ETHICS IN MEDICAL RESEARCH & INTRODUCTION TO THE GCP

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…the justification…

The primary purpose of

medical research (involving human subjects) is

to understand the causes, development and effects of diseases and **to improve** preventive, diagnostic and *therapeutic interventions* (methods, procedures and treatments).

WMA Declaration of Helsinki, v 2013: A6

..even the best, have to be challenged..

Even the best proven interventions

must be evaluated continually through research

for their safety, effectiveness, efficiency, accessibility and quality.

WMA Declaration of Helsinki, v 2013: A6

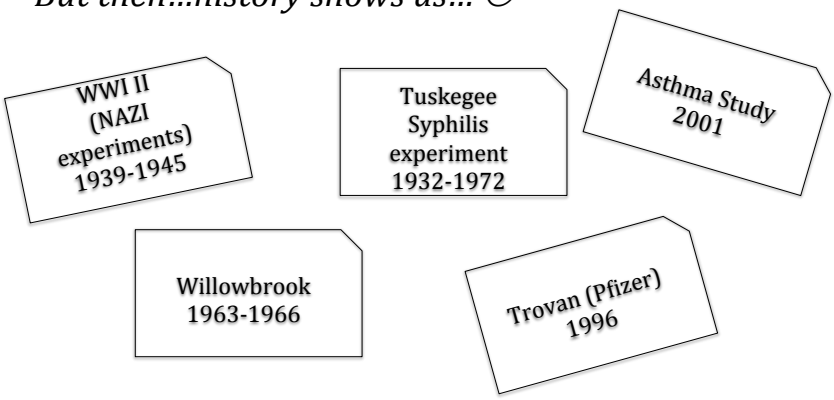
…ethical issues…

How can the rights of individual persons be reconciled with the demands of medical research?

- Benefits of medical research have come with ***a heavy price***
  - There are many examples of studies that have violated the rights and dignity of participants
  - In some cases, costing participants their health or even their lives

…a brief look at history…

- The good physician, first, do no harm
- *But then…history shows us…* ☹



Scandal & Tragedy in the History of Medical Research

- NAZI doctors (WWII)
- The Tuskegee Syphilis Study (1932-1972)
- Willowbrook Hepatitis Study (1950s)
- The Jewish Chronic Disease Hospital (1960s)
- San Antonio Contraception Study (1970s)
- The Thalidomide Experience
- John Hopkins Study

1935 – 1945

NAZI Experimentation (World War II)

- Experimentation to Holocaust Victims
- **No voluntary consent**
- Subjects not killed by experiments would be killed and dissected
- **1947: Doctor's trial at Nuremberg**

1947: the Nuremberg Code

1963 – 1966

Willowbrook Hepatitis Experiments

- Mentally compromised children at the Willowbrook State School in NYCwho were ***purposely exposed*** to hepatitis virus.
- Problem of hepatitis (the risk of having hepatitis is 30-50%).

- Healthy **children** intentionally given hepatitis C virus
  - Monitored to see effects of γ-globulin

"They will get it anyway"

1963:

Jewish Chronic Disease Hospital Case

- 22 elderly chronically ill (old) patients injected with live cancer cells
- Purpose was to "discover the secret of how the bodies fight the invasion of malignant cells"
- Covered-up by hospital administration

"They will die anyway"

1970's

San Antonio Contraception Study

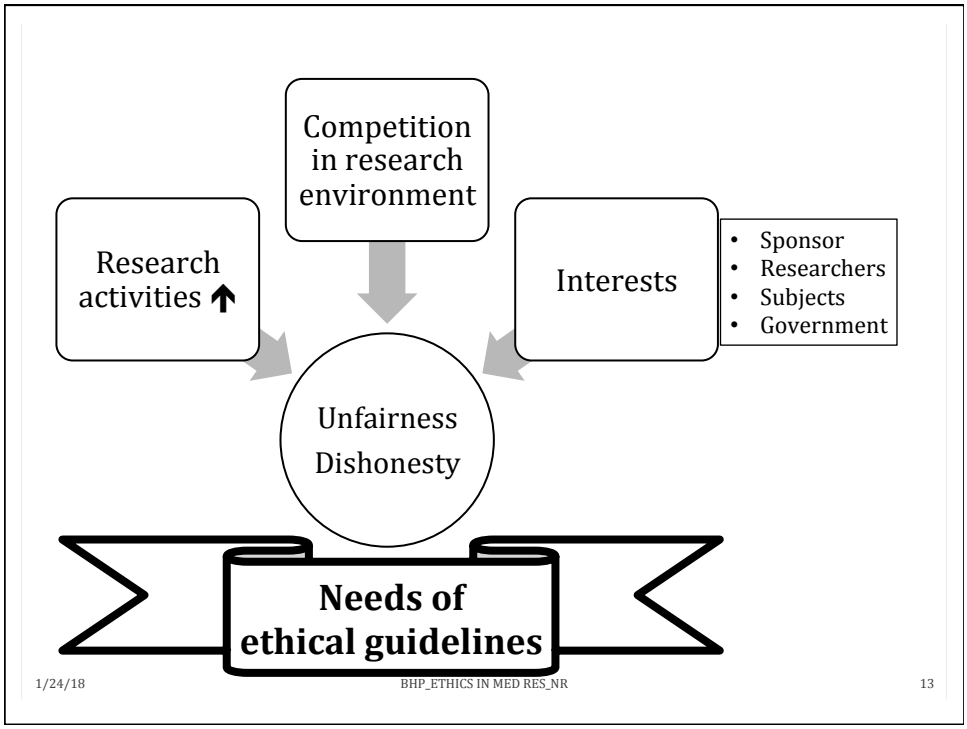
- Evaluate the effectiveness of female birth control pills.
- Indigent patients with no other place to go for advice or medication but the clinic.
- Randomized: active contraceptive and **PLACEBO.**
- **Women not informed.**
- ***Results***: High number of unplanned pregnancies in placebo group.

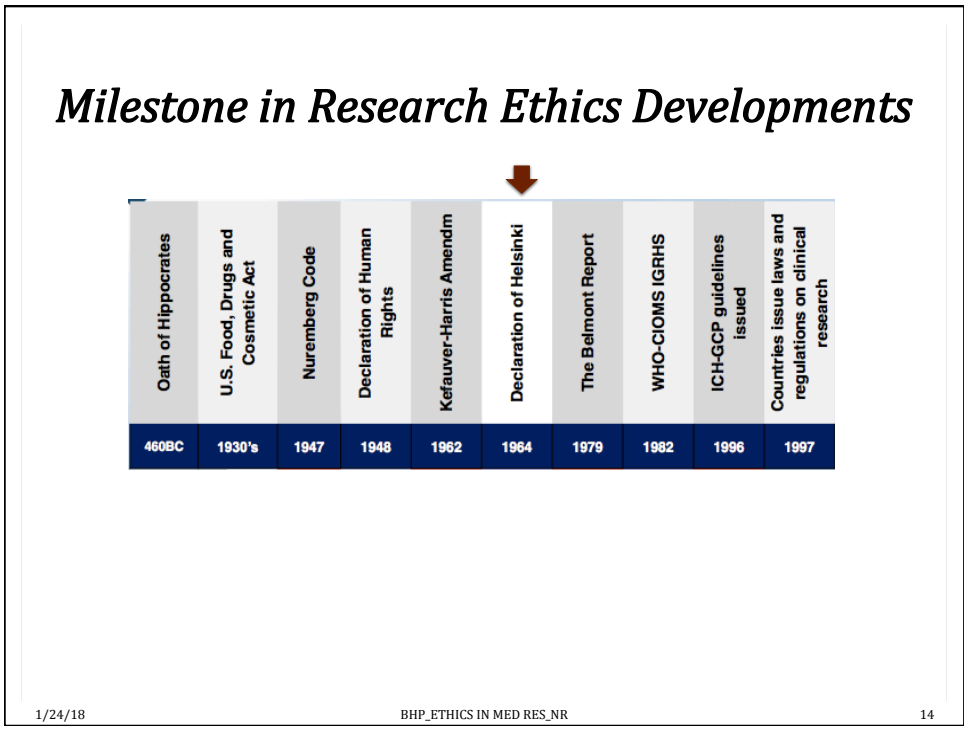
1950's
The Thalidomide Experience

- **Safety in pregnant women** has not been established.
- It caused 10,000 - 20,000 birth defects WITHIN YEARS

1/24/18

THE ESSENCE & LESSONS LEARNT


Competition in research environment
Research activities
Interests
Sponsor
Researchers
Subjects
Government
Unfairness
Dishonesty
Needs of ethical guidelines
1/24/18
BHP_ETHICS IN MED RES_NR
13


Milestone in Research Ethics Developments
Oath of Hippocrates
U.S. Food, Drugs and Cosmetic Act
Nuremberg Code
Declaration of Human Rights
Kefauver-Harris Amendm
Declaration of Helsinki
The Belmont Report
WHO-CIOMS IGRHS
ICH-GCP guidelines issued
Countries issue laws and regulations on clinical research
460BC
1930's
1947
1948
1962
1964
1979
1982
1996
1997
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BHP_ETHICS IN MED RES_NR
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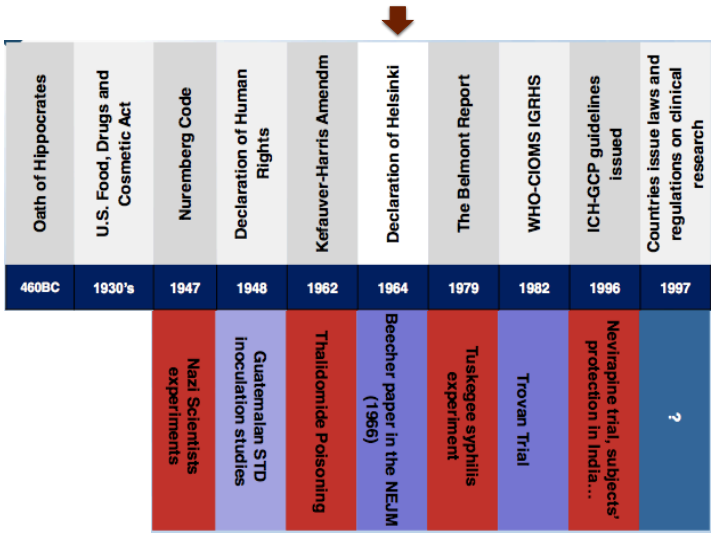
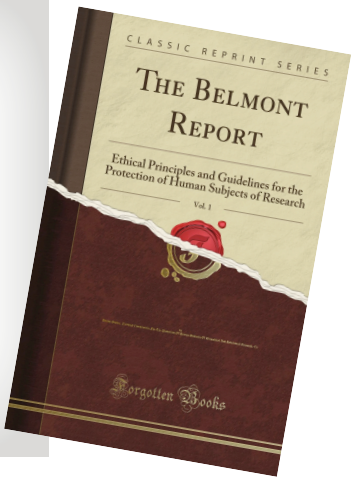
...Even though the guidelines are there...



The Belmont Report

National Commission for the Protection of Human Subject of Biomedical and Behavioral Research



1. Respect for Persons

- Treat individuals as autonomous agents (**Autonomy**) & **self determination**
  - **Voluntary**
  - **Informed consent**
  - **Confidentiality**
  - **Can stop participation anytime**
- persons with **diminished autonomy** (vulnerable subjects)

Research on Vulnerable Populations

- **Children**
- Mentally Challenged
- Institutionalized Individuals
- Subordinates/ Staff/ employee
- **Students**
- Prisoners
- Pregnant/ Lactating women
- Disease/condition
- **Poor**
- Military
- Tribal
- Uneducated
- Ethnic minorities/refugees
- Homeless/frail and old

- Not to include unless the study demands special groups
- Informed consent from the legal guardians
- Informed consent from the individuals wherever possible
- No inducement of guardians
- Assent from minors
- Respect their right to refuse participation

2. Beneficence

- DO NO HARM
- Maximize possible benefit and minimize potential risk

"Do unto others as you would have them do unto you"

3. Justice

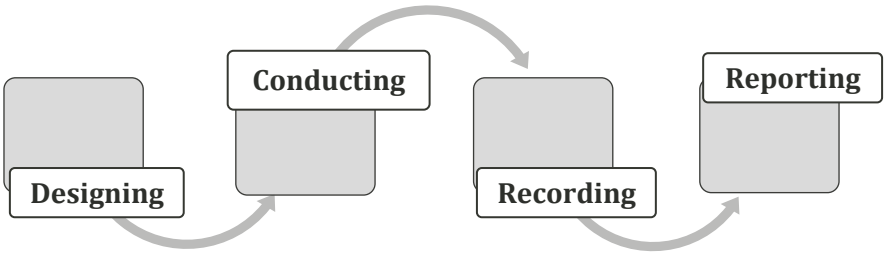
- To treat each person according to **what is morally right and proper**
- **Equitable** distribution of both **burdens and benefits** of the research
- Individual justice & Social justice *(we'll discussed in the next topic)*

…from ethics to GCP…

- The Helsinki Declaration, the Belmont Report & other documents give "**ethical principles**" **to guide** decision-making in medical research.
- This principles are **translated** in practical standards of working in the Good Clinical Practices (GCP) guidelines
  - World Health Organization, 1995
  - International Conference of Harmonization, 1996
  - National Guidelines

So..what is ICH-GCP?

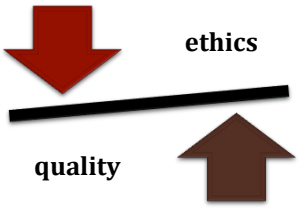
GCP (Good Clinical Practices) is
***an international standard (ethical & scientific quality)* in:**



trials that involve participation of human subjects

…reasons for GCP…

- Ensure **patients' protection**
- Ensure **quality of data**



When is GCP applicable?

This guideline should be followed:

generating CT data that intended to be submitted to regulatory authority/be published — **critical**

any research that may have an impact on the ***safety & well-being of human subjects*** — **always**

13 principles in GCP

1. **ethical principles in conducting clinical trial (CT)**
2. **Perform risk-benefit analysis before initiation of the trial**
3. **Safeguarding the participants**
4. **Adequate data (pre clinical data) to support proposed CT**
5. **Scientifically sound → clearly described in protocol**
6. **Comply with protocol when conducting the CT**

13 principles in GCP

7. **Medicare for participant (qualified physician)**
8. **Qualified trial personnel**
9. **Freely given informed consent (before and during the study)**
10. **Quality of the data**
11. **Respect participant confidentiality**
12. **Investigational Product**
13. **Quality assurance**

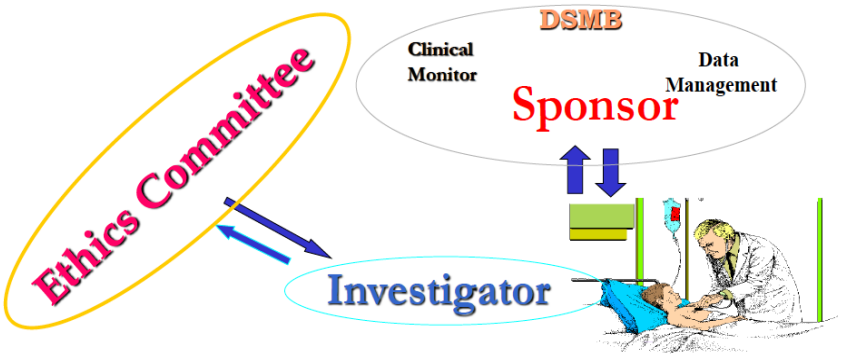
…to know more about GCP…

- a-3-days course
- by a competent trainer/institution

- it is encouraged that all researcher & supervisors of researchers take the course
- in-house training is possible (capacity building)

more and more offers come from the CRO
to conduct the CT (phase 2-3 CT)
→ And this is one of the requirement

…in applying GCP…



Researcher or IRB members

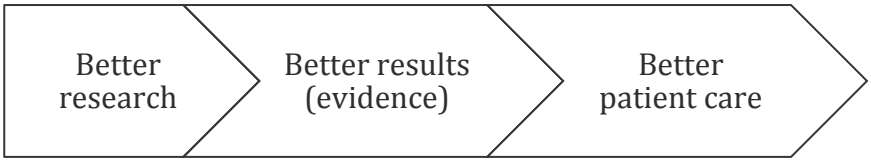
renewal every 2 years

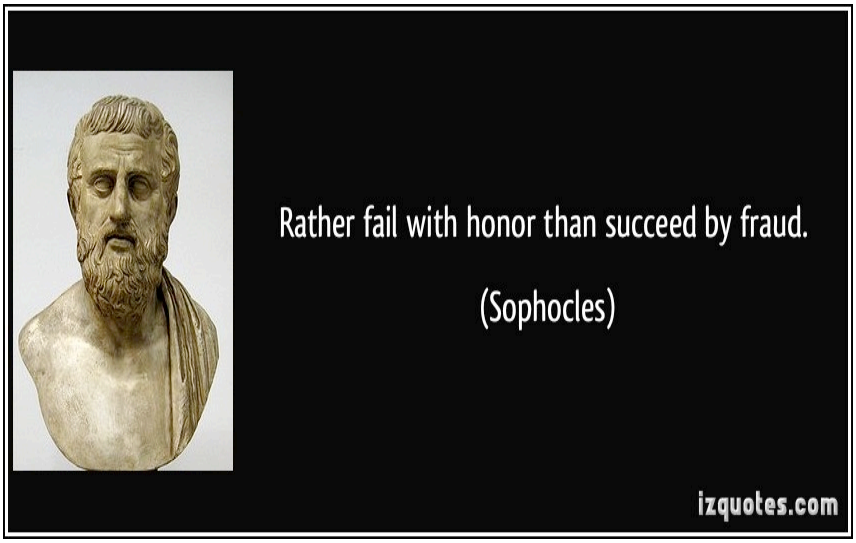
So…Research Ethics is devoted to

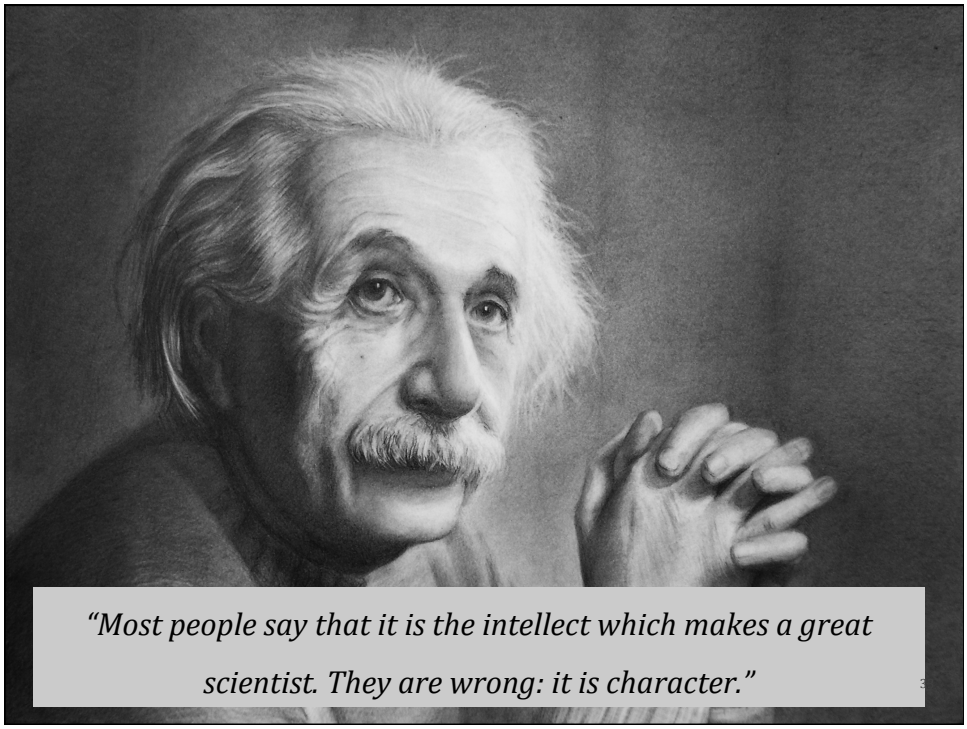
the **systematic analysis** of such questions
<u>to ensure</u> that study participants are protected,
and ultimately, that **<u>clinical research is conducted</u>** in a way that serves the needs of such participants and of society as a whole.
(Weijer, Dickens & Meslin, 1997)

…to summarize…

- Clinical Trial is a part of medical research (involving human subject)
- In doing so…
  - ICH-GCP is the international ethical & scientific quality standard
  - all investigators should be aware of this






"Most people say that it is the intellect which makes a great scientist. They are wrong: it is character."

THANK YOU