

# Study generates Soviet anthrax pathogen genome from autopsy specimens

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A new study by the Translational Genomics Research Institute (TGen) and Northern Arizona University (NAU) used deep DNA sequencing methods to generate the anthrax genome sequence from the victims of the 1979 anthrax outbreak in Sverdlovsk, Russia, when it was part of the USSR.

The Soviet Union produced [anthrax spores](#) on an industrial scale but repeatedly denied the existence of their biological weapons program. This study, to be published in the September issue of the journal *mBio*, represents a precise and detailed examination of the anthrax strain used in their weapons development, and includes an anthrax genetic database that puts the weapons strain into a global context.

"I have been studying this [anthrax outbreak](#) and these specimens for more than 20 years. Finally, using genomic technology, we could comprehensively characterize this pathogen genome," said Dr. Paul Keim, Director of TGen's Pathogen Genomics Division, a Regents Professor of Biology and the Cowden Endowed Chair of Microbiology at NAU, and the study's lead author.

"This is the signature agent of the world's largest biological weapons program and now we have it in our genetic databases. Anywhere this strain shows up again, we will be able to identify it and track it back to its source. This is now an essential part of our forensic arsenal," said Dr. Keim, who also is Director of NAU's Microbial Genetics & Genomics Center (MGGen).

The anthrax bacterium produces small capsules, or spores, that can lie dormant for decades. After settling inside the human lung, for example, it can cause a severe disease that, if not treated with antibiotics, kills 90 percent of those it infects.

Anthrax is found in many parts of the globe and dispersed through the human movement of animal parts contaminated with spores. Wool and hair from goats and sheep are moved globally as textiles or their precursors. When these originate in anthrax endemic regions, they can carry the spores, which are long-lived. While this bacterium has little variation from strain to strain, whole genome sequencing has identified DNA fingerprints that enable molecular epidemiology, tracing it to its source. When anthrax outbreaks occur, their whole genome profile are now routinely compared to the genetic database to identify possible sources and exclude others. This type of analysis was used by the FBI to track the spores in the 2001 anthrax letter attacks, which infected 22 people and killed five.

The Soviet Union had signed the Biological Weapons convention that prohibited the use of biological agents, including anthrax, as weapons. The United States' [biological weapons](#) program was eliminated in a decree by President Richard Nixon in 1969, but the Soviet program was maintained and expanded in a covert fashion for decades.

In 1992, an investigative team from the United States led by noted Harvard biologist Dr. Matt Meselson characterized the 1979 Sverdlovsk outbreak by interviewing local physicians, visiting cemeteries and examining autopsy specimens. This investigation, along with accounts by Ken Alibek, a former Soviet scientist, revealed that the Sverdlovsk anthrax outbreak was due to an industrial accident. A faulty filter at a Soviet spore production facility allowed anthrax spores, in a silent plume, to drift with the wind over the city and into the nearby countryside. Nearly 70 Sverdlovsk inhabitants died as far as three miles

downwind from the facility, but more anthrax-susceptible farm animals died over 25 miles away. It remains the world's deadliest human outbreak of inhalation anthrax.

The bacterial genomes were generated from autopsy tissue specimens of two Sverdlovsk anthrax victims. These tissues were moved to the United States with permission of Sverdlovsk pathologists to continue the investigation into the disease outbreak. From these, it was established that the anthrax pathogen was detected within their tissues and the victims died from inhaling the spores.

The Sverdlovsk anthrax genome was compared to the global genome database maintained by NAU to identify its close relatives and to look for evidence of genetic engineering. The Flagstaff research team found that this strain was closely related to other Asian isolates with very few differences to naturally occurring anthrax. There were no signs of genetic engineering.

Dr. Keim notes that the Soviets had to be very meticulous to avoid mutant variants from dominating their production stock. Invariably when wild anthrax strains are grown extensively in the laboratory, they adapt to those conditions and lose the killing power.

"The Sverdlovsk strain's genome looked very much like those of wild strains we see across Asia," Dr. Keim said.

Dr. Meselson, who was not part of the current paper, notes: "If this strain had been grown repeatedly in the laboratory, it would have mutated to a form that had less virulence and less capacity to cause [anthrax](#). The Soviet scientists must have been very meticulous in their maintenance of the natural form."

Dr. Meselson, who is the Thomas Dudley Cabot Professor of the Natural

Sciences at Harvard, is known for his 1961 discovery of messenger RNA.

Provided by The Translational Genomics Research Institute

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