History, Scandals and Tragedies: Beecher, Tuskegee, Willowbrook and the Rest

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U.S. legislation as response to tragedy
The Patent Medicine Evil
Safety of the food supply
Food and Drug Act 1906

[Image of book cover and movie poster]
Diet dangers c. 1930s
Elixir of Sulfanilamide tragedy

107 deaths
Food, Drug and Cosmetic Act of 1938

- Drugs or cosmetics must be tested for toxicity before marketing.
- Adequate directions for use needed to be on package.
- Some drugs are designated “by prescription only.”
Cranberry crisis of 1959

- Concerns about safety of pesticides used on Cranberries
1960-1961

83 children were born with unusual birth defects, not linked to thalidomide use.

A German scientist makes connections between thalidomide use and thousands of babies born with birth defects.
Kefauver-Harris Amendments to FDA

Frances Kelsey, FDA

FDA can demand scientific data to determine the drug works
Congress passes Animal Welfare Act, 1966
Fets for sale cheap—no questions asked

CONCENTRATION CAMPS FOR DOGS
Why do we have federal regulations for human experimentation?
In response to scandals and tragedies Congress passes the National Research Act

1974
Both the history of human experimentation and history of controversy over human experimentation much older
United States Congress, 1900

considers Senate bill 3424:

a law that would require investigators to disclose in advance the purpose and procedures of any non-therapeutic experiment involving human beings.
Senate bill 3424 calls for explicit ban on experiments using those persons deemed unable to consent, including infants, children under the age of twenty-one, and pregnant women.
Reed and his colleagues introduce written permission forms available in both English and Spanish.
The undersigned understands...

perfectly well that in case of the development of yellow fever in him, that he endangers his life to a certain extent but it being entirely impossible for him to avoid the infection during his stay in this island, he prefers to take the chance of contracting it intentionally in the belief that he will receive from the said Commission the greatest care and the most skillful medical service.
Subjects receive $100 in gold, $200 if death occurs
“A written consent was obtained from each one, so that our moral responsibility was to a certain extent lessened. Of course, only the healthiest specimens were experimented upon . . .”

Aristides Agramonte
Medical research in US

continuing social support for American researchers

celebrating the heroes and martyrs of medical research

self-experimentation and volunteers
Contaminated Blood Injection Kills Youth
In Seattle Preservation Research Project

SEATTLE, March 24—An 18-year-old college honor student died yesterday of an injection of bacterially contaminated blood given during an experiment connected with war research on blood preservation by the University of Washington.

James Stanley Leedom, a freshman at Seattle University, was one of forty volunteers who participated in the project seeking better ways to preserve whole blood.

He died three days after the injection despite every effort to save his life.

Dr. Robert H. Williams, head of the Department of Medicine at the University of Washington, said the blood had become contaminated by some phenomenon after it had been refrigerated.

"The only way we can explain it," said Dr. Williams, "is that the bacteria was able to grow in some manner while the blood was at freezing temperature and not at body temperature."

Both Dr. Williams and Dr. Clement A. Finch, Associate Professor of Medicine in charge of hematology at the university, said they would "gladly participate in the same experiment tomorrow."

They said the bacteria had not yet been identified, but they believed it to be a saprophyte (any organism living on dead or decaying organic matter) that does not grow at body temperature but thrives when chilled. It produces shock and high fever.

The father, Stanley P. Leedom, said he held no one at fault for his son's death.

"I don't blame anyone for this," he said. "I just don't want this tragedy to deter in any way from the blood donor program or these experiments."

The boy had planned to major in medicine.
Polio Epidemics
Polio epidemic c. 1952
PARENTAL REQUEST FOR PARTICIPATION OF CHILD IN POLIOMYELITIS VACCINATION FIELD TRIAL

The National Foundation for Infantile Paralysis, Inc., in cooperation with state and local health, medical and educational authorities, is conducting a nation-wide field study of the effectiveness of a vaccine which may be protective against paralysis due to poliomyelitis. The vaccine consists of chemically killed poliomyelitis virus of all three known types. For purposes of this study, several thousand children will be given three injections of this vaccine into the arm over a period of several weeks; at least an equal number of unvaccinated children will be observed so that a comparison can be made between the two groups. The children in each group, those who are vaccinated and those who are not, are equally important to the study. In certain instances it will be necessary to test small samples of blood at intervals during the study to determine the amount of antibodies against poliomyelitis that are present.

I HEREBY REQUEST that my child, ________________________________________, be vaccinated if selected, or otherwise be permitted to participate in the procedures described above without cost to me.

Date______________  Signed________________________

Relationship to Child _____________________________
(Must be parent or legal guardian)

School______________________________

Grade______________________________

(Street Address or Rural Location)

(City, Town or Township)  (State)

NFIP Form FT-1
By the 1960s no longer faith in medical researchers

Revelation of apparent abuses of human subjects, especially the Tuskegee Syphilis Study

Henry Beecher’s bombshell
HENRY K. BEECHER, M.D.

Professor of Anesthesia Research at Harvard Medical School

Convener of the Harvard Ad Hoc Brain Death Committee
“Ethics and Clinical Research”

New England Journal of Medicine 1966
22 examples of “questionable” research practices

Not from fringe BUT from mainstream researchers and institutions
Publication of the 22 examples

the rest from

Science, Cancer, J. of Urology, Surgery, Gynecology and Obstetrics, American J. of Medicine, Anesthesiology, and American J. Med. Sciences
Why HENRY K. BEECHER?

Christian faith?

anesthesia?

experience with human subjects research?
1946-47, prosecution of 23 Nazi medical personnel
United States v. Karl Brandt et al
Permissible Medical Experiments

The Nuremberg Code
First principle

The voluntary consent of the human subject is absolutely essential.
Strictly interpreted, the first principle would eliminate experiments on children, prisoners, the dying, the mentally ill.

efforts to create a more workable code
The Declaration of Helsinki (1964)
Beecher concerned about new researchers who fail to understand their responsibilities
Who were the research subjects in Beecher’s 22 examples?

“mentally defective” children
mentally retarded and delinquent children
the very elderly
soldiers in the armed forces
charity patients
terminally ill
alcoholics
children and newborns
patients at the NIH Clinical Center
Example 4

Study of effects of new antibiotic for treating acne using juvenile delinquents

the drug associated with liver problems

teenagers undergo repeated liver biopsies
Dr. Saul Krugman et al begin studies to acquire information about the natural history of hepatitis and work toward vaccine
Newly admitted children (whose parents give consent) are given intramuscular injections of hepatitis or “milkshakes” with hepatitis.
Krugman continued to defend the studies but issues persisted about informed consent, coercion, and study design (withholding gamma globulin)
Example 17

Jewish Chronic Disease Hospital case

Funded by USPHS and American Cancer Society

Injections of live cancer cells into elderly patients without consent

"did not wish to stir up any unnecessary anxieties in the patients" who had "phobia and ignorance" about cancer.
WASHINGTON, July 25—For 40 years the United States Public Health Service has conducted a study in which human beings with syphilis, who were induced to serve as guinea pigs, have gone without medical treatment for the disease and a few have died of its late effects, even though an effective therapy was eventually discovered.

The study was conducted to determine from autopsies what the disease does to the human body.

Officials of the health service who initiated the experiment have long since retired. Current officials, who say they have serious doubts about the morality of the study, also say that it is too late to treat the syphilis in any surviving participants.

Doctors in the service say they are now rendering whatever other medical services they can give to the survivors while the study of the disease's effects continues.

Dr. Merlin K. DuVal, Assistant Secretary of Health, Education and Welfare for Health and Scientific Affairs, expressed shock on learning of the study. He said that he was making an immediate investigation.

The experiment, called the Tuskegee Study, began in 1932 with about 600 black men.
This is a no-treatment study by your public health service.
Study begins in 1932
PHS Surgeon General Thomas Parran,

*Shadow on the Land*

Head of PHS, 1936-1948
INCIDENCE OF SYphilis AMONG NEGROES

MACON COUNTY, ALA.

BOLIVAR COUNTY, MISS.

ALBEMARLE COUNTY, VA.

MEHARRY UNIVERSITY, TENN.

Each symbol represents 3% of all Negroes studied
From treatment to “a study in nature”

Dr. Raymond Vonderlehr offers Negro men “last chance for special free treatment” for their “bad blood”
Lumbar puncture (to obtain spinal fluid for diagnosis)
World War II

• PHS asks Tuskegee draft board to exempt the men in the study from the draft

• They serve in another war
Nurse Eunice Rivers
Nurse Rivers obtains permission for autopsy easier when a burial stipend of $50 is provided. Only one refusal in 140 requests.


<table>
<thead>
<tr>
<th>Study population composition</th>
<th>ALABAMA</th>
<th>NORWAY</th>
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</thead>
<tbody>
<tr>
<td>Control</td>
<td>Rural Negro men</td>
<td>White men and women</td>
</tr>
<tr>
<td>Percentage autopsied of those who have died</td>
<td>Nonsyphilitic controls observed 63.3 per cent</td>
<td>No controls 24.3 per cent</td>
</tr>
<tr>
<td>Patient motivation for study participation</td>
<td>Volunteers with social incentives</td>
<td>Sickness and disability</td>
</tr>
<tr>
<td>Treatment status</td>
<td>Small amounts, especially in younger men</td>
<td>Less treatment available, especially in early years of study</td>
</tr>
<tr>
<td>Clinical facilities</td>
<td>Newer x-ray, EKG, and serologic techniques</td>
<td>Best medical facilities of the time (1925-1927)</td>
</tr>
<tr>
<td>Spinal fluid examination</td>
<td>Most of the syphilitic patients had spinal fluid examinations at start of study</td>
<td>No routine spinal fluid examination reported</td>
</tr>
<tr>
<td>Selection of patient material</td>
<td>Acute syphilis and younger patients treated and omitted at start of study; early and late latent patients studied and followed</td>
<td>Only early, untreated syphilis included</td>
</tr>
</tbody>
</table>
1954

"for the first time, men in the study identified as "volunteers with social incentives"
U.S. PUBLIC HEALTH SERVICE

25

This certificate is awarded to

In grateful recognition of 25 years
of active participation in the
Tuskegee medical research study.

Awarded 1958

Surgeon General
1969

CDC convenes a blue-ribbon panel to determine whether Tuskegee study should continue. Only physician not familiar with the Study argues that the experiment should end and the men receive treatment. The Study continues until 1972.
Study Revealed July 25, 1972
• Kennedy holds hearings on human experimentation including the TSS

• Legislation passed 1974

• National Research Act
1974 National Research Act

creation of a National Commission to study the moral issues posed by human experimentation

new federal regulations for IRBs and written informed consent
Television

FEBRUARY 16-22

Sacrificed to Science

A Docudrama Reopens
A Cruel Chapter
In the Annals of Race

BY MICHEL MARRIOTT
Persistent stories about the deliberate infection of the men in Tuskegee with syphilis
The AIDS ‘Plot’ Against Blacks

Bizarre as it may seem to most people, many black Americans believe that AIDS and the health measures used against it are part of a conspiracy to wipe out the black race.

A survey of black church members in 1990 found that an astonishing 35 percent believed AIDS was a form of genocide. A New York Times/WCBS-TV News poll in 1990 found that 1 black in 10 believes the AIDS virus was “deliberately created in a laboratory in order to infect black people” and an additional 2 in 10 thought that might be so. A Gallup/Newsweek poll in March produced similar results.

Even some dedicated black health workers engaged in the fight against AIDS decline to disavow these fears. Testifying before the National Commission on AIDS, one said that “until proven otherwise” she considered AIDS a man-made disease.

Worse yet, the treatments and preventives against AIDS have become suspect. Some blacks believe that AZT, the harsh drug used to combat the disease, is a plot to poison them ... that campaigns urging use of condoms, the best way to prevent sexual transmission, are a scheme to reduce the number of black babies ... that distributing clean needles to slow transmission among addicts is a plot to encourage drug abuse.

At its most destructive, the paranoia causes many blacks to avoid medical treatment. Unless black and Hispanic leaders play a more vigorous role in countering the fears and mistrust, it will become ever harder to slow the epidemic.

The task is urgent because the disease is now spreading most rapidly among minorities. Last year, for the first time, the number of AIDS cases reported for minorities exceeded the number for whites. Most worrisome for the future, blacks account for a majority of AIDS cases in women and children. “AIDS in future generations may be primarily a disease of black people,” the New York Department of Health warned last month.

Yet the response to this growing crisis has been sluggish. Financially pressed minority organizations and local governments have little energy for fighting AIDS, especially given the stigma attached to its main victims, homosexuals and drug addicts. But whether financing for minority AIDS programs has lagged behind white programs, as some black leaders charge, is not clear. Federal and state funds to minority AIDS organizations have gone up, and the Government’s central programs, like counseling and testing services, have huge minority caseloads.

No programs, even if well financed, will succeed without a change in attitudes. Thus it is welcome news that the New York State Health Department, with the help of black politicians and community leaders, has started a media campaign to encourage blacks to mobilize against AIDS.

The campaign rightly stresses that AZT and condoms are not plots against blacks. But it refuses to counteract the paranoia about AIDS as genocide, saying only that no matter how AIDS got started, there are ways to stop it. Campaign officials reasoned that few blacks would believe government denial anyway. But surely black leaders and public figures with high credibility, such as Magic Johnson, the basketball star, could do much to discredit the pernicious and dispiriting rumors.

Meanwhile, Federal, state and local health officials need a far better assessment of the flow of AIDS money into minority communities and stronger programs to fight the disease there. Costly drug treatment ought to be provided to all who seek it, an investment that would yield dividends far beyond slowing the spread of AIDS. And more vigorous outreach programs might persuade more individuals to avoid risky behavior.

As white Americans, shaken by the riots in Los Angeles, search for ways to help afflicted and distrustful minorities, there’s no wiser way to start than AIDS. A failure to treat and prevent AIDS among minorities: That would be the true genocide.
Presidential apology 1995

The Human Radiation Experiments

Final Report of the President's Advisory Committee
White House Apology for the Syphilis Study, May, 1997
Wielding the “Tuskegee Analogy”

In 1997 NEJM acting editor Marcia Angell compares placebo-controlled trials for preventing vertical transmission of HIV from mothers to infants to the Tuskegee Study
2001

Maryland State Supreme Court rules that families can sue the Kennedy-Krieger Institute (JHMI), comparing the research on effects of lead paint on children to both Nazi experiments and the Tuskegee Study.
President Bush vetoes stem cell research bill, summer 2006

research on human stem cells
“constitutes a grave violation of human rights just as we saw in the Tuskegee experiments here in the United States and in the Nazi experiments of World War II.”
Scandal, tragedy and revelation continues
2011
“ETHICALLY IMPOSSIBLE”
STD Research in Guatemala from 1946 to 1948

Presidential Commission for the Study of Bioethical Issues

September 2011
Diagram of a cisternal puncture.
From Alexander G. Reeves, M.D. and Rand S. Swenson, M.D., Ph.D., “Disorders of the Nervous System”
“I saw Doctor Parran on Friday [February 14] and he wanted to know if I had had a chance to visit your project. Since the answer was yes, he asked me to tell him about it and I did so to the best of my ability. He was familiar with all the arrangements and wanted to be brought up to date on what progress had been made. As you well know, he is very much interested in the project and a merry twinkle came into his eye when he said, ‘You know, we couldn’t do such an experiment in this country.’”
Learning the past, living with the past, forming the future