INFORMED CONSENT
What is it?
Why do we need it?
From whom do we get it?
How do we get it?
How can we be sure we’re doing it right?

I. What is it?

Informed Consent is not a legal document or a risk management tool for the investigator or the institution

It is a process

“The goal of the informed consent process is to provide people with sufficient information so they can make informed choices about whether to begin or continue participation in clinical research.”

“The process involves a dynamic and continuing exchange of information between the research team and participant throughout the research experience.”

“The document acts as a starting point for the necessary exchange of information between investigator and potential research participant. It is a resource and reference throughout the trial and is considered the foundation not the entirety”

II. Why do we need it?

Respect for persons
Respect for autonomy of decision making
True limit on investigative authority
Sense of formality

A. Historical Perspective

Most research ethics policies result from singular events and the reactions to them
Rarely proactive

Major events:
Nazi war crimes
Human radiation experiments, etc.
Tuskegee Syphilis study and others
1948: Nuremberg trial
1963: Declaration of Helsinki
1977: National Commission (Belmont Report)

Nuremberg Trial December 9, 1946, to August 20, 1947.
At the conclusion of the trial the Nuremberg Code was issued:
Defines basic human rights of medical research subjects
  Requirement for voluntary consent prior to participation
  Investigator responsibility to obtain consent
  Information gained by using human subjects would be unprocurable any other way

Declaration of Helsinki
  Articulated ethical principles for use by physicians conducting human research
  Affirmed the autonomy of the individual
  Universally adopted to ensure the rights and welfare of human subjects of research

1974 US Congress passes National Research Act
  Created National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
  Ethical foundation for US federal regulations on human subject’s research

Belmont Report
  3 basic principles that should govern all research involving human subjects
  Respect for persons (autonomy, right to factual information, right to withdraw, special protections for those with limited autonomy)
  Beneficence (maximize benefits, minimize risks, avoid harm)
  Justice (benefits and burdens equally distributed among all population groups)

B. Federal regulations (DHHS)
  Adopted by all agencies which conduct, supervise, regulate, fund or sponsor human research
  Informed consent requirements
  IRB approval of any research done

III. What does someone need to know?

Elements of informed consent
  Disclosure (what’s going to happen)
  Risks
  Benefits
  Alternatives
  Confidentiality
  Compensation
Standards
   Reasonable person
   Negligence
   Subjective

   “The reasonable volunteer”

IV. How do we get it?

A. Voluntariness:
   Freely coming to a decision
   Free from coercion or undue influence
   Assumes capacity
   Capacity
   Understand nature and ramifications

Who is not able to do this?

B. Vulnerable populations
   Children ?
   Prisoners?
   Pregnant women?
   Mental retardation
   Dementia
   Mental illness
   Coma/Vegetative state
   Severe pain

C. Assent - We are obligated
   If child can understand
   Age > 6 years (?)
   Can parents overrule?
   With possibility of benefit
   More than minimal risk?
   Not without prospect of benefit

D. Other vulnerable populations
   Research on individuals who lack capacity also requires prospect of benefit
   Not promulgated in federal regulations
   Consistent with state law
   Family member can consent

E. No standard methods for obtaining informed consent

Approach
Verbal vs. Written
Do patients want to know?
How seriously do they take it?

V. How do we do it right?

Informed consent gone wrong?
Examples:
Jesse Gelsinger (gene transplant)
James Quinn (artificial heart)
Hopkins asthma death (hexamethonium)

A. “The tragic case of Jesse Gelsinger”

“Jesse really wanted to participate in the study... Not because he thought it would improve his own health — he knew the test would probably make it impossible for gene therapy to help him later. He wanted to be a hero.”

“…he did not learn about any of the serious dangers his son was facing until it was too late. He didn’t know that two Rhesus monkeys had died in tests involving a gene delivery system similar to the one used with Jesse; he didn’t know that four other human patients had suffered toxicity to their livers earlier in the study.”

Reactions

The Food and Drug Administration (FDA) put all gene therapy trials at University of Pennsylvania — plus other experiments ongoing in several other institutions — on hold.

Hearings to investigate the quality of government oversight and safety enforcement in gene therapy studies.

President Clinton demanded improvements in patient consent procedures and access to information about gene therapy research across the board.

Issues

Truly informed consent may still be impossible. … it’s very difficult for anyone, whether a member of the general public or a skilled scientist, to learn details about the problems cropping up in gene therapy studies.

No guidance on when researchers ought to inform prospective participants about studies not directly related to the trial in question.

Quotes from the bioethics world
‘The privatization of science, combined with patients’ ardent desire for a cure, conspire to prevent meaningful protections for participants in all kinds of studies. Trade secrets,
financial conflicts of interest and overloaded review committees obstruct informed consent by keeping news about ongoing studies beyond the reach of patients and researchers alike. – Art Caplan, University of Pennsylvania

B. James Quinn Case

World's fifth recipient of a self-contained artificial died three days after suffering a stroke. Survived almost 10 months with the AbioCor heart. Of the seven people implanted with the device in a year, only one was still alive. At the time that he received the artificial heart, doctors estimated that he had as little as a week to live.

Artificial Heart Recipient Dies at Age 52
I understood that I would be a pioneer... if this thing worked or if it didn't work, I would be giving something to mankind."
-James Quinn, on his decision to have the artificial heart implanted

Artificial Heart Implant Leads to Suit Over Consent Process

Recipient's Widow Says She and Her Husband Were Misinformed and Misled on Risks, Benefits and the potential for pain and suffering
There was no quality of life. It was too painful. He said he wished he'd never done it.”

The informed-consent process failed," said Quinn's attorney…”They didn't understand what it meant to volunteer for a human subject experiment. They thought this was his only chance, that it was a therapeutic option, and not that he was a human guinea pig.”

Was it wrong?
13-page document detailing "significant risks" as stroke leading to brain and organ damage, loss of mental function, device failure, liver and kidney failure, impaired breathing and discomfort and pain.
As a “new and experimental surgical operation, complications could occur which were previously unknown or currently unforeseeable.”
Potential benefits of implanting the AbioCor heart are “uncertain and have not been proven to exist.”

Quotes from the bioethics world

“To some extent, this is human nature. People are desperate, there is no good alternative, and they may develop unreasonable hopes.”
Thomas H. Murray, president of the Hastings Center
“The informed-consent process for many trials is a sham. Clinical trials are set up in such a way that patients are misinformed and misled. Patients and families are not told what the actual and foreseeable risks are, and what they may expect in the way of pain and suffering.”
Vera Hassner Sharav, president of the New York-based Alliance for Human Research Protection

C. Volunteer in Asthma Study Dies After Inhaling Drug
   24 hours after inhaling hexamethonium, the volunteer reported dry cough, shortness of breath on exertion, muscular aches and fever. Two days later was admitted to the hospital, with concern about a possible reaction. Died one month later

Response
   Institution suspended the research
   Federal government (OHRP) temporarily shut down most of Johns Hopkins's research involving human subjects.
   Hexamethonium was not approved by the FDA an internal review board did not provide adequate oversight.
   “Action is unwarranted, unnecessary, paralyzing and precipitous.” -JHU University did take steps to correct problems

Healthy volunteers
   Volunteers may not stand to benefit directly, but could ultimately contribute to development of a new therapy that the participant might then use.
   Require particularly close monitoring, because they can pose a risk to a volunteer's health or life.

D. Why do people participate?
   Altruism
   Free medical care and medications
   Trust
   Self-interest
   Attention
   Do we want to constrain people if they are doing things for the wrong reasons?

E. Role of the IRB
   Protect the institution
   Can introduce complexity
   Responsibility of PI to terminate if they sense the patient is not really involved in the process
   No one knows how risk is really determined
   Ask questions after reading?

F. EM research consent forms
   94 forms analyzed from 96 EM programs performing research
Mean readability index (years of education needed to understand the content) was 10.
Length and complexity of consent increases with risk to subject.
Prospective subject would need at least a high school grade level education.
Average EM consent forms may be too difficult for the average prospective participant to understand.

G. Strategies for simplification
- Short sentences, short paragraphs
- Eliminate jargon
- Limit abbreviations and acronyms
- Active voice
- Conversational style (“you” not “I”)
- Large type (12-14 pt)
- Upper and lower case
- Sans serif font
- Don’t justify right margin
- Bold headings
- Double space
- 6th grade reading level

Readability & other discrepancies
- 82 documents from 3 IRBs, 16 specialties
- Mean Flesch grade level 8-17
- None below 4th grade (recommended for general US population)
- Two at 8th grade level (general recommendation for consent documents)
- 37% met >90% requirements in code of federal regulation

H. Probabilities
- How severe?
- How likely?
- Most severe and most likely should be brought to attention

VI. Special issues in Emergency Medicine Research

Waiver of Consent

Original waiver (1981 common rule) not relevant to patients with acute life-threatening illness or injury
Did not anticipate modern resuscitation research
FDA provided some regulatory guidance but meant to apply to one-time emergency treatments and not research

Resuscitation research
- Performed for many years without formal prospective informed consent
“Deferred consent”
Patient enrolled without consent
Family or surrogate asked for continued participation
Used in NIH Brain Resuscitation Clinical Trials 1984-86

Halt of resuscitation research
Office for Protection from Research Risk halted all resuscitation research using waiver of informed consent
Trials affected
Cardiopump study, vest-CPR study, PEG-SOD for head trauma

Response from EM community
Established Coalition of Acute Resuscitation and Critical Care Researchers
Consensus document drafted and endorsed by many organizations
Presented in public forum January 1995


Important Elements
Increased and documented role by investigator to attempt to contact family members or legally authorized patient representatives
Prestudy consultation with community representatives
Public disclosure before and after the study
Independent safety and data monitoring boards
Investigational New Drug/Device applications filed with FDA allowing close supervision
If prospective informed consent is not possible, investigator must inform patient or representatives as soon as possible

Points to consider
Does the new rule show respect for autonomy?
Impossible to know a patient’s thoughts at times of critical illness or injury
Focus should be on preservation of life (best interest)

Application of the rule
Limited experience
Lack of specific guidelines for how to satisfy the requirements
Community consultation and notification
Local variation
Flexibility for IRB

Summary
Past abuse of patients in the name of science is well-documented and must continue to be avoided. One way to ensure this is absolute compliance with human subjects protection requirements. Physicians perform research on a mandate from society to advance the quality of health care. Community involvement is essential for the public to continue to support scientific endeavors.