FIRST ENCOUNTERED THE CREATURE.
NEVER HAD THE GIRL BEHELD ANYTHING LIKE IT.
HELLO. WHAT KIND OF THING ARE YOU? WOULD YOU LIKE TO COME HOME WITH ME?

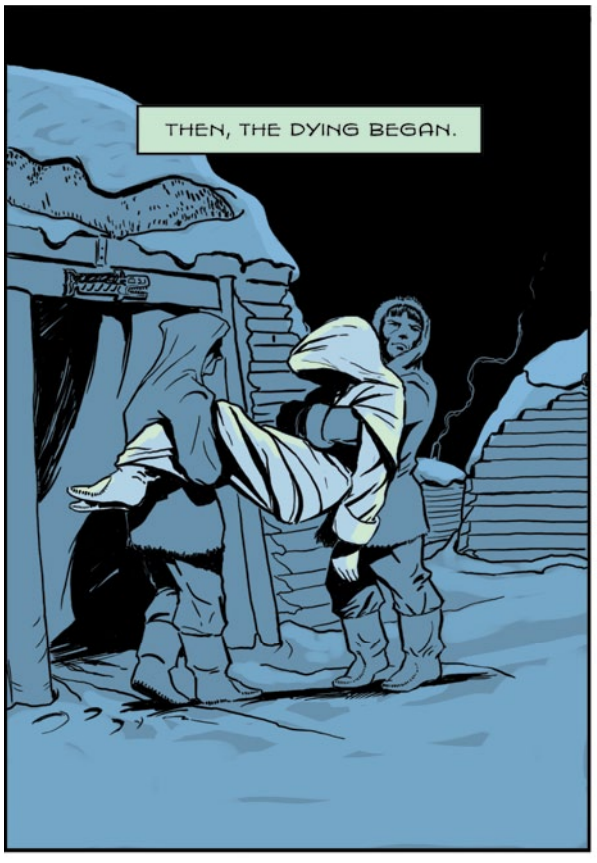

IT WAS A FRIENDLY, AFFECTIONATE LITTLE BEING AND DID NOT PROTEST WHEN THE CHILD CARRIED IT AWAY BACK TO THE VILLAGE.


AT FIRST SIGHT, EVERYONE WAS QUITE FOND OF THE CREATURE, BUT THEN THE STRANGENESS STARTED.
WHAT A HANDSOME BIRD! AND SO FRIENDLY!


JUST LOOK AT THIS BRIGHT-EYED LITTLE PIG! HE LOOKS AS THOUGH HE CAN UNDERSTAND EVERY WORD WE SAY.


BUT IT WASN'T A GOOSE, OR A PIG, THAT THE GIRL HAD BROUGHT INTO HER VILLAGE.


SOMEHOW THE CREATURE HAD TRICKED EVERYONE, MAKING THEM SEE WHATEVER IT WISHED. ONLY THE CHILD KNEW SOMETHING OF THE TERRIBLE TRUTH...
...THAT THE BEAST WAS NOT WHAT IT APPEARED TO BE.


THEN, THE DYING BEGAN.

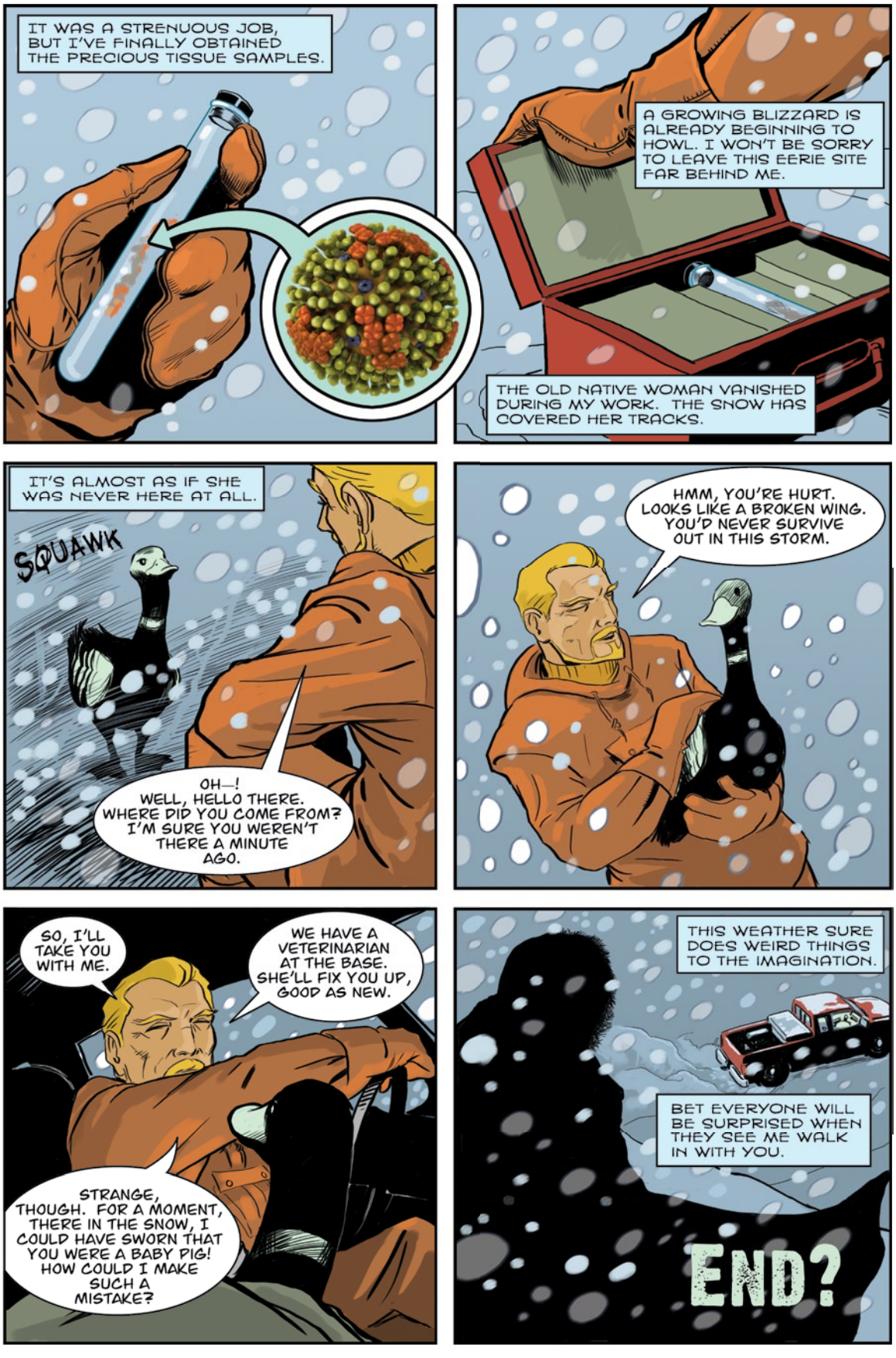

QUICK, CRUEL AND BRUTAL.


UNRELENTING.


NEARLY EVERYONE WAS AFFECTED.
MOTHER...? MOTHER, CAN YOU HEAR ME...?


AT THE END OF SIX SHORT DAYS, THE ENTIRE VILLAGE WAS A GRAVEYARD.
ONLY THE GIRL, HER OLDER SISTER, AND THEIR GRANDPARENTS REMAINED.
THE CREATURE, AND ITS POISONOUS PLAGUE HAD VANISHED, LEAVING FOREVER A HOLLOW ACHE IN THE HEARTS OF THE FEW SURVIVORS.


WHAT A DREADFUL STORY.
I CAN FULLY UNDERSTAND WHY THIS TERRIBLE TRAGEDY HAS GROWN INTO SUCH A FRIGHTFUL LEGEND.
HOWEVER, THERE WAS NOTHING SUPERNATURAL ABOUT WHAT HAPPENED IN THIS DOOMED VILLAGE. LET ME TRY TO EXPLAIN.
THIS HAS ALL THE ASPECTS OF AN OUTBREAK OF A NEW STRAIN OF INFLUENZA, ONE OF THE MOST LETHAL VIRUSES IN THE HISTORY OF HUMANITY. AS A SCIENTIST, I'M HERE TO TRY TO SOLVE THE MYSTERY.
YOU SEE, FLU GENES SHOULD STILL BE PRESENT IN THESE FROZEN GRAVES, AND WE CAN DETERMINE WHAT TYPE OF NEW DEADLY STRAIN THIS IS. FLU VIRUSES CREATE NEW STRAINS BY REASSORTING THEIR GENES WITH OTHER FLU STRAINS, SUCH AS THOSE FROM PIGS AND BIRDS.
WE SHOULD BE ABLE TO DEDUCE THE ACTUAL GENETIC CODE OF THE VIRUS.
THIS EXPERIMENT MAY EVEN HELP US TO UNDERSTAND WHAT MADE THIS FLU STRAIN SO VIRULENT. THEN WE CAN CREATE VACCINES AGAINST A FUTURE OUTBREAK.
WE HAVE THE CHANCE TO DO SOME REAL GOOD HERE, AND FINALLY PUT TO REST THAT GHOST STORY OF THE LITTLE GIRL AND HER SHAPE-CHANGING CHIMERA.
LISTEN, I'M SORRY. PLEASE FORGIVE ME, I GOT CARRIED AWAY. I'M AFRAID YOU DON'T COMPREHEND MUCH OF WHAT I JUST SAID—
IT IS YOU WHO FAILS TO UNDERSTAND. THIS IS NO MYTH. I SAW THE BEAST WITH MY OWN EYES, EVEN AS I SEE YOU NOW.
I, HINSHLAI, WAS THAT LITTLE CHILD OF FIVE.


IT WAS A STRENUOUS JOB, BUT I'VE FINALLY OBTAINED THE PRECIOUS TISSUE SAMPLES.
A GROWING BLIZZARD IS ALREADY BEGINNING TO HOWL. I WON'T BE SORRY TO LEAVE THIS EERIE SITE FAR BEHIND ME.
THE OLD NATIVE WOMAN VANISHED DURING MY WORK. THE SNOW HAS COVERED HER TRACKS.
IT'S ALMOST AS IF SHE WAS NEVER HERE AT ALL.
SQUAWK
OH—! WELL, HELLO THERE. WHERE DID YOU COME FROM? I'M SURE YOU WEREN'T THERE A MINUTE AGO.
HMM, YOU'RE HURT. LOOKS LIKE A BROKEN WING. YOU'D NEVER SURVIVE OUT IN THIS STORM.
SO, I'LL TAKE YOU WITH ME.
WE HAVE A VETERINARIAN AT THE BASE. SHE'LL FIX YOU UP, GOOD AS NEW.
STRANGE, THOUGH. FOR A MOMENT, THERE IN THE SNOW, I COULD HAVE SWORN THAT YOU WERE A BABY PIG! HOW COULD I MAKE SUCH A MISTAKE?
THIS WEATHER SURE DOES WEIRD THINGS TO THE IMAGINATION.
BET EVERYONE WILL BE SURPRISED WHEN THEY SEE ME WALK IN WITH YOU.
END?

Influenza:
Looking Down From the Stars

BY CARL ZIMMER

INFLUENZA: if you close your eyes, forget what the word means, and say it aloud, it actually sounds lovely. With its lilting rhythm, Influenza might be the name of an ancient Italian village. The word is, in fact, Italian, meaning INFLUENCE. And it is in fact an ancient name. In the Middle Ages, Italian physicians believed that stars influenced the health of their patients, sometimes causing a mysterious fever that periodically swept across Europe. Over the centuries, influenza has continued to wreak havoc. Global epidemics have periodically emerged; in 1918, an outbreak of the flu killed an estimated 20 million people. But even without an epidemic, influenza is a dangerous disease. Each winter, 36,000 people die of the flu in the United States alone, and somewhere between 250,000 and 500,000 people die worldwide each year.

Today scientists know that influenza is not the work of the stars. It's caused by a minuscule virus. Remarkably, the influenza virus can cause all this suffering with just 10 genes. We humans, by contrast, have about 20,000 genes. But 10 genes are all it takes for the influenza virus to sneak into our bodies and thrive, even as we get deathly ill.

Star-Forming Region LH 95 image courtesy NASA, ESA, and the Hubble Heritage Team (STScI/AURA)-ESA/Hubble.

Flu viruses spread in the droplets sick people release with their coughs, sneezes, and runny noses. A new victim may accidentally breathe in a virus-laden droplet or pick it up on a doorknob and then bring now contaminated fingers in contact with the mouth. Once a flu virus gets into the nose or throat, it can latch onto a cell lining the airway. It manipulates

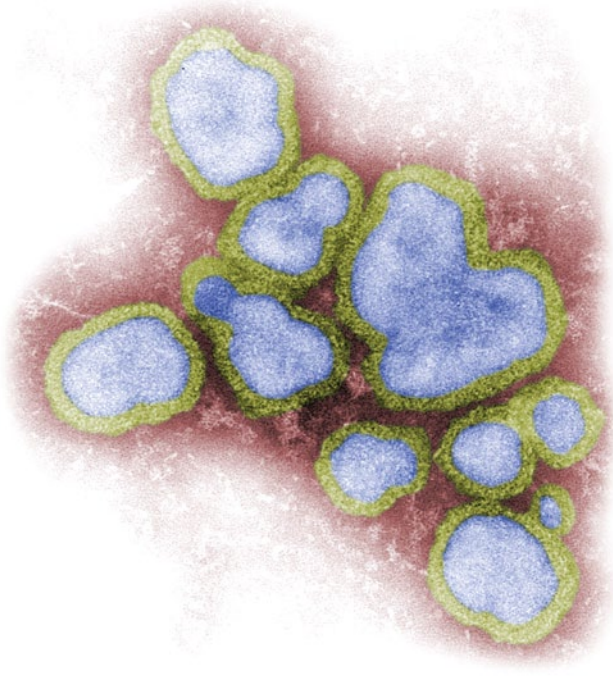
Image courtesy CDC/Brian Judd; photo by James Gathany.

the cell to swallow it up, whereupon it releases its genetic material. The virus uses the cell's own proteins to build new genes, along with the protein shells that encase them. Once new viruses have formed, they rip open holes in the host cell in order to escape and infect other cells.

As flu viruses spread from cell to cell in the lining of the airway, they leave destruction in their wake. The mucus and cells lining the airway gets destroyed, as if the flu viruses were a lawn mower cutting grass. In healthy

people, the immune system is able to launch a counterattack in a matter of days. In such cases, the flu causes a wave of aches, fevers, and fatigue, but the worst of it is over within a week. But in some people, the flu virus opens the way for more serious infections. Normally, the top layer of cells serves as a barrier against a wide array of pathogens. The pathogens get trapped in the mucus, and the cells snag them with hairs, swiftly notifying the immune system of intruders. Once the influenza lawn mower has done its damage, the pathogens can slip in and cause dangerous lung infections, some of which can be fatal.

For a virus that has caused so much death in the past and continues to claim so many victims each year, the flu virus remains surprisingly mysterious. Seasonal flu is most dangerous for people with weak immune systems that can't keep the virus in check—particularly young children and the elderly. But in flu pandemics, like the 1918 outbreak, people with strong immune systems proved to be particularly vulnerable. Scientists don't know why the flu switches targets this way. One theory holds that certain strains of the flu provoke the immune system to respond so aggressively that it ends up devastating the host instead of wiping out the virus.

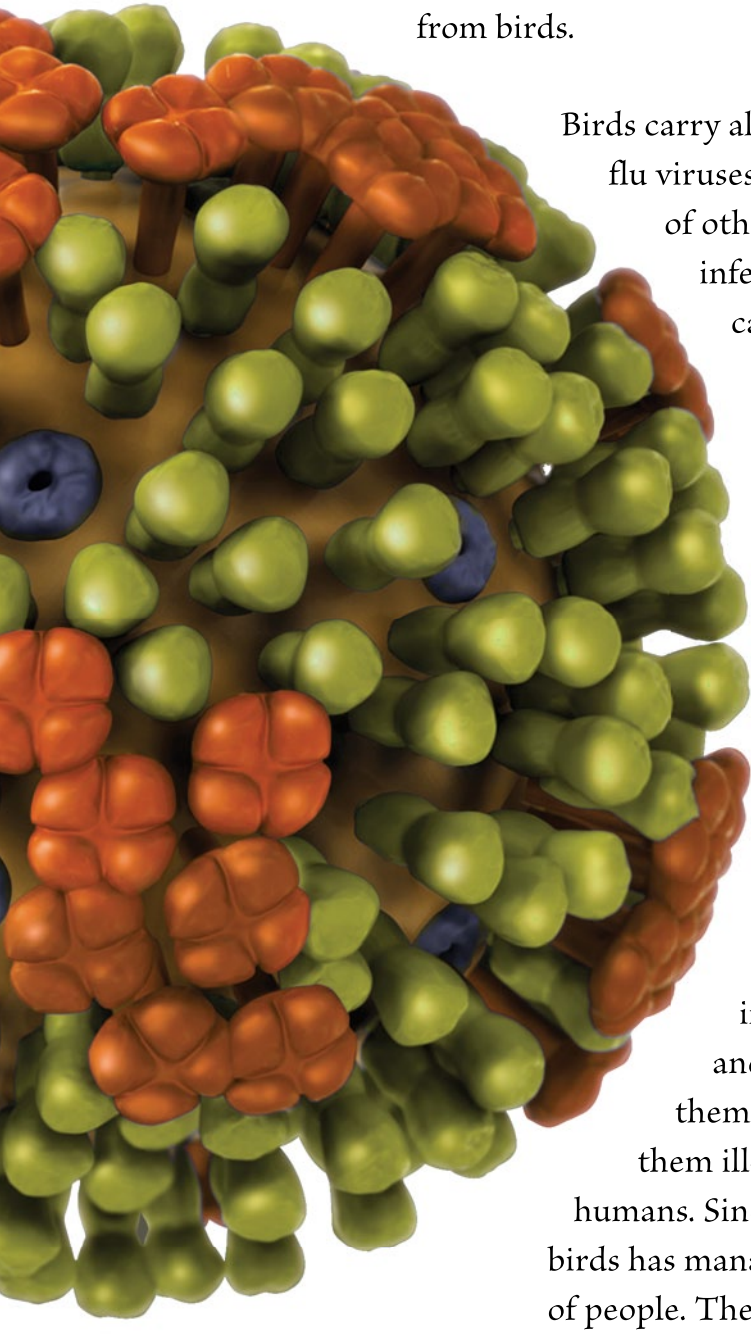


THIS IS A TRANSMISSION ELECTRON MICROGRAPH OF INFLUENZA VIRUS PARTICLES.

Image courtesy CDC/F. A. Murphy.

Scientists also don't know when influenza first started making people sick. There certainly are historical records of outbreaks of deadly fevers going

back thousands of years, but it's impossible to know whether influenza viruses caused them or a virus with similar symptoms. But amidst all the mysteries of the flu, it's clear where it came from. It came from birds.



THE INFLUENZA VIRUS.

Image courtesy CDC/Douglas Jordan; illustration by Dan Higgins. Recolored.

Birds carry all the known strains of human flu viruses, along with a vast diversity of other flu viruses that don't infect humans. Many birds can carry the flu without getting sick. Rather than carry the virus in their airway, many birds are infected in their guts and shed new viruses with their droppings. When other birds ingest virus-laden water, they get infected as well. The transition from bird to human probably was preceded by a number of failed crossings. Bird flu viruses are well-adapted to infecting their avian hosts and reproducing quickly inside them. Those adaptations make them ill-suited to spreading among humans. Since 2003, a strain of flu from birds has managed to sicken hundreds of people. The bird flu is often deadly to human hosts, so public health workers have been tracking it closely and taking measures to halt its spread. But for now, at least, this

strain of bird flu can only move from a bird to a human. It has shown little ability to spread from one human to another.

Unfortunately, a poorly adapted flu virus can evolve into a well-adapted one. Flu viruses are particularly sloppy at replicating their genes, so that many new viruses acquire mutations. These mutations are like random changes to the letters in the flu's recipe. Some of the mutations have no effect on viruses. Some leave them unable to reproduce. A few give flu viruses a reproductive advantage. Natural selection favors these beneficial mutations, and as mutation after mutation accumulates, flu viruses can become better suited to infecting humans. Some mutations alter the shape of the proteins that stud the virus shell, allowing them to grab human cells more effectively. Other mutations help the flu virus cope with human body temperature, which is a few degrees cooler than that of birds.

Human viruses have also adapted to a new route of transmission. In birds, the viruses travel from guts to water to guts. In people, the virus moves from airways to droplets to airways. This new route also causes the flu to become a seasonal disease. In places like the United States, most flu cases occur during the winter. According to one hypothesis, the air is dry enough in those months to allow virus-laded droplets to float in the air for hours, increasing their chances of encountering a new host. In other times of the year, the humidity causes the droplets to swell and fall to the ground.

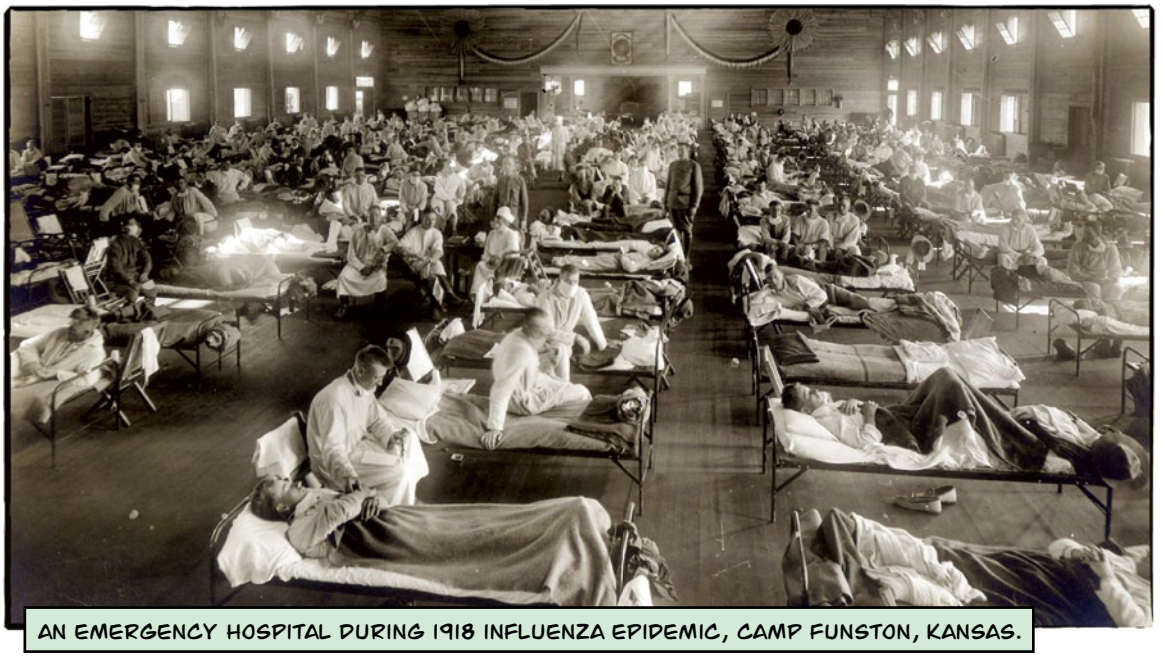
Thanks to their peculiar biology, flu viruses can also change their genes in a far more dramatic fashion. While many other viruses have genes arrayed in a single loop, flu viruses store their genes on eight separate segments. Sometimes two flu viruses will infect the same cell, and the cell will start producing the segments of each strain at the same time. Each new virus produced in the cell will have eight segments, but the segments may come from both of the original viruses. Instead of tweaking flu genes with small mutations, this process (called reassortment) can give a flu virus some entirely new genes.

As scientists get a closer look at the genes of flu viruses, they're discovering that reassortment has played a major role in the natural history of the flu. A quarter of all birds with the flu have two or more virus strains inside them at once. The viruses swap genes through reassortment, and as a result they can move easily between bird species. The great fear about the current outbreak of bird flu in southeast Asia is that reassortment will endow that strain with genes from a human flu virus, immediately giving it the ability to spread from person to person.

Such reassortments aren't just important on the rare occasions when flu viruses jump from birds to humans. Human flu viruses also swap genes among themselves during every flu season. The longer a flu strain circulates, the more familiar it becomes to people's immune systems, and the faster they can squelch its spread. But thanks to reassortment, an old flu strain can pick up some somewhat different genes and become harder for people to fight off.

Humans are not the only hosts who have picked up flu viruses from birds, however. Horses, dogs, and several other mammals have also picked them up. And in April 2009, the world became painfully aware that flu viruses also infect pigs. An outbreak of so-called swine flu spread from pigs to humans in Mexico and soon spread over the entire planet.

The history of this particular flu strain, called Human/Swine 2009 H1N1, is a tangled tale of genetic mixing and industrialized agriculture. Pigs seem to have just the right biology for reassortment; some of their receptors can easily accept human flu viruses, while other receptors welcome bird flu. Over the past century, pig farms have grown in size and density, so that flu viruses can easily move from host to host and swap genes with other strains. The oldest known swine flu strain emerged around the same time the 1918 pandemic strain entered humans; this so-called "classical strain" is still making pigs sick. In the 1970s a bird flu strain in Europe or Asia evolved into a new swine flu strain. A different pig-bird mix arose in the



AN EMERGENCY HOSPITAL DURING 1918 INFLUENZA EPIDEMIC, CAMP FUNSTON, KANSAS.

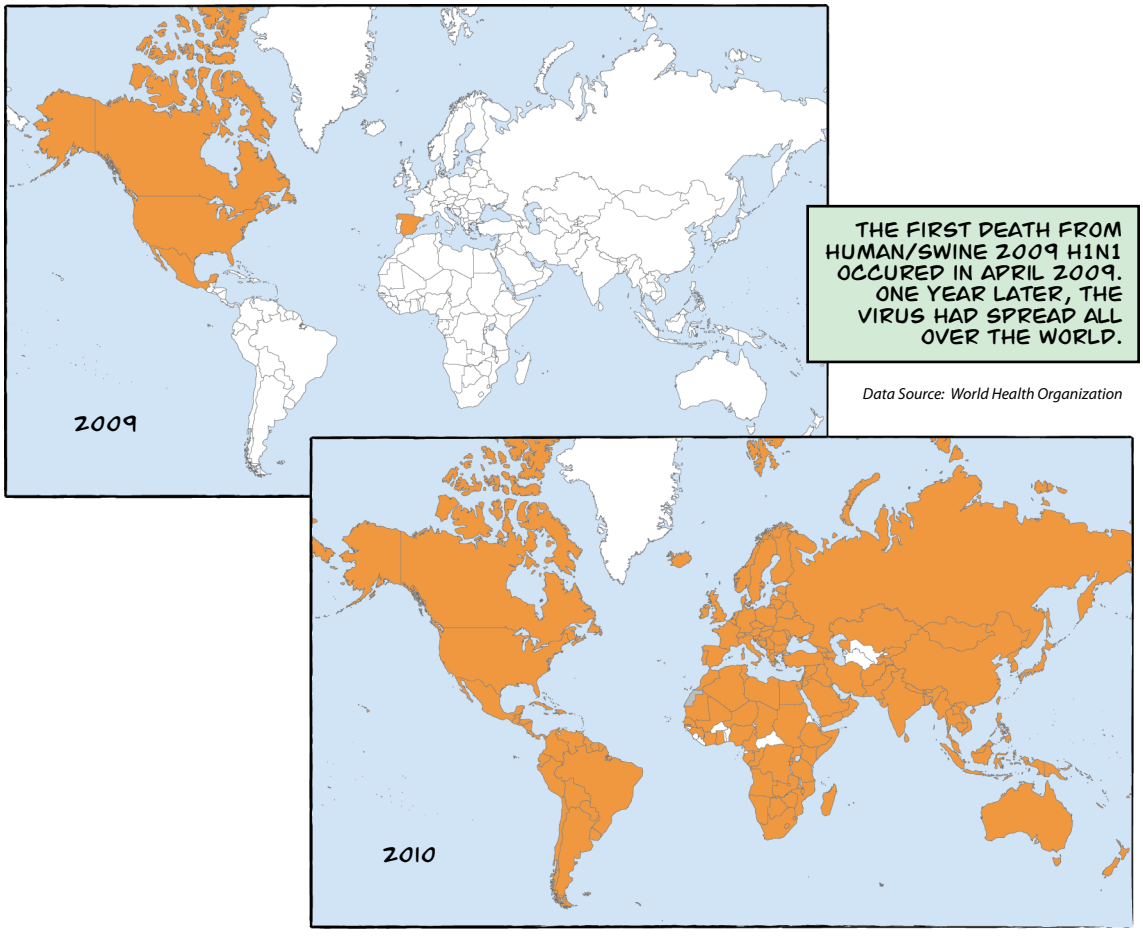
Image courtesy The National Museum of Health and Medicine.

United States. And in the late 1990s, American scientists discovered a "triple reassortment" that mixed genes from classic swine flu with genes from bird viruses and human viruses.

Once scientists sequenced the genes of the new Human/Swine 2009 H1N1, they realized that it was the product of two different flu viruses: the triple reassortment, and the Eurasian bird-to-pig strain. By comparing the new mutations that have arisen in the viruses infecting different patients, researchers have estimated that this new virus first evolved in the fall of 2008. It circulated quietly before coming to light in the spring of 2009.

Because Human/Swine 2009 H1N1 was such a new virus, public health authorities quickly swung into action. The Mexican government essentially shut down the entire country for a time, to reduce the chances that the new virus could find new hosts. As Human/Swine 2009 H1N1 turned up in other countries, their governments took actions of their own, which included shutting down many schools. By May 2009, it was clear that the new virus was not noticeably more dangerous than typical seasonal flu viruses. It claimed lives, but sadly typical flu viruses claim many lives each year without garnering headlines.

As the 2009 flu season ended in the northern hemisphere, scientists anticipated that Human/Swine 2009 H1N1 would make its way to the southern hemisphere, where the flu season was just getting started. No one can say if the strain will fade away, outcompeted by other flu strains. On the other hand, it may mutate into a more dangerous form, or experience even more reassortment and pick up new genes along the way. We are not helpless as we wait to see what evolution has in store for us. We can do things to slow the spread of the flu—most importantly, washing our hands. Meanwhile, vaccine developers are working on a new Human/Swine 2009 H1N1 vaccine. It may not provide perfect protection from the virus, but it will help slow its spread. We may not have the upper hand over the flu yet, but at least we don't have to look to the stars to defend ourselves.



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WORLD OF VIRUSES: FLU PANDEMIC
(28:30 MIN.)
PRODUCED BY LAKSHMI SINGH

CHECK OUT WHAT SCIENTISTS, RESEARCHERS AND PUBLIC HEALTH OFFICIALS ARE DOING ABOUT THE JUMP OF FLU VIRUSES BETWEEN ANIMALS AND HUMANS. HEAR THE STORY IN THE SOUNDPRINT RADIO PROGRAM ONLINE AT HTTP://SOUNDPRINT.ORG/FLU.

World of VIRUSES is an alliance of science educators, media professionals, virology researchers, and public libraries working to increase public understanding about viruses and infectious disease. For information about the World of Viruses project, contact our Web site at www.worldofviruses.unl.edu or contact project directors, Judy Diamond (jdiamond1@unl.edu) and Moira Rankin (moira@soundprint.org).

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Supported by the National Center for Research Resources, a part of the National Institutes of Health

These materials were funded by a Science Education Partnership Award (SEPA) from the National Center for Research Resources (NCRR) at the National Institutes of Health (NIH). Grant No. R25 RR024267-01 (2007- 2012). Its content is solely the responsibility of the authors and does not necessarily represent the official views of NCRR or NIH.