Future Uses of the Department of Defense Joint Pathology Center Biorepository

As the Civil War raged across America, the Army Surgeon General, Brigadier General William Hammond, sought to learn from the bloodshed. Through Hammond’s initiative, the Army Medical Museum was established to collect, catalog, and make available for study the specimens obtained from medical and surgical procedures performed on combatants.

The facility evolved over the following decades, expanding and diversifying, and establishing registries for specific organs and medical conditions. By the end of the 20th century, it had amassed the world’s largest collection of human pathologic specimens and was considered a premier consultation, education, and research facility. Samples from the renamed Armed Forces Institute of Pathology (AFIP) have been instrumental in helping to solve public health mysteries. When researchers sought to sequence the genome of the 1918 influenza virus that caused a pandemic that killed more than 40 million people worldwide, some biospecimens came from the AFIP, and one of its investigators led the research. (See Box.)

In 2005, the federal Base Realignment and Closure Commission (BRAC) recommended that the AFIP be closed, and its biorepository was transferred to the newly created Joint Pathology Center (JPC). During this transition in 2010, the Department of Defense (DoD) asked the Institute of Medicine (IOM) to provide advice on operating the biorepository, managing its collection, and determining appropriate future use of specimens for consultation, education, and research. The IOM committee’s report, Future Uses of the Department of Defense Joint Pathology Center Biorepository, provides this guidance.
Tissue Repository

As of 2011, the JPC held about 7.4 million accessions—tissue specimens and, in many cases, associated medical information—derived from about 3.2 million people. Some specimens are preserved and enclosed in containers; others lie beneath glass slides, are embedded in paraffin, or are stored in ultra-low temperature freezers.

Some 4.2 million of these accessions were transferred from military medical facilities closed under BRAC authority. These include the complete range of biologic materials collected in the course of providing routine medical care.

The remaining 3.2 million accessions constitute what is called the Central Collection, which is composed of specimens submitted by military, government, and civilian medical providers to repository pathologists for consultation or research. These accessions may include the patient’s name, social security number, and details of the patient’s medical history. The usefulness of Central Collection specimens for research purposes depends, in part, on their age. More recently acquired accessions, in general, have more associated clinical data and fewer condition problems, such as deteriorated or contaminated tissue.

The collection also includes a number of war and cohort registries, research collections that contain specimens and data from service members sharing a common military experience, such as participating in Operation Iraqi Freedom, spending time as a prisoner of war, or being exposed in wartime to Agent Orange.

Past Practices, Future Challenges

Many of the challenges that complicate transforming the JPC into a modern biorepository have their roots in how its existing collection of biospecimens and medical data were obtained. An overarching challenge, the committee writes, is uncertainty regarding the utility of the collection’s materials. Unlike biological samples gathered during a controlled clinical trial with consent forms signed by participants, the JPC specimens were collected in the absence of a purposely designed protocol and without explicit permission for subsequent use in research. Further, because of variations in how specimens were handled—before, during, and after they were prepared for long-term storage—as well as missing documentation, some biospecimens are unsuitable for some types of analysis.

Thus, the committee recommends that the JPC first evaluate the strengths and limitations of its collection and consider how to enhance the repository’s value, and then tailor its sample retention policies accordingly.

Biospecimen Retention, Maintenance

The committee notes that tissue analysis technology continues to advance, making it difficult to confidently predict the future scientific value of specimens. The JPC, however, is under no obligation to store the entirety of its collection indefinitely in the expectation of a possible future research need. Rather, the committee recommends that the JPC develop protocols to guide its decisions regarding when to retain potentially useful materials and when to dispose of specimens that have neither clinical use nor unique research or educational value. Items that could be discarded include wet tissue specimens and slides that are contaminated, dried, or otherwise damaged; tissue blocks that have deteriorated; frozen specimens with signs of freezer burn or that have melted and refrozen; and samples that lack a data record. Specimens that meet the disposal criteria could be purged. Because rules governing sample retention evolve, the committee recommends that the JPC consult with the DoD Office of the General Counsel before implementing its policy.

Since it would be costly and time-consuming to audit the JPC’s vast holdings, the committee recommends that the condition of samples be evaluated when they are retrieved for clinical, educational, or research purposes. If it becomes cost-effective to conduct an audit, the committee recommends that the JPC prioritize review of wet tissue specimens, since a 2008 report by an outside contractor indicated that most of these
samples had desiccated. Likewise, because frozen tissue is vulnerable to melting and ultra-low temperature freezers are expensive to maintain properly, the committee suggests that the JPC consider a targeted audit of its frozen holdings.

The specimens transferred from military health care facilities closed under BRAC authority have no greater value for education or research than materials held by hospitals, university pathology departments, or military health care facilities that remain open. For this reason, the committee recommends that the BRAC additions to the JPC repository be kept only for the amount of time needed to satisfy rules and regulations governing the retention of clinical specimens.

"BOX: Biorepository Samples Advance Public Health"

- **Sequencing the 1918 influenza virus.** In 1995, a team led by Jeffery Taubenberger, chief of the Division of Molecular Pathology of the Armed Forces Institute of Pathology (AFIP), extracted RNA fragments from repository tissue specimens to study this strain, which was responsible for a pandemic that killed more than 40 million people. The researchers examined more than 100 autopsy cases, finding one that tested positive for the presence of the virus. Samples from the repository were ultimately instrumental in sequencing four of 11 gene segments from the 1918 influenza.

- **U.S. Army Lieutenant Colonel Joseph Woodward,** the first pathologist at the Army Medical Museum, generated tissue sections from autopsies of Civil War victims who suffered from chronic diarrhea. Woodward used those sections to revolutionize the field of histology in the United States by establishing, in 1865, that synthetic dyes could be used to facilitate the study of particular tissues—a practice that had been independently developed earlier in Germany but had not reached the United States.

- **In 1983, researchers examined** AFIP biorepository cases of children who had Reye’s syndrome, which damages the brain and liver. They found that the syndrome was linked to using aspirin to treat chickenpox and upper respiratory infections. The Food and Drug Administration subsequently warned the public about aspirin use in children and teenagers who had or were recovering from chickenpox or flu-like symptoms, leading to a decline in the occurrence of Reye’s syndrome.

- **AFIP researchers reviewed** and performed autopsies from 2003 to 2005 on U.S. Marines who died in Iraq and Afghanistan. The data have been influential in protecting and treating our troops. After researchers determined that body armor protecting the shoulder, back, chest, and side can prevent most fatal injuries, the Department of Defense (DoD) developed more effective armor. Body scans also revealed that needles and tubes inserted into soldiers suffering from collapsed lung were too small for about half of military personnel. That finding led DoD to switch to thicker tubing.
Committee on the Review of the Appropriate Uses of AFIP’s Tissue Repository Following Its Transfer to the Joint Pathology Center

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Conclusion

While the biorepository was created more than a century ago, its recent reorganization prompted the DoD to ask the committee to take a fresh look at its myriad shelves filled with numbered boxes, asking fundamental questions about the repository’s utility and role, both today and in the future. In answering those questions, the IOM committee proposes a series of protocols, standards, safeguards, and guidelines that could help to ensure that this national treasure continues to be available to researchers in the years to come, while protecting the privacy of the people who provided the materials and maintaining the security of their personal information.