didactic session: thursday, march 9

Genetics and Informed Consent: Process and Content at the Millennium

Historical perspective of informed consent in ethics and the law. M.K. Pelias. Louisiana State Univ. Health Sciences Center, New Orleans.

The Doctrine of Informed Consent derives from dual origins in clinical medicine and in biomedical research. Early development of **informed consent in clinical practice** arose as a result of the expansion of medical and surgical treatment options in the early 20th century. As patients became more aware of their choices, they became increasingly quick to claim injury in tort when various options, and the possible consequences of the options, were not fully disclosed prior to making decisions about treatment. The concept of medical malpractice grew out of **civil litigation** in a series of lawsuits that significantly shifted the traditional emphasis in the physician-patient relationship from one of professional beneficence to one of patient autonomy. Patients acquired the right to disclosure of all "material" information as they pondered the course of treatment they wished to pursue, and health care professionals acquired the obligation to disclose sufficient information to support a truly informed decision. The somewhat later development of **informed consent in biomedical research** was first formulated by the Military Tribunal that presided over the criminal trial of Nazi physicians and scientists after World War II. The Nürnberg Code delineated both ethical and legal criteria for consent to participation in medical experimentation, including voluntary, competent consent, given without coercion or duress, with appropriate knowledge of the purposes and risks of the proposed research. These and other criteria in the original code were subsequently echoed by the World Medical Assembly in the 1964 Declaration of Helsinki and became the foundation of **legislation and regulations** that now govern the conduct of research with human subjects. As experiments on uninformed patients with syphilis and retarded children with hepatitis were exposed in the United States, Institutional Review Boards became the judges of the merits of research with human subjects. The **current expansion of technologies in medical genetics and genetics research** has generated novel questions that now compel new examination of the **interests of patients and subjects**. As clinical practice continues to interdigitate with biomedical research, new options for the present and future use of human tissue samples must be presented to patients and subjects. These options should include information about the unique nature of DNA samples with respect to personal identification and genotype information, both current and prospective. With appropriate caution, protection of personal privacy and autonomy may well coexist with broad latitude for continuing clinical and basic research activities.

45 CFR 46: Federal Regulations and Institutional Review Boards. Yoder FE, Office for Protection from Research Risks, National Institutes of Health, Rockville, Maryland.

The Department of Health and Human Services (DHHS) regulations, codified at Title 45, Code of Federal Regulations, Part 46 (45 CFR 46), provide a multilevel framework for protecting the rights and welfare of human subjects of biomedical and behavioral research. These regulations embody the guiding ethical principles of the Belmont Report that include respect for persons, beneficence, and justice. Subpart A of this policy, the Common Rule, applies to all human subject research conducted or supported by federal departments or agencies and to research that is subject to regulation by the Food and Drug Administration; DHHS regulations give additional protections to certain potentially vulnerable populations. The Institutional Review Board (IRB) plays a central role in implementing the protections provided by the regulations. The IRB has the authority to approve, disapprove, or require modifications to proposed research. All research proposals involving human subjects must be reviewed and approved by the designated IRB, prior to the conduct of the research. The regulations specify requirements for IRB membership and the criteria for IRB review and approval of research. The IRB must be qualified to evaluate proposed research in terms of institutional commitments, regulations, applicable law, and standards of professional conduct and practice. As a prerequisite to approving proposed research, the IRB must ensure, among others, that: (1) selection of subjects is equitable; (2) risks to subjects are minimized and that risks are reasonable in light of anticipated benefits; (3) adequate provisions exist to protect the privacy of subjects and confidentiality of data; (4) informed consent will be sought in a language understandable to the subjects and under conditions that minimize the possibility of coercion or undue influence; (5) informed consent includes all the key elements required under 46 CFR46.116; and (6) informed consent is documented as required under the regulations at 45 CFR 46.117. The regulations at 45 CFR 46 reflect minimum requirements for protection of human subjects of research. An IRB may determine that additional protections are needed for certain types research.

The UCLA experience in developing protocols for informed consent. L.L. McCabe[1,2], W.W. Grody[2,3], B. Henker[4], C. Jaenicke[5], S. Peckman[5], R.S. Sparkes[6], F. Wiley[2] and E.R.B. McCabe[2]. [1]Human Genetics; [2]Pediatrics; [3]Pathology; [4]Psychology; [5]Office for Protection of Research Subjects; and [6]Medicine, UCLA, Los Angeles, CA.

Our objective was to provide guidance for investigators in use of human samples for genetic research. Genetic investigation involves all areas of research, since genetic information may be quite sensitive, and is contained in sources as diverse as family histories and pathological specimens. Informed consent for human genetic research involves complex issues for research subjects and investigators. The Executive Vice Chancellor for UCLA created a Subcommittee of the Human Research Policy Board to develop a consistent, complete approach to prospective human tissue research. The subcommittee addressed a variety of issues, including the nature of genetic information, privacy and confidentiality of genetic information, sharing tissue and/or information with other investigators, feedback to participants, and sample ownership. Standard approaches and language were developed to insure appropriate consideration of genetic issues by all investigators. The work of the Human Subject Institutional Reviews Boards has been enhanced by a unified approach to genetic research. Investigators who are not geneticists have been sensitized to the issues of genetic testing of tissue samples. While the Subcommittee recognized that issues of genetic testing are evolving, the standard language was an attempt to deal with current issues and to anticipate future concerns.

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"Neurofibromatosis, the Elephant Man's disease. Is there anyone else in your family with this? What are you worried about, you are an intelligent young woman and we don't know enough about this disease to say whether your baby will be born with neurofibromatosis."

These words remain with me although I first heard them spring of 1975. It was during the first trimester of my pregnancy several small growths developed on my stomach. The physician in the health center where I attended college recommended I go into the county hospital free clinic, which was associated with a teaching university. Little did I know the experience and the diagnosis of that appointment would be life changing! As the clinic neurologist explained the Elephant Man's disease, I was advised to count my blessings, previous cases he had seen were imbeciles in a New York state institution. During the appointment, the door to the examining room opened and half a dozen students from the medical school circled around me in the middle of the room. When the dressing gown dropped, I became painfully aware of two things: my rounded belly and my comparable age with the men in the room. One student raised my arm and said, "Axillary freckling just like in the books," another student commented, "Café au lait markings on the stomach," and another noted numerous neurofibromas. My defense to this extremely uncomfortable situation was to wisecrack, "I guess this is as close as I've ever come to becoming a Playboy Bunny." For just an instance the circle of students froze and then cleared the room leaving me alone to get dressed. I felt traumatized by the humiliation of being viewed with such curiosity. The mental image of the Elephant Man from the best seller *Ripley's Believe it or Not* was permanently ingrained in my mind's eye. A week later, my husband and I consulted with a neurologist in private practice for a second opinion. This doctor's exact word were, "Have an abortion and never have children." Jim tells me I was hysterical when he carried me to the car.