

Science Watch Medical detectives close in on a killer

By M.A.J. McKenna/Staff

On paper, the image is unimpressive: Smudgy lines of black and white, compressed and slanted like a layer cake that a clumsy guest has leaned on, dotted with pale gaps and dense, uneven fractures. Scientific notes crowd the perimeter: "Depth $m(v)=0.110$ "; "Perimeter (m)"; "Edge . . . marker . . . marker . . . edge."

To a casual viewer, the dry notations and dim markings are incomprehensible. To scientists who can read them, they are a treasure map.

The image is a computer generation, built out of hundreds of radar readings: a cross section, 14 feet deep, of a piece of earth on a Norwegian island 720 miles below the North Pole. It shows a mass grave dug 80 years ago in the town of Longyearbyen high above the Arctic Circle: a straight-sided pit with a smooth, level bottom, surrounded by stable, frozen ground.

Three days from now, an international team of scientists will stand by that grave in Longyearbyen's cemetery and sink shovels into the spongy tundra. They hope to uncover what the radar wasn't sensitive enough to show: seven bodies, frozen into the permafrost of the high Arctic, that harbor one of the worst viruses known to history --- the influenza of 1918.

In the center of the group will be Kirsty Duncan, the driven Canadian geographer whose obsession with the deadly 1918 pandemic created this expedition to the top of the globe.

"It is so exciting to start getting some work done," she said recently while preparing for the trip. "The only thing I can think of now is getting this done properly. It has taken so long."

Duncan, only 31, has planned for five years for the opportunity that she and her team --- some of them twice her age --- will embark on this week. Science has waited much longer. No one has ever known what made the so-called "Spanish flu" so deadly, but it killed millions, sometimes within hours. Historical accounts describe young, healthy victims turning slate-gray from oxygen starvation and hemorrhaging beneath the skin, drowning on body fluids as their lungs filled from within. Many cities banned public meetings in a vain attempt to reduce the spread of infection; some ran out of coffins.

Virologists have predicted for years that an equally deadly variety of flu could emerge without warning --- but they have been hampered by not knowing just what made the 1918 variety so bad. The organism that causes flu wasn't identified in the lab until 1933, long after circulating strains of the virus had mutated into milder forms. Understanding the virus, scientists agreed, would take the near-miraculous recovery of a sample from a 1918 victim.

But even in science, miracles do sometimes happen. In 1997, a Washington scientist, Dr. Jeffery Taubenberger, recovered scraps of the 1918 genome from autopsy samples saved by the Army. In early 1998, a San Francisco

pathologist and adventurer, Dr. Johan Hultin, announced that he had retrieved tissues that still harbored pieces of the virus from a body buried in Alaska in 1918.

Now, Duncan's team hopes to complete the picture. After four years of negotiation, she has received permission from the Norwegian government and funding from the National Institutes of Health of the United States to exhume the bodies of six miners --- Magnus Gabrielsen, Hans Hansen, Tormod Albrigtsen, Johan Bjerck, William Henry Richardsen and Kristian Hansen --- who died in Longyearbyen in 1918. (A seventh victim, Ole Kristoffersen, lies buried alongside them, but his relatives have not agreed to his body's being retrieved.)

If the team accomplishes everything it has planned, it will leave Longyearbyen three weeks from now with samples of the tissues from all six bodies --- and it will find, possibly as much as a year from now, that the tissues contain complete copies of the virus of 1918. They would have the genetic key to the worst epidemic of this century --- and knowledge that may help public health authorities hold off an equally bad one in the years to come.

"If we could have a confirmed genetic sequence of the 1918 strain," said Dr. Dominick Iacuzio of the National Institutes of Health, "it would be a fantastic achievement."

The story of the 1918 flu is both numbingly tragic --- it is almost impossible to imagine up to 40 million dead --- and bewilderingly unfamiliar. Relatively few of those now living have heard of the Spanish influenza; flu historian Alfred Crosby has said that schoolchildren learn more about the Black Death of the 14th century than the pandemic flu of the 20th, though each disease claimed the same number of victims.

Perhaps because of that cultural unconsciousness, the lonely deaths of Duncan's seven miners have a peculiar power. They were mainland Norwegians who had signed on with the island's mining company for the winter; with fishing and agriculture over for the year, they would spend the 24-hour winter darkness underground. Their plans were disrupted by the flu, which broke out on board ship after it left the Norwegian coast for the island community on the Svalbard archipelago, hundreds of miles away. They died soon after arrival, in the first days of October, and were buried in the Longyearbyen cemetery far from home. No one remembers when or how their deaths were memorialized; six white crosses and a stone plinth, all installed in 1985 for a royal visit, mark their resting place now.

Duncan, a university professor in Toronto who first heard of the Spanish flu only six years ago, has told the miners' story hundreds of times now; nevertheless, at every retelling her eyes still grow wet. "When we were there in October, we had the local minister come to the cemetery for a short service," she said. "We laid a wreath and took a few minutes to remember them. It was hard, and I imagine this visit will be much harder." Photographs taken by team members show her turning away from the graves and weeping.

For the rest of the team --- a mix of Norwegians, British, Canadians, Americans and a New Zealander --- undertaking the excavation has meant balancing the emotional burden of the flu's history against the detachment needed for difficult scientific tasks. Most of them visited Longyearbyen for the first time last October, to survey the site using ground-penetrating radar --- a backbreaking process that required dragging heavy pieces of equipment in precise parallel lines over the uneven ground.

“It feels like a dance --- we called it ‘The GPR Shuffle,’ “ the team’s pathologist, Dr. Charles Smith of Toronto, said with a grimace. “It was tedious, awkward, fidgety stuff. The neat part was sitting in the little hotel rooms at the end of the day, watching all the data come together and form patterns.”

The recordings were brought back to Canada and analyzed by the radar’s manufacturers, Sensors and Software Ltd., and Alan Heginbottom, a scientist retired from the Geological Survey of Canada. After several months of massaging, the radar returns yielded key pieces of data: The area below the crosses was a 6-foot-deep pit with straight sides and a flat bottom wide enough to hold seven coffins. The earth close to the surface had obviously been disturbed, possibly dug out and then piled into the hole again. And, most important, the active layer --- the portion closest to the surface that thaws every summer --- was only 34 inches thick; the permafrost below had not melted.

If the bodies were in the grave, they were likely to have remained frozen since they were buried.

But the readings failed to answer the most important question: whether the miners are where they were supposed to be.

“The radar showed there is something there,” Duncan said. “We don’t know what. We assume it’s the bodies. So we are planning for every scenario: Are they in shrouds? Are they in coffins? Are the coffins filled with ice?”

Led by Heginbottom, a geologist well-acquainted with permafrost, and Smith, who has done exhumations in some of Canada’s northernmost areas, the team has devised a set of protocols that will guide it painstakingly through each step of the next three weeks: when to begin digging, how to protect the ecosystem, how to conduct the autopsies once the bodies are found, how to close the site again.

Each step addresses the same primary concern: preventing any virus that remains in the miners’ tissues from contaminating the scientists or the environment. Whether the bodies contain an organism that is still infectious -- or merely intact enough to study, but inert --- is a question that cannot be answered in advance.

“The risk is very small,” said Dr. Peter Lewin, a medical archaeologist and student of ancient diseases. “But it is not zero.”

Publicly, the group has maintained that the chance of the virus remaining infectious is low. But members have agreed to behave as though the virus is infectious, using protective housing around the excavation and operating on the bodies only after donning high-level protective gear.

“We want to make sure this is an absolutely super-safe procedure,” said Dr. Tom Bergan, a medical microbiologist who is the team’s Norwegian co-director. “We do not expect there to be any risk, but we are not willing to take any chances.”

In its work this past winter, the team began to consider an additional possible risk: that some of the 1918 victims may have been simultaneously infected with several bacteria that may also persist in the miners’ tissues.

“We want to know: Can we isolate these germs? Are they viable? And what are the molecular interrelationships between the virus and these bacteria?” said Lewin, whose identifications of disease organisms in Egyptian mummies spurred Duncan to invite him onto the team. “There is no doubt that in some cases bacteriological components were involved. There may be fungi, there may be other factors; we just don’t know.”

No matter what’s found in the graves, plans call for the same ending to the expedition: In the first week of September, four members of the team will leave Longyearbyen on four separate flights. Each will carry a

separate

set of samples, destined for one of four laboratories: Oslo, where bacterial components will be evaluated;

Winnipeg,

where the Canadian government is completing a new lab with the highest biosafety rating, P-4; and Mill Hill

near

London and Fort Detrick in Maryland, both P-4 labs where biological weapons research was once conducted.

Once there, the samples will be chemically disassembled; using recently developed techniques, virologists will pick through the samples' genetic sequences, searching for a match to what is already known of the virus of 1918.

One lab not on the list is possibly the best-known P-4 lab of all: the one belonging to the Centers for Disease Control and Prevention in Atlanta. Members of the public health agency's flu branch were initially involved in Duncan's project; others reviewed her successful request for \$150,000 in NIH funds. But CDC's scientists withdrew from participation in the team a year ago, and though watching things closely, have not yet stepped back

in.

"Initially it made sense for us to be involved, but as more and more virologists with international reputations became attracted to the project, it became obvious our participation wasn't essential," said Dr. Nancy Cox, the flu

branch chief. "There are others who can do this work very well, though we'll be happy to review the work or critique it if the opportunity arises."

Though team members expect news quickly, other scientists warn that the process may take awhile.

"I think it will take at least a year to find something; it might take longer, because P-4 labs are limited in number and their workloads are high," said Iacuzio, who is influenza program officer at NIH. "It will depend on how good

the samples are and how much the labs coordinate."

The international community of flu scientists, already alert after last winter's outbreak of a previously unknown flu

in Hong Kong, is watching closely. The recovery of a complete 1918 virus would be a stunning accomplishment. With Taubenberger already working on several samples, it has become something of a race.

Still unanswered --- possibly never to be answered --- is whether analysis of the 1918 virus will help scientists predict how bad a future pandemic might be. Global outbreaks have not been identical, and predicting the quality of

the next pandemic strain may remain out of reach.

"Knowing what we know about flu, I don't believe there will be only one answer to the virulence of the Spanish flu," Iacuzio said. "The information we learn about it may be predictive of other strains that will circulate in the future. On the other hand, we may learn that this was a unique event."

Which Duncan's team knows well. Its members take comfort in the recognition that, though their findings may contribute significantly to influenza research, the story of 1918 will not end with them.

"This isn't the climax of our work," Smith said just before leaving. "The climax will come weeks and months from now, when --- or if --- the virus is found in the lab. This is only the end of the beginning."

A delicate, difficult task

Researchers must protect a fragile environment --- and themselves

By M.A.J. McKenna/Staff

Superficially, the task of the team pursuing the 1918 flu virus is uncomplicated: Fly to an island accessible to large aircraft. Drive and then walk to a cemetery that's reachable by road. Locate graves that are already marked by large monuments. Dig down to bodies. Remove pieces of bodies. Cover bodies up. Go home.

But the devil always is in the details --- and some details of the upcoming expedition have proved particularly devilish. Among the complications: The victims' living relatives do not all support the exhumations. The environment around the cemetery is extremely fragile. The local and national governments have imposed strict conditions.

And --- though the possibility is remote --- the virus that killed up to 40 million people may still be alive in the miners' tissues. So the team must act at all times with the precision of the most secure labs at the Centers for Disease Control and Prevention --- even though they will be working, in sweaters, boots and gloves, in a tent pitched on one of the most inhospitable landscapes in the world.

"I think we'll be ready," Dr. Charles Smith, the expedition's chief pathologist, said recently. "We have done a tremendous amount of work on the paths the excavation process will take, depending on what we find when we open the graves. There are uncertainties, but we're prepared."

The Svalbard archipelago that holds the Norwegian town of Longyearbyen and its Russian sister city of Barentsburg was once a major coal mining center; coal was the reason the seven men went there in 1918, contracting the deadly flu along the way. But the mining industry never recovered from shelling by German battleships in World War II. Since the 1970s, Svalbard's major moneymaker has been tourism and adventure travel.

So the state of its landscape is extremely important to authorities.

That's why the team was denied permission to drive containerloads of equipment from the fiord at the town's base all the way to the cemetery on the side of the mountain; each piece will be carried part of the way by hand. And the pit itself must be dug by hand, using power tools but no earth-moving equipment --- a detail that persuaded the team to hire professional excavators rather than dig themselves.

"I've done frozen-ground exhumations in the past, but always with a backhoe," Smith said. "That's easy. I stand next to the site and direct the backhoe operator. . . . This is more complex."

Concern for the condition of the cemetery is so acute that the team will spend Monday and Tuesday photographing the site from every angle. When they are done, said Dr. Tom Bergan, the group's Norwegian co-director, what they leave behind must match the photos exactly. As soon as they have finished the shots, and probably before they break ground, the protective tent will go up. All the earth removed from the pit will remain inside the tent while the excavation goes on --- not only to reduce the risk of spreading disease organisms, but to remove stress on the surrounding ecosystem as well.

"It is extremely, extremely fragile vegetation," Smith said. "If you walk in one place on your lawn too often, you'll create a scar in the grass, but it will grow back. But tundra is the opposite: In 50 years, the scar will still be there, and bigger, not smaller. And you can't go out and buy a bag of tundra seed if you make a mistake."

The demand that the team respect the landscape has become entwined with the medical need to minimize contagion and the political and emotional necessity of respecting the dead. So the team has agreed to do all its work in the bottom of the pit it creates. The coffins, if there are any, will be uncovered and opened. But the bodies they contain will not be lifted to the surface; Smith and his crew will work on them in place.

Think about it: How do you take samples out of a body that has been solidly frozen for 80 years? Standard autopsy tools won't do it: They go through bone but balk on ice. Power tools are out of the question: The heat they generate could thaw the flesh, possibly releasing the virus into the air. Even a saw blade is questionable, since the fine dust shaken off its teeth could carry viral particles to the mouths and noses of observers.

Months of planning

The only power source Smith and his crew can rely on is their own muscle --- and the farther they get from the bodies, the less efficient their efforts will be. At one point, Smith thought he might have to lie on top of the corpses, protecting them from his body heat with a blanket of spongy insulating material and operating on the frozen flesh through windows cut in the sheet of foam. Next he considered dangling above them, slung from a rope like Tom Cruise in "Mission: Impossible" --- but unless he could brace himself against the walls of the pit, he would have become the weight at the end of a yards-long pendulum, swinging helplessly whenever he tried to exert some force.

The current plan calls for the excavators to clear enough space for him to crouch alongside the bodies, an awkward position that minimizes reliance on gadgetry but makes it more likely he will tire quickly. In the pit with him will be Barry Blenkinsop, a Toronto technician whom Smith relies on for messy infectious disease autopsies. Conditions are likely to make them clumsy --- to protect against disease organisms, both will wear full-body "spacesuits" with a contained air supply --- but they have worked together so frequently that both know where tools and equipment are likely to be and when to get out of each other's way.

Devising the appropriate tools took months of planning. The result, designed by scientists at the National Institute for Medical Research outside London, was a steel tube almost a foot long and about a half-inch wide, toothed at one end and pierced at the other to allow a handle for better torque and grip. It resembles the tubular saws Smith uses to gauge the health of hardwood trees on his family farm near Toronto; those produce narrow cylindrical cores of bark and heartwood, but the newer version is designed to withdraw layers of skin, fat, bone, muscle and organ without allowing the tissues to thaw. (Smith and the designers tested the tool --- successfully --- on frozen pigs.)

Blenkinsop and Smith will take hundreds of the tubes into the pit with them. On each body they will bore slowly into the abdomen, chest cavity, heart, throat and brain. As each core is withdrawn, it will be slid into a steel storage tube, sealed and frozen. Every time Smith takes a sample, he will take four more from the same spot on the body, as close as possible to the initial hole he created; one will go to each of the four labs that will analyze the samples, and the fifth will be retained as a reference.

If things go well, Smith and Blenkinsop will fill the tubes quite quickly, so at least one crew member and possibly two will remain in the tent to help them. The plan works like an operating room with clean and contaminated areas reversed: The two in the pit are the surgeon and scrub nurse, but dirty where they would be sterile; the “circulating nurse” at the lip of the pit will hand tools and equipment to the crew below, but stay clear of potentially infectious material. A fourth team member will probably carry messages between the autopsy crew and the tent entrance, but everyone else, by Bergan’s order as the responsible medical officer, will remain outside.

Though the precaution is sensible, it poses a poignant challenge for Kirsty Duncan, the young scientist whose passionate interest in the flu of 1918 spurred the expedition. She is a geographer, not a doctor; under the team’s strict rules, she has no place in the autopsy area. Though she spent five years pursuing permission to exhume the miners, she can never come closer to them than the closed flap of the tent.

It troubles her, she said recently, that she will never look on the faces of the dead.

“You know how I feel about disturbing a cemetery,” she said. “I believe it is a sacred place, and I am haunted by the necessity of doing it. So I would like to show my respect to the victims. I want to tell them thank you.”

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Science Watch

Threat of flu once again moves to center stage

By M.A.J. McKenna/Staff

It has been an extraordinary year for flu.

The unpredictable virus has been a human menace for millennia; it takes its name from the pre-Renaissance notion that illness was “influenced” by the stars. Several times a century, flu’s genetic code changes so abruptly that the human immune system has almost no defense against it; the subsequent pandemics --- epidemics that spread across national borders or arise in many places simultaneously --- kill hundreds of thousands.

There have been three pandemics this century, in 1968, 1957 and 1918; 1918 was one of the worst outbreaks of disease in history, killing from 20 million to 40 million around the globe and up to 675,000 in the United States (750 in Atlanta).

Yet most people think of flu --- if they think of it at all --- as something that sends them to bed for a week or two in midwinter and that may imperil grandparents in a nursing home if they fail to get a flu shot in time. And individual indifference to flu is mirrored on a national level; virologists almost universally complain that flu research and surveillance receive far fewer funds than they need.

Over the past 12 months, for the first time in decades, the fear of flu began to revive. Much of that was due to Kirsty Duncan and her team: Their Arctic venture, combining the romance of a 19th-century scientific expedition and the technology of a late 20th-century genetics lab, has caught the public imagination. But some of it is due,

as well, to an extraordinary confluence of events that brought the threat of flu back to public notice.

In March 1997, two researchers in Washington --- Dr. Jeffery Taubenberger and Ann Reid, of the Armed Forces Institute of Pathology --- announced in a scientific journal that they had recovered fragments of the 1918 virus from autopsy samples in U.S. Army archives.

In August, the Centers for Disease Control and Prevention announced that a 3-year-old child in Hong Kong had died of a flu never before seen in humans --- a strain so unusual that the first researchers to analyze it assumed it was a laboratory mistake.

By January 1998, the outbreak had sickened 18 and killed six. Health authorities at the CDC and in Hong Kong successfully contained the virus after a month, spending more than \$800 million and eventually slaughtering every one of the 1.4 million chickens in Hong Kong. In late January, Dr. Robert Webster of Memphis --- one of the world's experts in nonhuman flu --- warned that otherwise, the dangerous infection would have gone worldwide.

Simultaneously, the U.S. flu season became unexpectedly bad, thanks to the arrival of an unanticipated bug dubbed influenza A/Sydney via a cruise ship that had sailed in the South Pacific. Passengers from Australia and New Zealand infected the crew; they passed it to new passengers from Montreal whose leaf-peeping tour of New England seeded the strain up and down the East Coast. Flu shots, prepared as usual far in advance of the season, were only partial protection.

In February, to the scientific community's shock, Taubenberger announced a further advance: Months in advance of Duncan, he had obtained his own frozen body, courtesy of a San Francisco pathologist who had found and unsuccessfully analyzed Alaskan flu victims in 1951. The pathologist, Dr. Johan Hultin, took a weekend trip back to the same western Alaskan village, re-excavated the grave, found a body, retrieved the lung tissue and mailed it to Washington. Taubenberger, several weeks later, found scraps of virus that matched what he had already seen from 1918.

And as Duncan and company prepared to leave for Norway, the CDC and Canadian authorities jointly announced that an unknown flu had sickened more than 400 tourists in Alaska and the Yukon, killing at least one. Native areas might be at risk, the agencies said; and since many of the sick were boarding ships with passengers from around the world, the unidentified strain could spread.