7e Symposium de la Swiss Clinical Trial Organisation

Promotion de la relève en recherche clinique

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Regulating clinical research: why?

Bully?
Regulating clinical research: why?

Or friend?
ITP: a historical perspective:

Immune thrombocytopenia

Previously known as

Idiopathic thrombocytopenic purpura
ITP: a historical perspective:

- Werlhof’s disease (1735): a clinical syndrome of spontaneous formation of bruises (purpura) and petechiae (tiny bruises), especially on the extremities, bleeding from the nostrils and/or gums, and menorrhagia.
Idiopathic thrombocytopenic purpura (ITP)

• 1882: description of the platelets by Julius Bizzozero

• 1880s several investigators linked the purpura with abnormalities in the platelet count (Brohm, Denys, Hayem)

• 1916: first report of a successful therapy for ITP: a young Polish medical student, Paul Kaznelson, described a female patient's response to a splenectomy
Mechanism for thrombocytopenia in ITP: impaired production or peripheral destruction?
If humoral antiplatelet factor will cause thrombocytopenia

Test: inject blood from ITP patient in healthy volunteer:
Patient O+, as it happens Harrington is also O+...
ITP: The Harrington–Hollingsworth Experiment

- **Before experiment:**
  - Harrington platelet count: 250 x 10^9
  - Patient’s (with chronic purpura) count: 5 x 10^9

- **Experiment:**
  - Harrington received 500 ml of blood from the patient
  - Within three hours Harrington’s platelet count drops to 10 x 10^9
  - Harrington experiences a major seizure
  - For three days his platelet levels remain dangerously low
  - Presence of petechia and bruises
  - After 5 days platelets increased
  - Normal megakaryocytes throughout the experiment
ITP: The Harrington–Hollingsworth Experiment

• **Conclusion:**

• Don’t do this?

• No, repeated on all suitable staff of the hematology department

• ...including the department’s head!
The Harrington–Hollingsworth Experiment

Harrington’s platelet count

Harrington’s colleagues platelet count

Harrington’s time of seizure

Harrington’s platelet count
Malariatherapy

• Invented by Julius Wagner-Jauregg

• Austrian Physician

• won the Nobel Prize in Physiology or Medicine 1927

• "for his discovery of the therapeutic value of malaria inoculation in the treatment of dementia paralytica"
Malariatherapy

• Julius Wagner-Jauregg was a controversial figure as also used electrotherapy on soldiers suffering from post-traumatic choc.

• Inhumane and painful treatment, resulting in many death, suicides,...

• Had to face court for his barbaric treatment of soldiers in 14-18, saved by his friend Sigmund Freud

• Also became a Nazi eugenecist who advocated the forced sterilization for people regarded as genetically impure
Malariatherapy

- Wagner-Jauregg's main work, throughout his life, was related to pyrotherapy: treatment of mental disease by inducing a fever.

- He tried erysipelas (Streptococcus infection, causes skin rash and fever) and M. tuberculosis infection, but with no success.
Malariatherapy

• In 1917 he tried inoculating neurosyphilis patients with malaria parasites.

• Neurosyphilis, at that time, was a terminal disease, causing dementia paralytica (general paresis of the insane (GPI)).

• Plasmodium vivax could be treated by quinine.

• Mararia produced prolonged and high fevers which killed the thermosensitive Treponema pallidum.

• Limited success, with high death toll due to malaria (>15%)

• Does not work on other psychoses
Malariatherapy

• Treatment for GPI abandoned after the discovery of penicillin and the advent of bioethics.

• Henry J. Heimlich (from the choking «Heimlich maneuver») controversially proposed to treat Lyme disease and HIV patients by malariatherapy.

• In the 1990s and 2000s malariatherapy for HIV studies were conducted in China (not randomized controlled studies, and not very ethical either)

• Heimlich was widely condemned by CDC, NIH and others