Ethical Issues in Research Involving Children

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Is it ethical to do research involving children?

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- ***Are we willing to place a child at any risk or discomfort today for the sake of other children who might benefit in the future?***

- ***If so, how do we protect the children to assure they are not placed at undue risks?***

Children are Unique

- Diseases
- Development
- Growth
- Metabolism
- Toxicity

Why are Studies Avoided in Children?

- Small number of subjects
- High costs
- Complex consent process
- Limited economic gain
- High liability risk

The Nuremberg Code
(1947)

"The voluntary consent of the human subject is absolutely essential"

“Ethics and Clinical Research”

Henry K. Beecher , M.D. (NEJM, 1996)

- **Many of the patients never had the risks explained**
- **Hundreds never knew they were subjects of experimentation**

Is it ethical to do research involving children?

- **Paul Ramsey-protestant theologian:**

  only if the research furthers the medical interests of the child

- **Richard McCormick-catholic theologian:**

  parents may consent even if there is no therapeutic benefit

National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (1974-1978)

- The Belmont Report
- Research involving children
- Institutional Review Boards
- Research involving those institutionalized as mentally infirm

BELMONT Report (1978)

Practice: ***intervention to enhance the well being of an individual patient***

Research: ***protocol to test a hypothesis and contribute to generalizable knowledge***

BELMONT Report (1978)

Ethical Principles and Guidelines for the Protection of Human Subjects of Research

- Beneficence\Non-maleficence
- Respect for persons
- Justice

BELMONT Report (1978)

Beneficence:

"effective ways of treating childhood diseases and fostering healthy development are benefits that serve to justify research involving children…

research also makes it possible to avoid the harm that may result from the application of previously accepted routine practices…that may turn out to be dangerous"

Respect for Persons

- **Individuals with capacity…**
  treated as autonomous

- **Persons with diminished autonomy…**
  entitled to protection

BELMONT Report (1978)

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Federal Policy for the Protection of Human Subjects (45CFR46)

Subpart A(§46.1):

- Basic policy
- IRBs
- Informed consent

Subpart B(§46.2):

- Special populations
  - Fetuses
  - Pregnant women
  - In vitro fertilization

Federal Policy for the Protection of Human Subjects (45CFR46)

Subpart C(§46.3):

- Prisoners as subjects

Subpart D(§46.4):

- Children as subjects

“Children”

Children are persons who have not attained the legal age for consent to treatment or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.

45 CFR §§46.402

Permissible Research in Children

- **Minimal risk**
- **Greater than minimal risk and prospect of direct benefit**
- **Minor increment over minimal risk and no prospect of direct benefit**
- **Significant risk and special opportunity (Secretary HHS review)**

Minimal Risk

"That the risks of harm anticipated in the proposed research are not greater, considering probability and magnitude, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests"

45 CFR §§46.401-409

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Minor Increase Over Minimal Risk

- **Experiences to subjects commensurate with actual or expected medical situations**
- **Likely to yield generalizable knowledge of vital importance about subject's disorder**
- **Assent of child and permission of parents**

45 CFR §§ 46.406

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Subpart A(§46.1):

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IRBs and Pediatric Clinical Research

- **Expertise in pediatrics**
- **Knowledge of regulations**
- **Appropriate community members**
- **Credentialing/monitoring/accountability**

Pediatric Informed Consent

- **Parental permission**
- **Child assent**

Child Assent in Research

- **Developmentally appropriate**
- **Inform about study/procedures**
- **Solicit expression of willingness**

Adolescent Consent in Research

- **Emancipated minor**
- **Mature minor**

Adolescent Consent In Research

- **Parental permission (??)**
- **Adolescent consent/assent**

Waive Parental Permission

If the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects…it may waive the consent requirements…

45 CFR §§46.408(c)

Federal Policy for the Protection of Human Subjects

Subpart B(§46.2) - revised Dec 13, 2001

Additional protections for pregnant women, human fetuses and neonates involved in research

NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects (1998)

- **Presumption that all research studies will include children**
- **Protections for Children unchanged**