

Sommer Lectures 2023

The History of Human Experimentation

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“Those who cannot remember the past are condemned to
repeat it”

George Santayana (1863-1952)

Ethics 倫理

**Ethics is what we do
when no one is watching.**

**It is the guide inside each of us to tell us
what is right and wrong.**

SOMMER
Why do we have IRBs?
MEMORIAL

The First Published Human Experiment

- In the Bible
- About 3500 years ago
- Daniel 1:8-15
 - Rationale: (verse 8) Daniel was to eat the king's food but did not want to defile himself with it.
 - Method: (verse 12) : "Let them give us kosher food to eat and water to drink. Then let our countenances be looked upon and the countenances of the youths that eat of the kings food"
 - Results (verse 15): "at the end of 10 days their countenances appeared fairer and they were fatter in flesh than all the youths that did eat of the kings food"

Why are the British Referred to as “Limeys”?



Thomas Percival (1803)

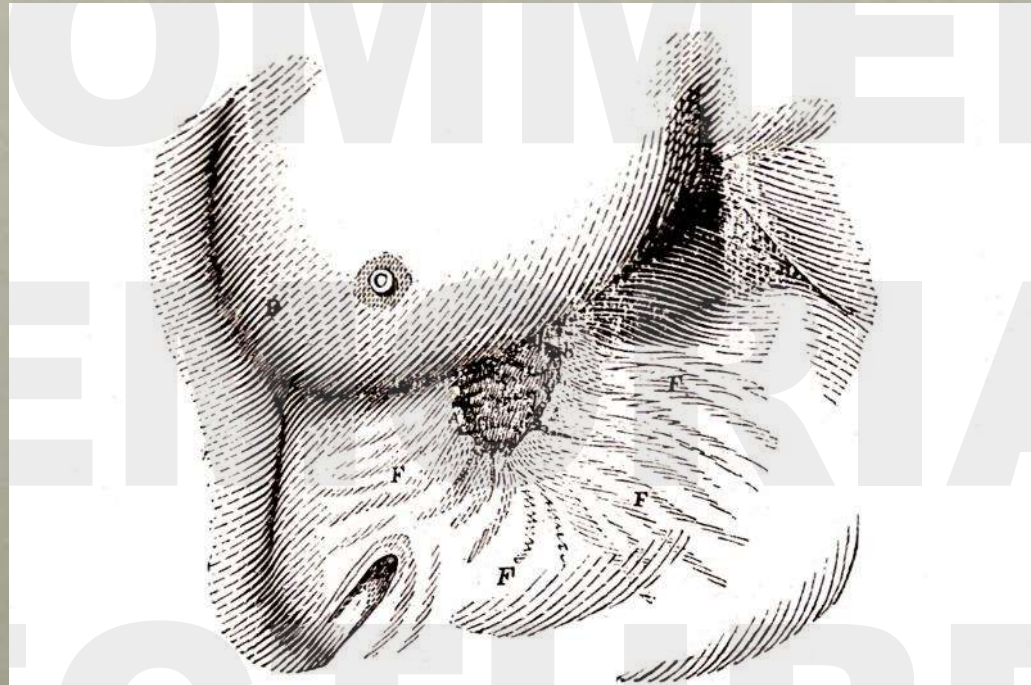
- British Physician (1740-1804) who coined the expression “Medical Ethics”
- First Modern code of Ethics: *Medical Ethics, or a Code of Institutes and Precepts, Adapted to the Professional Conduct of Physicians and Surgeons*
- This was used as the basis for an AMA Code of Ethics in 1847

Dr. William Beaumont



Figure 20. William Beaumont (1785–1853). From Myer's *Life and Letters of Dr. William Beaumont* (St. Louis: C.V. Mosby, 1912).

The Wounds of Alexis St. Martin



*Figure 23. St Martin's wound. This illustration of St. Martin's wound is from Beaumont's *Experiments and Observations*. The letters A and B outline the aperture, C is the nipple, D is the anterior portion of the breast, and E and F show surrounding scar tissue.*

Beaumont's Notebook

Alex. Lamala, a Canadian had about
19 years old, family, robust & healthy, was
accidentally shot by the voluntary discharge
of a gun, on the 6th of June 1822.
The whole charge, consisting
of powder & duck shot, was received in the
left side, about more than 2 or 3 feet
distance from the middle of the breast, in a
posterior direction, obliquely forward & out-
wards - carrying away by its force, the integ-
uments more than the size of the palm of
a man's hand, blowing off & fracturing the
5th rib, from about the middle anteriorly
fracturing the 5th rib posteriorly, the lower part
of the left lobe of the lung - & penetrating
the stomach, by a fissure of the rib, there
was blown through it - beyond the deep
wounding fire & among the fracture ribs & clavicle
muscles & cartilages, & having the clothing
it stuck to a crisp - I was called to him
immediately after the accident, found the
a portion of the lung as large as a turkey
between the 5th rib & the sternum
Blount, & below the another protrusion, remain-
ing a portion of the stomach, which was not
well, I could not believe possible to be
the organ in that situation with the
subject surviving - but on closer ex-
amination I found it to be actually the
stomach, with a penetration in the posterior
portion large enough to receive my fore
finger, though I had a portion of his
food, that he had taken for breakfast,
had come out & lodged among the
apertures - In this dilemma, I crossed
my attempt to save his life, & I was
then attending at a church, & was every moment
in my power to save his life when called to
administer relief, I proceeded to clean
the wound, & give it a superficial dressing
not believing it possible for him to survive
the penetrating nature of the wound, I found the Lung, was

Figure 22. Beaumont's notebook describing St. Martin's wound. This is the first page of Beaumont's original case record on the wound of Alexis St. Martin. From Myer's *Life and Letters of Dr. William Beaumont* (St. Louis: C. V. Mosby, 1912).

William Beaumont

- Wrote a book in 1833 about his experimental results
- Included an early code of ethics for human experimentation
- “Voluntary Consent is Necessary”

AMA Code of Ethics

- Philadelphia, 1847 Meeting of the AMA

Auto-Experimentation: Two Nobel Prizes!

- By 1972, there were more than 137 experiments performed on themselves by 185 people
- 1580- Sanctorius of Padua
- 1767- John Hunter
- 1847- Simpson
- Tragic Stories
 - Lazar- Yellow fever
 - Carian- Oroya Fever
 - Halstead- Cocaine

Werner Forssmann (1904-79)

- Started out as a Surgery resident
- His boss was Sauerbruch, who fired him
- He then went to a small town as a radiologist



Human Right Heart Catheterization: 1929



Nobel Prize-1956

- Forssmann (Germany), Coumand (France) and Richards (US)
- Based on Forssmann's original paper
- Prize was for cardiac catheterization

Nobel Prize-2005

- Dr. Barry Marshall
 - Born 1951, Australia
 - In 1984 after attempts in pigs failed, he drank H. Pylori, developed gastritis quickly and then treated it with antibiotics.
 - Med J Aust 1985. 143:319
- Dr. J. Robin Warren
 - Met Marshall in 1981 in Perth and studied ulcer disease together



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The Era of Nazi Medicine

Law for the Prevention of Genetically Diseased Offspring: 14 July 1933

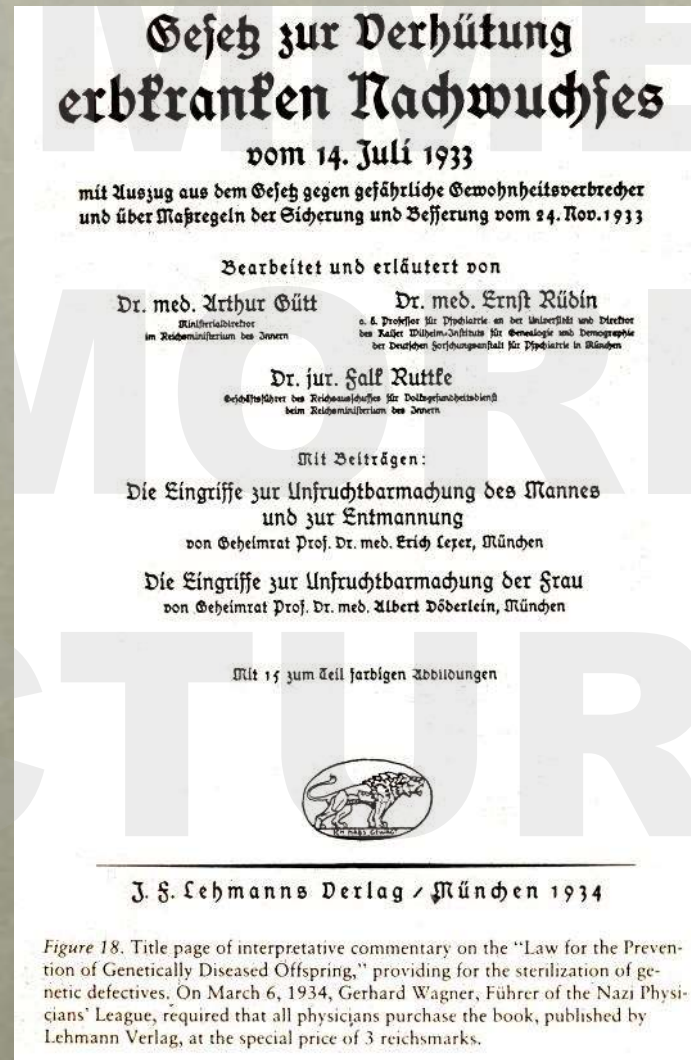


Figure 18. Title page of interpretative commentary on the "Law for the Prevention of Genetically Diseased Offspring," providing for the sterilization of genetic defectives. On March 6, 1934, Gerhard Wagner, Führer of the Nazi Physicians' League, required that all physicians purchase the book, published by Lehmann Verlag, at the special price of 3 reichsmarks.

“We do not stand alone”



The cost of bringing up a sick child



The cost to the government for a child with needs



Organized Medicine was Deeply Involved

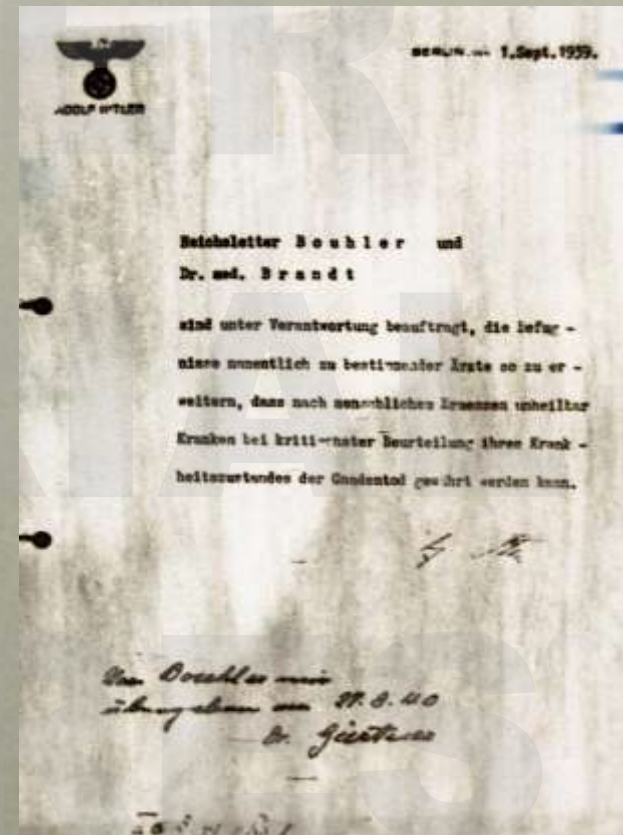


The Doctor of the German People



T4 Program

- Put the ideas of “Racial Hygiene” into practice
- Authorized directly by Hitler
- Lebensunwertes lebens “Lives unworthy of living”
- prisoners, "degenerates", dissidents,
- people with congenital cognitive and physical disabilities feeble-minded", epileptic, schizophrenic, manic-depressive, cerebral palsy, muscular dystrophy, deaf, blind, homosexual, idle, insane, and the weak
- Who performed these executions?



T4 Program

- Eventually about 300,000 people were killed
- Killing was performed by doctors authorized by the government
- Served as a “killing laboratory” which later enabled mass killings in concentration camps

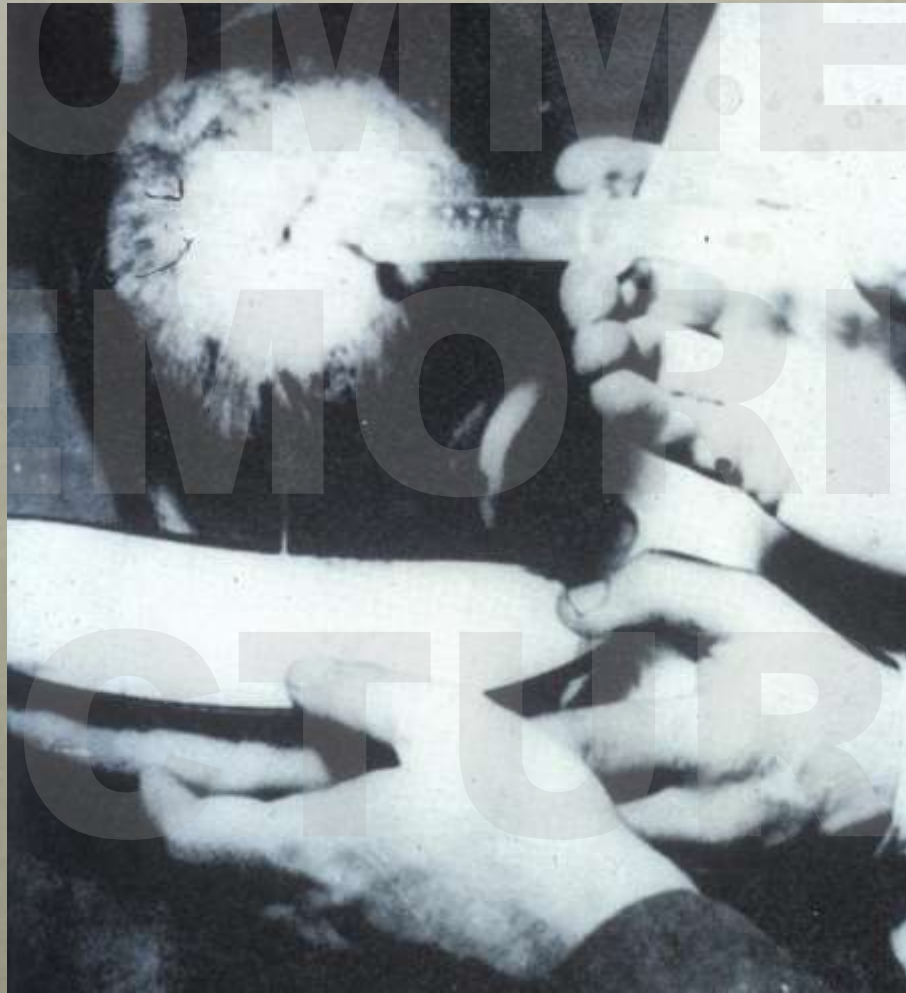


Dachau 1933-1945











This work was not a secret

Originalmitteilungen

Aus der III. Chirurg. Universitätsklinik am Städt. Robert-Koch-Krankenhaus
Berlin (Direktor: Prof. E. Gohrbandt)

Auskühlung

Von E. Gohrbandt

Generalarzt und beratender Chirurg bei der San.-Inspekt. d. L.

Mit Auskühlung, fälschlich auch »Unterkühlung« genannt, bezeichnet man den Kälteschaden, der den ganzen Organismus betrifft, bei dem die Herabsetzung der gesamten Körpertemperatur mit ihren Folgeerscheinungen ohne besondere lokale Schädigungen im Vordergrund steht. Es hat sich nicht nur ganz allgemein aus verschiedenen Gründen für zweckmäßig, sondern therapeutisch auch als notwendig erwiesen, diesen den Gesamtorganismus treffenden Kälteschaden von den rein lokalen Kälteschädigungen (den Erfrierungen) abzutrennen. Gerade die Aus-

NEJM 1990

Vol. 322 No. 20

DACHAU HYPOTHERMIA EXPERIMENTS — BERGER

1435

SPECIAL ARTICLE

NAZI SCIENCE — THE DACHAU HYPOTHERMIA EXPERIMENTS

ROBERT L. BERGER, M.D.

IT is widely recognized that the experiments performed on prisoners in German concentration camps during the Second World War were in fact brutal crimes committed under the guise of medical research. There is controversy, however, about the use of the results obtained from those studies. Among the approximately 30 known projects, the controversy has focused most intensely on the experiments involving hypothermia in humans that were performed at the Dachau concentration camp.¹ The debate among scientists and ethicists has spread to the public through the print and broadcast media.²⁻⁶ Positions range from a total ban to advocacy of the uninhibited use of the material. At one pole, Arnold Relman, editor-in-chief of the *Journal*, has noted that the Nazi experiments

its scientific rigor is needed to shed light on the reliability of the results and on the need to pursue the ethical debate about their use. This paper presents a critical analysis of the experimental protocol and the results reported, and an examination of the credentials and reliability of the investigators.

THE DACHAU HUMAN HYPOTHERMIA STUDY

The immersion-hypothermia project was conducted at the Dachau concentration camp between August 1942 and May 1943. Its purpose was to establish the most effective treatment for victims of immersion hypothermia, particularly crew members of the German air force who had been shot down into the cold waters of the North Sea.¹⁴ The subjects in the experiment

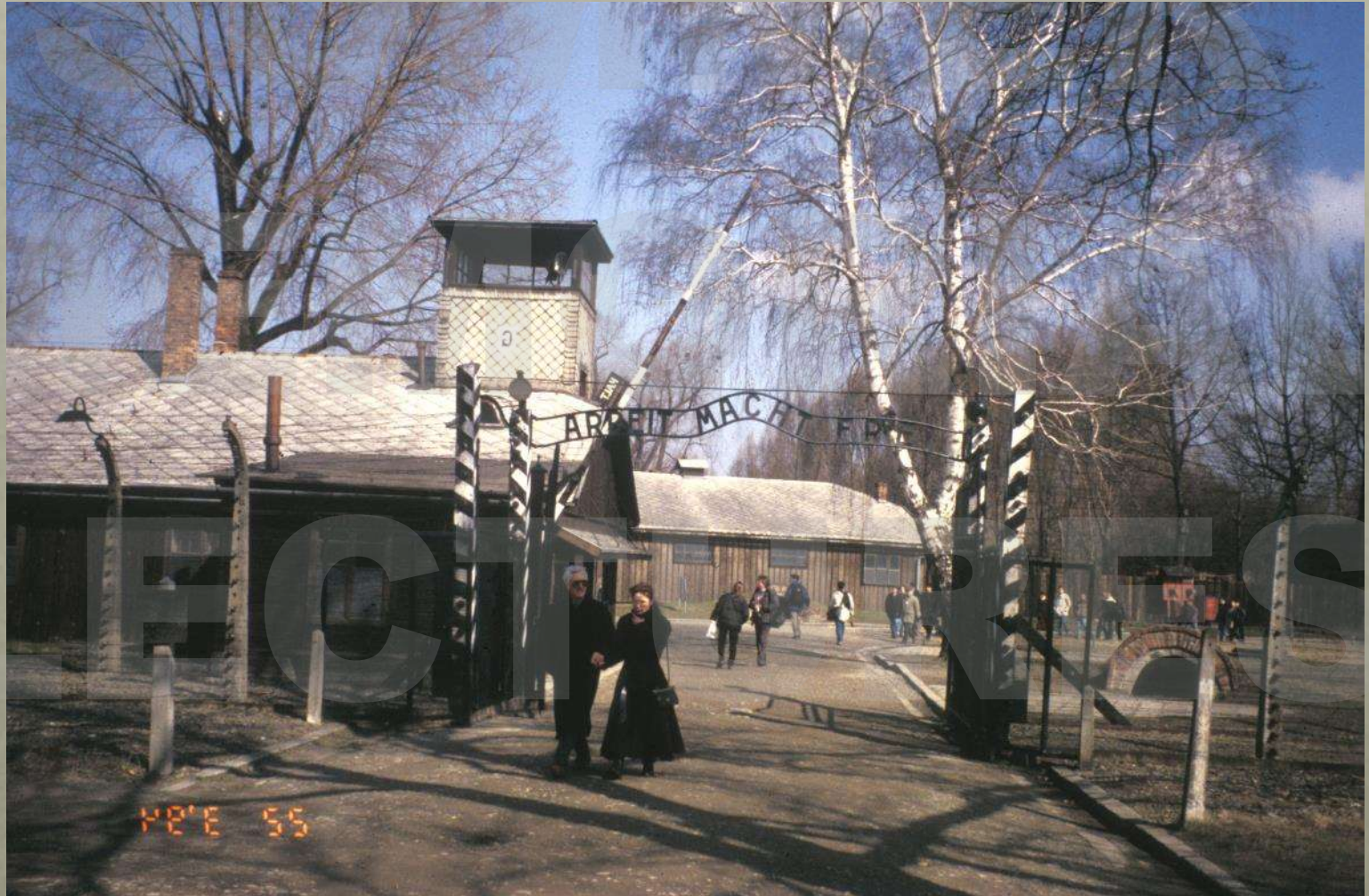
Auschwitz 1941-1945



Arrival Platform









HAFTL-KRANKENBAU
CHIRURGISCHE-ABT.
EINTRITT VERBOTTEN

HOLANDIA
ITALIA



HOLANDIA

22 3'94

WYWIADK I PRZEKRYWANIENIE BADANIA
WYKONYWANE W OBOZIE KL. W LAZAROWIE
PRZEZ LEKARZA SS DR. J. MENZLE
W DNIU 10.06.1942 R.

11. August 1942

Scheim

Meiner Verehrten, Sie sind von 1933 bis 1940 in
Frankfurt am Main im Städt. Krankenhaus, wo ich
beruhte, tätig gewesen. Ich habe Sie dort
als Leiterin der Frauenabteilung kennen gelernt.
Im Februar 1942 bin Sie nach Auschwitz
überführt worden. Ich habe Sie dort
als Leiterin der Frauenabteilung kennen gelernt.
Ich habe Sie dort als Leiterin der Frauenabteilung
kennen gelernt. Ich habe Sie dort
als Leiterin der Frauenabteilung kennen gelernt.

WYWIADK I PRZEKRYWANIENIE BADANIA
WYKONYWANE W OBOZIE KL. W LAZAROWIE
PRZEZ LEKARZA SS DR. J. MENZLE
W DNIU 10.06.1942 R.

PISMO H. HIMMLERA DO F. BRACKA, POLE-
CAJACE ROZPOCZECIE SERII EKSPERYMENTÓW
STERYLIZACYJNYCH W OBOZACH KONCENTRA-
CYJNYCH

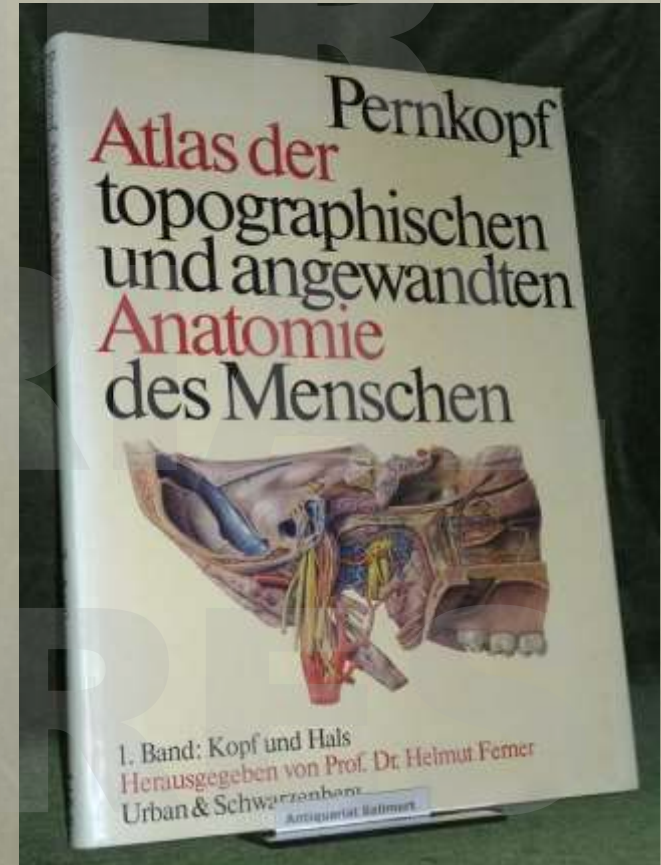
PISMO LEKARZA SS DR. K. CLAUBERGA
DO H. HIMMLERA DOTYCZĄCE MOŻLIWOSCI
PRZEWODZENIA MASOWEJ STERYLIZACJI

H.K. 6 - Brief Dr. Dr. Dr. H. Himmler
Klin. Diagnost. Nr. 12
Durchsuchungsbefund:
Die Frau ist eine gesunde, geistig entwickelte
Person. Sie ist eine gebildete Frau.
Sie hat eine gesunde, geistig entwickelte
Persönlichkeit.



The Pernkopf Atlas

- Controversy started in 1996, published in JAMA
- In 1997, University of Vienna investigated and found that the bodies of 1377 executed people had been delivered in the Nazi era.

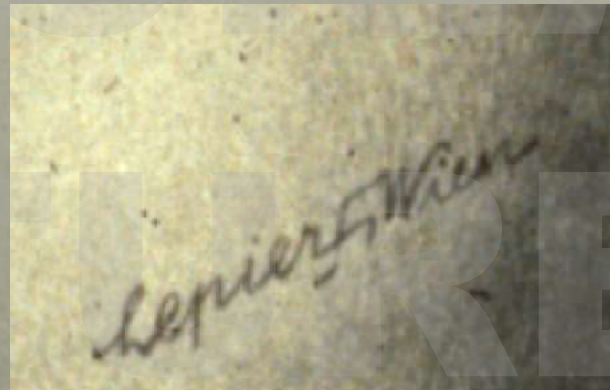


The Pernkopf Atlas

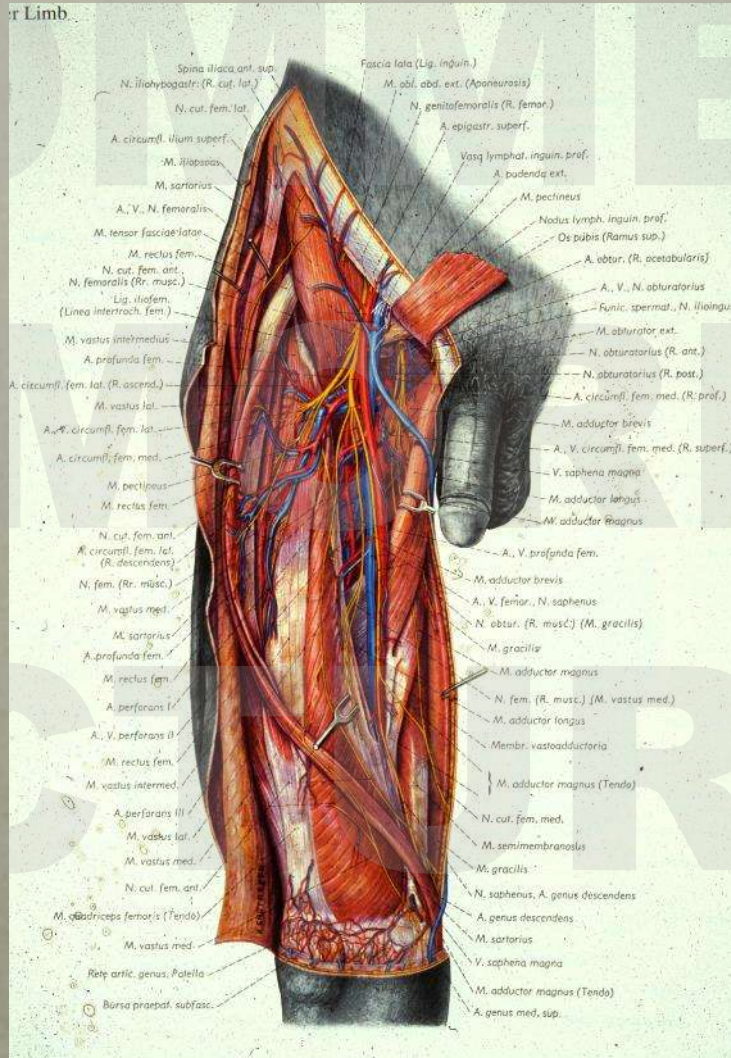
- Who was Pernkopf?



The Pernkopf Atlas



The Pernkopf Atlas



The Doctors' Trial: Nuremburg 1946



*The "Dock" of defendant physicians at the "Doctor's Trial," November 1946
(UPI/Bettmann Newsphotos)*

Moral Failures of Doctors in Nazi Germany

1. Embracing a false science—eugenics—that was coupled with racism.
2. Collusion in the exclusion of Jewish physicians from medical practice.
3. Forced sterilization.
4. Implementation of the Nuremberg Race Laws.
5. “Euthanasia” of lives “not worth living.”
6. Participation in mass extermination.
7. Medical experiments performed without consent, and sadistically.
8. Postwar distortions of the truth.

The Nuremburg Code

- Voluntary Consent
- Yield fruitful results otherwise unobtainable
- Based on animal experiments
- Avoid physical and mental suffering
- Not done if injury expected
- Risk is less than the importance of the problem
- Protect subject from injury
- Conducted by qualified people
- Termination at any time by the subject
- Termination at any time by the investigator

Declaration of Helsinki

- 1964, World Medical Association
- Ethical Principles for Human Experimentation
- Guidelines but not Regulations
- Built on the Nuremberg Code
- Amended 6 times since 1964

Shame for the United States

The Tuskegee Trial












'NOW can we give him penicillin?'

Testing Radiation on Humans in the USA- After World War II



Testing Radiation on Humans
Radiation studies under review by the Energy Department.

| Location(s) | Date | People affected | Experiment |
|--|-------------|---|--|
| Vanderbilt University, Nashville | Late 1940's | About 800 pregnant women | Subjects were studied to determine the effect of radioactive iron on fetal development. A follow-up study of children born to the women found a higher-than-normal cancer rate. |
| Oak Ridge National Laboratory, Oak Ridge, Tenn. | Mid-1970's | Nearly 200 patients with leukemia and other cancers | They were exposed to high levels of radiation. The experiments ended after a 1974 Government memorandum, later uncovered by Mother Jones magazine, said the study had done little to benefit the patients. |
| University of Rochester, Oak Ridge Laboratory, University of Chicago, and the University of California Hospital in San Francisco | 1945-1947 | 18 people | Subjects were injected with high concentrations of plutonium, apparently without their informed consent. Many patients were chosen because medical specialists believed they suffered life-threatening illnesses. Last month, The Albuquerque Tribune identified five of the subjects. |
| Oregon State Prison | 1963-1971 | 67 inmates | Prisoners' testicles were exposed to X-rays to help researchers understand the effects of radiation on production and function of sperm. The inmates signed consent statements indicating that they were aware of some of the risks, but the statements did not mention that radiation could cause cancer. |
| Washington State Prison | 1963-1970 | 64 inmates | A similar study, begun after an accident at the Hanford nuclear site exposed three prisoners to high levels of radiation. The purpose was to determine the minimum dose that would cause healthy men to become temporarily sterile. |
| Columbia University and Montefiore Hospital in the Bronx | Late 1950's | 12 terminally ill cancer patients | Subjects were injected with concentrations of radioactive calcium and strontium-85, another radioactive substance, to measure the rate at which radioactive substances were absorbed into various human tissues. |

Sources: The Department of Energy, The Atomic Energy Commission, Congress, The Albuquerque Tribune, The Government Accountability Project, Mother Jones Magazine.

Belmont Report

- Issued in 1979
- Written into US Law
- Three Principles: Respect for persons, Beneficence and Justice
- Applications of Ethical Principles: Informed Consent, Assessment of Risks & Benefits and Selection of participants
- Required IRBs, which began in 1981

Why do we have IRBs?

- Historical Milestones
 - Thomas Percival “Medical Ethics” (1803)
 - AMA Code of Ethics (1847)
 - Nuremberg Code (1947)
 - Declaration of Helsinki (1964)
 - Beecher article (1966)
 - Tuskegee experiment (1972) which was followed by a US Senate investigation
 - Belmont Report (1979)- written into US Law
- Some of our colleagues are unable to control their urge to collect data at any cost, usually for their own professional benefit.
- Perhaps, this is an innate trait in human nature.

...for more information...

Lefor AT. Scientific misconduct and human experimentation: Historical parallels and moral implications. *Nutrition*. 21:878-82 (2005).

