Pros and cons of phage therapy

- Why did phage therapy become unpopular?
- Why is it becoming popular again?
- What are its pros and cons?

History of phage therapy

Figure 2 Phage pioneers. In 1923, French Canadian physician Felix d'Herelle, the discoverer of bacteriophage (seated) and Soviet microbiologist Giorgi Eliava (right) founded an institute dedicated to phage research, later named Eliava Institute (Tbilisi, Georgia). While

Reasons that phage therapy fell out of favor

- Phage therapy was being piloted before clinical trials were rigorous, controlled, and randomized
- Use of antibiotics becomes widespread
  - Phage were not prepared or stored as easily as antibiotics
  - Phage were not as "broad spectrum" as antibiotics
- People didn't know what phage were, or whether they were alive or not, and were thus skeptical & scared of them

Reasons that phage therapy fell out of favor

- People came to see phage therapy as un-American (e.g. the Soviet Union)
- D'Herelle disassociated himself from the Eliava Institute after Eliava's execution
- To this day, phage therapy is used throughout the former Soviet Union, for wound & burn care, GI tract disorders, etc

http://samegrelo.geguchadze.com/images/G.Eliava2.jpg

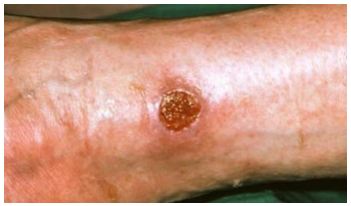
Reasons why phage therapy may return to the US

- Phage may now become popular again due to:
  - The rise of resistance to antibiotics
  - The narrow spectrum of phage

"Among their numerous advantages, phages are exceedingly specific: the viruses possess tail fibers that only bind with a particular strain of bacteria. That gives producers the power to target only pathogenic bacteria and leave those that don't cause illness unharmed. That's especially important for foods that depend on bacterial cultures to develop—for example, yogurt or some pungent cheeses like Munster."

Reasons why phage therapy may return to the US

- 2009, the first Phase I randomized trial in the US is published
  - for chronic venous leg ulcers
  - using a mixture of phages against *E. coli, Staph aureus,* and *Pseudomonas aeruginosa*



http://www.nhs.uk/Conditions/Leg-ulcer-venous/PublishingImages/M280096-Close_up_of_ankle_showing_venous_ulcer_342x198.jpg

Clinical trials to obtain FDA approval

- Average length is 5-8 years
- Average cost of a trial is $868 million
- Used to approve drugs, diagnostic tests, medical devices, vaccines, treatments & procedures (but not supplements)

http://www.ciscrp.org/patient/facts.html

Four phases of a clinical trial

- **Phase I**: (20–80 people) to evaluate its **safety** & identify side effects – not as a treatment
- **Phase II**: (100–300 people) to determine its **effectiveness**, & to further evaluate its safety
- **Phase III**: (1,000– 3,000 people) to confirm its effectiveness, monitor side effects, & to **compare** it with standard or equivalent treatments

- Phase IV: After a drug is approved by the FDA and made available to the public, researchers continue to track its safety

Required elements of Informed consent

- Purpose, duration, and what procedures are involved
- Risks
- Benefits
- Alternative procedures or treatments that might be advantageous to the subject
- If confidentiality will be maintained
- If compensation or treatment is available, if injury occurs
- Who to contact with questions
- Voluntary, so can discontinue any time

A Brief History of Informed Consent

- 1947, Nuremberg Code
- 1957, "informed consent" appears in court documents
- 1971, NIH publishes a full definition of **informed consent**
- 1974, **Common Rule** requires informed consent for all federally funded human-subject research

The principal defendants (front row from left to right): Hermann Göring, Rudolf Hess, Joachim von Ribbentrop and Wilhelm Keitel.

http://www.von-nuernberg-nach-den-haag.de/en/wp-content/uploads/2012/01/A_historic_milestone.jpg

History of human experimentation in the US

- 1930s-1963, "Mississippi Appendectomies" (forced sterilizations)
- 1944, John Cutler infects Terre Haute, Indiana prison inmate volunteers with STDs
- 1946-1948, Cutler runs Guatemala experiments injecting 1308 people with STDs
- 1953, Cutler injects syphilis into inmate volunteers in Sing Sing prison in NY
- 1956, Start of a 15-year study at Willowbrook State School in NY, where children with mental disabilities are infected with hepatitis
- 1972, Halt of Cutler's 40-year Tuskegee Alabama experiment where 400 African American men with syphilis were observed without treatment

http://www.nature.com/polopoly_fs/7.2752.1328719117!/slideshowimage/g04-1.jpg_gen/derivatives/fullsize/g04-1.jpg

Ethics of Informed consent

- Self-testers

- Children
- Severely ill
- Those who are impoverished (& will receive compensation)
- People with Down's, Schizophrenia, or a psychiatric disorder
- People with Alzheimer's, Huntington's, or a degenerative disorder
- Those living in developing countries
- Prisoners