Introduction to Experimental Medicine

Peter P Doran
Experimental Medicine

- Studies that provide information on health and disease

- Major goal is to identify
  - How we stay well?
  - Why we get sick?
  - How we can treat disease

- Whilst type of studies within experimental medicine are very broad ranging the above goals are consistent
Principles and Practices Course

• Objective of the 3 days
  – Provide an introduction to core principles
  – Provide practical advice on initiating research programmes
  – Introduce research language / terminology
  – Primer for those commencing research programme
  – Emphasise research embedded within healthcare system
360 View of Disease

- Population Studies
- Molecular Mechanisms
- Diagnosis
- Disease Sub Groups
- Treatment
- Impact of the disease
Beginnings

- The earliest documented study is described in the Old Testament

- King Nebuchadnezzar II prescribed a diet of meat and wine; but Daniel followed a diet of pulses and water

- Daniel remained healthy while his companions became ill

- Nebuchadnezzar revised his dietary advice
Willow Bark

- Hippocrates noted that chewing leaves and bark of salix (willow) relieved chronic pain
- Salicyclic Acid, Aspirin
Scurvy

- James Lind was the first to introduce control groups into his experiments.
- Lind carried out trials while at sea on board the Salisbury in 1747.
- All scurvy patients were given the same general diet +
  - cider,
  - vinegar
  - seawater
  - nutmeg
  - oranges and lemons.
- In just six days, those patients taking citrus fruits were fit for duty
Evolution of Experimental Medicine

- From 1800 onwards, clinical trials began to proliferate and more attention was paid to study design.
- Placebos were first used in 1863
- Randomisation was introduced in 1923.
- The first trial using properly randomised treatment and control groups was carried out in 1948 by the Medical Research Council, and involved the use of streptomycin to treat pulmonary tuberculosis.
- This trial also featured blind assessment
Medical Research’ Darkest Hour
Josef Mengele

- Medical officer in Auschwitz

- “Research” programme on camp detainees

- Changing eye colour by directly injecting chemicals into the eye

- Creation of conjoined twins by sewing two gypsy children together

- Determination of amount of force needed to crush a human skull
Alex Dekel- Auschwitz Prisoner

I have never accepted the fact that Mengele himself believed he was doing serious work — not from the slipshod way he went about it. He was only exercising his power. Mengele ran a butcher shop — major surgeries were performed without anesthesia. Once, I witnessed a stomach operation — Mengele was removing pieces from the stomach, but without any anesthetic. Another time, it was a heart that was removed, again, without anaesthesia. It was horrifying. Mengele was a doctor who became mad because of the power he was given. Nobody ever questioned him- Why did this one die?, Why did that one perish?

The patients did not count.

He professed to do what he did in the name of science, but it was madness on his part.
Regulating Experimental Medicine

• Since 1945, ethical considerations have been prioritised in experimental medicine

• Strict regulation of experiments to protect human subjects

• Regulations
  - Nuremberg Codex (1947) and the
Current Experimental Medicine

• Medical research has evolved into a standard procedure, focusing on patient safety and requiring informed consent from all participants.

• There will always be a balance between medical progress and patient safety, and the regulation of clinical trials helps to ensure that this balance is acceptable.

• Research embedded in the healthcare system
Dublin Academic Medical Centre

- Patient Care
- Education
- Research
Drug Discovery Pathway

- Discovery
- Preclinical
- Phase 1
- Phase II
- Phase III
- Phase IV
Research Overview

• Basic Research
  – Attempts to discover the mechanisms of disease
  – Identify molecular mediators which underpin initiation and progression of disease
  – Target discovery
  – Drug development

• Applied Research
  – Application of basic research findings
  – Animal models
  – Clinical studies

• Translational Research- accelerate translation of basic research findings to applied clinical setting
Basic Research

- Cell biology
- Proteomics
- Genomics
- Metabolomics
- Genetics
- Transcriptomics
- Medicinal chemistry
- Pharmacology
- In vivo studies
- etc
Population Studies

• Broad group of studies aimed at
  – Tracking the occurrence of disease in a population
  – Identifying contributors to disease
  – Determining natural history of disease
  – Identifying interventions to modulate disease course
  – Preventing disease
Observational Studies

- Follow group of people over time to find out what happens to their health.

- E.g. Framingham Heart Study

- This study was the first to demonstrate association of heart disease with
  - Elevated cholesterol
  - Elevated blood pressure,
  - Cigarette smoking
  - etc
Epidemiological studies

- These studies look at patterns of disease in large populations

- E.g Flu epidemiology studies

- Can describe both the existing burden of disease and also model how disease dynamics is changing in the population
Prevention studies

• Focus is on the prevention of the disease in the first place.

• These studies often involve people who are at risk for a particular disease.

• E.g modifying risk factors in at risk heart disease population
Clinical Trials

• Testing of drugs in human population
• begin only after results from laboratory and animal studies show that the new, investigational treatment is
  – safe to test and
  – likely to be effective in people.
• Very highly regulated environment
• Separated into Phases
  – Phase 1
  – Phase II
  – Phase III
  – Phase IV
Clinical Trials

- Discovery
- Preclinical
- Phase 1
- Phase II
- Phase III
- Phase IV
- Time
Drug Discovery Pipeline Vs. 360 View

- Discovery
- Preclinical
- Phase I
- Phase II
- Phase III
- Phase IV

Time

Feedback / Learning
System wide inquiry

- Population Studies
- Molecular Mechanisms
- Impact of the disease
- Treatment
- Diagnosis
- Disease Sub Groups

Disease
Developing knowledge

• Overview of the major elements of medical research

• Understand how these activities link together to effect improvements in health

• Rest of the week will build further on these individual areas
Overview of Course

Disease

- Population Studies
- Molecular Mechanisms
- Diagnosis
- Disease Sub Groups
- Treatment
- Impact of the disease
Clinical Research Centre

Excellence in Clinical and Translational Research
Clinical Research Centre
Enabling High Quality Research

CRC

MMUH Campus

SVUH Campus

Core Infrastructure / Enabling Resources
Clinical Research Centre
Operational Areas

- Clinical Trials (Phase I-Phase IV)
- Medical device studies
- Population studies
- Biocollections
- Translational research programmes
- Biomarker studies
- Qualitative Studies
- Pharmacokinetic Studies
Clinical Research Centre

What We Do

- Study design
- Study Sponsorship
- Core laboratory
- Obtaining regulatory approval
- Patient consent and interview
- Collection of biological samples
- Conducting clinical trials
- Sample Management, Processing & Analysis
- Data collection, management and storage
- Laboratory research programme development and support
Patient Visits

- 5,124 visits in 2008
- 11,212 visits since opening in April 2006

Activity Profile
- 2007 - 51% growth
- 2008 - 23% growth

Activity Type
- 10% Clinical Trials
- 27% Population Studies
- 63% Translational Research
Patient Visits by Year

- 2006
- 2007
- 2008
Patient Visits by Study Type

- Clinical Trial: 479 visits
- Population Study: 1290 visits
- Translational Study: 3355 visits

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CRC Investigators

- 67 Investigators now using CRC facility on a regular basis
  - 33 MMUH Campus
  - 23 SVUH Campus
  - 11 Other
- 114 other (non-principal investigator) users
- Total of 181 individuals using CRC resources
CRC Studies

• Study portfolio increased to 125

• Core Areas
  – Clinical Trials
  – Biocollections
  – Population Studies
  – Mechanisms of disease

• Phase 2 Clinical Trials

• Pharmacokinetics

• Nutrition Studies
Clinical Disciplines

- CRC supporting research across all DAHC clinical disciplines
- 24 different specialties now represented by CRC users
- Major areas
  - Respiratory
  - Neurology
  - Cardiovascular
  - Rheumatology
  - Infectious Disease
Industry Relationships

• Ongoing work at CRC involves partnership with 21 individual pharma and biotech companies
• These relationships to be further developed into research partnerships
Research Partners

• UCD Conway Institute
  – Ireland’s largest biomedical research institute
  – Research Themes
    • Neuroscience
    • Infection, inflammation and immunity
    • Vascular biology and diabetes
  – Core Technologies
    • Genomics
    • Proteomics
    • Animal Models
    • Imaging
Research Partners

- UCD Geary Institute
  - Leading Social Sciences research institute
  - Core Expertise
    - Outcomes
    - Healthcare Economics
    - Pharmacoeconomics
    - Quality of Life
    - Qualitative research