A Discovery-Based Approach to Understanding Clinical Trials

DESTINY

Subjects: English, Health, Science, Social Studies

Overview: In modern society, the drugs we take and the medical procedures we undergo are the result of extensive research. Most people have seen the ads for clinical trials, recruiting people with heart disease or high blood pressure or some other possible mental or physical ailment. Yet, many don't fully understand the procedures involved in clinical research. According to the US National Institute of Health website, ClinicalTrials.gov, clinical research is the "fastest and safest way to find treatments that work in people and ways to improve health." This lesson plan, designed to be covered in one 90 minute class (or at the end and beginning of two successive classes), will help students to learn about the make-up of clinical research and the provisions in place to ensure the safety of the human participants.

The lesson will also be useful in teaching critical reading and informational writing skills. Social Studies teachers may wish to expand on the content provided here by focusing on the history, ethics, and regulations of clinical trials. General information may be found at "The history of clinical testing and its regulation" (http://www.roche.com/pages/facets/18/histclinte.htm). Objectives: Students think critically about the ways in which scientific researchers approach health problems, while also learning to analyze texts and write informational, science-based compositions.

RESOURCES

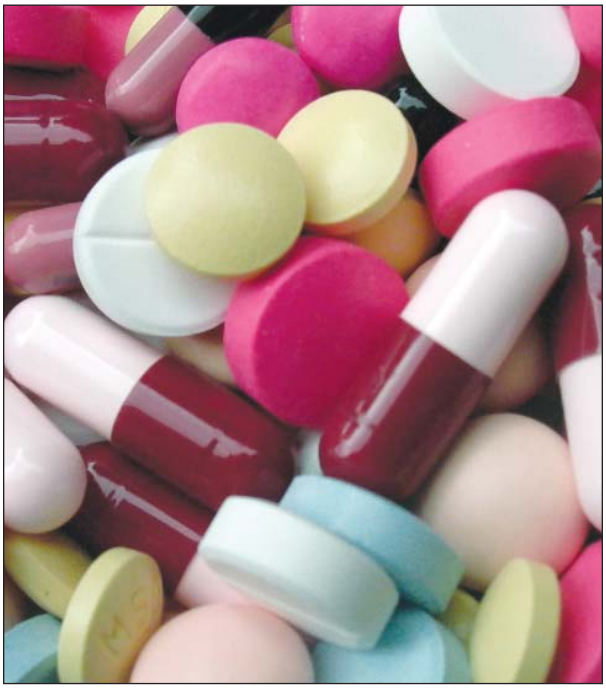
• 3 Handouts (attached): Engagement Activity, FAQ and Glossary (Understanding Clinical Trials), Exploration Activity ("Childhood-onset Growth Hormone Deficiency").
• Students and teachers may also wish to consult the website ClinicalTrials.gov.

ACTIVITIES/PROCEDURES

I. Engagement Activity (15 minutes)

a. At the beginning of class, provide each student with a copy of the attached "Engagement Activity" handout, which lists four different clinical trials. (Alternatively, place the handout on an overhead projector.)

b. Ask the students to look over the handout and jot down answers to the following questions:



i. What is the purpose of each of these trials?
ii. Would you consider participating in one of these trials, if you met the requirements? Why?
iii. Would you do it if you got paid?
iv. What questions would you want to ask the researchers before you agreed to participate?
v. Would you be interested in the results of any of these trials? Why?

II. Explore (this activity may also be assigned as individual or group homework) (45 minutes)

a. Divide students into small groups and provide each group with copies of the attached "Exploration Activity" handout — "Childhood-onset Growth Hormone Deficiency" and the attached "FAQ and Glossary" handout — "Understanding Clinical Trials" (or direct them to the ClinicalTrials.gov website).

b. Ask students to complete the "Student Activities" section of the "Exploration Activity" handout.

III. Explain (15 minutes)

a. Students share the answers to the "Student Activities" section of the "Exploration Activity" handout with the entire class.

IV. Elaborate (homework) – choose a or b
   a. Students may locate 2 additional clinical trial descriptions from either the unchealthcare.org website (clinical trials are listed under "Health & Patient Care") or the ClinicalTrials.gov website, and use the descriptions to answer questions 2, 3, and 4 from the "Student Activities" section of the "Exploration Activity" handout.
   b. Using the "Childhood-onset Growth Hormone Deficiency" as a model, students devise their own proposed clinical trial. They, of course, will not conduct this trial but will outline the protocol, exclusion/inclusion criteria, time-line and include a description of the proposed trial. Suggestions for possible trials:
      i. The effect of video games on violence in teenagers
      ii. The effect of fast food advertising on teenage food purchases
      iii. The correlations between wearing sandals and blistered and calloused feet

V. Evaluate
   a. Teachers may choose to evaluate students based on class participation and completion of the homework assignment(s)

ENGAGEMENT ACTIVITY

Think You Might Have Gum Disease?

RESEARCH PATIENTS NEEDED

UNC Center for Inflammatory Disorders
-and-
UNC Center for Oral and Systemic Diseases

Male and female subjects with periodontal (gum) disease are needed for a clinical research study. This study will assess the effect of gum treatments on general health. Eligible subjects will receive certain treatments at reduced fees or no charge.

For information please call or e-mail the
UNC School of Dentistry GO Health Center.

Lung study

Do you currently smoke cigarettes?

Have you quit smoking, but smoked for at least 10 years?

The Center of Environmental Medicine at UNC is looking for individuals for a research study. This study involves 1 visit and a total of 1½ hours of your time.

You will be reimbursed for completion of the study. If you participate, you will have a breathing test and learn more about your lungs. Participants that are interested in quitting smoking will be given information and guidance to help them quit.

Genetic Study of Anorexia Nervosa in Families

We are seeking families with at least two members who have or had anorexia nervosa, and who would be willing to participate. Experts from around the world are working to help identify the genes that might predispose individuals to develop anorexia nervosa.

UNC Eating Disorders Program

African American Couples Needed for a Research Study

If you have been living with your partner for at least 9 months, are not taking anti-hypertensive or anti-depressant medications, are between the ages of 18 and 50, and are willing to have blood samples and blood pressure taken, then you may qualify for a study about the benefits of partner relationships.

Receive up to $200 per couple for completion of 2 lab visits.

If interested, please call the UNC
Stress and Health Research Program.

All advertisements on this page were retrieved on April 27, 2005, from unchealthcare.org

UNDERSTANDING CLINICAL TRIALS

FREQUENTLY ASKED QUESTIONS

What is a clinical trial? (*from* University of Maryland's brochure "Thinking about Enrolling in a Clinical Trial")

A clinical trial is an experimental research study that evaluates the effect of a new drug or medical device on human beings. Clinical research is a process of discovery that is intended to improve medical care. Researchers attempt to answer questions such as "Which medication works better?" or "What is the best way to treat a medical problem?"

Who can participate in a clinical trial? (*from* University of Maryland's brochure "Thinking about Enrolling in a Clinical Trial")

All participants in a clinical trial are volunteers who have agreed to participate in a particular study. Some volunteers seek out clinical trials, and some are referred to clinical trial opportunities by their physicians. There are research opportunities in clinical trials for persons with specific diseases and conditions and for persons in generally good health. Volunteers participating in a study are referred to as "subjects" or "participants." Volunteers can leave a study at any time for any reason.

What are the benefits and risks of participating in a clinical trial? (*from* ClinicalTrials.gov)

Bene ts
• Play an active role in personal health care.
• Gain access to new research treatments before they are widely available.
• Obtain expert medical care at leading health care facilities during the trial.
• Help others by contributing to medical research.

Risks
• There may be unpleasant, serious or even life-threatening side effects to experimental treatment.
• The experimental treatment may not work for the participant.
• The trial may require more time and attention than standard treatment, including trips to the study site, more treatments, hospital stays or complex requirements.
• The participant may be placed in the "placebo" group

How is the safety of the participant protected? (*from* ClinicalTrials.gov)

The ethical and legal codes that govern medical practice also apply to clinical trials. In addition, most clinical research is federally regulated with built in safeguards to protect the participants. The trial follows a carefully controlled protocol, a study plan which details what researchers will do in the study. As a clinical trial progresses, researchers report the results of the trial at scientific meetings, to medical journals, and to various government agencies. Individual participants' names remain secret and are not mentioned in these reports.

Every clinical trial in the U.S. must be approved and monitored by an Institutional Review Board (IRB) to make sure the risks are as low as possible and are worth any potential benefits. An IRB is an independent committee of physicians, statisticians, community advocates, and others that ensures that a clinical trial is ethical and the rights of study participants are protected.

What should people consider before participating in a trial? (*from* ClinicalTrials.gov)

People should know as much as possible about the clinical trial and feel comfortable asking the members of the health care team questions about it, the care expected while in a trial, and the cost of the trial. The following questions might be helpful for the participant to discuss with the health care team.

• What is the purpose of the study?
• Who is going to be in the study?
• Why do researchers believe the experimental treatment being tested may be effective? Has it been tested before?
• What kinds of tests and experimental treatments are involved?
• How do the possible risks, side effects, and benefits in the study compare with my current treatment?
• How might this trial affect my daily life?
• How long will the trial last?
• Will hospitalization be required?
• Who will pay for the experimental treatment?
• Will I be reimbursed for other expenses?
• What type of long-term follow up care is part of this study?
• How will I know that the experimental treatment is working?
• Will results of the trials be provided to me?
• Who will be in charge of my care?
• What happens if I'm injured because of the study?

GLOSSARY

Blind — A clinical trial is "Blind" if participants are unaware on whether they are in the experimental or control arm of the study; also called masked.

Control group — In many clinical trials, one group of patients will be given an experimental drug or treatment, while the control group is given either a standard treatment for the illness or a placebo (See Placebo).

Double-blind study — A clinical trial design in which neither the participating individuals nor the study staff knows which participants are receiving the experimental drug and which are receiving a placebo (or another therapy). Double-blind trials are thought to produce objective results, since the expectations of the doctor and the participant about the experimental drug do not affect the outcome; also called double-masked study.

Efficacy — The maximum ability of a drug or treatment to produce a result regardless of dosage. A drug passes efficacy trials if it is effective at the dose tested and against the illness for which it is prescribed.

Expanded access — Refers to any of the FDA procedures that distribute experimental drugs to participants who are failing on currently available treatments for their condition and also are unable to participate in ongoing clinical trials.

Food and Drug Administration (FDA) — The U.S. Department of Health and Human Services agency responsible for ensuring the safety and effectiveness of all drugs, biologics, vaccines, and medical devices. The FDA also works with the blood banking industry to safeguard the nation's blood supply.

Inclusion/exclusion Criteria — The medical or social standards determining whether a person may or may not be allowed to enter a clinical trial. These criteria are often based on age, gender, the type and stage of a disease, previous treatment history, and other medical conditions. Inclusion and exclusion criteria are not used to reject people personally, but rather to identify appropriate participants and keep them safe.

Informed consent — The process of learning the key facts about a clinical trial before deciding whether or not to participate. It is also a continuing process throughout the study to provide information for participants.

Peer review — Review of a clinical trial by experts chosen by the study sponsor. These experts review the trials for scientific merit, participant safety, and ethical considerations.

Phase I trials — Initial studies to determine the metabolism and pharmacologic actions of drugs in humans, the side effects associated with increasing doses, and to gain early evidence of effectiveness; may include healthy participants and/or patients.

Phase II trials — Controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks.

Phase III trials — Expanded controlled and uncontrolled trials after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather additional information to evaluate the overall benefit-risk relationship of the drug and provide and adequate basis for physician labeling.

Phase IV trials — Post-marketing studies to delineate additional information including the drug's risks, benefits, and optimal use.

Placebo — An inactive pill, liquid, or powder that has no treatment value. In clinical trials, experimental treatments are often compared with placebos to assess the treatment's effectiveness. In some studies, the participants in the control group will receive a placebo instead of an active drug or treatment. No sick participant receives a placebo if there is a known beneficial treatment.

Protocol — A study plan on which all clinical trials are based. The plan is carefully designed to safeguard the health of the participants as well as answer specific research questions. A protocol describes what types of people may participate in the trial; the schedule of tests, procedures, medications, and dosages; and the length of the study. While in a clinical trial, participants following a protocol are seen regularly by the research staff to monitor their health and to determine the safety and effectiveness of their treatment.

Randomized trial — A study in which participants are randomly (i.e., by chance) assigned to one of two or more treatment arms of a clinical trial.

Single-blind study — A study in which one party, either the investigator or participant, is unaware of what medication the participant is taking; also called single-masked study.

Information on this page was retrieved on April 28, 2005, from the National Library of Medicine's website, ***ClinicalTrials.gov****.*

EXPLORATION ACTIVITY: COOL.CLICK™ ADOLESCENT TRANSITION STUDY: STUDY OF SAIZEN® IN SUBJECTS WITH CHILDHOOD-ONSET GROWTH HORMONE DEFICIENCY

This study is currently recruiting patients.

Sponsored by:	Serono
Information provided by:	Serono

PURPOSE

The primary objective is to evaluate the efficacy and safety of two different dose regimens of r-hGH (Saizen®) in subjects with childhood-onset growth hormone deficiency (COGHD) during the transition phase from childhood to adulthood.

Condition	Treatment or Intervention	Phase
Childhood-onset growth hormone deficiency Pituitary Dwarfism	Drug: Saizen®	Phase III

- Study type: Interventional
- Study design: , Randomized, Open Label, Dose Comparison, Single Group Assignment, Efficacy Study
- Official title: A Phase IIIb, Prospective, Multi-center, Randomized, Open-label Study to Determine the Safety and Efficacy of Two Different Dosing Regimens of Saizen® (recombinant human growth hormone (r-hGH), using cool.click™ in Subjects with Childhood-onset Growth Hormone Deficiency during the Adolescent Transition Phase (CATS)

Further Study Details:

- Primary outcomes: Increase in percent of trunk fat in COGHD
- Secondary outcomes: Changes in lean body mass and body composition parameters
- Expected total enrollment: 60
- Study start: August 2004; Expected completion: August 2006
- Last follow-up: July 2006; Data entry closure: July 2006

This is a phase IIIb, prospective, multi-center, randomized, open label study to determine the safety and efficacy of two different dose regimens of r-hGH with a dose escalation scheme. Screening assessments must be completed 30 days prior to SD1 (Study Day 1). Eligible subjects ages 13 to 21 years will be randomized in equal allocation in a 1:1 ratio to one of two treatment groups (30 subjects/group). Daily subcutaneous injections will be self-administered or received from a designated individual using cool.click™, the needle-free growth hormone (GH) delivery device. The study consists of three periods: screening (up to 30 days prior to Study Day 1), active treatment (up to 24 weeks), and follow-up (4 week safety evaluation after the last dose of study medication).

Each subject will be required to complete a daily treatment diary to assess dosing compliance, adverse events, and concomitant medications. Each subject will receive one treatment diary at SD1, weeks 8, 12, and 24. Subjects will be required to record daily diary entries that will capture dosing compliance, adverse events, and concomitant medications. Depending upon treatment allocation and subject tolerability, dose titration will be increased as follows:

- Group A: 0.005 mg/kg/day for 30 days then increasing, with the Investigator's approval, to 0.010 mg/kg/day from day 31 to week 24.
- Group B: 0.010 mg/kg/day for 14 days with the opportunity to dose escalate, with the Investigator's approval, on day 15 to 0.02 mg/kg/day and day 30 to 0.03 mg/kg/day.

Scheduled study visits include screening, baseline, and weeks 8, 12, and 24. Dosage adjustments will be based on subject tolerability and telephone assessments from study drug initiation through week 6. Trunk fat will be measured at SD1, weeks 12 and 24 (or early termination visit). Routine clinical laboratory assessments (hematology, blood chemistries, and urinalysis) will be performed pre-treatment (-30 to -1 SD1) and post-treatment on week 24 (or early termination visit). Special laboratory assessments include the central analysis of lipid panel, fasting insulin, fasting glucose, IGF-I, IGFBP-3, free T4 , total T4, CRP. Physical exams will be performed at screening, weeks 12 and 24. Safety evaluations will occur during scheduled study visits, through telephone assessments, and by the review of adverse events and concomitant events on the subject treatment diary.

ELIGIBILITY

Ages Eligible for Study: 3 Years-21 Years

Genders Eligible for Study: Both

Inclusion Criteria:

The day of entry or Study Day 1 is defined as the first day of study treatment. To be eligible for inclusion into this study, the subjects must fulfill all of the following criteria within 30 days prior to Study Day 1.

- Male or female from 13 to 21 years of age, inclusive
- Diagnosis of childhood onset GH deficiency and prior completed GH treatment as evidenced by bone age greater than 14 years for girls and 16 years for boys or no height increase > 0.5 cm in the 6 months prior to SD1.
- Have documented GH deficiency (acquired or idiopathic), established by a standard provocative test, such as insulin (<5 ng/mL) or growth hormone releasing hormone plus arginine (<9 ng/mL) within the past 6 months.
- If hypopituitary, must have been on adequate replacement therapy (if required) of glucocorticosteroids, thyroid and sex hormones (hormone levels on replacement being in normal/mildly elevated range) for at least 6 months prior to study entry.
- Be willing and able to comply with the protocol for the duration of the study.
- Have given written informed consent before any study-related procedure not part of the subject's normal medical care, with the understanding that the subject may withdraw consent at any time without prejudice to future medical care.
- Female subjects of childbearing potential must use a hormonal contraceptive, intra-uterine device, diaphragm with spermicide or condom with spermicide for the duration of the study. Confirmation that a female patient is not pregnant must be established by a negative hCG pregnancy test (urine or serum) within 7 days of study enrolment (SD1).

Exclusion Criteria:

To be eligible for inclusion in this study the subjects must not meet any of the following criteria:

- Known allergy or hypersensitivity to growth hormone or diluent.
- Previous treatment with GH within six months prior to study entry.
- Severe illness during the previous six months.
- Active malignancy (except non-melanomatous skin malignancies).
- Diabetes mellitus (type I or II).
- Seropositivity for human immunodeficiency virus (HIV), Hepatitis B surface antigen (HbsAg) and/or Hepatitis C Virus (HCV) serology.
- Pregnancy or lactation.
- History of drug and/or alcohol abuse or use of drugs for non-therapeutic purposes.
- Any medical condition that, in the opinion of the Investigator, would jeopardize the patient's safety following exposure to study drug.
- Clinically significant abnormal hematology, chemistry or urinalysis results at screening in the judgment of the Investigator.
- Have taken another investigational drug or had any experimental procedure in the six months preceding study entry.

ClinicalTrials.gov processed this record on 2005-06-07

STUDENT ACTIVITIES

1. Visit the "Resources" page of ClinicalTrials.gov, and click on "Glossary of Clinical Trial Terms" (or, use the handout provided by your teacher). Using this glossary, write down definitions for the three words underlined on page 1 of this handout.

2. Additionally, write down definitions for each of the following words
   a. Inclusion/Exclusion Criteria

   b. Protocol

3. Answer the following questions:
   a. What are the inclusion criteria for this study?

   b. What are the exclusion criteria?

   c. Who is sponsoring this trial?

   d. What is the trial's protocol?

   e. Why is protocol important?

4. On the front of the "Understanding Clinical Trials" handout, there is a list of questions that people should consider before participating in a clinical trial. Read over this list. (On the website, this list is under the question "What should people consider before participating in a trial?")
   a. Using the information provided in the description of the "Childhood-onset Growth Hormone Deficiency" clinical trial, answer the list of questions that people should consider before participating in a clinical trial.

   b. What questions can you not answer?

   c. What could you do to find the answers?

5. What are the possible benefits of conducting this trial, both to the participants and to the general public?

