Disclosures

• I have no relevant financial relationships to disclose as it pertains to the content of my presentation.

• I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation.
The Surgeon Scientist

- Huggins – hormonal treatment of cancer
- Gibbon and Lillehei – cardiopulmonary bypass and open cardiac surgery
- Murray and Starzl – solid organ transplantation
- Dudrick – development of TPN
- Carrel – organ culture
- Folkman – mechanism of dependence of tumors on blood supply

Nina Braunwald (1928-92)
Implanted 1st mitral valve, own design 1960
Surgeon-Scientist…

- Goal – to discover and apply new knowledge to problems affecting surgical populations
- In search of better ways of overcoming old problems
- Combination of genetic manipulation, gene therapy, conventional surgery, immunotherapy, chemotherapy
• Read the literature
• Develop a hypothesis
• **Design an experiment**
• **Methods**
Observations → Question → Hypothesis → Prediction

Test *does not support* hypothesis; revise hypothesis or pose new one

Test *supports* hypothesis; make additional predictions and test them

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Planning the Project

• Detailed literature review
• Developed a testable hypothesis
• Study design
  — Anticipation of a definitive result
  — Methodology – Innovation?
    ▶ Needs to be able to answer the question
  — Risk/benefit assessment
  — (Inclusion/exclusion criteria)
  — Statistical analysis (Power analysis)
Designing an Experiment
Experiment Type

• In vitro
• In vivo
  » Animal
  » Human
  • Case Report
  • Case Series/Retrospective Review
  • Natural History
  • Clinical Trial
Risk/Benefit Assessment

• Is the study properly designed?
• Does the “cost” justify the potential results?
• Are risks/use of animals/humans justified?
• What is the chance & severity of harm?
• Systematic assessment of risk/benefit
  — Risks limited to those necessary to achieve research objectives while protecting the subjects
  — Oversight- stopping a study if there is a clear benefit/risk/lack of anticipated contributory result
Methodology

• Be innovative
• Methodology needs to be specific step by step
• The Lab Notebook - document steps actually done carefully
• Be careful about changing proposed method midstream
The Laboratory Notebook – The Goals

• Diary of laboratory experiments of one individual
• Complete record of procedures, reagents, data, active thought process
• Enough detail to be able to repeat experiments
• Enough detail to understand how work was done
• Foster analysis of data
• Legal document - Establish invention conception, integrity
The Laboratory Notebook Documentation

- Record real time
- Add explanation for lapses in time
- Do not leave out (potential for new discovery)
  - Bad experiments
  - Mildest change in technique
  - Source of key materials
- Neat, legible hand writing, proper grammar
The Laboratory Notebook Documentation
Don’t Forget

- Lot numbers
- Centrifuge speed
- Incubation time
- # washes
- Delays
- Culture medium
- pH
- Percent gel (for western blots)
- Cell passage
- Cell quality
- Etc…………
Research Type

• Observational
• Experimental/Quantitative
  – Actively introduce a variable for study
    » Experimental conditions
    » Intervention
    » Treatment
    » Measureable outcome
Study Groups

• Comparison Groups
  — One intervention/treatment/condition vs. another with both being of interest

• Control Group
  — Customary care group or placebo group

• Placebo Group
  — Treatment group with no expected physiological effect
Selection Bias

- What is included?
- What is excluded?
- Is blinding done when/where appropriate?
- Will experimental and control groups be treated equally?
Proper Statistical Testing

• Determine test to be used when the study is designed (i.e., BEFORE experiments begin)
• Test used NOT necessarily the one that gives the best $p$ value
• Advent of computer programs may lead the wrong choices in analysis/Determine when a statistician is needed
• Alpha Value - Probability of a type 1 error – rejecting the null hypothesis when it is actually true
• Power - probability of getting a statistical difference if a true difference exists between groups
Findings

• Results should be presented accurately regardless of how they reflect on the hypothesis

• Conclusions must be based on the data obtained – loose interpretation must be avoided
Your Conclusions Can Only Address the Question Asked

Phil Witte, Piedmont, CA
Union of Concerned Scientists Cartoon Competition
Research Integrity

- Information needs to be complete, honest
- Follow the guidelines for documentation
- Be careful on extending the meaning of your results
- Reviewed for misconduct
Special Considerations
Animal-Based Research

• Non-animal alternatives
  —ALT Web - http://altweb.jhsph.edu/
  —UCDavis Center for Animal Alternatives Information

• Power analysis to determine sample size
  —PHS policy is that no animal life is wasted; the number of animals used in each project must be the minimum necessary to obtain valid and meaningful results
Special Considerations
Animal-Based Research

• Provision of humane care
  — Right thing to do
  — Approved animal care facility
  — Alleviation of pain, discomfort and needless suffering
  — Violation of animal care regulations can result in not only the shut down or research in the lab committing the violation but can lead to a halt of animal research at the institution
  — Follow the mandates
  — Listen to the Animal Care and Use Committee
Special Considerations In Clinical Research

- Protect Patient Rights and Clinical Needs
- Assessment of Risks and Benefits
- Power Analysis to Determine Sample Size
- Informed Consent
- Subject Selection
  - Vulnerable subjects e.g. incompetent, incapable of giving consent, minor
- Data protection/security
Institutional Review Board “The IRB”
Federally Mandated Committee

- Human Protocols
- A committee of physicians, statisticians, researchers, community advocates that ensures a clinical trial is ethical and that the study participants rights are protected
- Require ethics training for all researchers
- Provides initial approval and periodic review of the research to protect the rights of human participants
- Can approve, require modifications or disapprove the plan
Study Validity

• Internal validity
  – When study groups are comparable in terms of demographics and clinical characteristics

• External validity
  – When study groups are comparable to the target population such as the general public
In Summary……

- Knowing the literature/what has already been done and where the gaps in knowledge exist is essential

- Research should have a well-defined question to be answered and stated in a hypothesis

- The hypothesis determines the research design

- Research should contribute new information, be timely and relevant
• A series of small advances.

• Research is a continued development of learning from the work of others and yourself…

• Hypothesis development

• Experimental Design

• Experimentation

• Data analysis

• Hypothesis refinement

• Again and again and again……..

• Thomas Edison took $>1000$ attempts to get the light bulb right