Asthma Study Recruitment Flyer

Do you know this view all too well?
Do you SUFFER from ASTHMA?
Are you between the ages of 12 and 18?
Do you want FREE movie passes?

If you answered ‘yes’ to the questions above and use an inhaler at least once a week, you could be eligible to participate in a Clinical Research Study. All study related procedures will be at no cost to you.

Participants will receive movie passes as compensation for their time.

Interested?
Call: 1-800-555-1212
Email: volunteer@asthmarelief.com

Boston Clinical Research Unit
Asthma Simulation Outcomes

You were assigned to the **control** group, but first you (and everyone else who volunteered, including the experimental group) were asked to stop all your regular medications; you received an inactive placebo. Your asthma got worse.

You were assigned to the **control** group, but first you (and everyone else who volunteered, including the experimental group) were asked to stop all your regular medications; you received an inactive placebo. Your asthma stayed the same.

You were assigned to the **control** group, but first you (and everyone else who volunteered, including the experimental group) were asked to stop all your regular medications; you received an inactive placebo. Your asthma got better.

You were assigned to the **control** group, but first you (and everyone else who volunteered, including the experimental group) were asked to stop all your regular medications; you received an inactive placebo. Your asthma got worse.

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You were assigned to the **experimental** group. Your asthma improved, but you had a severe rash all over your body. You had to spend two days at the hospital to have the rash treated.

You were assigned to the **experimental** group. Your asthma improved with no serious side effects.

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You were assigned to the **control** group, but first you (and everyone else who volunteered, including the experimental group) were asked to stop all your regular medications; you received an inactive placebo. Your asthma improved, but you gained 10 pounds (4.5 kg).

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The Ellen Roche Case—Research with Healthy Volunteers

Ellen Roche was a 24-year-old healthy technician at a university asthma and allergy center. A researcher called her one day to ask her to participate in an asthma study because she had participated in studies before.

Asthma is a serious disease that is on the rise, especially in urban areas. The purpose of the study Roche volunteered for was to better understand how asthma affects the body. First, she took a drug designed to mimic the effects of asthma. Next, she inhaled a chemical (hexamethonium) that was supposed to block nerves the researchers believed were involved in asthma attacks.

The consent form called the hexamethonium a “medication” that had been “used during surgery, as a part of anesthesia”—giving the impression that it was approved by the Food and Drug Administration (FDA) as a medicine and was, therefore, safe. There was no mention that inhaling the chemical was experimental.

The day after receiving the experimental treatment, Roche developed a cough and started to feel ill. Four days later, she was hospitalized with a fever and abnormal chest symptoms, and the study was placed on hold. The air sacs in her lungs collapsed, then her lungs became stiff, and, finally, her other organs stopped working. Less than a month after the treatment, Roche died. If she had completed the study, she would have received up to $365.

Research involving humans must be reviewed by an institutional review board (IRB). The IRB determines whether studies are both scientifically sound and ethical. The university’s IRB had reviewed and approved the original research proposal.

One of the biggest criticisms of the IRB is that it did not request more careful review of the chemical. Many critics believed that researchers should have reevaluated the study when the first subject had troubling symptoms (before Roche’s treatment). That subject reported mild shortness of breath and coughing, but the symptoms got better on their own.

Before the experiment, the scientist who led the study looked at research going back 50 years and did not find any sign that hexamethonium would be harmful. However, after Roche’s death, investigators found earlier papers that warned about possible toxic effects. The chemical was also not approved by the FDA for the way it was used in this study. The role of the FDA in approving studies at research universities is not clear, but many people felt that the researchers should have sought the FDA’s opinion.

The U.S. Office for Human Research Protections stopped all research at the university for several days, until the university came up with a plan that included funding for more IRBs. Until then, the university had only two committees that were responsible for reviewing 2,400 proposals. The university accepted responsibility for the death and reached a financial settlement with Roche’s family four months later.

About 50,000 individuals participated as subjects in research at the university the year Roche died. The university was one of the most highly regarded medical centers in the nation. It had conducted trials for 100 years without any deaths of healthy volunteers. In an article about the case in the February 28, 2002, issue of the New England Journal of Medicine, the dean of the medical school expressed the difficulty of balancing the potential for learning new information that can help improve human health and the risks of harming people involved in experiments: “At a certain point some patient is going to die in clinical trials. There is no question about it.” But, he noted, the alternative is “not to do any clinical investigation...and still have children on ventilators after polio.”
Reflexion Questions

1. Aside from its focus on asthma, how is this case similar to or different from the experiment conducted in class?

2. What is the role of an institutional review board (IRB)?

3. Some ethicists noted that because Roche was an employee at the university, she may have felt unduly induced* to volunteer. A doctor called to ask her if she wanted to take part because she had participated in other studies. Do you think this is a concern? Why or why not?

4. How does this case illustrate the challenge of balancing research that may have health benefits and the risks that research participants face?

*Undue inducement refers to a situation where people are pressured into doing something harmful by the use of incentives. When inducements distort a person’s judgment, leading them to agree to do what they would not otherwise do, the inducements are considered undue.
Willowbrook Hepatitis Experiments

Background

Willowbrook State School in Staten Island, N.Y., housed and cared for mentally disabled children. Dr. Saul Krugman from the New York University School of Medicine and his coworkers began conducting hepatitis studies there in 1955 and continued for more than 15 years. Hepatitis was a major problem at Willowbrook for patients and staff, and Krugman believed that most newly admitted children became infected with hepatitis within the first year of residence in the institution. (More recent estimates put the risk of a child contracting hepatitis at Willowbrook at 30 to 50 percent.)

Hepatitis A is a relatively mild disease affecting the liver. Symptoms include jaundice, fatigue, abdominal pain, loss of appetite, nausea, diarrhea, and fever. It is usually spread from person to person when someone puts something in his or her mouth that has been contaminated with the feces of an infected person.

It was known at the time that the response to infection was milder in the younger children and that once infected, children were protected against the more damaging forms of hepatitis. Krugman was interested in using gamma globulin antibodies (taken from the blood of hepatitis patients) as a way to create immunity in others.

Antibodies are produced by the body's immune system in response to foreign substances. Krugman thought that if a child was infected with hepatitis after he or she had been injected with these protective antibodies, a mild case of hepatitis would result, and the child would have long-lasting protection against future, potentially more serious, infections. His goal was to find the best ways to protect children from hepatitis.

More than 700 children at Willowbrook were involved in the studies, which fell into two categories. The first used children who were already at Willowbrook. Researchers injected some with protective antibodies (the experimental group) and did not inject others (the control group). Then, they observed the children's degree of immunity to hepatitis.

In another series of studies, researchers gave newly admitted children protective antibodies. A subset of these children were then deliberately infected with hepatitis virus (obtained from sick children). Those who had received protective antibodies but were not deliberately infected served as the controls. The children in this experiment were housed in a well-equipped and well-staffed facility where they could be given special care and be kept away from the other types of infections at the institution.

As the studies progressed, researchers noticed differing symptoms caused by different virus samples. They concluded that there are two strains of hepatitis, A and B. Hepatitis B is more difficult to pass on to others because it is spread through blood and sexual contact. Hepatitis B can lead to long-term (chronic) infection.

The children who were deliberately infected with hepatitis A virus had a mild reaction (a swollen liver, yellowing of the skin and eyes, and a few days of vomiting and not eating). The researchers noted that many children would become infected during their stay at Willowbrook, anyway. Children who naturally got hepatitis from other children had worse symptoms than those who got it from the study.

The researchers obtained consent from the parents of each child. Parents of children who participated early in the study gave consent after receiving information provided by Willowbrook orally and in writing. Parents of children who participated later could meet the research staff, tour the facility, discuss the program with the staff and other parents, and speak with their own private physicians. Then, after several weeks, researchers asked for the parents' consent.
Letter to Parents

This is the letter parents received from researchers in the Willowbrook Study.

November 15, 1958
Willowbrook Study
Staten Island, New York

Dear Mrs. __________:

We are studying the possibility of preventing epidemics of hepatitis on a new principle. Virus is introduced and gamma globulin given later to some, so that either no attack or only a mild attack of hepatitis is expected to follow. This may give the children immunity against this disease for life. We should like to give your child this new form of prevention with the hope that it will afford protection.

Permission form is enclosed for your consideration. If you wish to have your children given the benefit of this new preventive, will you so signify by signing the form.

What Are the Relevant Ethical Considerations?

**Pro**

The benefits outweighed the potential harms. Researchers did not expose the children to greater risks than those they would otherwise have been exposed to (there was no “excessive risk”).

**Respect for Persons**

- Researchers chose Willowbrook for the study because there was such a high level of hepatitis there, not because the children were mentally disabled.
- When the school became too crowded, school officials told parents there was only space in the separate hepatitis research building. It is not unethical to require consent to participate in research as part of admission to a specialized facility.

**Harms and Benefits**

- The research provided valuable information about viral hepatitis and its treatment. It established that two types of hepatitis (A and B) occurred at Willowbrook and that injections of gamma globulin can have a protective effect against infection by hepatitis A virus.
- In addition to this larger benefit to society, the research benefited the participants and everyone in the institution. The research reduced the amount of hepatitis among patients and employees by 80 to 85 percent because of better care. Many of the children who participated lived in a special facility where they were less likely to get sick from other diseases that were common at Willowbrook and their health could be monitored closely. Some children benefited from the vaccination as well as from the better health conditions in the special facility.
- There was little additional risk of harm because there was so much hepatitis at Willowbrook—children were exposed to the same strain of hepatitis even if they were not in the study and had more serious symptoms if they got hepatitis naturally from other children. The researchers minimized risks by first observing the side effects of a low dose of virus.
- The research protocol was reviewed and approved by state, university, and federal review boards. The researchers also voluntarily chose to follow the guidelines of the World Medical Association’s Draft Code on Human Experimentation. It wasn’t possible to tell which children were infected, and children had lots of interaction with each other as part of their therapy, so isolating carriers wasn’t practical. Even under the most carefully controlled conditions, managing the spread of an infectious disease is difficult.
- At the time, specialized facilities with expert services were often seen as the best places for mentally disabled children, and parents were eager to get their children into them, including Willowbrook.
What Are the Relevant Ethical Considerations?

Con

Respect for persons and fairness were violated. The study provided an undue inducement because students were given a coveted spot in Willowbrook in a newer part of the facility if they participated in the research. Parents and their children were not truly informed about the risks of the study. Also, the study could have been done with adults in the facility instead of children.

Respect for Persons
- Children in a mental health facility can't fully understand the risks of a study they are participating in.
- The methods by which children were recruited are also questionable. Parents were unduly induced to give their consent. For example, when the main school was closed to new admissions in 1964 due to overcrowding, parents were told there were openings in the hepatitis unit for children who could participate in the study. The public outcry over this case was largely due to the impression that parents had little choice over whether or not to participate in the research. Parents who wanted care for their children may not have had any other options.
- It is not appropriate to use a vulnerable, institutionalized population for experiments. Feeding live hepatitis virus to mentally disabled children in order to deliberately infect them does not respect them as persons.

Unfair Aspects (Fairness)
- There is no compelling reason to study viral hepatitis in children before studying it in adults; none of the 1,000 adults working at Willowbrook was enlisted for the study. Why wasn't the research conducted on them first?
- Hepatitis was present at high levels because of overcrowding and unsanitary conditions, which the healthcare professionals had a duty to improve. Instead, they took advantage of the situation to conduct an experiment.
Willowbrook—Key Questions

(Fill out individually as homework.)

What is the ethical question?
Was the Willowbrook Study conducted ethically?

What are the relevant facts?

Who or what could be affected by the way the question gets resolved?
(Fill out with your partner.)

What are the relevant ethical considerations?

Group Participants (please list the names of those assigned to each position)

Those assigned to the Pro position: ____________________________________________
(You will argue that the researchers acted ethically.)

Those assigned to the Con position: ____________________________________________
(You will argue that the researchers did not act ethically.)

With your partner, develop two or three main points you wish to share with the opposing side. List these below. Record the main arguments of the students in the opposing side after they have shared them with you.

**Pro:** The benefits outweighed the potential harms. Researchers did not expose the children to greater risks than those they would otherwise have been exposed to (there was no “excessive risk”).

1. 
2. 
3. 

**Con:** Respect for persons and fairness were violated. The study provided an undue inducement because students were given a coveted spot in Willowbrook in a newer part of the facility if they participated in the research. Parents and their children were not truly informed about the risks of the study. Also, the study could have been done on the adults in the facility instead of the children.

1. 
2. 
3.
(Fill out individually.)

Conclusions from Group Discussion

Agreement (if any)—After listening to both sides, did most people in your group agree on any points? If so, list those points here:

Disagreement (if any)—Is there strong disagreement on any points? If so, list them here:
Your Own Views

After listening to all the arguments, what are your own views on the Willowbrook Study?

• Respect for Persons
  Was this study respectful of the individuals involved? Why or why not?

• Harms and Benefits
  Did the benefits outweigh the risks (potential harms)? Why or why not?

• Fairness
  Was this study fair to the individuals involved? Why or why not?

Do you think that researchers conducted the study ethically? Does it meet the guidelines for research that your class identified? If so, how? If not, why not?