Science at the heart of medicine

Emphasizing the potential for discovery of new information while assuring trust in the informed consent process

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Why Trust Us?

- Bad Blood: “The scandalous story of the Tuskegee experiment when government doctors played God and science went mad” by James H. Jones 1981.
- The Willowbrook Hepatitis Studies, 1966 H.K. Beecher, NEJM.
- The Immortal Life of Henrietta Lacks: “Doctors took her cells without asking. Those cells never died. They launched a medical revolution and a multimillion-dollar industry. More than twenty years later, her children found out,” by Rebecca Skloot 2010.

The Havasupai Indian Tribe Case- Lessons for Research Involving Stored Biologic Samples

Michelle Mello, J.D.,Ph.D., Leslie Wolf J.D., M.P.H. NEJM 6/15/10

- On April 20, 2010, Arizona State University agreed to pay $700,000 to 41 members of the tribe for improper use of blood samples in genetic research.
- The suit stemmed from a 1990 diabetes study in which ASU researchers collected >200 blood samples from tribe members in order to study: "the causes of behavior/medical disorders" but prestudy talks were focused on diabetes.
- Samples were used in multiple studies unrelated to diabetes, i.e.
  - Genetic basis of schizophrenia
  - Inbreeding: a taboo in the tribe
  - Evolutionary-genetics: theory for migration across Bering Sea vs tribe's beliefs
- Did the downstream uses of the samples fall within the scope of the donors' informed consent (IC)?

IC, Biospecimens & Future Use

- In the settlement, ASU agreed to return samples to the tribe.
- Questions remain as to what constitutes adequate IC for biospecimens collected for research to be stored and used in future, possibly unrelated studies?
- Case law states that biospecimen donors do not retain property interests in samples collected and used in accordance with properly obtained IC.
- Research on previously collected biospecimens is permitted without obtaining new IC when:
  - samples cannot be traced back to individuals
  - or when there is minimal risk to participants
  - does not adversely affect their rights or welfare
  - Could not practicably be carried out if new IC were required
  - And provides a mechanism for giving participants additional pertinent information when appropriate

IC, Biospecimens & Future Use

- Office for Human Research Protections states that IC for storing identifiable biospecimens should include a clear description of “the specific types of research to be conducted”
- Thus, what constitutes adequate IC for research on stored samples has both ethical and legal ramifications.

Approaches to IC for Research on Stored Biospecimens

Approach **How Consent Is Obtained**

- Specific consent: Research participants are recontacted and asked to consent for each new use of their specimen or for information that is outside the scope of their original consent.
- Tiered consent: At the time samples are collected, research participants are presented with a menu of options from which to choose, which may include general permission for future use, consent only for future uses related to the original study topic, consent for future uses unrelated to the original study topic, and specification that the investigators must obtain specific consent for any future use that differs from the original study.
- General permission At the time samples are collected, research participants are asked to permit all future uses that a qualified ethical review board determines to be scientifically meritorious and ethically defensible.
- Presumed consent At the time samples are collected, research participants are informed that their specimens will be used in future research unless they expressly deny permission.

Caveats

- Does general permission or blanket or global consent for future research uses constitute meaningful IC?
  - Potential for breach of confidentiality as with genomic data.
  - Avoid by labeling samples with code numbers and storing links to indentifying information separately.
- Does removing donors' indentifying information from samples eliminate the ethical dilemma?
  - Rationale is that analysis of samples does not involve risk
- Future projects will utilizing new techniques for discoveries.

Response to Caveats

- People have a right to control the uses to which their bodily tissues are put, regardless of risk.
- Thus, the donation of biospecimens for research involves a compact in which the participant agrees to donate samples and the researcher agrees to abide by the conditions regarding their collection and use.
- Allowing donors to grant general permission is ethically acceptable, but the use of even anonymized specimens for purposes beyond the agreed uses is not unless new IC is obtained.
- Tribe members would not have contributed samples for non-diabetes studies even if anonymized.

Best Practices for IC

- Determine what research participants want.
- A majority of the public finds general permission acceptable.
- However, there are populations that desire new specific consents for new uses especially if genomic information is obtained.
- Participants should be told that the biobank will allow research aimed at curing a certain disease or improving human health although this may not be sufficient to assure trust.
- The tiered consent offers the best example of respecting participants and providing opportunities for discovery.

Example of Language for Tiered Consent

- With your permission, we would like to store your blood sample for use in future research.
- You do not have to agree to this in order to be in the study, and your decision will not affect the care you receive from the study doctors.
- Please pick one of the choices below:
- My blood may be kept and used in research to learn about, prevent, or treat diabetes.
- My blood may be kept and used in research to learn about, prevent, or treat diabetes or

  other health problems (e.g., heart disease and mental illness).
- My blood may not be used in future research unless researchers contact me to tell me

  about the study and ask my permission.
- My blood may not be used in future research. I do not want researchers to contact me about future studies.
- * Adapted from the National Cancer Institute's informed consent template for cancer treatment

Best Practices for IC- Community Engagement

- Researchers need to ensure that the participant's perspectives are addressed.
- Consult the community first, advocacy group, etc., to identify potential areas of concern.
- Develop a partnership with community, participants, families, etc.
- Develop effective means to translate research discoveries that would be accepatble and adopted by individuals and communities that realized the value of the data, samples, and information that they provided at all stages of discovery and who demanded to engage as both partners and participants.
- Maintain ongoing communication and transparency of goals.

PedsHome Study: Do I Have to Take Part in This Research Study?

- Your participation is voluntary. This means that you decide whether or not you want to join the study after speaking with the researcher, or other member of the research team.
- If you decide to take part you will be asked to sign this consent form. Your signature means that you agree to be a subject in this research.
- After reading this form and having a discussion about what it says, you should ask all the questions you want to ask. You should take as much time as you need to make a decision.
- If you do not understand some of the terms used in this form, ask the person who is discussing the study with you to give any additional information that may make this easier to understand.
- You do not have to consent to participate in the study immediately, or ever. Take time to decide whether or not you wish to join. You may take home a copy of this consent form to think about it or discuss the information with family or friends before you decide.
- If you decide not to participate in this study, the care providers at this facility will give you all of the standard care that is appropriate for you.
- If you decide to participate in this study, you are free to withdraw at any time without any reason. This will not affect your care and you will continue to be treated at this facility.
- You will be given a copy of this form whether or not you agree to participate in this study. Do not sign the form unless you have had all your questions answered and understand exactly what is involved.

Genetic Testing

- **WILL THIS TEST INVOLVE GENETIC RESEARCH and /or TESTING?**
- Genetic means having to do with information that is passed on in families from parents to offspring through genes.
- Researchers and doctors know some of the genes that cause disease, but they do not know all of them. Your participation in this study may help identify genes that are related to high blood pressure in adolescents, which in turn, may help in the diagnosis and treatment of high blood pressure.
- Tests conducted under this research study may reveal genetic information.
- You may wish to obtain professional genetic counseling prior to signing the informed consent. A genetic counselor is a person qualified to provide information about what the results of this type of test may mean to you and your family. No formal genetic counseling will be provided under the research study. You or your insurance company will be responsible for the cost of these services.
- Since the significance of these tests is not known, we will not disclose the results of the genetic testing.

Biobanking

- **WILL ANY OF THE SAMPLES (BLOOD, TISSUE, DNA) TAKEN FROM ME BE USED FOR FUTURE RESEARCH STUDIES?**
- **USE OF DE-IDENTIFIED SPECIMENS FOR FUTURE RESEARCH:**
- In addition to the research you are consenting to under this research study, Dr. Frederick Kaskel or other researchers at this or other institutions may wish to study the samples in future research, including genetic analysis. These samples, taken from your body, would NOT be linked back to you. No one will know your name or protected health information.
- At this time, the researcher does not know what the future studies will be. Your specimens may also be submitted to a tissue/cell/DNA bank. The specimens may be kept for a long time and may exceed 50 years.
- In some research using human blood or tissue, the specimens and their parts may enable researchers to develop medical tests or treatments that have commercial value. You will not receive any money that may result from any such commercial tests or treatments. Your specimens may be used for future research, even though the purpose of the future research is not known at this time.

Consent Process

- **PARTCIPANT: PLEASE INDICATE YOUR CHOICE BY INITIALING ONE (1) OF THE FOLLOWING OPTIONS**
- ___ I consent to have my specimens used for future research studies.
- ___ I consent to have my specimens used for future research studies only for the study of _____.
- ___ I do NOT consent to have my specimens used for future research studies. (The specimens will be destroyed at the end of the study.)

The CCIR Website

26/Aug/2010

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Cystinosis is an "orphan" disease with about 500 people - mostly children - stricken with the disease in the United States and approximately 2,000 worldwide.

Cystinosis is a metabolic disease in which the amino acid cystine accumulates within the cells. The cystine slowly destroys the organs in the body including the kidneys, liver, eyes, muscles and the brain. With such a rare disease affecting such a small population, research money is scarce to nonexistent. Yet research on complicated diseases like cystinosis often leads to advancements in other rare diseases.

As proteins are degraded within the lysosomes of cells, the individual amino acids that make up the proteins are transported from the lysosome to the cell's cytoplasm via specific transporters. The transporter for cystine is defective in children with cystinosis and this defect causes the cystine to accumulate within tissue. The cystine content of the cell is 50-100 times the normal value.

Cystinosis is an autosomal recessive genetic disease. This means that both parents are carriers of the abnormal gene that leads to this condition. The parents do not exhibit any of the symptoms of cystinosis. In such couples, the odds are that one-in-four of their children will have cystinosis. The gene for cystinosis, CTNS, was mapped to chromosome 17p13.

Newsflash NEW

Phase 3 Study of Cysteamine Bitartrate Delayed-release Capsules (RP103)

Phase 3 Study of Cysteamine Bitartrate Delayed-release Capsules (RP103) is now open in three U.S. locations; Atlanta, Georgia, Chicago, Illinois and Stanford, California. This multi-center research...

Brain and Cognitive Development in Cystinosis

The Pediatric Neurology Research Group at the University of California, San Diego (UCSD) is conducting the following research study on cystinosis:

Stress and Coping in Cystinosis

The Pediatric Neurology Research Group at the University of California, San Diego (UCSD) is conducting the following research study on cystinosis

Executive Functioning in Cystinosis

The Pediatric Neurology Research Group at the University of California, San Diego (UCSD) is conducting the following research study on cystinosis:

www.cystinosisregistry.org

Registration
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