Thriving in Academia: Challenges in Clinical Research

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Sharing My Experiences in Clinical Research

- Conduct government-funded clinical research in infectious diseases
- Serve on advisory committees that translate clinical research findings into practice and public policy
- Mentor young investigators in research
- Provide care to children with infections
- Teach students about pediatric infections
Join a Team With the “Right Chemistry”

Find team members who have a reputation for:
- Doing what they say they will do
- Working well together
- Showing respect for colleagues
- Meeting deadlines
- Taking time to assist others before you
Factors Important in Choosing a Topic

- Choose a timely, important and interesting topic that has long-term potential
- Have passion and motivation for the topic
- Early in the project, solicit opinions from experienced researchers and biostatisticians
- Know what has been done before
My Personal Perspective
Reported Cases of Pertussis: United States, 1922–1980
General Concern About Safety of DTP Vaccine

- Current pertussis vaccines were inactivated whole pertussis organisms combined with diphtheria and tetanus toxoids (DTP)
- DTP vaccines were often associated with fever and local reactions in children
- DTP refusals increased
- DTP vaccines stopped in Japan and the UK
- Stimulated research on new vaccines
Generation of Acellular Vaccines (ACV) in 1980-90s

- ACV consisting of one or more pertussis antigens produced and evaluated
- Serologic responses to each antigen were measured by ELISA and functional assays
- ACV remarkably less reactive
Clinical Trials of New Pertussis Vaccines

- Phase 1 clinical studies in adults, children, and infants

- Phase 2 studies in infants
  - Multicenter NIH funded trial (MAPT)
  - Compared 13 ACV and 2 DTP in one trial
  - Common protocol

- Results of trial used to decide which ACVs used in efficacy trials in Europe and Africa
Phase 3 APERT Efficacy Trial

- Prospective, randomized, double-blind trial in adolescents and young adults
- Large multi-center, 2-year study
- 2781 subjects
- Vaccine groups (aP vs Hep A)
- Active cough illness surveillance (every 2 weeks)
- Culture, PCR and serologic evaluations

APERT = Acellular Pertussis (trial); PCR = polymerase chain reaction.
Efficacy of an Acellular Pertussis Vaccine among Adolescents and Adults


ABSTRACT

BACKGROUND

Pertussis immunization of adults may be necessary to improve the control of a rising burden of disease and infection. This trial of an acellular pertussis vaccine among adolescents and adults evaluated the incidence of pertussis, vaccine safety, immunogenicity, and protective efficacy.

METHODS

Bordetella pertussis infections and illnesses were prospectively assessed in 2781 healthy adults receiving placebo or a 3-dose pertussis vaccine regimen at 4 intervals. Clinical features and laboratory findings were characterized. The endpoints were the incidence of pertussis and the rate of vaccine-related adverse events.

RESULTS

The incidence of pertussis among the vaccinated group was significantly lower than in the placebo group. The vaccine was well tolerated, with a low rate of vaccine-related adverse events. The antibody response to pertussis was significantly higher in the vaccinated group compared to the placebo group.

CONCLUSIONS

The acellular pertussis vaccine is effective in reducing the incidence of pertussis in adolescents and adults. The vaccine is safe and well tolerated, with a high seroconversion rate. These findings support the use of pertussis vaccine in adults to control the rising burden of disease.
Reported Pertussis Cases: United States, 1922–2007*

Source: Centers for Disease Control and Prevention.
Live Attenuated *B. pertussis* as a Single-Dose Nasal Vaccine against Whooping Cough

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Tips for Trial Performance

- Never be “too good” to do what you ask of others
- Understand and perform all aspects of the trial
  - Recruit patients and obtain informed consent
  - Administer study drug
  - Perform data acquisition, entry and analysis
  - Write the manuscript
- Respect the expertise and suggestions of staff
- Manage problems immediately; they don’t disappear
“Science begins only when the worker has recorded his results and conclusions in terms intelligible to at least one other person qualified to dispute them.”

— B.M. Cooper, 1964
“Natural History” of an Immunization Program

- Prevaccine Coverage
- Increasing Coverage
- Loss of Confidence
- Resumption Confidence
- Eradication

- Disease
- Vaccine Coverage
- Outbreak
- Eradication
- Immunization Stopped
- Adverse Events
The Ten Commandments of Research

- Invest ample time and money in planning.
- Formulate your study protocol carefully.
- Seek input from your mentor and biostatistician.
- Carefully formulate the rationale for the size and composition of your sample and consider bias.
- Conduct your study carefully and maintain control of what is occurring.
The Ten Commandments of Research

Prepare your manuscript concisely; explain what is new, interesting, and useful about your study.

Answer the questions, “So what?” and “Who cares?”

Follow journal guidelines precisely.

Edit ruthlessly and write cautious but perceptive conclusions.

Treat others with respect.
Challenges that Remain

- Distributing vaccines to all that need them
- Developing vaccines for malaria, HIB, TB
- Ensuring vaccine safety
- Maintaining public confidence in vaccines
- Educating the new generation of scientists
- Educating a responsible public