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SHELVED

For decades, the Armed Forces Institute of Pathology has been a leader in disease diagnosis. Now it is closing, and its legacy is in jeopardy.

BY ALISON MCCOOK

The news took William Travis's breath away. The e-mail he had just opened revealed that the organization where he had worked for nearly 15 years — the Armed Forces Institute of Pathology (AFIP) in Washington DC — was to close. "I had cold chills," recalls Travis, now a thoracic pathologist at the Memorial Sloan-Kettering Cancer Center in New York City. "I was shocked. I thought, 'How could an institution like this be allowed to go away?' I had trouble breathing."

That was in the spring of 2005, just five months after Travis had left the institute. The storied medical centre had become a casualty in a wave of cost-cutting closures and consolidations at the US Department of Defense. And on 15 September, less than a year shy of its 150th birthday, the AFIP will shut its doors for good.

In its long history, the AFIP has become a stalwart of the international biomedical community. With its vast library of tissue samples and expertise at analysing tissues for the diagnosis of disease, it has been a valuable resource for researchers and clinicians alike. Every year, the AFIP received at least 50,000 requests for second opinions on difficult cases from external pathologists. The nearly 800 employees — including experts in many areas of human and animal pathology — made major or minor changes to roughly half of the cases they acted on.

The military has yet to decide whether academic scientists will continue to have access to the AFIP's unique tissue repository. The largest in the world, it holds 55 million glass slides, 31 million paraffin blocks and more than 500,000 wet tissue samples. Scientists had only just begun to apply modern molecular techniques, such as DNA and RNA sequencing, to the collection. "That repository is an international treasury. And that has got to be available to the community at large,"

With nearly 90 million samples, the AFIP's tissue repository is the world's largest.

A diary of death & disease

The Armed Forces Institute of Pathology built up a worldwide reputation for its tissue repository and expertise in disease diagnosis.

1862
THE BEGINNING
Brigadier General William Hammond, the Army surgeon-general, establishes the Army Medical Museum to collect specimens from the American Civil War.

1918
THE WAR
The First World War brings nearly 10,000 specimens. The institution starts transforming into a diagnostic pathology facility.

1944
STRANGE CASES
Samples flood in during the Second World War, as soldiers return with mysterious diseases. The military establishes the Army Institute of Pathology to gather and learn from the cases.

NATIONAL MUSEUM OF HEALTH AND MEDICINE (LEFT); CORBIS

says John Madewell, a former AFIP radiologist now based at the M. D. Anderson Cancer Center in Houston, Texas. So even as scientists mourn the loss of the institution, many are wondering what will become of the fruits of its labours. "I am very concerned," says Madewell.

HUMBLE BEGINNINGS

From the start, the AFIP had a mission that extended beyond military strategy. In the spring of 1862, three dried and varnished tissue specimens were placed on a shelf in the Washington DC office of Brigadier General William Hammond, the Army surgeon-general. It was the beginning of the Army Medical Museum (see 'A diary of death & disease'). Hammond wanted to collect and catalogue the specimens that had been accumulating from men fighting in the American Civil War. He wanted a collection that would "embrace all forms of injuries and diseases, so that eventually it would become a general pathological museum, accessible for study to all medical men who are prosecuting original inquiries".

The museum became increasingly important to the military during the two world wars, says Michael Rhode, an archivist and one of the few remaining AFIP employees, as soldiers came back with strange new diseases such as gas gangrene, in which bacteria produce tissue-killing toxins inside the body. The army decided it needed a central location to collect and learn from unique cases and in 1944, the museum established the Army Institute of Pathology. Five years later, the institute became the central laboratory of pathology for all branches of the armed forces, and adopted its current name.

Rhode says that "there was a strong tradition of involving civilians". It was in the military's interests to collect difficult cases from around the world, to learn more about the diseases troops could face. As the AFIP didn't initially charge for second opinions on difficult cases, the samples flooded in.

The institute's final home, on 16th Street in Washington DC, was built in the 1950s to accommodate the growing repository and the pathologists who wanted to work at the AFIP, drawn to the collection and the stream of unusual cases. Within the first five years in the new building, AFIP scientists conducted more than 200 investigations of misunderstood diseases.

AFIP pathologists also began producing the *Atlas of Tumor Pathology*, a set of frequently updated volumes that are considered "bibles" of the field, says Chris Kelly, a former spokesperson for the AFIP. "There is probably not a bookshelf in a pathology office that does not contain at least one of these."

But many clinicians would say that the AFIP had the most impact with its consultation service, in which resident experts provided a second opinion on cases submitted by external pathologists in which, for whatever reason, the original diagnosis was uncertain. For instance, says former AFIP pathologist Susan Abbondanzo, two high-grade lymphomas — lymphoblastic and Burkitt's lymphoma — can be difficult to distinguish using the typical tissue-staining method used by most pathologists. But each has a very different treatment, so an incorrect diagnosis could kill the patient. The AFIP could routinely diagnose these cases, relying on experts in conjunction with a molecular and immunohistochemical laboratory, which many small hospitals lack. "I'm not going to say every diagnosis is life-saving," says Abbondanzo. "But many of the things you see there are, potentially."

> *"That repository is an international treasury. And that has got to be available to the community."*

A PATHOLOGIST'S GOLDMINE

When pathologists extol the value of the AFIP, the conversation always returns to the tissue repository — all told nearly 90 million tissue samples, including some of the most rare and difficult cases ever encountered in the history of the field. A general pathologist might see one or a few cases of a rare tissue abnormality during a career. The repository often contains many, enabling researchers to categorize the diseased tissues and standardize diagnosis.

Abbondanzo joined the AFIP's department of haematopathology in 1990, and the first research project she collaborated on was investigating whether the anti-seizure drug Dilantin caused tumours in lymph nodes. "It was a huge concern," she says. Abbondanzo had been a pathologist for six years, but had never seen a case of enlarged lymph nodes in people taking Dilantin. When she arrived at the AFIP, there were 25, which allowed Abbondanzo and her colleagues to determine that the vast majority of cases were benign, not cancerous — showing there was no association between the drug and the cancer[1].

And in the 1990s, Jeffery Taubenberger (then chair of the AFIP's department of molecular pathology) and his colleagues began applying molecular techniques to the repository's paraffin-embedded tissue blocks containing lung samples from soldiers killed by Spanish flu during the 1918 pandemic[2]. From these samples, among others, they were able to analyse the genome of the virus and investigate why it was so deadly. They traced its virulence to multiple genes, and found that it triggers a dramatic inflammatory response.

OUT OF FAVOUR

Abbondanzo, who became the chair of the haematopathology department in 1994, began to suspect that the AFIP was in trouble during the first US war with Iraq in the early 1990s, when the Department of Defense began to take a closer look at its budget. Suddenly, research projects that would have been approved and encouraged in the past were being questioned. Abbondanzo and her colleagues had submitted a proposal to study follicular lymphoma, a type of cancer that is rare in children. The AFIP repository contained at least 20 childhood cases, providing an unprecedented opportunity to characterize the condition. But the board that approved proposals rejected the project, saying it had "no military relevancy", Abbondanzo says. During this same period, she attended a meeting at which someone from the department referred to the AFIP as an "obscure little agency".

Travis, too, was worried about the AFIP's future. In 2003, he and others asked pathologists from overseas to write letters urging the military to continue supporting the AFIP, and he worked with the office of Senator Edward Kennedy (Democrat, Massachusetts), a long-time supporter of the institute, which tried to get financial support from other agencies.

1949
GROWTH AND RECOGNITION
The facility is renamed the Armed Forces Institute of Pathology (AFIP), and later moves to a new building in Washington DC.

1997
DATA RESURRECTED
A team led by Jeffery Taubenberger starts using lung samples from soldiers killed by the 1918 pandemic flu to analyse the viral genome.

2001
GRIM TASK
The AFIP mobilizes a team of more than 50 experts to identify the victims of the 11 September plane crashes at the Pentagon and Shanksville, Pennsylvania.

2005
THE END NEARS
The AFIP is officially 'disestablished' by the US Department of Defense. One year later, it receives its 3,000,000th case.

(FROM LEFT) AP; K. KASMAUSKI/SCIENCE FACTION/CORBIS; NATIONAL MUSEUM OF HEALTH AND MEDICINE

"I spent countless hours," Travis says. "All those efforts were not going anywhere. It was very clear I had to look out for myself and my family." When a position opened at Memorial Sloan-Kettering, he applied.

Despite rumours that some services might be cut, the closure announcement in 2005 came as a shock. "We learned of it when everyone else did," says Kelly. Rhode, who has worked at the AFIP since the 1980s, heard the news in an auditorium full of other staff. "I don't remember people talking much. It seemed like we kind of just spilled out and went back to our offices in silence."

The AFIP was on a list of base closures and changes designed to save more than US$30 billion over 20 years. But the institute's budget in fiscal year 2004 was only $93 million — slightly more than 0.02% of the defence department's budget request for 2004 of $380 billion. The military had welcomed civilian pathology cases for decades. Clearly, something had changed. A spokesperson for the Department of Defense said the decision to "disestablish" the AFIP was "based on capacity, military value and scenario development after analysis of military and non-military workload, services available in the civilian sector and cost savings".

What really caused the demise of the AFIP, speculates Abbondanzo, is that the vast majority of its work had limited direct benefit to the military. "It's been a long time coming," she says.

LIFE AFTER DEATH

Not everything will disappear. A new entity, the Joint Pathology Center, has been created in Silver Spring, Maryland, to carry on the AFIP's military duties, including consulting on pathology cases for the military and other federal agencies.

The AFIP's museum, the National Museum of Health and Medicine, which includes such exhibits as the bullet that killed US President Abraham Lincoln, is being packed up and moved to Fort Detrick's Forest Glen Annex in Silver Spring — a "stressful" process, says Rhode. And Madewell has helped to move the radiological pathology training that the AFIP provided for the majority of US radiology residents to the American College of Radiology based in Reston, Virginia.

A 2007 report by the US Government Accountability Office concluded that the change in the AFIP's consultation and other services would have "minimal impact", because there are alternative sources of pathology expertise. In recent decades, some centres — such as the Mayo Clinic in Rochester, Minnesota, and Johns Hopkins University in Baltimore, Maryland — have developed strengths in particular fields of pathology, and have become sources for second opinions in difficult cases, says Colonel Vernon Armbrustmacher, one of the AFIP's former directors. "The world of pathology will survive without the AFIP," says Armbrustmacher. "I hate to say that, but it will."

Even so, these services could be more expensive than those of the AFIP, which charged from around $20 to just over $2,000 for consultations, depending on the procedure. Some pathologists will feel the hit more than others — especially those in developing countries, who frequently lack local services to diagnose emerging tropical diseases and can't afford to pay high fees. These were a minority of cases — perhaps between 5% and 10% of consultations, estimates Armbrustmacher. But "they were unbelievable cases", Travis recalls. "Really challenging, difficult problems."

> *"The world of pathology will survive without the AFIP. I hate to say that, but it will."*

And even when pathologists can afford second opinions from academic centres, what they receive may not be of the same calibre as what they would have got from the AFIP, says Timothy O'Leary, director of Clinical Science Research and Development at the US Veterans Health Administration in Washington DC, and a pathologist at the AFIP until 2004. "There are cases that are just not common. And at the AFIP, we saw a lot of those unusual cases, far more than you do at academic centres." It may only be "a few hundred, a thousand people each year" whose diagnoses might be significantly affected, he estimates. "But for those people, it can be a matter of life and death."

The fate of the tissue repository, which is now under the control of the Joint Pathology Center, remains unknown. It has been moved to two renovated buildings at Forest Glen Annex, one of which used to serve as the laundry facility for the AFIP and the Walter Reed Army Medical Center, which is also being relocated this year. Officials have asked the Institute of Medicine to recommend how best to use the repository, including who should have access to it, says the Joint Pathology Center's interim director Colonel Thomas Baker. Those recommendations are due in June 2012.

What's most important, many say, is that civilian pathologists continue to have access to the repository. New techniques in high-throughput genomics and proteomics could "now or soon" reveal even more clues about the deadly diseases preserved there, says Taubenberger, now at the National Institute of Allergy and Infectious Diseases in Bethesda, Maryland. The repository "is only of value to people who know what's in it", says Travis. If the top pathologists can't access the material, an untold amount of valuable knowledge will never be uncovered, he says.

Inside the AFIP, the mood is decidedly sombre as people watch the lights go out, says Rhode. "Every day, you see a little bit more furniture moving down the hallway." Little by little, more offices are emptied, cleaned, locked and fitted with 'do not enter' signs.

Florabel Mullick, the last director of the institute, declined to be interviewed for this article. But in the AFIP's final newsletter last winter, she lamented watching the institution become a "shell of its former self" and wrote that closing the AFIP "has been one of the most painful experiences of my life … How does one, after all, watch missions that have benefitted so many people fade away?"

"It is the passing of one of the greatest institutions in the entire history of medicine," agrees Travis. "And it is very painful to see that happen. But we all have to move on." ■

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1. Abbondanzo, S. L., Irey, N. S. & Frizzera, G. *Am. J. Surg. Pathol.* **19,** 675–686 (1995).
2. Taubenberger, J. K., Reid, A. H., Krafft, A. E., Bijwaard, K. E. & Fanning, T. G. *Science* **275,** 1793–1796 (1997).