Understanding Clinical Studies: Development of a new Drug

US275 Scientific Ethics
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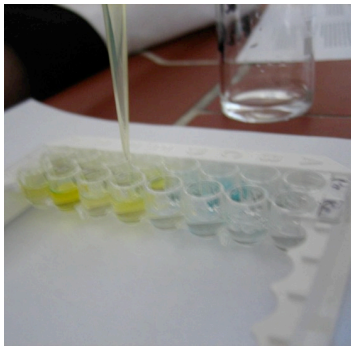
Potential new drugs are identified in Preclinical Research

- Research Laboratory
  - 5 - 10 years
- newly discovered chemical compound
  - usually after years of development through basic chemical and biomedical research
  - may involve synthesis of related molecules

Preclinical Testing determines the biological activity of a drug.

- laboratory and animal studies
  - approximately 3 - 4 years
  - show biological activity of the compound against the targeted disease
  - evaluated for safety



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Investigational New Drug Application (IND) filed with FDA

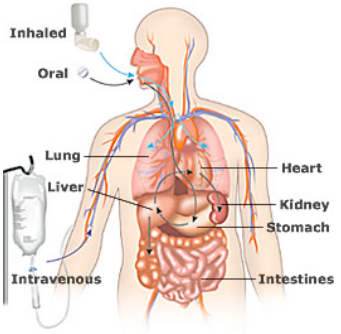
- shows results of previous experiments
- details new studies to be conducted
- describes how it works in the body
- documents toxic effects from animal studies
- approval of Institutional Review Board

Phase I clinical trials test the safety of the drug on healthy volunteers.

- Safety Profile
  - about 1 year
  - 20 - 80 normal, healthy volunteers
  - determine safe dosage range

The goal of Phase I clinical Trials is to understand how the body responds to the drug.

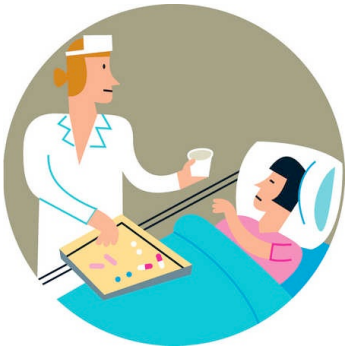
- Study activity of drug
  - how drug is absorbed
  - how drug is distributed in the body
  - how drug is metabolized and excreted
  - duration of drug action



A drug's life in the body.
http://publications.nigms.nih.gov/medbydesign/chapter1.html

Phase II clinical trials examine if the drug is safe and effective.

- Drug Effectiveness & Safety
  - controlled study
  - 100 - 300 volunteer patients
    - small study with people with the disease
- takes about two years



Phase III Clinical Trials examine the efficacy of a new drug.

- Efficacy studies
  - confirm effectiveness
    - compare with commonly used treatments
      - different dosages
    - ease of use
    - identify adverse reactions
  - involves 1,000 - 3,000 patients in clinics and hospitals
    - different populations
    - Physicians closely monitor patients

The FDA reviews the New Drug Application

- all scientific information presented in report to FDA
  - demonstrate safety and effectiveness
  - often 100,000 pages or more
  - FDA reviews application in
    - goal 6 - 10 months for review
    - 1993 - 27 months for review
    - 2001 - 19 months for review

After FDA approval, the new medicine is available for physicians to prescribe.

- company submits periodic reports to FDA
  - cases of adverse reactions
  - quality control records
  - Phase IV studies to evaluate long-term effects

U.S. Food and Drug Administration

Phase IV Clinical Trials continue to evaluate drug safety.

- post-marketing studies
  - collect additional information
    - risks
    - benefits
    - optimal use
  - long-term effects of drug use
- example:
  - Nonsteroidal anti-inflammatory drug Vioxx withdrawn from market in 2004

Cancer.gov

A placebo is a drug with no effect on the disease.

- Placebo: (Latin) "I will please"
- a medically ineffective treatment for a disease
  - inert substance such as a "sugar pill"
  - sham surgery
  - other procedures

Prescription placebos used in research and practice, National Institutes of Health

Many patients report a "placebo effect"

- a perceived or measurable improvement in health after receiving a placebo
- about 1 out of 3 patients will report improvement after receiving a placebo
  - example: pain relief
- some patients also report a nocebo effect
  - unpleasant side effects from placebo

Pygmalion Seeing His Statue Come to Life
François Lemoyne, 1729

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Expectation of improvement and positive attitude important in recovery.

- mind-body connections
  - conditioning to expect relief when receiving medication
- endorphins
  - natural pain relieving chemicals released by brain

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What does this mean for alternative medicine?

- Acupuncture
  - needles inserted into specific points stimulate flow of qi through meridians in the body
  - no histological or physiological evidence of qi, meridians, and acupuncture points
- scientific evidence supports acupuncture effectiveness in some pain treatment and post-operative nausea.

Acupuncture chart from the Ming Dynasty: The Pericardium Meridian of Hand-Jueyin
1368 - 1644

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Assignment

Cure Interrupted?

Patients Upset over end of Parkinson's Drug Trial: Risks associated with experimental drug leave patients in limbo. (December 28, 2004). ABC News. http://abcnews.go.com/Health/story?id=363348

Cure Interrupted? Human Guinea Pigs Bewail Withdrawal Of Experimental Drug. (September 11, 2005). CBS News. http://www.cbsnews.com/stories/2005/09/08/60minutes/main828098.shtml

Human Guinea Pigs: (video) (September 13, 2005). CBS News, 60 minutes. (approximately 3 minutes). http://www.cbsnews.com/sections/i_video/main500251.shtml?id=833966n

In your discussion group:
Discuss with other members of your group the question: *Must the sponsors of a clinical drug trial follow the absolute mandate and requirements established in the Belmont Report and the Food and Drug Administration and terminate a study, even though the subjects want to continue receiving access to the experimental drug. Assume that the experimental drug in question does not appear to have a documented therapeutic effect and does not appear to have any harmful side effects.*

Readings

Understanding Clinical Trials

ClinicalTrials.gov, U.S. National Institutes of Health.

http://clinicaltrials.gov/ct2/info/understand

Constantine the African examines patients' urine.

Any Questions?

Email me at:
hoffmanj@arcadia.edu

http://www.yippitbullkennels.com/images/animated-question-mark.gif