The Reading Club:
Enriching The Scientific Knowledge of Rheumatology Trainees

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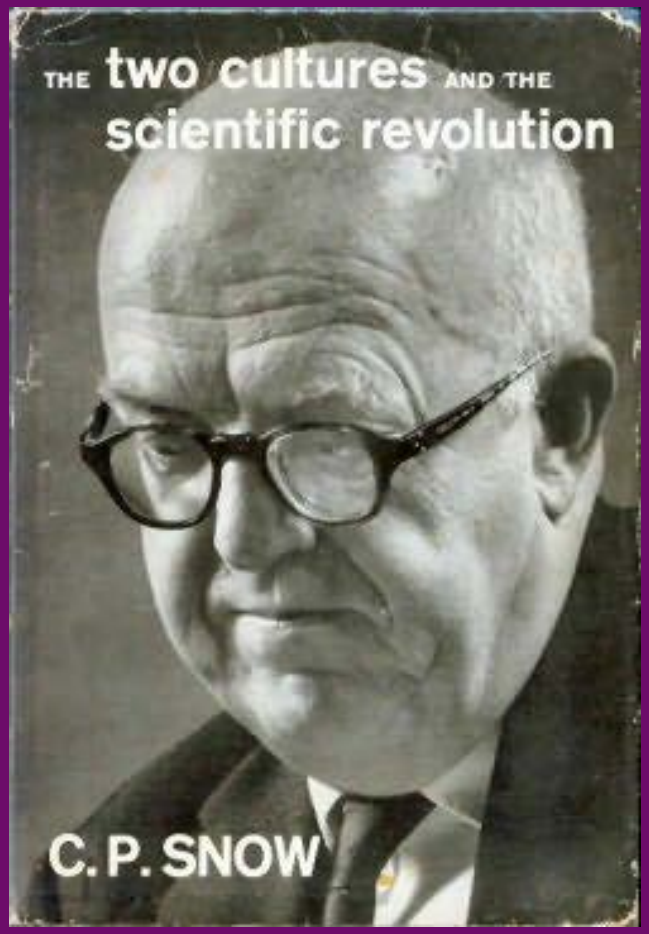
Medicine and Science:
A Cultural Sea Change

- Applicants to medical school come from a wider range of backgrounds than in the past-many do not come from strongly science-oriented backgrounds

- There is a crisis in science in the U.S., with fewer students opting for research careers

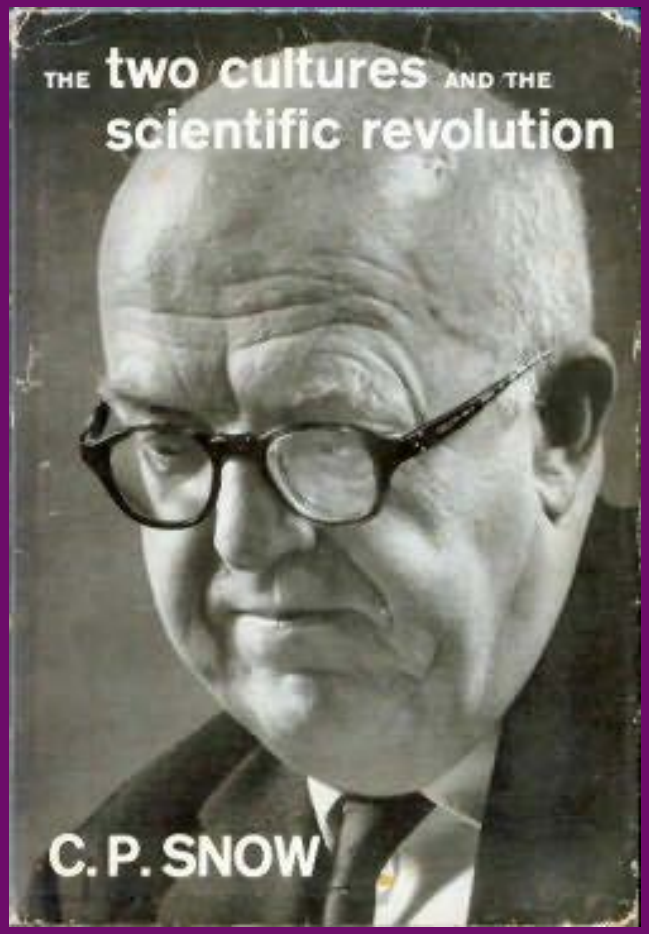
- The teaching of science in med school has become a major challenge--managing volume, speed of advancement, heterogeneity of skills and interests

Science and Clinical Practice: Two Cultures?



1959 (CP Snow): Scientific and humanistic knowledge have become fragmented, and people who are literate in one branch of human knowledge are frequently illiterate in the other. This is detrimental to the individual and dangerous for society.

Science and Clinical Practice: Two Cultures?



Scientific knowledge and clinical practice have become fragmented, and people who are literate in one branch of medical knowledge are frequently not adequately knowledgeable in the other. This is detrimental to the individual and dangerous for society.

The NYU Fellowship

- Take four fellows a year
- Basic philosophy-science and clinical medicine are inseparable
- We want to train clinicians, clinical scientists and basic scientists
- A mix of expertise and ability is considered desirable training- each enriches the other
- Our fellows come with diverse backgrounds and knowledge bases
- We expect that all fellows will have a basic literacy in science

This doesn't always happen, however…

Can we bring all of our fellows up to speed in basic science and ensure a common level of confidence and expertise?

(Can we do this without exhausting ourselves and our resources and driving our fellows to distraction?)

The Reading Club Model: A "Low Energy System"

Goal: To Improve Scientific Literacy and Comfort (not to make PhDs out of all the fellows!)

Method: A directed reading program, punctuated regularly by informal, non-threatening discussion

The Reading Club Model:

A Two-year *Non-linear* Curriculum Permits First and Second Year Fellows to Participate Together

Year A	Year B	Year A	Year B
Class of ‘07	Class of ‘07 Class of ‘08	Class of ‘08 Class of ‘09	Class of ‘09 Class of ‘10

The Basic Science Reading Club:
A Two Year Curriculum in Molecular Literacy

Year 1: A textbook of immunology

Year 2: Selected topics in basic science review

Basic Science Year A:

Reading An Immunology Textbook

Janeway's Immunobiology

- Extensive and inclusive
- Long but not overly long
- Very clear, frequently updated text
- A lot of redundancy and context
- Many and very clear figures
- A reasonable price (we buy!)

Janeway's Content

Ch1-Basic concepts in immunology
Ch2-Immunity
Ch3-Antigen recognition
Ch4-Generation of lymphocyte antigen receptors
Ch5-Antigen presentation to T lymphocytes
Ch 6-Signaling through immune system receptors
Ch7-Development and survival of lymphocytes
Ch8-T cell-mediated immunity
Ch9-The humoral immune response
Ch10-Dynamics of adaptive immunity
Ch11-Mucosal immune system
Ch12-16-Clinical and evolutionary aspects of immunity

Basic Science Year B (Part 1):

Selected Topics in Basic Science Review

Dempsy PW, Doyle SE, He JQ, Cheng G. The signaling adaptors and pathways activated by TNF superfamily. *Cytokines and Growth Factor Reviews* 2003;14:193-209.

Chen G and Goeddel. TNF-R1 signaling: a beautiful pathway. *Science* 2002;296:1634

Natoli G, Costanzo A, Guido F, Moretti F and Levrero M. Apoptotic, non-apoptotic and anti-apoptotic pathways of tumor necrosis factor signaling. *Biochemical Pharmacology* 1998:56:915-920.

Ghosh S, May MH and Kopp ER. NF-kB and Rel proteins: evolutionarily conserved mediators of immune responses. Annu Rev Immuno 1998;16:225-60.

Almawi WY and Melemedjian OK. Negative regulation of nuclear factor-kB activation and function by glucocorticoids. *J of Molecular Endocrinology* 2002;28:69-78.

Karin M and Lin A. NF-kB at the crossroads of life and death. *Nature Immunology* 2002;3(3):221-227.

Kumar S. ICE-like proteases in apoptosis. *TIBS* 1995:198-202.

Cohen GM. Caspases: the executioners of apoptosis. *Biochem J* 1997;326:1-16.

Vaux DL, Haecker G and Strasser A. An evolutionary perspective on apoptosis. *Cell* 1994;76:777-779.

Basic Science Year B (Part 2):

Selected Topics in Basic Science Review

Beere HM. Stressed to death: regulation of apoptotic signaling pathways by the heat shock proteins. Science STKE 2001.

Walter S and Buchner J. Molecular chaperones—cellular machines for protein folding. *Angew Chem Int Ed* 2002;41:1098-1113.

Shaulian E and Karin M. AP-1 as a regulator of cell life and death. *Nature Cell Biology* 2002;4:131-136.

Karin M, Zheng-gang L and Zandi E. AP-1 function and regulation. *Current Opinion in Cell Biology* 1997;9:240-246.

Karin M. The regulation of AP-1 activity by mitogen-activated protein kinases. *J Biol Chem* 1995;270(28):16483-16486.

Stewart SA and Weinberg RA. Senescence: does it all happen at the ends? *Oncogene* 2002;21:627-630.

Collins K and Mitchell JR. Telomerase in the human organism. *Oncogene* 2002;21:564-79.

Tsumuki H, Hasunuma T, Kobata T, Kato T, Uchide A and Nishioka K. Basic FGF-induced activation of telomerase in rheumatoid synoviocytes. *Rheumatol Int* 2000;19:123-128.

Stewart SA and Weinberg RA. Telomerase and human tumorigenesis. *Seminars in Cancer Biology* 2000;10:399-406.

Khosla S. Minireview: The OPG/RANKL/RANK system. *Endocrinology* 2001;142(12):5050-5055.

“Hey, what about the science of clinical investigation?”

Yusuf Yazici
Clifton Bingham III

The Clinical Science Reading Club:

A Two Year Curriculum in Clinical Research Literacy

Year A: Selected topics in clinical research methodology

Year B: A reading of important clinical articles (current and paradigm-forming) and related editorials, with regard to methodologic structure, strengths and weaknesses

Clinical Science Year A (Part 1):

Selected Topics in Clinical Research Methodology

Evans S. When and how can endpoints be changed after initiation of a randomized clinical trial? *PLoS Clin Trials* 2007; 2(4): e18.

Garattini S, Bertele V. Non-inferiority trials are unethical because they disregard patients' interests. *Lancet* 2007; 370: 1875-77.

Goekoop-Rulterman YPM, Vries-Bouwstra JK, Allaart CF, et al. Comparison of treatment strategies in early rheumatoid arthritis: a randomized trial. *Ann Intern Med* 2007; 146(6):406-415.

Kaul S, Diamond GA. Good enough: a primer on the analysis and interpretation of noninferiority trials. *Ann Intern Med* 2006; 145(1):62-69.

Rothwell PM. Subgroup analysis in randomized controlled trials: importance, indications, and interpretation. *Lancet* 2005; 365: 176-86.

Schulz KF, Grimes DA. Sample size calculations in randomised trials: mandatory and mystical. *Lancet* 2005; 365: 1348-53.

Schulz KF, Grimes DA. Multiplicity in randomized trials II: subgroup and interim analyses. *Lancet* 2005; 365: 1657-61.

Roland M, Torgerson D. Understanding controlled trials: What outcomes should be measured? *BMJ* 1998; 317: 1075-1080.

Clinical Science Year A (Part 2):

Selected Topics in Clinical Research Methodology

Welch HG, Woloshin S, Schwartz LM, et al. Overstating the evidence for lung cancer screening: the international early lung cancer action program (I-ELCAP) study. *Arch Intern* Med 2007; 167(21): 2289-2295.

Bland JM, Altman DG. Statistics notes: some examples of regression toward the mean. *BMJ* 1994; 309: 780.

Mamdani M, Sykora K, Li P, et al. Reader's guide to critical appraisal of cohort studies: 2. Assessing potential for confounding. *BMJ* 2005; 330: 960-962.

Normand ST, Sykora K, Li P, et al. Reader's guide to critical appraisal of cohort studies: 3. Analytical strategies to reduce confounding. *BMJ* 205; 330: 1021-1023.

Roberts C, Torgerson DJ. Understanding controlled trials: Randomisation methods in controlled trials. *BMJ* 1998; 317: 1301-1310.

Roberts C, Torgerson DJ. Understanding controlled trials: Baseline imbalance in randomized controlled trials. *BMJ* 1999; 319: 185.

Rochon PA, Gurwitz JH, Sykora K, et al. Reader's guide to critical appraisal of cohort studies : 1. Role and design. *BMJ* 2005; 330: 895-897.

American College of Rheumatology Committee to Reevaluate Improvement Criteria. A proposed revision to the ACR20: the hybrid measure of American College of Rheumatology response. Arthritis Rheum 2007; 57: 193-202.

Clinical Science Year B (Part 1):

Evaluating the Methodology of Clinical Studies

Haubitz M, Schellong S, Gobel U, et al. Intravenous pulse administration of cyclophosphamide versus daily oral treatment in patients with antineutrophil cytoplasmic antibody-associated vasculitis and renal involvement. Arthritis Rheum 1998; 41: 1835-1844.

Guillevin L, Cordier JF, Lhote F, et al. A prospective, multicenter, randomized trial comparing steroids and pulse cyclophosphamide versus steroids and oral cyclophosphamide in the treatment of generalized Wegener's granulomatosis. Arthritis Rheum 1997; 40: 2187-2198.

Juni P, Rutjes AWS, Dieppe PA. Are selective COX 2 inhibitors superior to traditional non steroidal anti-inflammatory drugs? BMJ 2002; 324:1287-1288.

Bombardier C, Laine L, Reicin A, et al. Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. N Engl J Med 2000;343:1520-8.

Silverstein FE, Faich G, Goldstein JL, et al. Gastrointestinal toxicity with celecoxib vs nonsteroidal anti-inflammatory drugs for osteoarthritis and rheumatoid arthritis, the CLASS study: a randomized controlled trial. JAMA 2000; 284: 1247-1255.

Curfman GD, Morrissey S, Drazen JM. Expression of concern: Bombardier et al., "Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis," N Engl J Med 2000;343:1520-8. N Engl J Med 2005; 353: 2813-2814.

Dieppe PA, Ebrahim S, Martin RM, et al. Lessons from the withdrawal of rofecoxib. BMJ 2004; 329: 867-868.

Clinical Science Year B (Part 2):

Evaluating the Methodology of Clinical Studies

Boers M, Verhoeven AC, Markusse HM, et al. Randomised comparison of combined step-down prednisolone, methotrexate and sulphasalazine with sulphasalazine alone in early rheumatoid arthritis. Lancet 1997; 350: 309-318.

Goekoop-Ruiterman YPM, de Vries-Bouwstra JK, Allaart CF, et al. Clinical and radiographic outcomes of four different treatment strategies in patients with early rheumatoid arthritis (the BeSt study): a randomized, controlled trial. Arthritis Rheum 2005; 52: 3381-3390.

Zeidler H, Hulsemann JL. How should best strategy and tight control be translated into clinical practice? Comment on the article by Goekoop-Ruiterman et al. Arthritis Rheum 2006; 54: 2338-2348.

Emery P, Fleischmann R, Filipowicz-Sosnowska A, et al. The efficacy and safety of rituximab in patients with active rheumatoid arthritis despite methotrexate treatment: Results of a phase IIb randomized, double-blind, placebo-controlled, dose-ranging trial. Arthritis Rheum 2006; 54: 1390-1400.

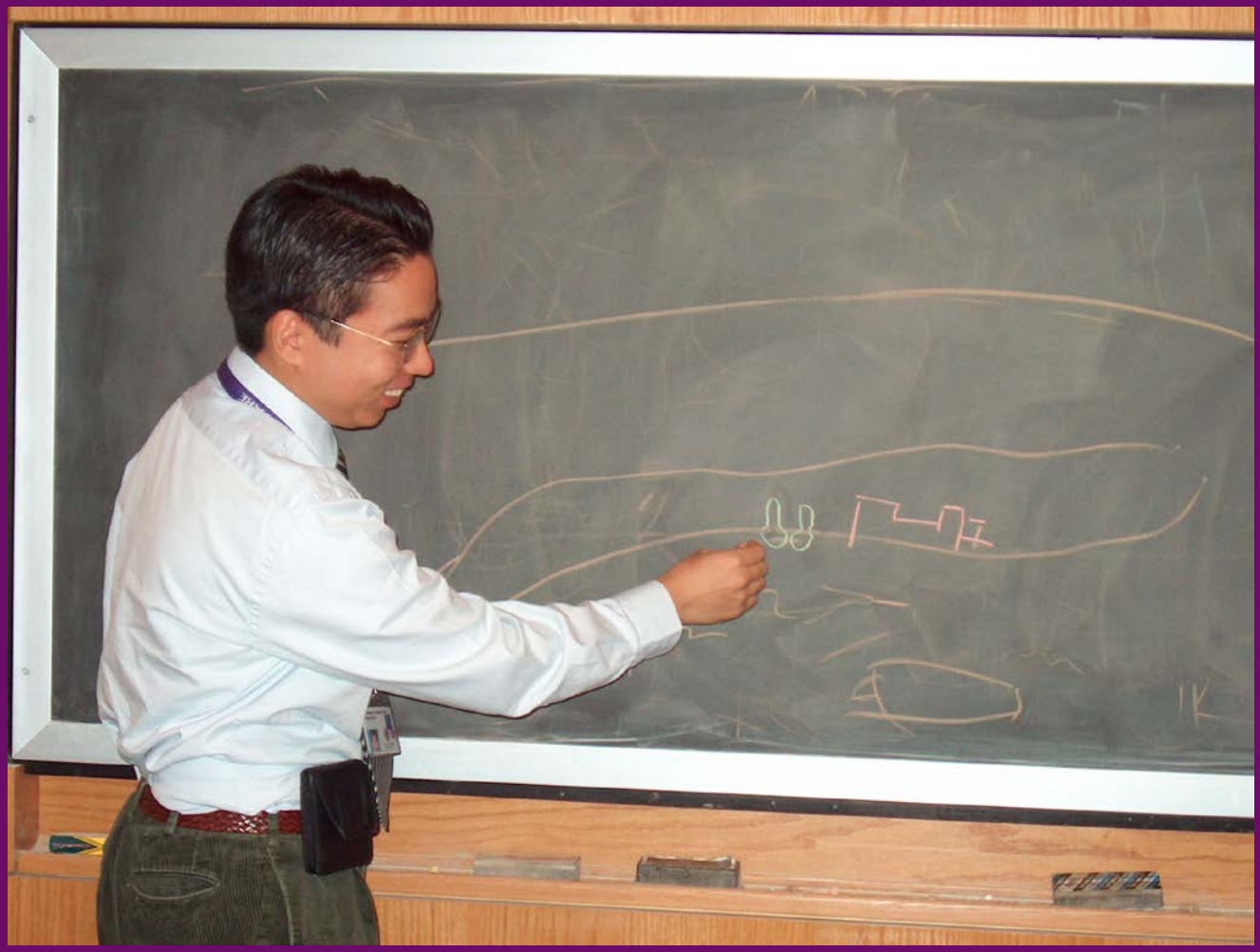
Cohen SB, Emery P, Greenwald MW, et al. Rituximab for rheumatoid arthritis refractory to anti-tumor necrosis factor therapy: Results of a multicenter, randomized, double-blind, placebo-controlled, phase III trial evaluating primary efficacy and safety at twenty-four weeks. Arthritis Rheum 2006; 54: 2793-2806.

Kremer JM, Genant HK, Moreland LW, et al. Effects of abatacept in patients with methotrexate-resistant active rheumatoid arthritis: A randomized trial. Ann Intern Med 2006; 144:865-876.

Boers, M. Abatacept in rheumatoid arthritis: A new branch on the “biologics” tree. Ann Intern Med 2006; 144:933-935.

How To Ensure Enthusiastic Fellow Participation

Basic Science Reading Club: Fellows Participate Directly In The Review and Discussion of the Material



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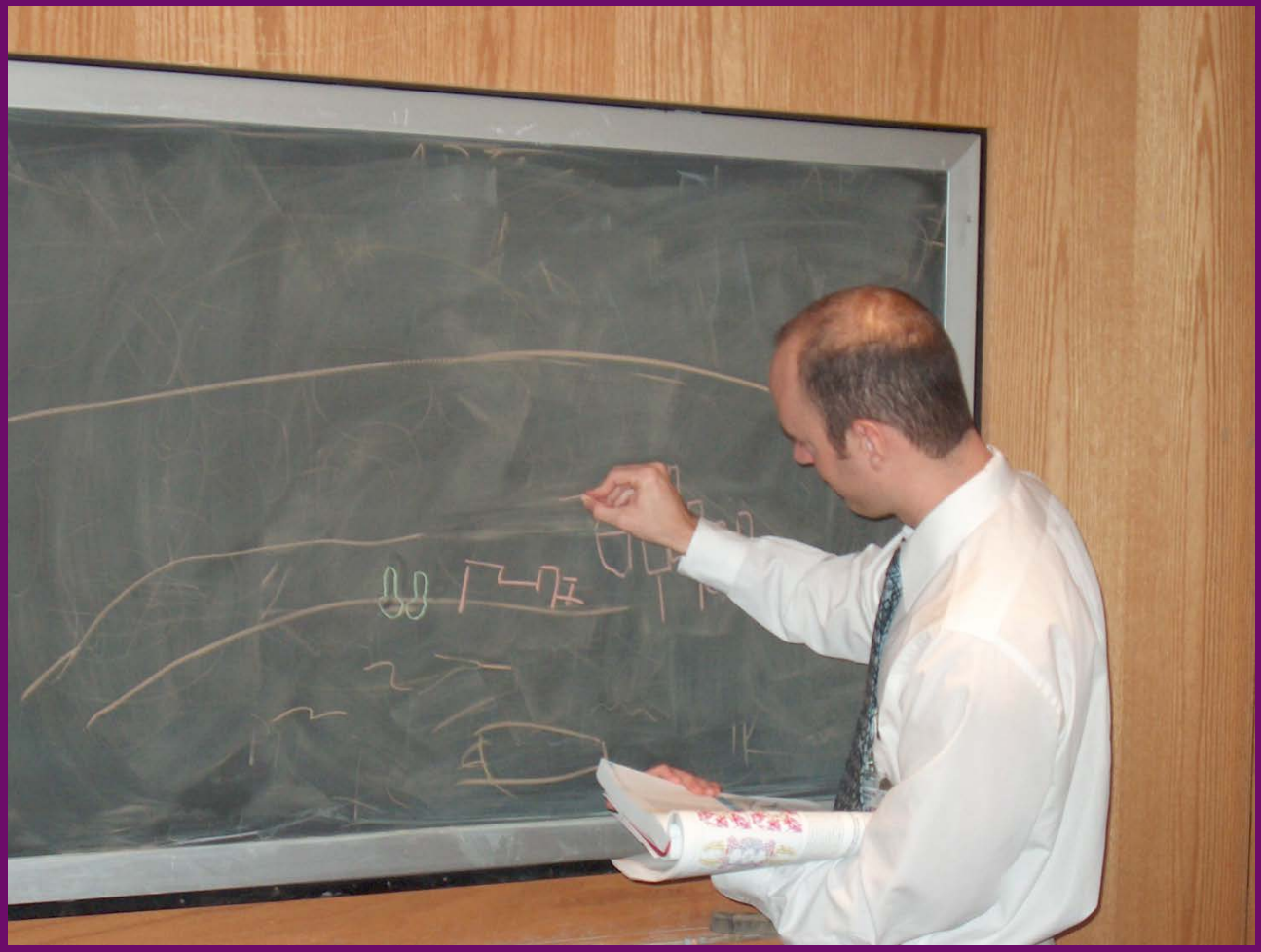
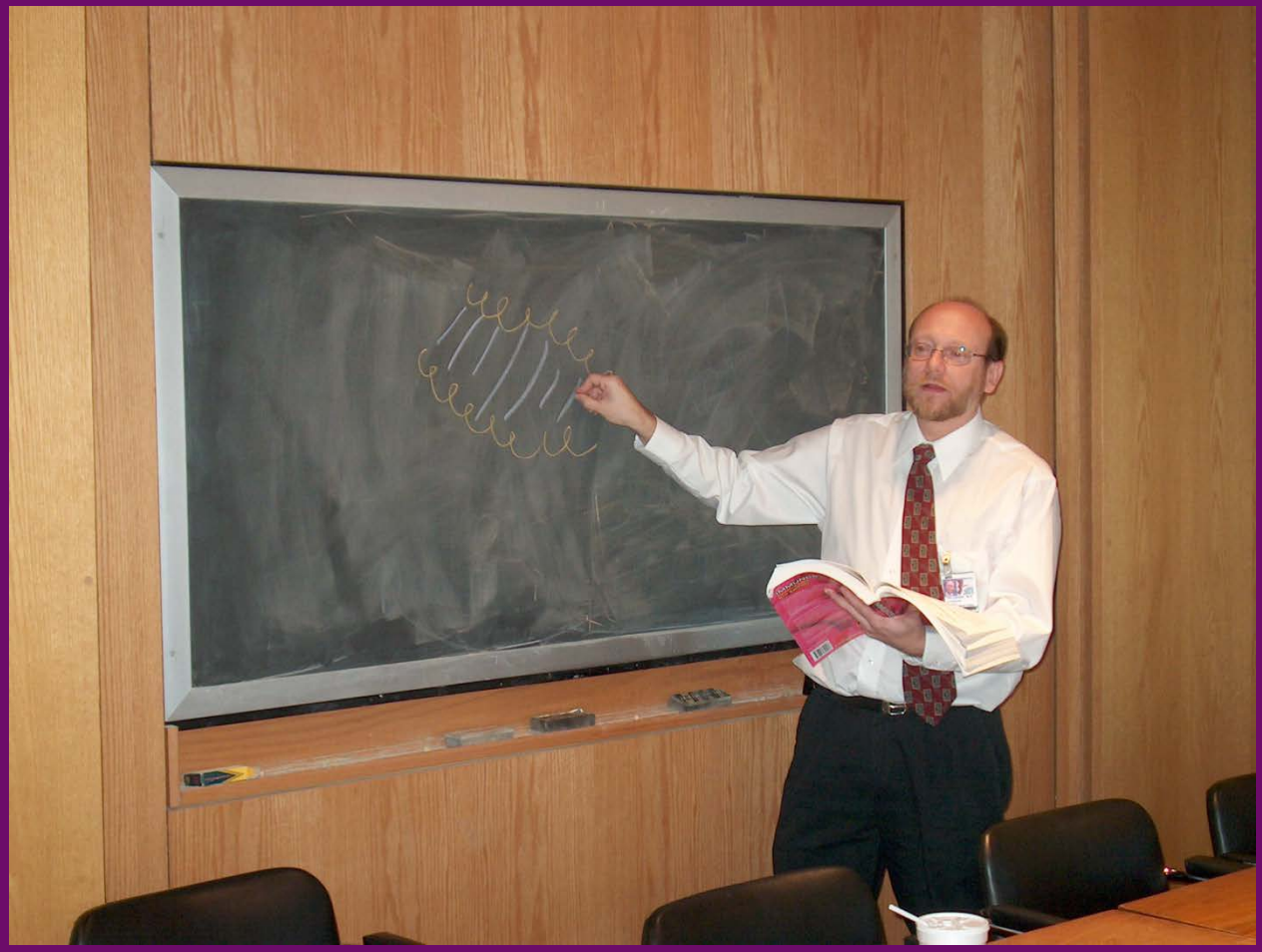
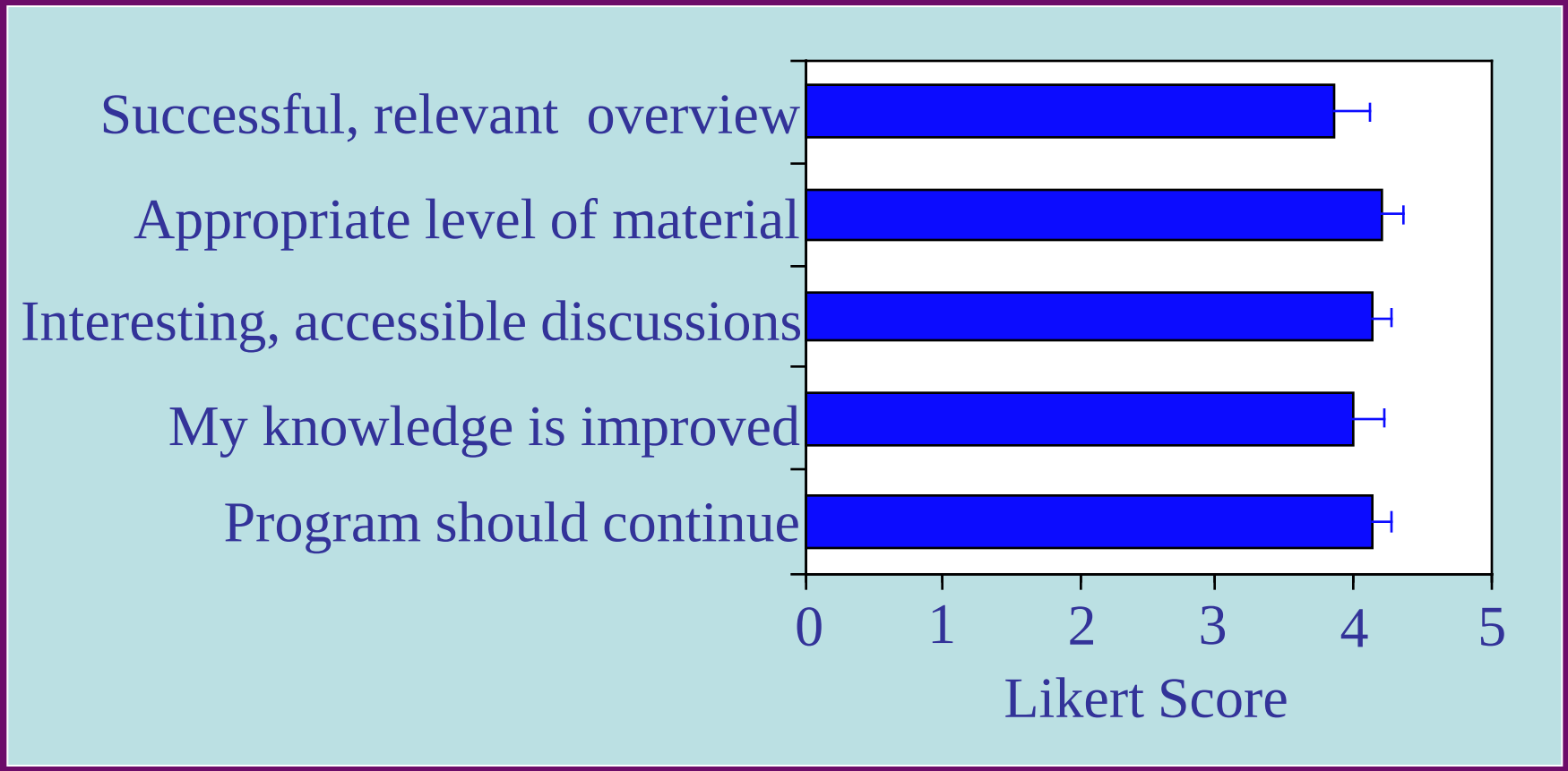


Basic Science Reading Club: Faculty and Fellows Share In The Review and Discussion of the Material



Basic Science Reading Club: Faculty and Fellows Share In The Review and Discussion of the Material

How Are We Doing?
Fellow Feedback on the Clinical Science Reading Club



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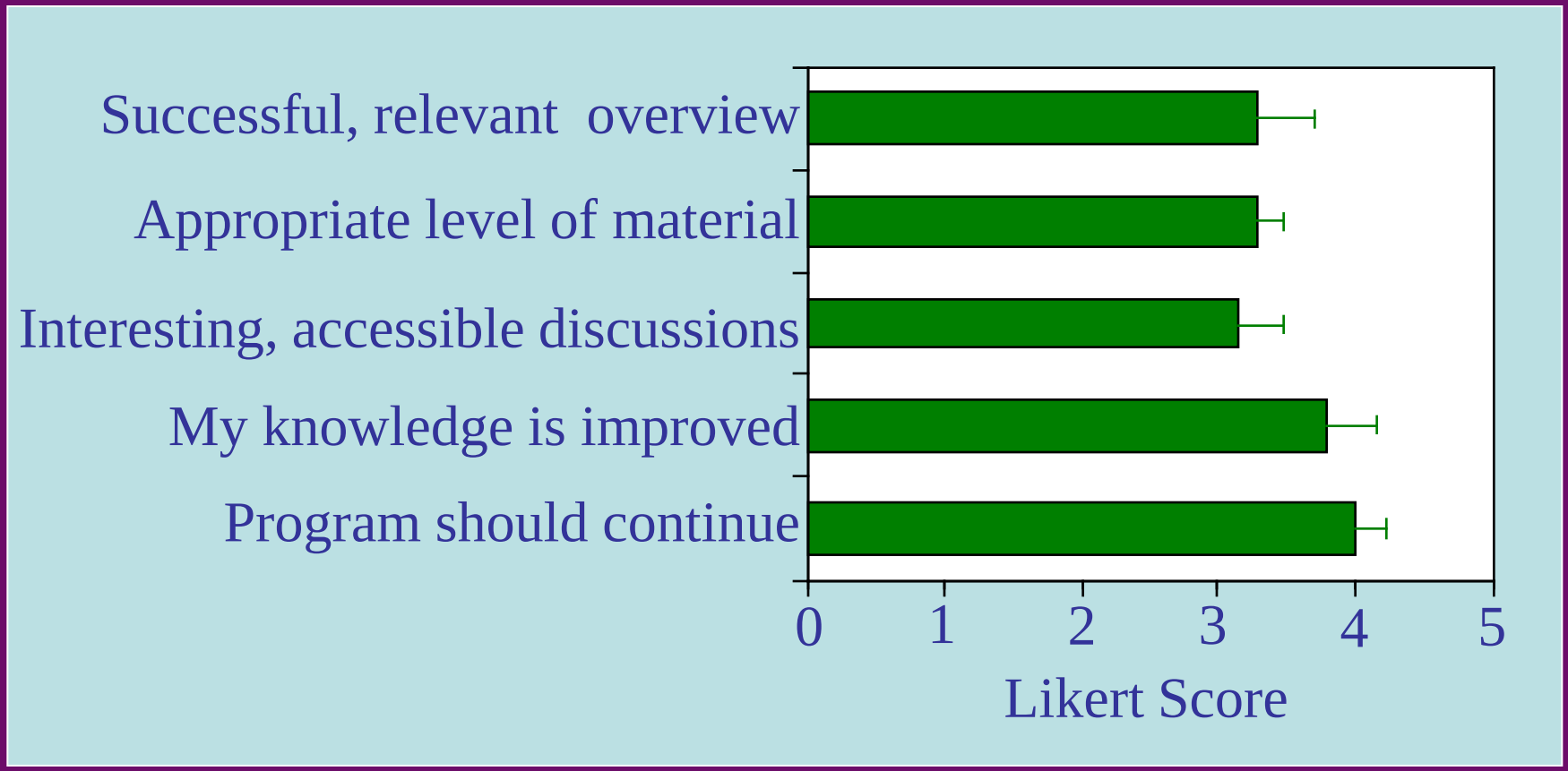
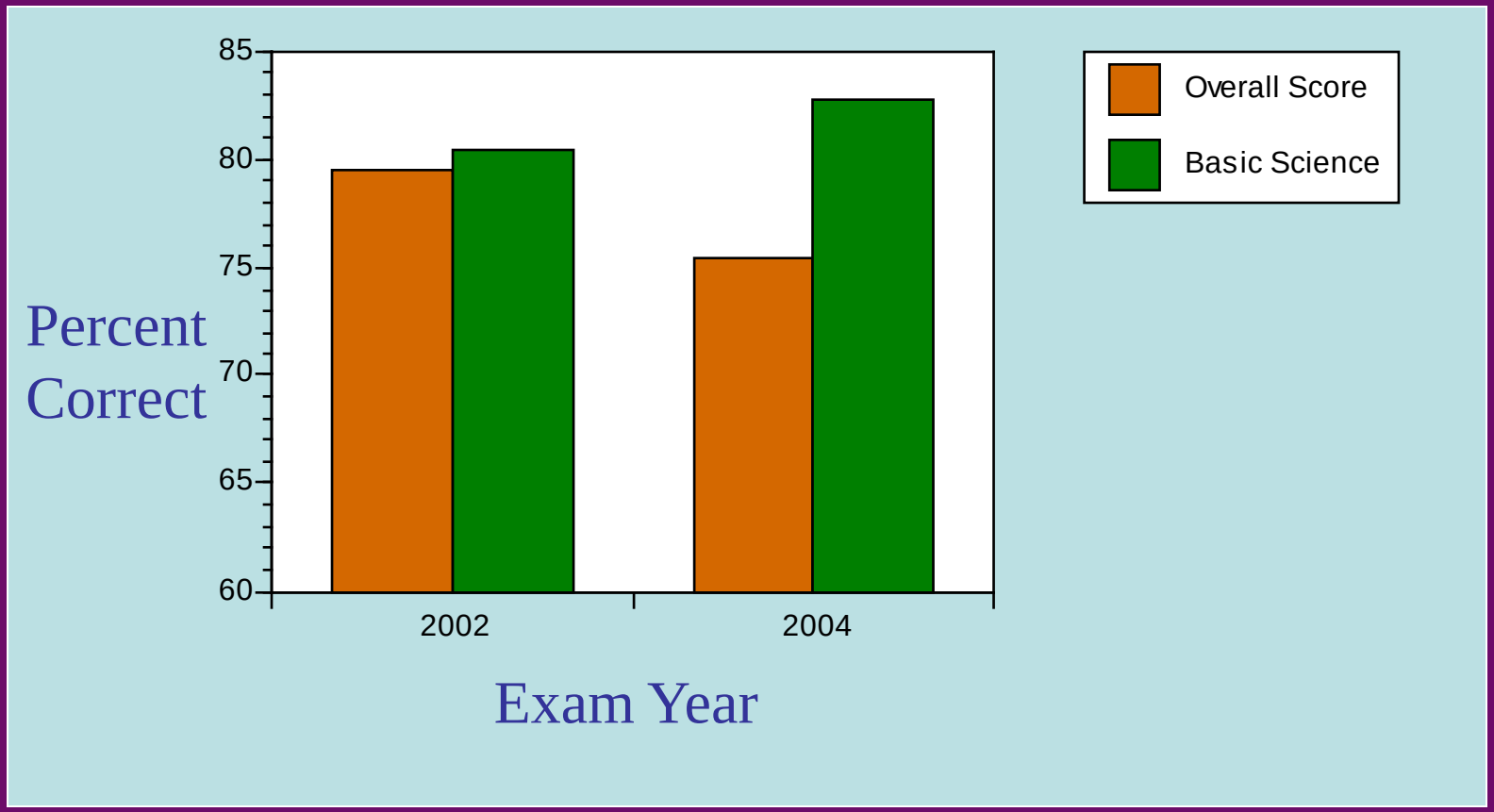


Fellow Comments-Basic Science Reading Club

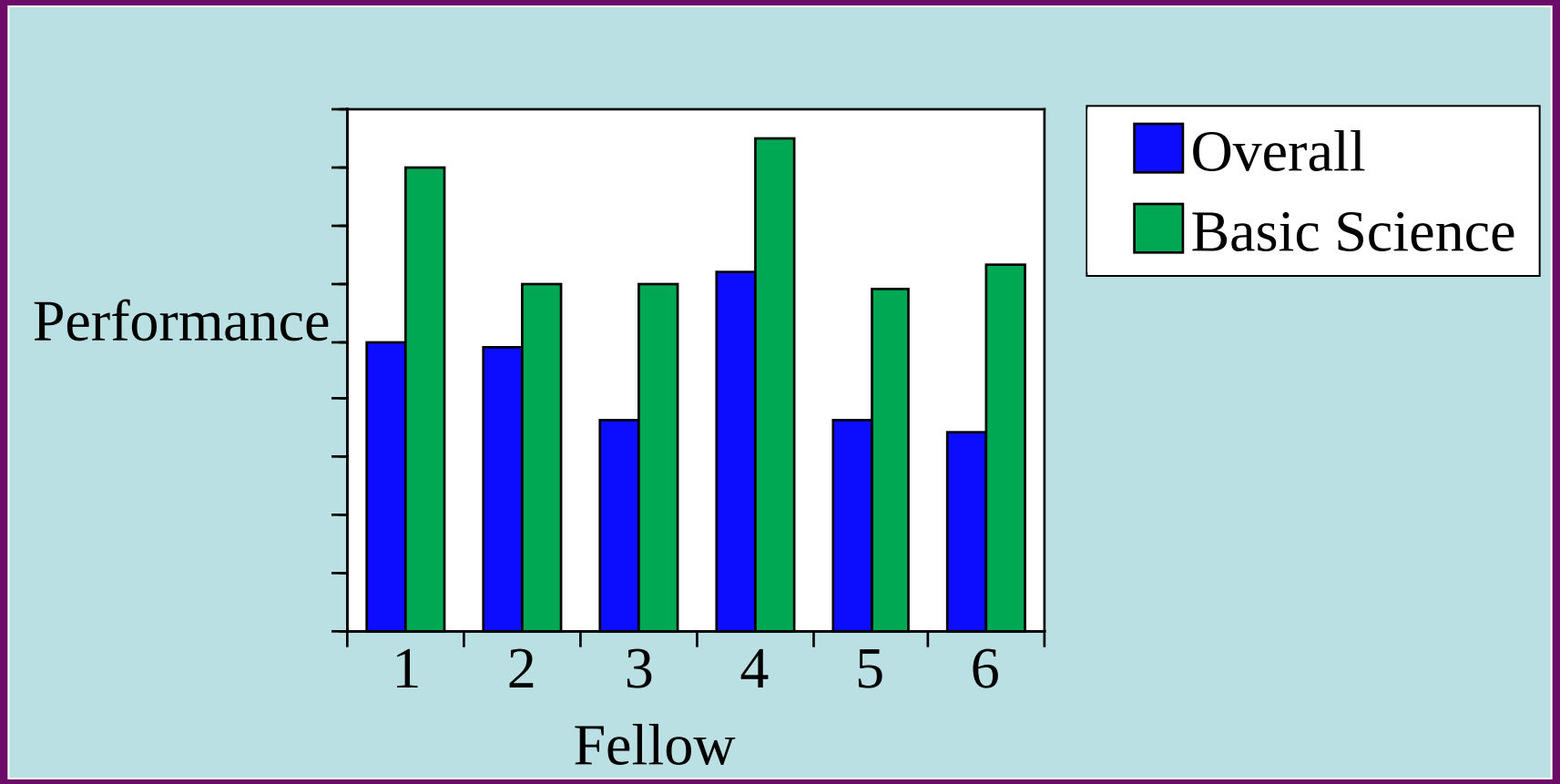
-Needs better articles

-Some of the articles chosen were too specific and not really as helpful in giving us an overview of the topics as maybe some other articles/reviews would

How Are We Doing?
Science Board Scores Pre- and Post-Reading Clubs



How Are We Doing?
In-training Exam: Overall vs Basic Science



How Are We Doing?
What Is the Objective Evidence for Possible Impact of Clinical Science Reading Club?

NONE

But…..

-The quality of fellows' clinical journal club presentations has unequivocally improved

-More fellows seem interested in a career in clinical research

Final Thoughts

The Reading Club Format…

-Requires *relatively* little planning and effort

But the participating faculty and fellows still need to do the reading (and some won't!)

-Is useful for improving knowledge base, and general fluency in a given area

But it will not turn your fellows into experts

-Sends a signal that you place value on the subject being covered

But may distract fellows from other areas of endeavor, particularly if the reading load is too heavy

The selection of the reading materials, and the enthusiasm of the fellows and faculty, are the key determinants of success

Thank You!!!