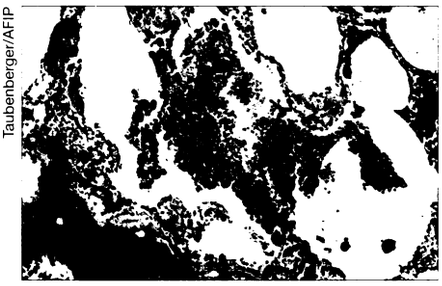
A Doughboy's Lungs Yield 1918 Flu Virus

On Sept. 19, 1918, an Army private destined for the trenches of World War I France reported to the base hospital at Camp Jackson, S.C. Although otherwise healthy, the 21-year-old complained of chills, fever, headache, backache, and a cough. "Opinion: Influenza," a doctor noted in the medical record.

Within a week, he was dead—1 of 21 million people worldwide who would succumb to the influenza pandemic of 1918. For almost a century, samples of the doughboy's lungs sat in a warehouse run by the Armed Forces Institute of Pathology (AFIP) in Washington, D.C. Hidden in his tissues lay RNA bearing the solution to an enduring mystery, the genetic code for the worst pandemic in human history.

Now, for the first time, the killer has been exhumed and fragments of its genes deciphered, say Jeffery K. Taubenberger and his colleagues at AFIP.

"This is not just a medical detective story," Taubenberger says. "This could happen again. It would be really useful to find out what happened in 1918 and apply that knowledge to protect us against future outbreaks."



Taubenberger/AFIP

Lung tissue that yielded 1918 influenza genes. Clumps of purplish cells in the white spaces are dead epithelial cells filled with flu virus. Black dots are white blood cells containing inhaled coal dust.

"This is a tremendous advance," says virologist Robert Webster of St. Jude Children's Research Hospital in Memphis, Tenn. "The 1918 virus represents the ultimate disease-causing agent—in a sense it's like ebola gone mad. We need to understand as much as possible about this virus because the world will get another pandemic, maybe late in this century or early in the next."

One pandemic was one too many. In the 1918 outbreak, nearly 700,000 people died in the United States. Historian Alfred Crosby has written that Washington, D.C., seized two train cars of coffins headed for Pittsburgh so that the capital's undertakers could bury the dead.

Taubenberger and his colleagues began their search for the virus' genes by selecting at random 28 of the 70 pandemic victims whose lung samples are stored at AFIP. Autopsy reports from 1918 disclosed that seven of these servicemen died soon after becoming ill, enhancing the likelihood that lung tissues might contain intact bits of RNA from the virus' unusual eight-strand genome.

People who live longer are less likely to harbor the virus, because the body's defenses eradicate the microbes, Taubenberger says. In such cases, bacterial pneumonia delivers the fatal blow. But in the seven servicemen who died quickly, the immune counterattack might not have had time to wipe out the virus.

The researchers drew a blank in six cases. The private from Camp Jackson, however, was unusual. His left lung had suffered extensive bacterial pneumonia, but his right lung had not. This raised the possibility that the right lung might still harbor the virus. To find out, the researchers removed some tissue from the paraffin in which it was stored. Step by step, they broke it down until only RNA remained.

"The people who preserved this tissue never imagined what might be possible down the road," says team member Ann H. Reid.

Reid made millions of copies of nine RNA fragments of five flu genes. Thomas G. Fanning of AFIP then deciphered the sequences of the fragments and compared them to every other known sequence of the flu gene.

"It's unique," Taubenberger says. The team has also confirmed prior evidence suggesting that the sequences most closely resemble those from swine flu. Their report appears in the March 21 SCIENCE.

Researchers disagree on whether it will be possible to rebuild the entire genome of the virus, perhaps yielding clues to its spectacular virulence. Most agree that the work might permit the making of a vaccine, if needed. "If this fossil were to reemerge," says Webster, "we could use this information to get a best-match vaccine that would probably protect us quite well." —*S. Sternberg*

X-ray microprobe unveils biostructures

Proteins play a crucial role in binding a sperm to an egg to begin fertilization. The absence of these proteins in defective sperm may contribute to infertility.

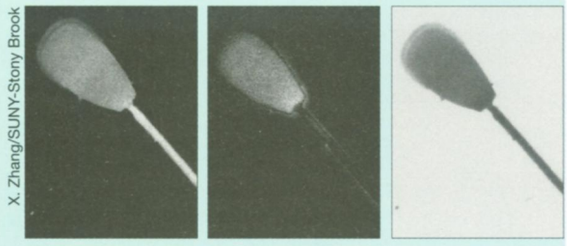
Now, researchers have developed a new form of X-ray microscopy that can locate and map proteins in and on sperm cells. The technique can also probe a variety of biological structures to determine the distribution of DNA and other molecular constituents.

The method involves passing intense X rays, generated by a particle accelerator (SN: 5/4/96, p. 276), through a system of mirrors and lenses that focuses the rays into an extremely narrow beam. Developed by physicist Janos Kirz and his coworkers at the State University of New York at Stony Brook, the system generates a shaft of X rays only 50 nanometers wide at a wavelength between 2.3 and 4.4 nm.

"We think this is the smallest beam of focused electromagnetic radiation of any wavelength [anyone has yet produced]," Kirz says. He described the technique this week at an American Physical Society meeting in Kansas City, Mo.

By tuning the X-ray wavelength, it's possible to map specific molecules. With scientists from the Lawrence Livermore (Calif.) National Laboratory, Kirz and his team used an X-ray microbeam to determine the distribution of protein and DNA in bull, mouse, stallion, and hamster sperm. Though the individual proteins vary from species to species, their arrangement proved remarkably similar.

The researchers hope to develop an X-ray microscope that will enable them to image cellular structures in three dimensions without having to stain or thin-slice samples. Such a tomographic technique would require taking a large number of images, which would normally damage the sample. Recent experiments, however, show that flash-freezing to liquid-nitrogen temperatures lessens dramatically the damage inflicted by X rays, opening the way for developing nanotomography. —*I. Peterson*



X. Zhang/SUNY-Stony Brook

Images at slightly different X-ray wavelengths reveal the distribution of protein (left) and DNA (center) in bull sperm (right).