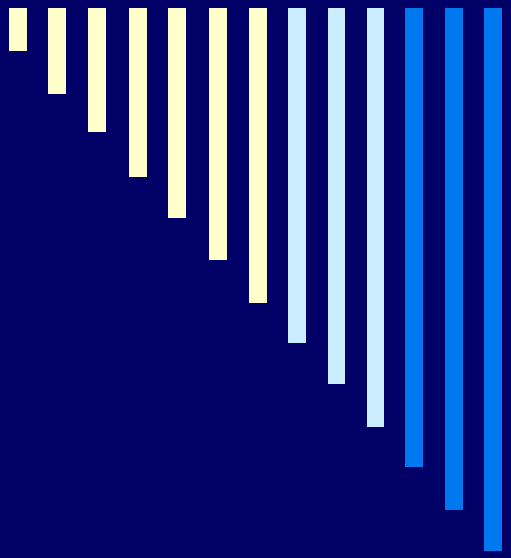


Balancing Residency and Research

Resident Research Forum

Benjamin Wang, M.D., FRCPC
Department of Medicine
University of Tennessee Health Science Center
June 11, 2007

Doing Research in Residency: Indications

- To establish a record of publications
- To answer one's own clinical questions and satisfy one's own curiosity
- To learn about the process and skills needed to conduct scientific investigation
- To be able to appreciate and critically appraise the scientific literature
- To realize the strengths and limitations of current knowledge

Doing Research in Residency: Contraindications (Relative)

Remember: None of these are “terminal diseases!”
With some effort, they can all be remedied

- Not enough time
- No mentor
- Not deeply curious
- Not able to commit long-term time and effort
- Not strong in self-directed learning and independent work
- No perseverance

Potential Rewards

- You'll know more than your colleagues
- You'll be able to master the scientific literature
- You'll become an expert in your field and are called upon as such
- You'll belong to a community of experts and investigators
- You'll make valuable scientific insights that contribute to knowledge in the field

Potential Sacrifices

- Research requires committed time
- Research can be “unproductive” for long periods (especially clinical research)
- Research careers are often (read: always) less financially lucrative than purely clinical careers
- Funding is often uncertain and requires ongoing effort to obtain

Why residency is a good time for research

- Dedicated period for learning
- Abundance of clinical material and observations
- Ready access to experts and mentors
- Variety of research options available

Goals for residency research

- Learn how to access the medical literature
- Learn how to read and appraise the literature
- Learn the fundamentals of biostatistics, epidemiology, clinical study design, and ethical principles of research
- Publish original scholarly works
- Be introduced to the scientific community
- Forward-looking career mentoring in research
  - Academia
  - Industry
  - Integrated into private practice

My own experience

When you're starting out, you have little idea what you want to do and little direction.

There are three key words for residents in doing research:

-- Curiosity, from yourself

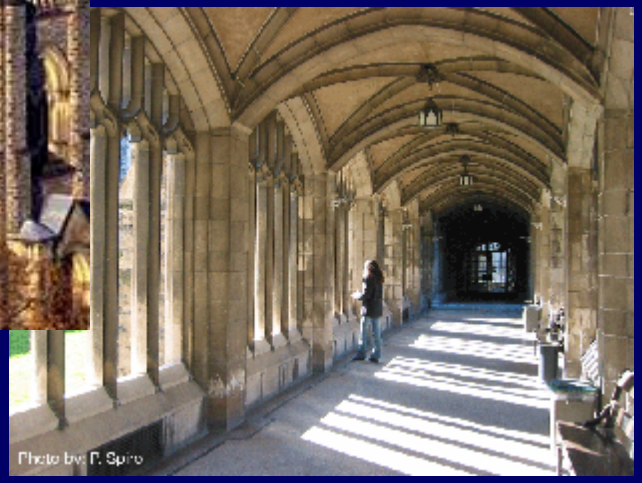
-- Mentorship, from others

-- Planning, from both

University of Toronto

I got interested in
research here (**curiosity**!).
In fact, I was ready (and funded)
To do a PhD in Immunology!

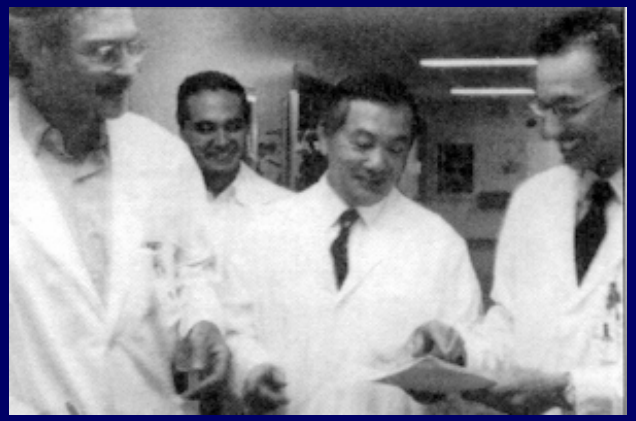
Then I applied for med school…



Faculty of Medicine, University of Toronto

A wonderful institution and a great experience! Although I didn't have the time to pursue lab work, I was still interested in research

My Mentors – Internal Medicine



Dr. Herbert Ho Ping Kong
A master clinician and role model

Dr. Allan Detsky
Always asking questions and proposing ways to answer them

Dr. Howie Abrams
Humane! What knowledge!

There was a strong culture of clinical investigation in the department during my residency in Internal Medicine. Drs. Singer and Detsky ran a great course in critical appraisal of the literature (with lunch).

Dr. Peter Singer
Outstanding young professor and bioethicist

Others: Drs. David Naylor, Maria Bacchus, Daniel Panisko, David McNeely (a real live “House”), Ken Robb

My Mentors - Rheumatology

I was a Fellow from 1995-1997 at the University of Toronto

Dr. Ed Keystone
(RA)

Dr. Claire Bombardier
(Epidemiology)

Dr. Dafna Gladman
(Lupus, PsA)

Dr. Joan Wither
(Immunology)

Dr. Rob Inman
(Spondyloarthropathy)

Dr. Murray Urowitz
(Lupus)

Dr. Adel Fam
(Gout)

Others: Drs. Arthur Bookman, Peter Lee, Duncan Gordon, Hugh Smythe, Jack Reynolds, etc.

Stanford University Fellowship in Epidemiology, Health Services Research

Dr. Jim Fries
Rheumatologist

I loved sitting in Jim's office and just talking. A true "change agent" in modern medicine.

Stuff like this takes advance **planning**. It's good to start exploring possibilities early in your training.

Thanks: Drs. Monica Oertendahl, Yuko Matsuda, Mark Genovese; Cindy Williams, Jared Schettler, Dena Ramey

ARAMIS

investigators

research

publications

HAQ

pharmaceutical collaborations

STANFORD UNIVERSITY MEDICAL CENTER

ARAMIS: investigators

University of Pittsburgh

Thomas A. Medsger, MD

Professor of Medicine, University of Pittsburgh and ARAMIS Project Director, University of Pittsburgh.

Mary Chester M. Wasko, MD, MSc

Assistant Professor of Medicine, University of Pittsburgh. Dr. Wasko's research interests include:

- Epidemiology of cardiovascular diseases in rheumatoid arthritis
- Cancer epidemiology in rheumatoid arthritis
- New pharmacologic therapies for rheumatoid arthritis

University of Saskatchewan

John Sibley, MD

Professor, Department of Medicine, University of Saskatchewan, Saskatoon, Canada and ARAMIS Project Director, University of Saskatchewan.

University of Tennessee

Benjamin Wang, MD, FRCP(C)

Assistant Professor, University of Tennessee Health Sciences Center, Division of Rheumatology. Dr. Wang's research interests include:

- Optimal deployment of disease-modifying agents in the treatment of rheumatoid arthritis
- Outcome measures in arthritis
- Long-term efficacy and toxicity of drugs used to treat arthritis

My Classmates from Toronto

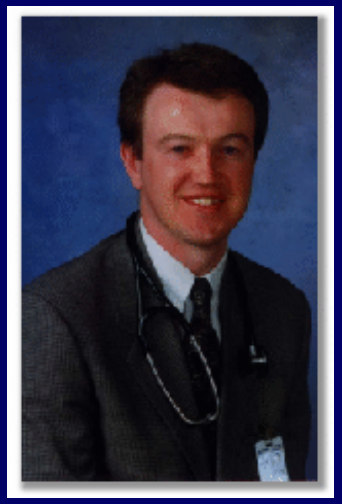
These folks have all become successful clinical investigators – check out their papers in JAMA and NEJM. It can be done!

Dr. Sophie Jamal
Endo-Osteoporosis
University of Toronto

Dr. David Alter
Cardiology-Epidemiology
University of Toronto

Dr. Shreyasee Amin
Rheum-Epidemiology
Mayo Clinic, Rochester

Dr. Proton Rahman
Rheum-Epidemiology-Genetics
Memorial University School of Medicine
St. John's, NF



Dr. Carl van Walraven
GIM-Epidemiology
University of Ottawa
(Carl and I published a paper together as 4th yr med students)

Practical Projects for Residents

- Basic Science
  - Ongoing lab projects
  - Learning laboratory techniques
- Clinical Science
  - Case reports
  - Narrative reviews
  - Systematic reviews
    - Qualitative systematic review
    - Meta-analysis
  - Data collection and abstraction
  - Statistical analysis

Annals of Internal Medicine

Review

Narrative Review: The Pathophysiology of Fibromyalgia

Aryeh M. Abeles, MD; Michael H. Pillinger, MD; Bruce M. Solitar, MD; and Micha Abeles, MD

Primary fibromyalgia is a common yet poorly understood syndrome characterized by diffuse chronic pain accompanied by other somatic symptoms, including poor sleep, fatigue, and stiffness, in the absence of disease. Fibromyalgia does not have a distinct cause or pathology. Nevertheless, in the past decade, the study of chronic pain has yielded new insights into the pathophysiology of fibromyalgia and related chronic pain disorders. Accruing evidence shows that patients with fibromyalgia experience pain differently from the general population because of dysfunctional pain processing in the central nervous system. Aberrant pain processing, which can result in chronic pain and associated symptoms, may be the result of several interplaying mechanisms, including central sensitization, blunting of inhibitory pain pathways, alterations in neurotransmitters, and psychiatric comorbid conditions. This review provides an overview of the mechanisms currently thought to be partly responsible for the chronic diffuse pain typical of fibromyalgia.

Ann Intern Med. 2007;146:726-734. www.annals.org

For author affiliations, see end of text.

Differences between Narrative Reviews and Systematic Reviews

Feature	Narrative Review	Systematic Review
Question	Often broad in scope	Often a focused clinical question
Sources and search	Not usually specified, potentially biased	Comprehensive sources and explicit search strategy
Selection	Not usually specified, potentially biased	Criterion-based selection, uniformly applied
Appraisal	Variable	Rigorous critical appraisal
Synthesis	Often a qualitative summary	Quantitative summary*
Inferences	Sometimes evidence-based	Usually evidence-based

* A quantitative summary that includes a statistical synthesis is a meta-analysis.

Cook, D. J. et. al. Ann Intern Med 1997;126:376-380

Annals of Internal Medicine

Rheumatology 2007;46:529–532
Advance Access publication 29 September 2006

doi:10.1093/rheumatology/kel326

Concise Report

Dose escalation of the anti-TNF-α agents in patients with rheumatoid arthritis. A systematic review

R. Ariza-Ariza, F. Navarro-Sarabia, B. Hernández-Cruz, L. Rodríguez-Arboleya, V. Navarro-Compán and J. Toyos

TABLE 1. Main characteristics and results of the included studies

Study [reference]	Type of study *n*, biological agent	Main outcomes and results	Quality assessment
Abarca [1]	Based on medical records $n=224$ Infliximab ($n=89$) Etanercept ($n=128$) Both ($n=27$)	Initial and last mean dose of INF: 3.38 and 4.51 mg/kg ($P<0.001$) Initial and last mean dose of ETN: 25.0 and 25.8 mg ($P=0.16$)	Based on review of medical records. Evidence level: IV
Durez [2]	Prospective, clinical study $n=513$ Infliximab	Dose increase at week 30: 106 patients (22%) ACR response after dose increase (from week 30 to week 54): ACR 20: 27% (from 34 to 61%). ACR 50: 13%	Interventions and outcomes clearly described. Uncontrolled study. Evidence level: IV
Edrees [3]	Clinical study $n=55$ Infliximab	Dose increase: seven patients (12.7%) Decreased interval between infusions: 11 (20%) Total dose escalation: 18 (32.7%) ACR 20 post-dose increase response: 29% ACR 20 post-frequency decrease response: 36%	Uncontrolled study. Collection data was not clearly prospective. Evidence level: IV
Etemab [4]	Based on registries Infliximab ($n=424$) Etanercept ($n=690$)	55% of the patients experienced a dose increase Mean dose increase was 29% 11% of the patients experienced a dose increase	Limited by the design based on records. Insufficient information about the outcomes. Evidence level: IV
George [5]	Based on records $n=201$ Infliximab	Mean initial dose of infliximab: 307 mg Mean dose at eighth infusion: 434 mg (increase of 41.3%)	Limited by the design based on records. Insufficient information about the outcomes. Evidence level: IV
Gilbert [6]	Based on registries Infliximab ($n=598$) Etanercept ($n=950$)	57.9% of patients with dose increase in a year 18.1% of patients with dose increase in a year	Limited by the design based on records. Insufficient information about the outcomes. Evidence level: IV
Harley [7]	Based on registries Infliximab ($n=141$) Etanercept ($n=853$)	36.9% of the patients with dose increase 22% of the patients with dose increase	Limited by the design based on registries. Evidence level: IV
Ollendorf [8]	Retrospective Based on records $n=1236$ Infliximab	Dose escalation: 762 (61.7%) Dose increase: 482 (63.3% of 762) Frequency increase: 79 (10.4% of 762) Dose and frequency increase: 201 (26.4% of 762) Median time to escalation: 254 days	Limited by the design based on records. Interventions and outcomes clearly described. Evidence level: IV

Annals of Internal Medicine | Review

Meta-analysis: Diagnostic Accuracy of Anti–Cyclic Citrullinated Peptide Antibody and Rheumatoid Factor for Rheumatoid Arthritis

Kunihiro Nishimura, MD, MPH; MS; Daisuke Sugiyama, MD, MPH; Yoshinori Kogata, MD; Goh Tsuji, MD, PhD; Takashi Nakazawa, MD, PhD; Seiji Kawano, MD, PhD; Katsuyasu Saigo, MD, PhD; Akio Morinobu, MD, PhD; Masahiro Koshiba, MD, PhD; Karen M. Kuntz, ScD; Isao Kamae, MD, DrPH; and Shunichi Kumagai, MD, PhD

Background: Rheumatoid factor (RF) and autoantibodies against cyclic citrullinated peptide (CCP) are markers that might help physicians diagnose rheumatoid arthritis.

Purpose: To determine whether anti-CCP antibody more accurately identifies patients with rheumatoid arthritis and better predicts radiographic progression than does RF.

Data Sources: MEDLINE through September 2006 and reference lists of retrieved studies and review articles.

Study Selection: Studies in any language that enrolled at least 10 participants and that examined the role of anti-CCP antibody and RF in the diagnosis or prognosis of known or suspected rheumatoid arthritis.

Data Extraction: Two authors independently evaluated studies for inclusion, rated methodological quality, and abstracted relevant data.

Data Synthesis: The DerSimonian–Laird random-effects method was used to summarize sensitivities, specificities, and positive and negative likelihood ratios from 37 studies of anti-CCP antibody and 50 studies of RF. The pooled sensitivity, specificity, and positive and negative likelihood ratios for anti-CCP antibody were 67% (95% CI, 62% to 72%), 95% (CI, 94% to 97%), 12.46 (CI, 9.72 to 15.98), and 0.36 (CI, 0.31 to 0.42), respectively. For IgM RF, the values were 69% (CI, 65% to 73%), 85% (CI, 82% to 88%), 4.86 (CI, 3.95 to 5.97), and 0.38 (CI, 0.33 to 0.44). Likelihood ratios among IgM RF, IgG RF, and IgA RF seemed to be similar. Results from studies of patients with early rheumatoid arthritis were similar to those from all studies. Three of 4 studies found that risk for radiographic progression was greater with anti-CCP antibody positivity than with IgM RF positivity.

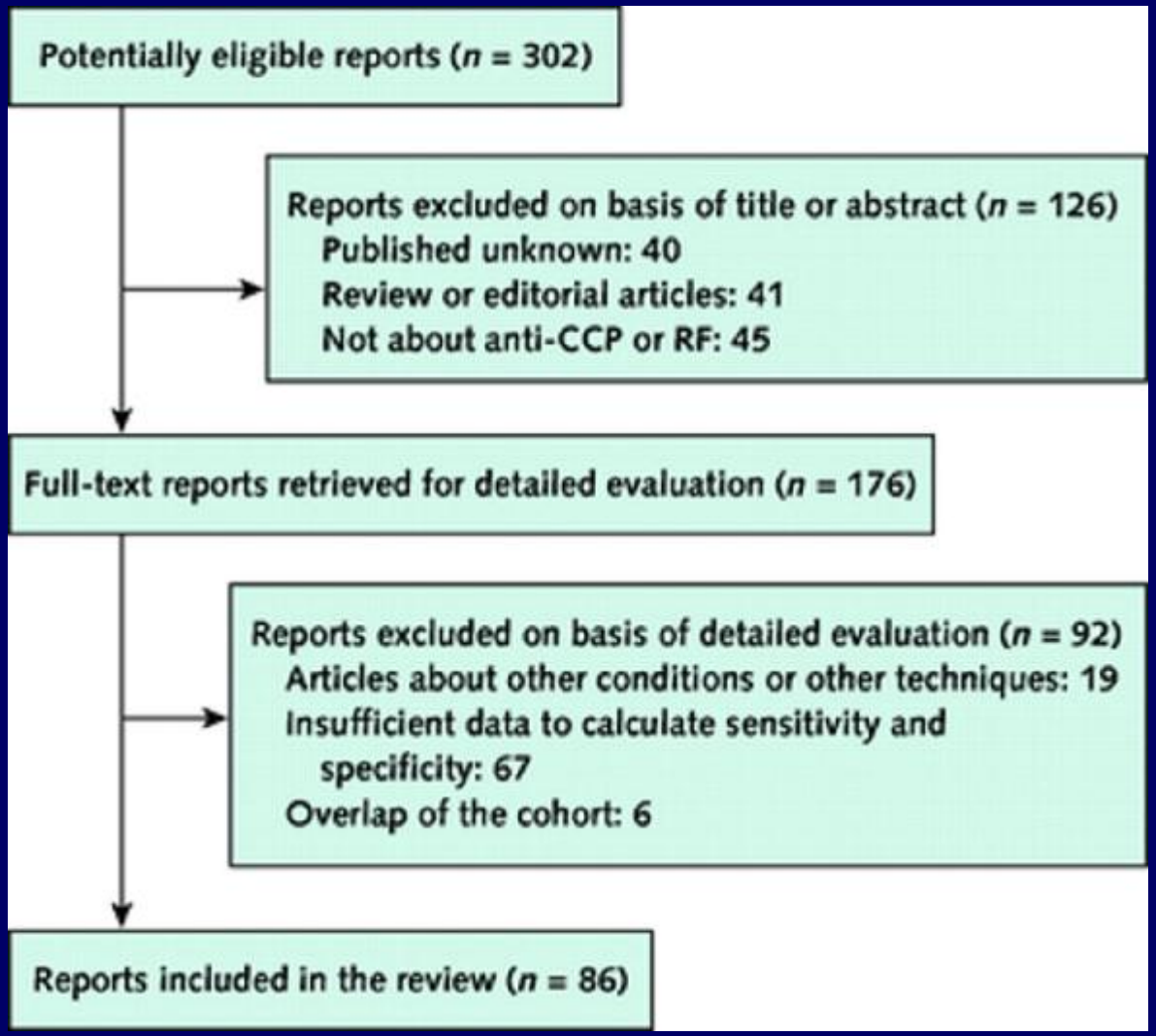
Limitations: Many studies had methodological limitations. Studies of RF were heterogeneous and had wide ranges of sensitivity and specificity.

Conclusions: Anti-CCP antibodies are more specific than RF for diagnosing rheumatoid arthritis and may better predict erosive disease.

Ann Intern Med. 2007;146:797-808. www.annals.org

For author affiliations, see end of text.

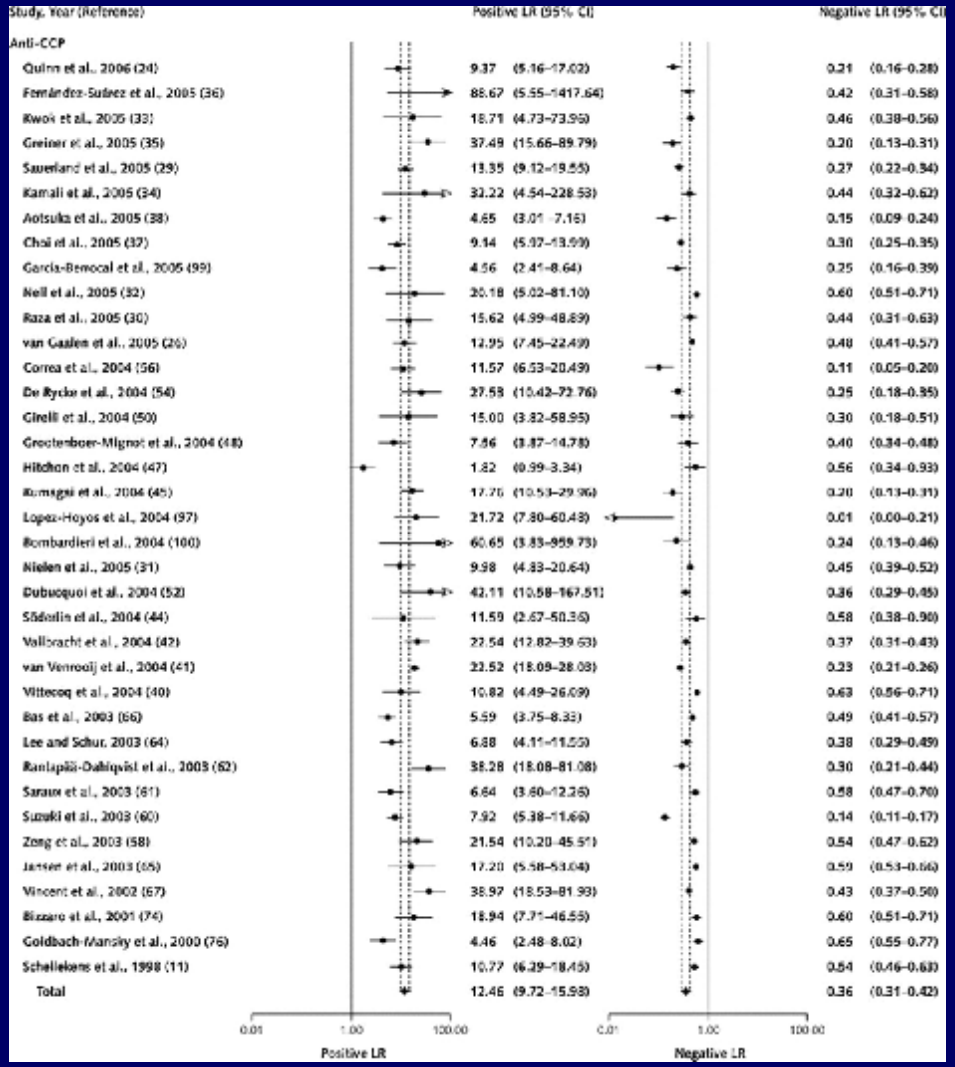
Study flow diagram



Nishimura, K. et. al. Ann Intern Med 2007;146:797-808

Annals of Internal Medicine

Likelihood ratio (LR) for autoantibodies against cyclic citrullinated peptides (anti-CCP)



Nishimura, K. et. al. Ann Intern Med 2007;146:797-808

Annals of Internal Medicine

When it comes to achieving the balance, All I Ever Really Needed to Know…

Excerpts from
"All I Ever Really Needed to Know I Learned in Kindergarten"
as applied to research (with apologies to Robert Fulgham)

- **Concerning conducting research:**
  - Play fair
  - Clean up your own mess
  - Don't take things that aren't yours
  - Say sorry when you hurt somebody
  - Flush
- **Concerning your life**
  - Live a balanced life
  - Learn some and think some and draw and paint and sing and dance and play and work every day some
  - Take a nap every afternoon
- **Concerning needing good mentors**
  - When you go out into the world, watch for traffic, hold hands, and stick together
- **Concerning our attitude as physicians**
  - Be aware of wonder
  - Remember the little seed in the plastic cup? The roots go down and the plant goes up and nobody really knows how or why, but we are all like that
  - And then remember the book about Dick and Jane and the first word you learned, the biggest word of all: LOOK

Some Final Thoughts

- As physicians, whatever our career in medicine may be, should have a little bit of academia in our blood
- The current health care environment works against us, preventing us from taking time, thinking things through, studying, making our own decisions, and being scholars and teachers
- We need to resist the trend of being swept up in the confusing and demanding atmosphere of health care today, and take time and effort to study and be constant learners
- Some experience in research helps us in our ability to gather, appraise, and synthesize information throughout our career
- Always keep eyes, ears, brain, and time open for your patients' sake