

## Long-frozen body may yield flu clues

By M.A.J. McKenna/STAFF WRITER

A frozen body found in a mass grave in remote Alaska has yielded portions of the virus that caused the 1918 flu epidemic, the worst natural disaster of this century.

Working from lung tissue taken in August from the partially preserved body of an Alaskan native woman, a team at the Armed Forces Institute of Pathology in Washington has identified and begun to genetically analyze the 1918 virus, which killed 40 million people, 675,000 of them Americans, within 11 months.

The recovery of the virus, and the one-man weekend expedition that quietly produced the sample, has surprised and thrilled the tightly knit community of flu scientists worldwide. Though the 1918 virus has been glimpsed before ---the same group reported last March that they had isolated 7 percent of it from a long-lost autopsy sample ---it has never been recovered from unadulterated buried tissue.

The finding could give scientists a deeper understanding of what made the 1918 strain so lethal and help them devise strategies for another flu pandemic if the virus turns deadly again.

“This is very exciting,” said Dr. Edwin Kilbourne of New York Medical College, a leading U.S. flu expert. “It is very fragmentary data, but it is pointing us in the right direction.”

That goal, experts agree, is vitally important. No other flu has matched 1918 for virulence: It killed in days and took overwhelmingly the young and healthy. But flu scientists worry that an equally severe variety could be produced at any time by the viral roulette of flu’s constant mutation, a concern that contributed to the deep alarm over the Hong Kong flu outbreak this winter. They hope that analysis of the 1918 flu ---such as the work the Washington group has done on the Alaska sample and two from their own archives ---could help prepare for the next pandemic.

“We should be able to see if there was diversity among the viruses that were circulating at the time; that could help account for some of the differences in pathogenicity,” said Dr. Nancy Cox, chief of the influenza branch at the Centers for Disease Control and Prevention.

“If a new pandemic arises, we’ll have to deal with planning on the basis of what populations are affected by whatever virus emerge. We certainly can learn from the past, though it is difficult to say specifically how it would change anything we have done in planning so far.”

The 1918 virus vanished long before medical technology achieved methods to analyze it, so retrieving a sample has become an internationally sought scientific goal: A Canadian-led team hopes to exhume bodies of flu victims in the Norwegian Arctic next fall. The Washington research team, led by Dr. Jeffery Taubenberger, were given the new sample as a gift by Dr. Johan Hultin, a retired pathologist living in San Francisco who has a long acquaintance with the 1918 flu. In 1951, he was part of an expedition from the State University of Iowa that exhumed and

sampled bodies in Brevig Mission, Alaska, not far from Nome ---a town where 85 percent of its population, 199 people, died within one week.

That mission aimed to recover a live virus that could be cultured in the lab, but was unsuccessful: Though buried in permafrost, the bodies had thawed and refrozen, and the virus' fragile genetic structure had fractured, making it inert. But when Hultin read the results of Taubenberger's work with the autopsy sample, published last year in the journal *Science*, he realized that more sophisticated analysis was possible; he volunteered to return to Alaska to speak to his contacts of 47 years ago.

"The speed at which he did this was really incredible," Taubenberger said. "He flew up on a Friday, got permission from the village leaders Friday evening, staked out the site Saturday, began to dig Saturday evening, by Monday reached several bodies, and by Tuesday was filling the grave up."

Of the 11 bodies Hultin found ---part of a mass grave in which 72 flu victims were once buried ---most had been reduced to skeletons; on four of them, though, some soft tissue remained. Hultin biopsied their lungs and sent the material to Taubenberger, who found viral fragments in tissue from one woman whose plumpness in life protected her organs after death. Her name is unknown, but Hultin has nicknamed her Lucy. "It comes from the Latin for 'light,'" Taubenberger said, "and he hopes she will shed some light on the 1918 flu."

Taubenberger and his colleague Ann Reid, a molecular biologist, are comparing the Alaskan viral material against their other two samples. "All three deaths occurred within a week of infection, at the height of the fall wave of the epidemic," he said. "Very little is known about what kind of genetic variability occurs in an influenza pandemic ---the last one, in 1968, occurred before genetic sequencing was possible ---so we believe this is going to be very interesting."

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Section: Reader Letter: C Page: 1 Words: 1384

## **THE 1918 FLU: TRACKING A KILLER**

### **UNLOCKING LUCY'S SECRET A woman dead for 80 years aids medical science**

By M.A.J. McKenna/Staff

They are calling her Lucy.

No one knows her real name: She and almost everyone who knew her died in one icy winter week almost 80 years ago. Rescuers who came much too late found her and her neighbors, some already arranged for burial, others still tangled in their beds. They laid the frozen corpses in a mass grave above the seashore, shot the starving household animals, and took the orphans away.

They are calling her Lucy because the name comes from the Latin word for light, and because the man who retrieved her body hopes she will illuminate the disease that killed her, along with most of the Alaskan town she

lived in and millions of people around the world: the devastating influenza of 1918.

Science has waited 80 years to understand that epidemic. Dr. Johan Hultin, who found Lucy in August, has pursued its secrets for 46 years. "I am enormously privileged," he said recently. "It has been an adventure."

The 1918 flu is one of medicine's enduring mysteries. When it swept across the globe --- killing as many people in 11 months as the Black Death took in a century --- the influenza virus had not yet been isolated in the lab. By the time science achieved that skill, the 1918 variety had disappeared, transformed into a milder strain by flu's nonstop mutation. No one has ever been sure what made that flu so lethal, but the knowledge is desperately needed: Each year, the probability increases that a similarly deadly strain will return.

The only hope of understanding what made the 1918 flu so deadly lies with those who died from it, whose bodies might still harbor fragments of the fragile and elusive virus. Recovering it has become a scientific rivalry: Washington, Toronto and London researchers have been ransacking medical archives for autopsy samples and racing to plan exhumations of graves far above the Arctic Circle.

Two weeks ago, Hultin, a 73-year-old pathologist living in retirement in San Francisco, brought the competition to a shocked stop. He announced that, working alone and using his own money, he had flown to Alaska on a late-summer weekend, excavated the mass grave in the town of Brevig Mission, recovered samples from four bodies and given them to one of the leading researchers in the field. The researcher, Dr. Jeffery Taubenberger of the Armed Forces Institute of Pathology in Washington, made a simultaneous announcement: Tissues that Hultin had given him, taken from the victim he called Lucy, did indeed contain small portions of the 1918 flu.

The search for the flu is far from over: Taubenberger and his competitors are still pursuing the complete virus, and the Canadians have scheduled an excavation in October. But Hultin grabbed the early glory because he had an edge. He knew where to look, because he had been there before. He knew he was in no danger from the virus buried there, because he had already been exposed to it without being affected. And he had an undiminished zest for the goal that had eluded him 46 years ago.

"When I spoke to Jeff Taubenberger to let him know I would try this, he told me another expedition had been in the planning stages for four years," Hultin said. "He asked when I could go. I think he expected me to say, 'Next year sometime.' And I told him, 'I cannot go this week. But next week, I will.' "

And he did --- as matter-of-factly as if he were arranging a weekend jaunt to the wine country instead of a one-man expedition within spitting distance of Siberia. Within days, he took a commercial flight to Anchorage, rode a freight plane as far as Nome, found a bush pilot to land him on the foggy beach of a still largely Eskimo town with only a duffel bag and a set of sketches for his proposed excavation, and persuaded the local Lutheran pastor to intercede for him with the village elders.

Hultin has a verifiable taste for adventure: He has climbed in the Andes and Himalayas, supervised archaeological digs in Sweden, and built --- with hand tools --- a multistory log structure modeled on a seventh-century Norwegian house. And he had made this same trip before, under even less friendly conditions. In June 1951, for a Ph.D. thesis

that is still unfinished, he hiked into Brevig Mission with three other researchers, dragging sleds of equipment across six miles of tundra, bent on excavating the grave described in diary accounts of the 1918 flu.

They found the site, after melting the permafrost by lighting fires in the ditches they dug; took samples of the bodies, chilling the tissues with foam from fire extinguishers they had hauled behind them; and toiled back to the State University of Iowa, where Hultin was studying virology. But they couldn't reproduce the flu from the tissues they had retrieved, and Hultin had always hoped to return to try again. Incredibly, when he did, the villagers remembered him.

"I had heard the story of his excavation before he arrived," said Brian Crockett, the 39-year-old pastor of the Brevig Memorial Lutheran Church, who helped Hultin on his return. "The village elders remember making the decision to allow him to dig. Some of the elders remember the flu: They lived in the church, which was made into an orphanage. Not just anyone could have walked in here and done this, but he could."

Within two days of arriving, Hultin met with the City Council, representatives of Brevig Mission's 265 Inupiat and Caucasians. By 4 o'clock on the same day, digging had begun.

"It took us an hour, maybe a couple of hours, before we decided he could do this," said Gilbert Tocktoo, Brevig's 35-year-old mayor. "We thought, if he could get some samples from these bodies, we could keep the virus from spreading to the whole country the way it did before."

It took five days for Hultin and four helpers to dig through the permafrost, using the long summer days to work from 9 a.m. until almost midnight. They found bones, hair and clothing; wrapped around one unknown victim was a rare and lovely albino reindeer skin. And then they found a body.

"On the right side was a skeleton; on the left, a skeleton," Hultin said. "In between was a woman, in an amazingly good state of preservation, maybe 25 to 35 years old. I sat on an upside-down pail and looked at her, and I began to see the reason: She had been obese, and her skin and fatty tissue were so thick that they protected her body from thawing and freezing and decay."

Three other skeletons had some flesh still attached. Working with a scalpel and rib cutters, Hultin took samples of the major organs; from Lucy, the best preserved, he took both lungs. The partially frozen tissues were placed in preservative Taubenberger had sent and then reburied nearby to keep them cold. That evening, using the wood shop in the local high school, Hultin built replicas of the original crosses, 5 feet and 9 feet tall so they could be seen from the sea. Before he left Brevig, he and the high school students hoisted them above the refilled grave as a memorial.

In 1918, Alaska had been quarantined to preserve it from the disease ravaging the lower states. The strategy almost worked --- but they forgot to exclude the mail, and the mail, it is thought, brought the flu. In an ironic echo, the mail brought the flu back from Alaska as well: Hultin retrieved his still-frozen samples, divided them and mailed them --- in four separate lots to protect against accidents --- to the lab in Washington. Three weeks later, a phone call confirmed it: In the lungs Hultin had retrieved from Lucy, Taubenberger had found fragments of the virus of 1918.

Taubenberger continues to work on the Alaskan samples, using the portion of virus he has isolated to verify other fragments found in autopsy samples from his institute's archives. In San Francisco, Hultin is creating a bronze plaque for one of the crosses he built, containing the names of the 72 Brevig victims; sometime this summer, he will return to present it to the town. He is still not sure of Lucy's identity, though he has narrowed it down to one of 15 victims.

"The first body to be called Lucy, a 3 million-year-old skeleton in Ethiopia, illuminated the mysteries of human evolution," Hultin said. "This Lucy may shed light on the mystery of the 1918 pandemic, and that will be her legacy even if we never find her name."

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## **THE 1918 FLU: TRACKING A KILLER A GENETIC WHODUNIT Payoff for solving mystery may be improved vaccines**

By M.A.J. McKenna/Staff

The fragments of influenza virus found in the corpse of a Brevig Mission flu victim will help to solve one of the most enduring medical mysteries of the century: why the 1918 flu pandemic, one of the worst outbreaks of infectious disease in history, was so lethal.

That knowledge is needed not only to understand the past, but to protect the future. Virologists are increasingly sure that another vicious flu will emerge soon --- past pandemics have occurred several times a century, and the last was 30 years ago. The "bird flu" outbreak in Hong Kong this winter only underscored the urgency of the threat.

If the genetic analysis performed on the Alaskan samples explains why the 1918 flu was so lethal, it could help researchers identify dangerous characteristics in the next major flu strain.

"The scientific question has been, was there something unique about that strain that the genetic sequence will provide a clue to?" said Dr. Dominick Iacuzio, influenza program officer at the National Institute of Allergy and Infectious Diseases. "The hope is that we would be able to identify some unique characteristic that can be associated with higher virulence."

Researchers at the Centers for Disease Control and Prevention found such a marker --- a chain of basic amino acids at a particular point on the virus' coat --- in samples from the Hong Kong flu outbreak this winter. That strain, which appears to have passed to humans from chickens, sickened 18 people and killed six. Though it had never been seen in humans before, it was already known to be lethal to fowl, and the genetic analysis at the CDC's Atlanta labs explained why: The additional amino acids allowed the virus to attack unusual sites in the birds' bodies.

Finding a similar feature in the 1918 strain will allow advance preparation for another lethal strain.

“We need it so we can project how to make a future vaccine, and so we can ask whether the anti-viral agents we have now are likely to work on a virus like that if it appears again,” said Dr. Robert Webster of Memphis, an internationally recognized flu scientist.

Dr. Johan Hultin, the retired 73-year-old pathologist who exhumed and sampled the Alaskan body, is not the only scientist in pursuit of flu from frozen corpses. A Canadian team, led by medical geographer Kirsty Duncan of Toronto, is preparing to excavate in October in a former mining camp in the Norwegian Arctic. Their goal is the same as Hultin’s: to locate a 1918 flu victim who died soon after infection and whose body was preserved by frozen ground. But because their victims were infected in a different month and in a different part of the world, their work could illuminate whether the virus mutated as it swept across the globe.

The Alaskan findings “give us even more reason to do the Norway study,” said Webster, who is advising the Canadian team. “The bottom line is that we need the whole genetic sequence of this virus, and we need it from multiple isolates to make comparisons.”

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## THE 1918 FLU: TRACKING A KILLER A GENETIC WHODUNIT

ìFor three weeksí time, I was the only person walking.î

M.A.J. McKenna

*In November, 1918, Teller Mission, Alaska (later renamed Brevig Mission), was an isolated subsistence village of about 100 Inupiat Eskimos and four Caucasians: Oluf Fosso, a Lutheran missionary; Clara, his wife; their four-month-old son; and a teacher, Jorgine Enestvad. That year’s influenza pandemic was deadly everywhere, but it struck natives with extraordinary force: 85 percent of the village died. At the height of the epidemic, Clara Fosso was the only adult not affected. Years later, she rewrote her diary into a narrative of the terrible winter; it was edited and published by her daughter, Alalie Fosso Johnson. The following is an excerpt from her account:*

ìWe did not know what the sickness was. It seemed to affect its victims in three different ways: some the brain, some the lungs, others had intestinal trouble. ...

ìMy husband determined to go for help. Though feverish and somewhat delirious, he hitched up the dogs and drove the 14 miles to Teller. He returned with the word that the situation there was no better than ours. They promised us only that someone would visit us up at the mission as soon as they were able ...

ìFor three weeksí time, I was the only person walking. Each day more and more sick people were added to our number at the mission until I wondered what spot the next one would occupy. It was a long, cumbersome stairway when it came to making the many daily turns with fuel and care of the sick with no toilet conveniences. ... I was hauling fuel to run six stoves at 35 degrees below zero. The November daylight at Teller Mission is hardly 4 hours long, so I worked into the twilight to finish my outdoor chores. ... When these tasks were being done, a tub of dog food was cooking on the stove. There were 17 dogs to feed. ... On my way to the doghouse many hungry Eskimo dogs which had torn loose from their stakes would lurch around and follow me as they smelled food. ...

ìThe long arctic nights dragged on and grew longer and deeper. Although the mission home was filled with people, I was alone. There was no one to converse with. My husband was deliriously driving dogs in his sleep. The sick were constantly moaning and groaning. Outside, the loose wild dogs howled like wolves. ...

îA scouting party came from Teller to help us. One day was spent shooting the loose dogs and looking for signs of life in the igloos. One place had as many as 25 dead bodies. Alalukís igloo, in which the dead from the mision had been placed, struck them with a scene of horror. Dogs had broken in and eaten them, leaving only a gory mess of human bones. They could only gather the remains into sacks.

îAnother igloo had its seal-gut window in the roof broken. As the party of men looked down through the opening they saw several corpses. Much snow had drifted in. ... As they shouted down, three frightened children popped from under the deerskins screaming. They ... had kept themselves alive on a package of oatmeal. ...

îIn another igloo, a girl was living alone with the rest of her family dead around her. In an outlying settlement four children were found alive, several adults having died. ... The children had kept warm in their bedding of skins. The little girl of 7 years had saved her baby brotherís life by keeping cans of milk thawed by their body heat.

îThese and other children increased our mission family to 46 orphans. Only eight grown-ups were left.î