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## **CONNECTIVE TISSUES: ETHICAL GUIDELINES FOR BIOHISTORICAL RESEARCH**

Nancy Buenger

### **1. Introduction**

Biomolecular technologies offer new frontiers for interdisciplinary research with historical human biological artifacts. Academic, commercial, and private investigators are seeking access to bone fragments, locks of hair, preserved organs, and bloodstained garments for biomolecular research, particularly DNA analysis (Fig. 1).

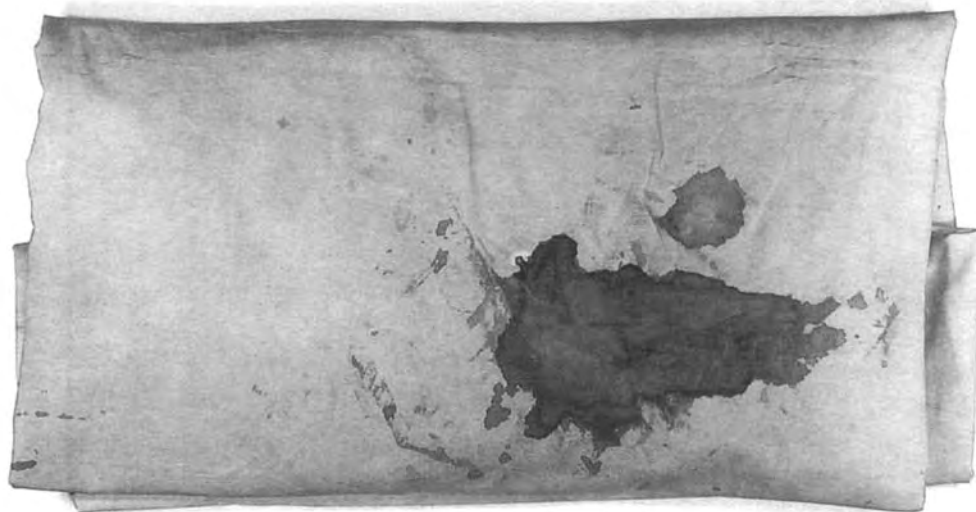


Figure 1. Bloodstained sheet attributed to Abraham Lincoln's deathbed. Courtesy of the Chicago Historical Society (Accession number 1920.253).

Biohistorical research proposals have raised significant social and methodological questions as well as the public profiles of would-be investigators. Does biomolecular analysis yield meaningful evidence for historians? What safeguards are necessary to protect living descendants as well as human remains and cultural biological artifacts?

The rapid development of biotechnologies in the 1990s, particularly DNA analysis, was accompanied by a wave of highly publicized investigations of historical human biological tissues or traces, also known as biohistorical research. Biohistorical investigators have included a range of specialists in anthropology, forensics, genetics, and molecular biology as well as documentary film companies, commercial DNA marketers, private collectors, armchair historians, and individuals seeking information on their family or cultural heritage; academic historians have been notably absent in these endeavors. Custodians of cultural collections and historical sites entered the arena as researchers sought access to new sources of non-indigenous biological samples in the wake of the 1990 Native American Graves Protection and Repatriation Act (NAGPRA).

Biohistorical research proposals have generated historical, scientific, and social concerns, including the justification for the proposed research, appropriateness of the study design, destruction of fragile museum specimens, the relevance of informed consent, potential harm to living relatives, cultural respect for the dead, confidentiality of medical and genetic information, and the interpretation of study results. The ambiguous legal status of human remains contributes to these debates. Human subject protections are codified for federally funded research with the living but do not apply to the dead. State protections vary but have progressively allowed tissue retention and analysis as the research value of cadaver tissue increases (Nelkin and Andrews 1998). Although NAGPRA strengthened federal protections for indigenous skeletal remains, forensic anthropologists have launched legal and research initiatives challenging the statute (Bonnichsen 1997; Jantz and Owsley 2001; Bonnichsen 2002).

Custodians of cultural collections and sites face considerable difficulties when evaluating research requests involving their historical human biological holdings. Codes of ethics and practice are splintered between professional specialties and do not adequately address biological tissue analysis. Caretakers of cultural collections typically lack the specialist knowledge necessary for evaluating genetic research proposals. The politicization of research with the dead, funding offered by commercial companies and the lure of biotechnology publicity further complicate the decision-making process.

The Chicago Historical Society (CHS) and the Institute for Science, Law, and Technology (ISLAT) at the Illinois Institute of Technology have initiated a multi-year project, with funding from the National Science Foundation, to develop ethical guidelines for biohistorical research. The project is an outgrowth of requests for access to historical human biological materials at CHS and ISLAT's mission to provide a forum for dialogue among academics, scientists, policy-makers, lawyers, professionals and students about critical issues at the intersection of law and technology. While primarily focusing on the implications of bioanalysis for historical as opposed to anthropological research, the CHS-ISLAT collaboration is encouraging an interdisciplinary and intercultural dialogue to consider common concerns. Genetic analysis is a central consideration because of its implications for living descendants as well as the preservation of cultural materials. An evaluation of historical, scientific, and social concerns raised by recent studies has generated preliminary suggestions for evaluating biohistorical research proposals. CHS and ISLAT are soliciting case studies as well as commentary on the project to promote a national dialogue on biohistorical research.

## **2. Historical Concerns**

The Chicago Historical Society houses one of the largest historical collections in the United States. Biological holdings include the most comprehensive collection of artifacts associated with Abraham Lincoln's assassination, the remains of one of Chicago's earliest homicide victims, hair attributed to various historical figures, and cultural artifacts stained with body fluids. Requests for bioanalysis of CHS's Lincoln relics exemplify biohistorical quests that typically involve the authentication of historical remains and artifacts, the resolution of speculative medical history or paternity disputes, or the commercial potential of genetic analysis.

Many of CHS's Lincoln assassination relics were originally purchased by Charles Gunther, a Chicago confectioner and politician, for his popular Libby Prison Civil War Museum in the 1890s. Typical of early American museum collectors, he gathered a hodgepodge of relics, both genuine and sham (Fig. 2).



Figure 2. Charles Gunther collected authenticated Lincoln artifacts as well as this “Skin of the Serpent who Tempted Eve in the Garden of Eden”. Courtesy of the Chicago Historical Society (Accession number 1920.1714).

A CHS museum administrator initially suggested genetic analysis of stains on a cloak allegedly worn by Mary Lincoln on the night of the assassination to determine its authenticity. The society hosted a 1999 conference of historians, scientists, and conservators who concluded that DNA research was inappropriate as currently available DNA extraction techniques would damage the artifact and there was no established Lincoln genetic profile for comparative analysis. CHS found itself at the center of massive international media coverage following the conference. “Keeping Facts Cloaked is Lousy Reasoning” screamed one headline while a support group for Marfan syndrome patients published an irate letter on the Internet: “I thought that a ‘historical’ society wanted to ferret out truth. Where is that line in the sand drawn – what we ignorant heathens are permitted to learn about historical figures and what is off limits to us? And who draws that line – the Chicago Historical Society?” (Cortese 1999).

CHS declined a number of biohistorical research proposals from outside investigators. The BBC Discovery cable broadcasting network offered to underwrite DNA analysis of the cloak associated with Mary Lincoln in exchange for information on whether Lincoln suffered from Marfan syndrome, a connective tissue disorder. StarGene Inc., the brainchild of Nobel Prize laureate and polymerase chain reaction (PCR) patent holder Kary Mullis, made a similar proposition in exchange for the right to replicate any genetic material found on the garment. StarGene embeds the “‘genetic essence’ of the stars” in GeneStones (TM), “a gem-like resin, that will encapsulate

and visually preserve” DNA, for a line of jewelry products and collectibles (StarGene 1996). Self-identified Lincoln relatives volunteered blood samples in exchange for confirmation of their patrimony; one gentleman even offered to exhume his grandmother to facilitate a genetic analysis. Other descendants supported the request of a retired college administrator with an education degree who hoped to conduct Y-chromosome analysis to investigate Lincoln’s paternity (Hyatt 2003).

Biohistorical investigations sometimes appear to be more closely associated with political agendas than significant historical inquiries. Davidson has questioned the timing of a high-profile 1989 request for genetic analysis of bone fragments linked to Abraham Lincoln’s assassination at the National Museum of Health and Medicine. Investigators associated with the Human Genome Project hoped to determine if the president had a genetic predisposition to Marfan syndrome at a time when Congress was in the process of authorizing funds for the project. A panel of experts considering the investigation initially approved the request although they agreed that Lincoln’s medical history was not a major historical question and that there was no substantive medical evidence that he had suffered from Marfan syndrome (Davidson 1996). Reilly has suggested that the Department of Defense ultimately squelched plans for the analysis because of public concern over its DNA bank for military personnel (Reilly 2000).

The articulation of meaningful questions lies at the heart of all historical research. Substantive historical queries should reflect an extensive knowledge of related scholarship and a critical examination of multiple sources of evidence, including an assessment of their reliability. Bioinvestigators frequently assume the authenticity of museum specimens although historical artifacts rarely have the detailed provenance associated with more commercially valuable fine art works. The interpretation of historical figures or events from a single source of physical evidence smacks of biological determinism. More readily available textual and oral sources, which may be sufficient to answer the historical question, are often ignored.

### 3. Scientific Concerns

The significance of historical questions must be carefully weighed against the obligation to conserve cultural materials and the complexities of biological research, particularly destructive sampling for genetic analysis. Minimally invasive visual or microscopic examinations that could provide sufficient historical evidence are often ignored in favor of “cutting-edge” technologies. An interdisciplinary team should design protocols for biohistorical testing and consider whether the proposed analysis can accurately answer the historical question.

Researchers should be familiar with the unique properties of aged biological samples and fragile cultural artifacts. Bioarchaeological methodologies for extracting and analyzing ancient human DNA (aDNA) are destructive and biological traces pose special challenges. Extraction and analysis of aDNA from stains on historically important textiles such as CHS’s Lincoln assassination cloak have not yet been validated (Gaensslen 1999). Enough DNA must be extracted to permit multiple independent amplifications as well as external replication to confirm the presence of aDNA; additional sample material should be reserved for future testing or to apply new techniques not available at the time of an initial study (Kaestle and Horsburgh 2002). The presence of blood on fragile cultural artifacts should be confirmed prior to destructive sampling; a suitable micro-scale Takayama test has not yet been developed for aged textile blood stains (Gaensslen 1999).

Contamination from modern DNA remains a significant problem for aDNA analysis. Despite

general agreement on standard protocols to prevent and detect contamination, aDNA researchers regularly experience failure rates of over fifty percent due to contamination problems. The cloak associated with Mary Lincoln has been extensively handled by museum staff and even worn by a society member in the 1930s. (Fig. 3); each has left contaminating DNA deposits on presumed blood stains.



Figure 3. Chicago Historical Society Member modeling the cloak attributed to Mary Lincoln. Photo c. 1930. Courtesy of the Chicago Historical Society (Accession number 1920.976).

Standard procedures developed for decontamination of aDNA samples from bone, including surface removal with sandpaper, soaking in bleach, or UV irradiation, are often inappropriate for other materials. A biohistorical investigator who requested permission to conduct Y-chromosome analysis of CHS's Lincoln relics included a testing proposal from a private laboratory that provides modern DNA analytical services for genealogists. Laboratories performing aDNA analyses must be physically separated from modern DNA facilities and dedicated solely to aDNA extraction and analysis to avoid contamination (Kaestle and Horsburgh 2002).

#### 4. Social Concerns

The social implications of biohistorical research encompass cultural, ethical and legal considerations. The social concerns of living family members have not received adequate attention in recent bioanalytical studies of historical celebrities (Fig. 4).



Figure 4. Although there are no living direct descendants of Abraham Lincoln, an analysis of his DNA could reveal the medical history of related family members and affect on-going paternity disputes. President Lincoln and family circle, published by John Smith, 1865. Courtesy of the Chicago Historical Society.

Biohistorical investigations of Native Americans and African Americans have generated national debates concerning cultural affiliation and consent. The potential negative consequences of biohistorical knowledge production as well as the proprietary or commercial interests of investigators should be identified.

Research with the living is subject to institutional and federal human subject regulations for informed consent and confidentiality, but amateur biohistorical investigators can circumvent these requirements. Genetic analysis of tissue from relatives can reveal information about the paternity, health status, and predispositions of family members (Nelkin and Andrews 1998). Retired pathologist Eugene Foster did not publish consent and confidentiality provisions in conjunction with his 1998 comparative Y-chromosomal study of the descendants of Thomas Jefferson and his slave Sally Hemings although he published his subjects' genetic sequences. The private lives of the Jefferson and Hemings families were disrupted by the intense media coverage generated by Foster's study, which improperly discredited some African-American descendants' long-standing belief that they were related to Thomas Jefferson (Foster et al. 1998; Davis 1999; Andrews and Nelkin 2001). Princeton Hospital pathologist Thomas Harvey has been criticized for failing to obtain consent for his studies of scientist Albert Einstein's brain, published in the

1990s. Harvey removed Einstein's brain during his 1955 autopsy, divided it, and distributed samples to several colleagues although Einstein had expressly rejected the use of his body for scientific research and his family assumed that his entire body had been cremated. Unauthorized use of body tissues can also violate religious beliefs. Orthodox Jews believe that the body must be buried whole; rabbis requested Einstein's brain for burial so that the scientist could rest in peace (Anderson and Harvey 1996; Nelkin and Andrews 1998; Witelson et al. 1999). Other individuals may object to the patenting of body tissues or their use by for-profit enterprises such as StarGene or documentary filmmaking companies.

Anthropologists have grappled with the problem of obtaining consent for research with the dead, which is exempt from regulations concerning the use of human subjects. Some form of proxy consent for the deceased is recommended, typically from culturally affiliated living descendants. However, identifying appropriate individuals or groups who can provide proxy consent is difficult at best. Most discussions of consent for research with the dead have concerned indigenous peoples; protections developed for these populations are difficult to apply to less cohesive communities, especially when they lack recognized political authorities (Kaestle and Horsburgh 2002). The results of genetic studies may have implications for group members even if they did not participate in the research.

The debates surrounding biohistorical analysis of "Kennewick Man" and excavated remains from New York's African Burial Ground highlight the continuing potency of human remains as symbols of cultural integrity and colonial oppression. When Native Americans opposed the investigation of a skeleton excavated near Kennewick, Washington, forensic scientists argued that its measurements were inconsistent with previously documented local indigenous remains. In an ongoing legal dispute, Smithsonian Institution scientists have suggested that cranial dimensions should trump notions of cultural affiliation (Bonnichsen 2002). The excavation of New York City's colonial African Burial Ground became a microcosm of African American concerns regarding racism and economic exploitation. Members of the black community objected to white researchers' analysis of bones from the burial ground, anticipating interpretations that would reflect white social stereotypes, and eventually gained control of the project (Harrington 1993). While Native American communities are generally opposed to scientific analysis of human remains on religious grounds, many African Americans have expressed considerable interest in biohistorical research to obtain additional information about their ancestry. The mixed genealogical heritage of many cultural communities, particularly those of colonial-era Native American and African American slaves, complicates notions of cultural consent and control of biohistorical investigations.

## **5. Evaluating Biohistorical Research Proposals**

CHS-ISLAT investigators have drafted a preliminary set of questions to facilitate the evaluation of biohistorical research proposals; ethical guidelines will be published at a later date. The questions were developed following a review of published biohistorical studies and human subject regulations, consultation with a range of specialists, and analysis of codes of ethics and practice for a selected group of professional associations.

### **5.1. Protocol Development**

- Who will assume primary responsibility for evaluating the proposed investigation?



- Has an appropriate interdisciplinary and/or intercultural team of consultants been assembled for planning and implementing the project as well as interpreting and disseminating project results?
- Has adequate consideration been given to the historical, scientific, and social implications of the proposed investigation?
- Have potential conflicts of interest been identified?
- What federal, state, or local laws are applicable?
- What provisions have been made for the responsible stewardship for cultural artifacts?

## **5.2. Historical Analysis**

- Have the investigators critically engaged previous historical scholarship and existing evidence?
- What are the investigators' motivations for the proposed research?
- Can the historical question be answered with non-biological evidence?
- Is the provenance of proposed biological samples reliable?
- Does the significance of the historical question justify destructive sampling or analysis of cultural artifacts?

## **5.3. Scientific Investigation**

- Can the proposed methodologies answer the historical question?
- Have non-destructive methodologies been adequately considered?
- Do the investigators have previous experience and a reasonable success rate with the proposed materials and methodologies?
- Is the laboratory facility appropriate for the proposed investigation?
- If genetic testing has been proposed:
  - » Have preliminary tests confirming the nature of suspected biological traces been performed?
  - » Does the condition of biological materials suggest that aDNA is more likely to be present than not?
- Have the proposed sampling and testing techniques been validated on similar aged and fragile materials?
- What are the likely sources of contamination and can they be controlled by standard protocols?
- Is an authenticated DNA reference sample available for comparative analysis?

- Is the laboratory facility solely dedicated to aDNA analysis?

#### **5.4. Social Considerations**

- Who are the stakeholders in the proposed investigation and have the investigators demonstrated a commitment to initiating and maintaining a dialogue with them?
- What are the potential negative consequences of biohistorical knowledge production for human subjects as well as their relatives and communities?
- Are appropriate safeguards in place to protect human subjects as well as their relatives and communities?
- Provisions for informed consent and confidentiality should consider:
  - » Who will be asked to provide consent and why?
  - » What provisions have been made for securing identifying information?
  - » Who will have access to test results and control of acquired data?
  - » How and where will samples be stored and for how long?
  - » What provisions have been made for destruction of test materials?

#### **6. Conclusions**

Despite the problematic nature of biohistorical investigations completed to date, historians should not dismiss the potential of laboratory analysis to yield significant evidence. Historians and scientists have rarely undertaken collaborative research projects, which offer the potential for unusual analytical perspectives as well as new evidentiary sources. Comprehensive research methodologies as well as an interdisciplinary and intercultural dialogue on the implications of biohistorical investigations are sorely needed. Biohistorical researchers should consider revamping their methodologies by a century or two – basic techniques such as detailed visual and microscopic examination can yield a level of evidence that is far richer and more useful than genetic analysis. Historical biological tissues and traces should be preserved for the future development of less invasive and more accurate sampling and analytical techniques.

CHS and ISLAT welcome case studies and comments as they develop ethical guidelines for biohistorical investigations; the author's contact information follows below. The guidelines will be distributed to professional and cultural associations for commentary to promote a national dialogue on the implications of biohistorical research.

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