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Genetic Research among the Havasupai: A Cautionary Tale

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Imagine that you donated a bit of blood to a researcher whom you believed intended to identify a genetic link to a disease ravaging your community, only to discover years later not only that you had been misled, but that other researchers were mining your DNA for reasons that were never disclosed to you. What would you do? This was the case for the Havasupai Tribe in Arizona, who learned that researchers at Arizona State University (ASU) had gathered blood samples from them to search for a link to diabetes but used the samples to look for other diseases and genetic markers, thereby violating the basic tenets of human subject research. To determine where the breakdown between the Havasupai Tribe and ASU occurred, let's look at community-based participatory research and its underlying principles of informed consent.

Background

The Agency for Healthcare Research and Quality (AHRQ) defines community-based participatory research (CBPR) as a “collaborative research approach that is designed to ensure and establish structures for participation by communities affected by the issue being studied, representatives of organizations, and researchers in all aspects of the research process to improve health and well-being through taking action, including social change” [1]. CBPR, as AHRQ describes it, further entails shared decision-making power and mutual ownership between the community and the researchers. Over time, researchers have come to recognize that, with community commitment, they could work effectively to assist in identifying and resolving health care disparities [2].

Topics for community studies have ranged from asthma in urban populations to genetic propensities to develop various types of cancer. Well-known CBPR studies include those that helped identify the BRCA1 gene prevalence in the Ashkenazi Jewish population and the sickle cell trait among African Americans. Certain fundamental principles apply in conducting CBPR, regardless of the group in question. It is vital that a researcher respect the community and its values and beliefs and follow the principles of human subject research, namely, obtaining informed consent from the community. Not only can failure to adhere to informed consent protocols be devastating to a community, it can permanently damage the credibility of a researcher or institution.

The Principle of Informed Consent

Informed consent has been a point of debate and concern since its origin in the post-World War II Nuremberg Code, which is a set of guidelines drafted to ensure that harms to humanity like those in Nazi “medical” experiments would never occur again in the name of science [3]. Informed consent is achieved when a competent individual agrees to participate in a study or procedure after having expressed clear understanding of all material facts related to the activity in question. These facts are provided by the researchers and empower the individual to make an informed choice, in full recognition of the nature and consequences of the decision.

The Tuskegee Syphilis Study, which began in 1932, involved approximately 400 African American men infected with syphilis. The U.S. Public Health Service tracked these men for roughly 40 years without providing them with a diagnosis of their disease or any opportunity for treatment [4]. This was a direct violation of informed consent principles and the antithesis of how CBPR should be performed. As a result of their lack of treatment and lack of knowledge, hundreds of the men and their families lost their lives to a treatable disease.

Congress responded with the National Research Act in 1974, which created the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research [5]. In 1979, this commission published the Belmont Report to identify the minimum ethical principles required for human subject research, which included informed consent as a basic tenet [6].

The federal government did not stop with the Belmont Report. In 1991, the U.S. Department of Health and Human Services published the Common Rule, which mandated that researchers obtain informed consent before engaging in most types of human subject testing [7]. The elements of informed consent have been codified within the Common Rule to include: a statement that the study involves research; the purpose of the research, the duration of the research and the procedures that will be followed, a description of any potential benefits to the subject or to others which may result from the research, a statement describing how the confidentiality of the subject will be maintained, and an explanation of whom to contact for answers about the research and research subjects’ rights [8]. These elements are vital to ensuring that an individual can truly make an informed choice.

Obtaining informed consent from a community for CBPR can be difficult, time-consuming, and fraught with challenges. Sometimes, for example, an individual is not only consenting on his or her own behalf but must secure the approval of a community leader before participating in any type of study. Therefore, a researcher must take the time to establish a trusting relationship between herself and the community and its leaders, which includes following through on promises and maintaining contact with the community [9]. A community leader can be the head of a Native American tribe, the head of a church or synagogue, a spokesperson for an informal community of individuals with a common interest, and so on. Lines of

communication must remain open to these leaders and the community as a whole to ensure dialogue and participation throughout the study and the relationship.

Perhaps the most crucial element is making sure that the community is truly informed about the full extent of the research and consents to it. The Havasupai Tribe's claim against Arizona State University illustrates what can happen when researchers—either intentionally or through negligence—do not make the full extent of their research goals known.

The Havasupai Tribe CBPR Experience

In 1989, members of the small tribe of approximately 650 poverty-stricken people approached ASU anthropology professor John Martin, with whom the tribe had a preexisting and trusting relationship [10], seeking to learn why the incidence of diabetes within their community was increasing. Genetic links to diabetes had been identified in another tribe, and, if a similar gene could be located among the Havasupai, it might provide a tool for addressing risk factors. Professor Martin approached a colleague, Therese Markow, a geneticist at ASU, to assist in the study. Dr. Markow's previous work had touched upon other diseases, specifically schizophrenia, and she wished to expand the study to include mental disorders [11]. Professor Martin is said to have responded that he did not believe there would be interest in Dr. Markow's research on the part of the tribe, but Dr. Markow continued with her mental disorder research based on the samples provided by the tribe [11].

Approximately 100 tribal members signed a broad consent document to “study the causes of behavioral/medical disorders” [12]. Most of them had not completed high school, and, for many, English was a second language [12]. All of the tribe members believed that they were donating blood solely for the purpose of looking for a link to diabetes to improve the health in their community [13]. ASU researchers determined that the genetic link to diabetes found in the other tribe did not exist among the Havasupai but continued their research into medical disorders without seeking additional consent from the tribe. Other ASU researchers also utilized the Havasupai samples for their work and published papers about inbreeding, alcoholism, and the origin and migration of the tribe from Asia. Although the hard data published in these studies may have been accurate, the studies violated informed consent, and theories about the tribe's origin conflicted with their core beliefs.

The complaint in the case of *Havasupai Tribe vs. the Arizona Board of Regents* listed six charges that included lack of informed consent, violation of civil rights, and intentional or negligent infliction of emotional distress. ASU paid for a private investigation to keep the suit out of the courts, and, after seven years of litigation, 41 members of the Havasupai Tribe settled in April 2010. ASU is reported to have spent upwards of \$1.7 million defending itself against the allegations. The terms of the settlement were a payment of \$700,000, the return of the blood samples, and additional assistance including scholarships and help in obtaining federal funding for a health clinic for the impoverished tribe [12]. The Havasupai tribe's experience demonstrates the extensive harm that can be done to a community—some of it

irreparable—through violation of informed consent. The research subjects were not adequately informed about how their DNA would be used at the university, and this significantly impacted the integrity of their community and their trust of outsiders.

The April 2010 settlement initiates a healing period for the tribe, yet ASU's reputation—along with that of the researchers—seems to have been permanently undermined by the informed consent violation. Some tribes still refuse to work with ASU [12]. This situation could have been avoided if the informed consent documents had been clear, and if information had been properly and patiently conveyed in full to the tribe. Moreover, those looking to engage in further study of the original samples should have gone back to the community to obtain new informed consent for the additional research. It appears unlikely that the Havasupai would have consented to research related to schizophrenia and other disorders, which would have saved the tribe much of the emotional distress they experienced. What can be gleaned from this glaring example of research gone wrong is that, by failing to follow proper protocols and regulations, a researcher engaging in CBPR may inflict permanent harm on the participating community and chill future research among disadvantaged populations.

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