Why Medicine Needs Physician Scientists and How to Train Them

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Rowe Neurology Institute
Former CEO Verrow Pharmaceuticals, Inc.
Adjunct Professor of Neurology, University of Kansas Medical School

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Physician Scientists Can Develop Novel Drugs and Devices

- **We need more PS's, because we need new drugs and devices to improve the quality of life for our patients**
- Definition--**Physician Scientist--any physician trained in basic laboratory science—a broad definition to define impact**
- Not necessarily a "physician who is independent and lists research as his or her full time occupation"—MSTP: MD-PhD definition
- Physician Scientists can be part-time or full-time researchers, and work in practice, industry, regulatory, legal, academic, or be in other careers in medicine
- Important for **novel drug and device development**—something they are uniquely qualified to do

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Novel Drug Discovery-Why Pharma Can't Do It

- Success Limited and they know it—Pfizer abandoned research on DMT's for Neurodegenerative Dz, Glaxo changes direction
- Big Pharma companies are engines of profit for shareholders
- Profits come from sales, so they spend their money on marketing
- Prefer Me-Too drugs
- Prefer to buy pipelines from Academia, Startups, and Small Pharma—"de-risk" development
- Bench to Patent to Business to Bedside (***Push* Technology**) pathway
- But—novel drug developers at all levels must play by Industry rules, and go for the **patent**, not the **paper or presentation**, since Pharma is an integral part of our medical care system

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What About Academia for Drug and Device Development?

- The **currency** of **academics** involves **grants and publications**, whereas the currency of **drug and device development** in startups and pharma involves **capital and patents**
- **Tradeoff** is possible: Example: papers required for academic promotion, but for patents, publication and presentation possibilities limited. Val Stella-KU vs NIH suit over inventorship.
- **Technology Transfer** process to commercialize discoveries in academia can be long and tedious
- Funding in Life Sciences frequently driven toward **trendy research** in areas like
  - Stem Cells
  - Genetics
  - Proteomics
  - CRISPR
- Despite much funding, these areas have **produced little** in new drug development
- **NIH budget just too small** (Industry R&D 2X NIH)
- **NIH Grant Process fosters competition, rarely cooperation**

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NIH Mission Statement—Has the NIH Lost Its Way?

Table 1. The Purpose of Biomedical Research: From the Original National Institutes of Health Mission Statement

The ultimate purpose is to help provide the practicing physicians of this nation and of the world with better means for ameliorating physical suffering and emotional imbalance, for prolonging human life, and for making all the years of that span more useful both to the individual and to society.

From Topping NH, The United States Public Health Services Clinical Center for Medical Research. JAMA 150:541–545, 1952.

But Now, First-Time Grants Go To PhD **Competition, Not Cooperation**

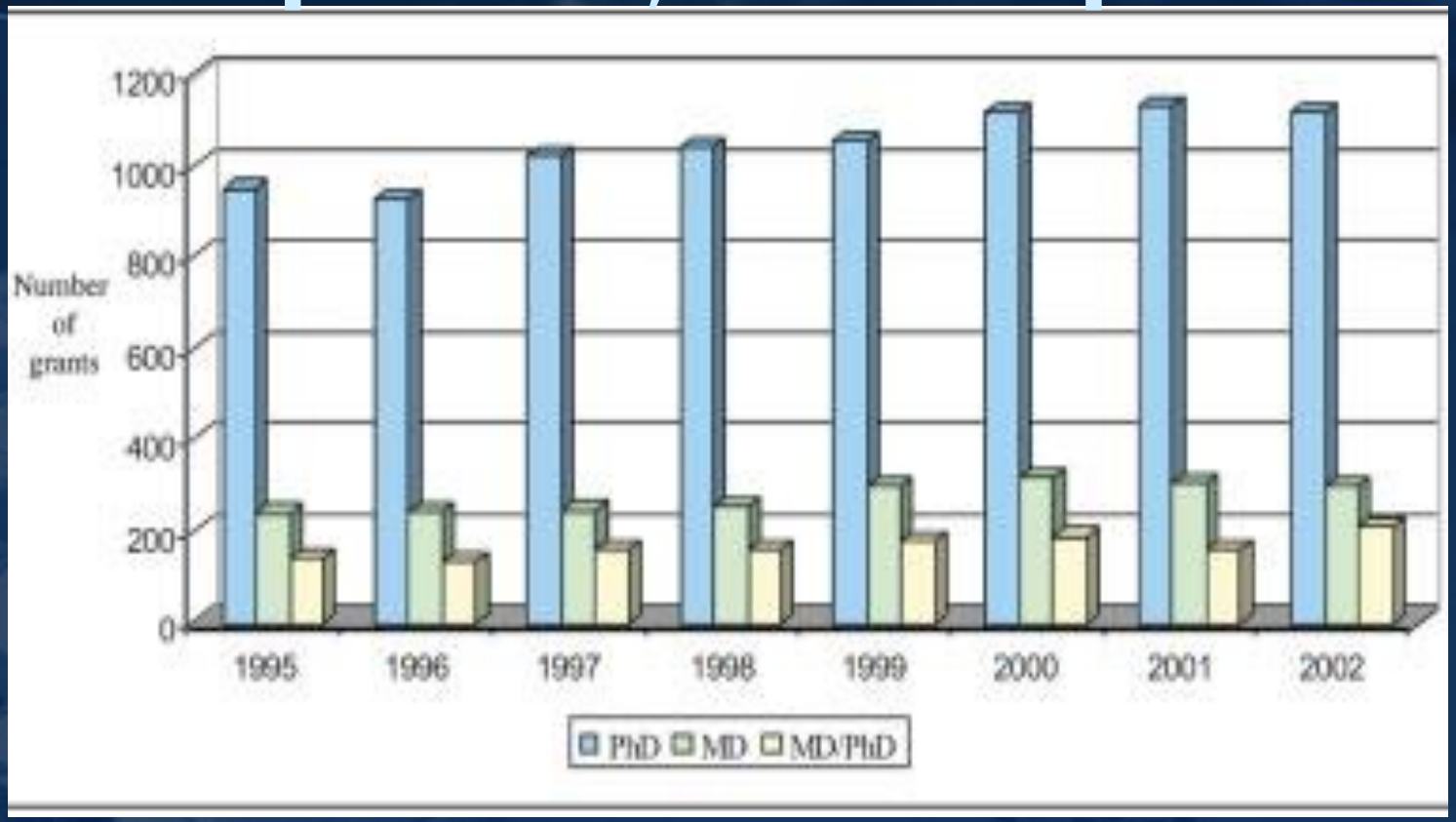

Fig 3. First time applicants for NIH Research Project Grants.

Ann Neurol 2006;60:278–285 Saving the Clinician-Scientist: Report of the ANA Long Range Planning Committee

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Everyone Seems to Agree More Physician-Scientists Needed

- **But: Clinical, Not Basic, Research emphasized**
- **MD-PhD Not a substitute—scientists first, and physicians second**
- **NIH K08 and K23 Mean Age 38, R01, 45, and even with altered grant structures, little can be shaved off this incredibly long time line with current training schedules**
- **Huge untapped gender and diversity opportunities**
- **Debt load to Medical Students Increasing**
- **($177-240 k)**

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RNI-Verrow—An Example of How Physician Scientists Can Develop Novel Drugs

- Start-up spun out of modular RNI (Marcus Welby on steroids concept), to commercialize discoveries of nephroprotective re-formulations
- Sold 2018 to Ligand Pharmaceuticals
- An example of a company, founded by a Physician Scientist, that moved beyond the start-up phase to Intermediate Pharma for clinical development
- Others locally—Nick Franano, MD, Physician Scientist, Proteon and others
- You can do it too

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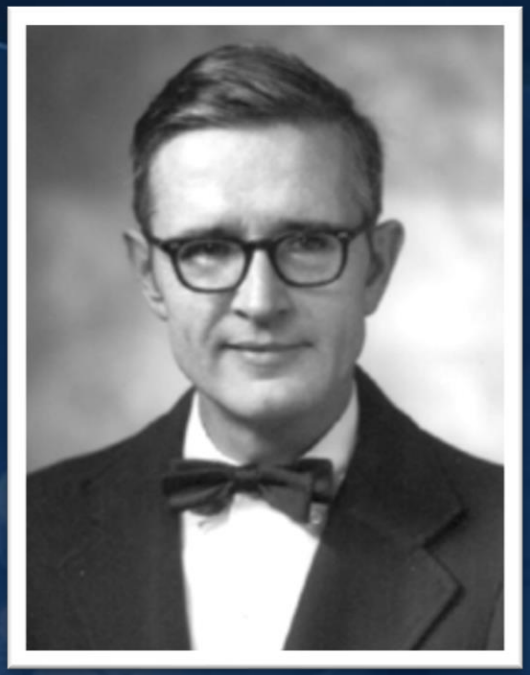
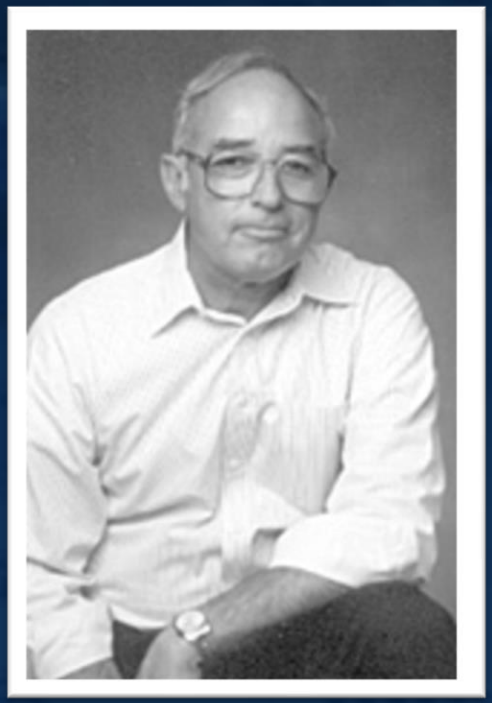
Example-How I Became a Physician Scientist Mentoring and Associates Key

- **Jim Sidbury, MD**, Duke, and the RTP—year-long license to do research on a particular problem, cataract formation. Stanley Appel, MD, Neurology
- **CORD program**—Research Associate, NIH Bethesda
- **Gordon Guroff, PhD** at the NIH: animal models, Parachlorophenylacetyl Glycine, NGF, "The problem is the problem, and look where the light isn't"
- **Guy McKhann, MD** Johns Hopkins program director, Physician Scientist
- **Dewey Ziegler, MD**, KU, VA support, R01, and TIAA early in career and **Barry Festoff, MD**
- **Branch point to Practice**, actively carrying out pharma protocols
- **Charles Conrad, MD**., a neuro-oncologist, joined our group to develop the Blood Brain Barrier Disruption program. He also set up a **basic lab** adjacent to our practice location, to study a **telomerase inhibitor he invented** and was helping to **commercialize**
- **Elizabeth Rowe, PhD, MBA**—joined RNI after long independent career as biochemist

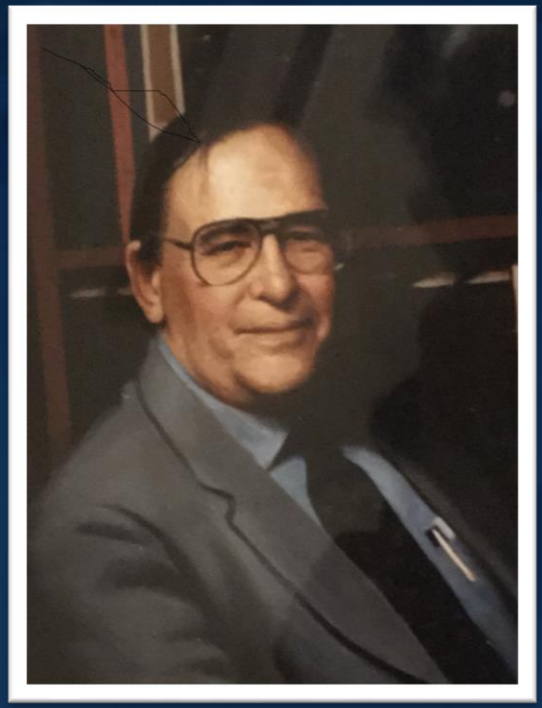
Mentors



James B. Sidbury MD Duke
Research Training Program
Professor of Pediatrics, Duke
Scientific Director, NICHD



Gordon Guroff, Ph.D
Intermediary Metabolism, NICHD
Scientific Director, NICHD



Guy McKhann MD
Chair of Neurology Johns Hopkins
Physician Scientist

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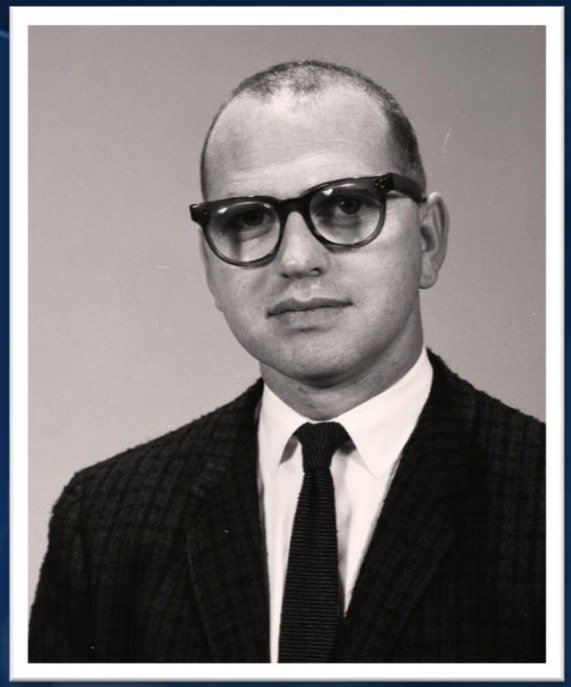
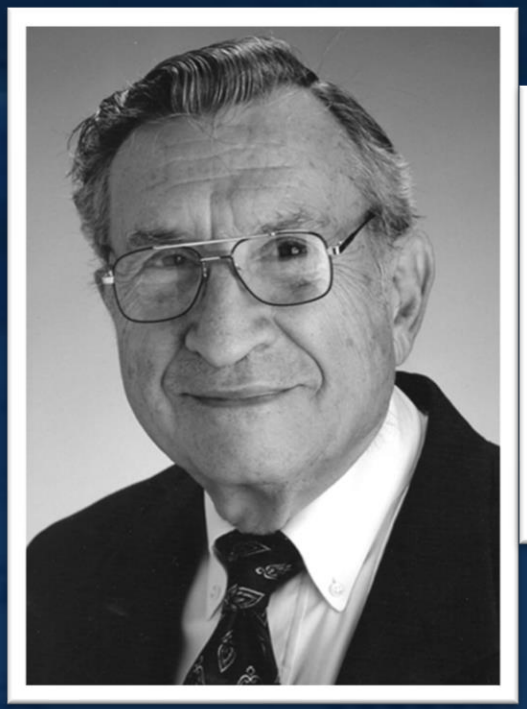
Mentors



David V Cohn, Ph.D.
Chief of Research, KCVA
Barry Festoff, M.D.
Chief of Neurology, KCVA
Physician Scientist



Dewey Ziegler, MD
Chair of Neurology KUMC
Sponsored Career Development Grant

Geoffrey O. Hartzler, MD
Interventional Cardiologist
Entrepreneur Investor.
Business mentor
Verrow Board Member

Verrow Pharmaceuticals

Colleague

Elizabeth Rowe, PhD, MBA

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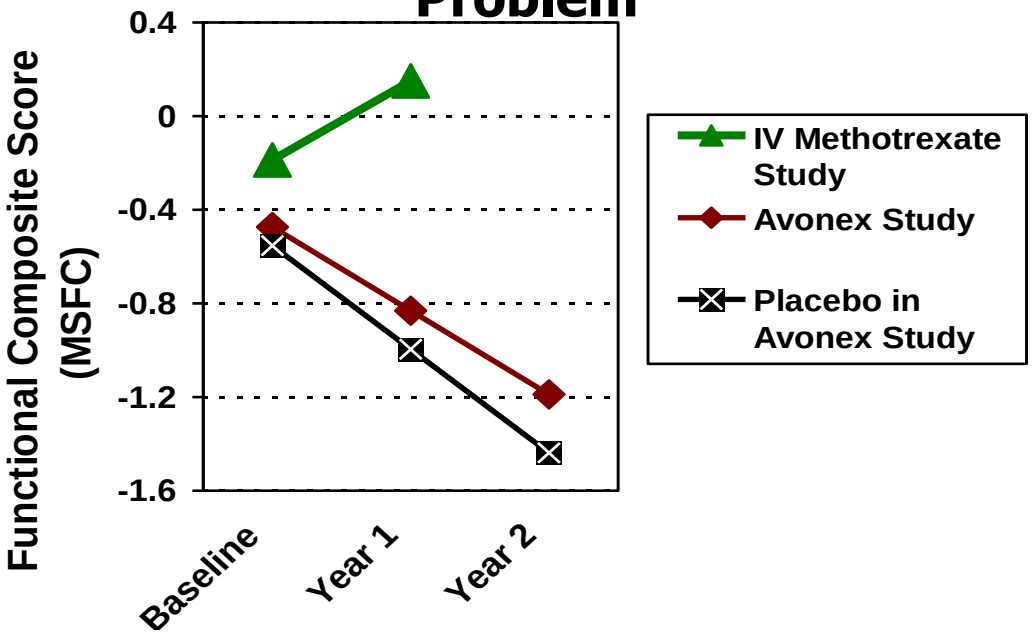
Here's How Verrow Was Born

In Early 2000's,Physicians At RNI Used IV Methotrexate with Leucovorin Rescue to Treat Multiple Sclerosis

High Dose IV Methotrexate By Itself Helps MS

But Kidney Toxicity Is a major Problem



1. Cohen JA, et.al. *Neurology*. Sep 10 2002;59(5):679-87.

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US006903100B2

(12) **United States Patent**
Rowe

(10) **Patent No.: US 6,903,100 B2**
(45) **Date of Patent: Jun. 7, 2005**

(54) **USE OF REGULARLY SCHEDULED HIGH DOSE INTRAVENOUS METHOTREXATE THERAPY, WITH INTERIM ADMINISTRATION OF IMMUNOMODULATORY AGENTS, TO TREAT MULTIPLE SCLEROSIS AND OTHER DISEASES OF THE CENTRAL NERVOUS SYSTEM**

(75) Inventor: **Vernon D. Rowe**, Kansas City, MO (US)

(73) Assignee: **MidAmerica Neuroscience Research Foundation**, Kansas City, MO (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 274 days.

(21) Appl. No.: **10/128,947**

(22) Filed: **Apr. 24, 2002**

(65) **Prior Publication Data**

US 2003/0008875 A1 Jan. 9, 2003

Related U.S. Application Data

(60) Provisional application No. 60/288,567, filed on May 3, 2001.

(51) **Int. Cl.**[7] **A61K 31/525**; A61K 31/555; A61K 31/275; A61K 39/38; A61K 45/00

(52) **U.S. Cl.** **514/251**; 514/186; 514/521; 514/638; 514/742; 424/184.1; 424/279.1

(58) **Field of Search** 514/251, 186, 514/521, 903, 889, 638, 742, 825; 424/184.1, 810, 279.1

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High-dose methotrexate with leucovorin rescue: For monumentally severe CNS inflammatory syndromes

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ABSTRACT

Background: At sufficiently high doses, methotrexate (HDMTX) achieves substantial CNS penetration, whereas other tissues can be rescued from the effects of HDMTX by leucovorin rescue (LR), which does not penetrate the blood-brain barrier.
Objectives: To report on the efficacy and safety of HDMTX with LR (HDMTX-LR), in the treatment of acute demyelinating inflammatory CNS syndromes refractory to conventional immunotherapy.
Methods: We performed a retrospective chart review of 12 patients treated (6 multiple sclerosis [MS], 4 neuromyelitis optica [NMO], and 2 Sjogren's syndrome myelopathy [SSM]) with HDMTX-LR after failing to improve, or exhibiting worsening following conventional immunotherapy. 11 patients were followed for a total of 6 months following HDMTX-LR (one was lost to follow up after 1 month); and clinical findings were documented at 1 month, 3 months, and 6 months following HDMTX-LR therapy.

Answers to Questions About Methotrexate Led to Other Discoveries

- How can we make high dose iv methotrexate safer ?
- How does it work in MS?
- **Captisol** by John Siebert, then CEO of **Cydex**
- To answer these questions, we needed a **basic science laboratory, and close cooperation between PhD and MD investigators.**
- Results of the laboratory work led to **Nephrotoxicity Reduction** for **Other Drugs and Pipelines—a "platform" technology**
- But **which ones** should we develop first? Complex question involving **science, regulatory, and cost** factors
- Long story short—**Iodinated Contrast:** Captisol-enabled iohexol
- **Geoff Hartzler--**mentorship during startup formation

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Verrow: An Example of the Bedside-To-Bench-To-Bedside Approach To Drug Development

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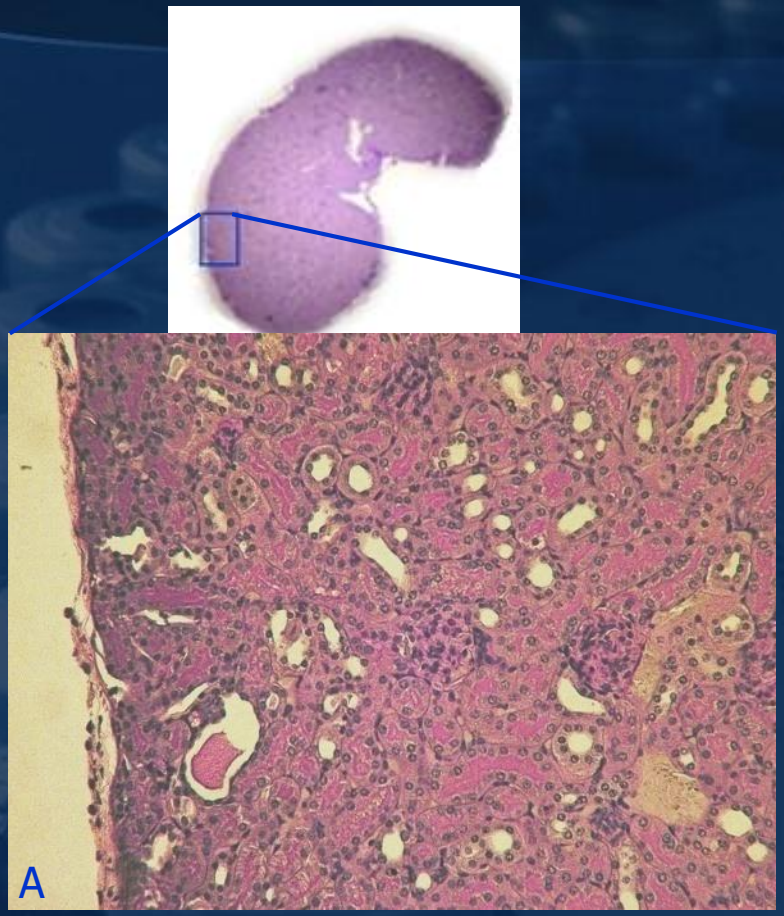
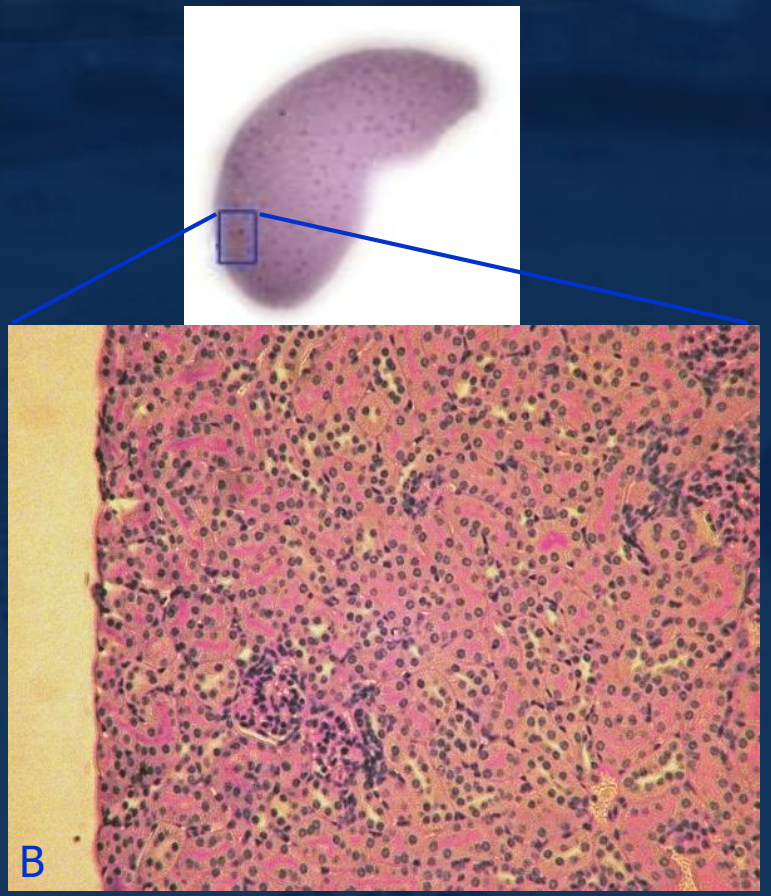
Captisol Blocks Kidney Damage by Methotrexate and Other Nephrotoxic Drugs, Like Iodinated Contrast



Tubular dilatation, degeneration, and cast formation 48 hours after 1.5 gI/kg **Iohexol** administration



Absence of renal pathology 48 hours after 1.5 gI/kg **Captisol-Enabled Iohexol** administration

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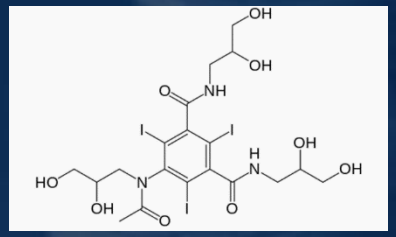
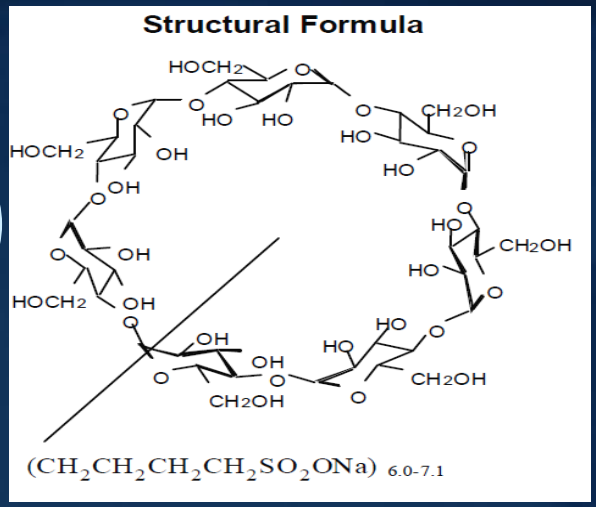
Contrast-Induced Acute Kidney Injury: Iohexol and Captisol



Iohexol

Captisol



Captisol-Enabled Iohexol

Captisol-Enabled Iohexol
1 molecule of Captisol per 40 molecules of Iohexol.

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US008277779B2

(12) **United States Patent**
Rowe

(10) **Patent No.: US 8,277,779 B2**
(45) **Date of Patent: *Oct. 2, 2012**

(54) **COMPOSITIONS USEFUL FOR REDUCING NEPHROTOXICITY AND METHODS OF USE THEREOF**

(76) Inventor: **Vernon D. Rowe**, Shawnee, KS (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 431 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **12/641,708**

(22) Filed: **Dec. 18, 2009**

(65) **Prior Publication Data**

US 2010/0093664 A1 Apr. 15, 2010

Related U.S. Application Data

(63) Continuation of application No. 11/753,883, filed on May 25, 2007, now Pat. No. 7,658,913, which is a continuation-in-part of application No. 11/562,924, filed on Nov. 22, 2006, now abandoned.

(60) Provisional application No. 60/740,142, filed on Nov. 28, 2005, provisional application No. 60/778,037, filed on Mar. 1, 2006.

(51) **Int. Cl.**
A61K 49/04 (2006.01)

(52) **U.S. Cl.** **424/9.43**; 424/9.4

(58) **Field of Classification Search** 424/9.43, 424/9.4

See application file for complete search history.

(56) **References Cited**

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WO	WO 03/053475	7/2003
WO	WO 2007-062403	5/2007

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US008192721B2

(12) **United States Patent**
Rowe

(10) **Patent No.: US 8,192,721 B2**
(45) **Date of Patent: Jun. 5, 2012**

(54) **COMPOSITIONS USEFUL FOR REDUCING TOXICITY ASSOCIATED WITH GADOLINIUM-BASED CONTRAST AGENTS**

(75) Inventor: **Vernon D. Rowe**, Shawnee, KS (US)

(73) Assignee: **Verrow Pharmaceuticals, Inc.**, Lenexa, KS (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 596 days.

(21) Appl. No.: **12/333,168**

(22) Filed: **Dec. 11, 2008**

(65) **Prior Publication Data**

US 2009/0155181 A1 Jun. 18, 2009

Related U.S. Application Data

(60) Provisional application No. 61/013,456, filed on Dec. 13, 2007.

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Years Later the Mechanism of Action Finally Found Captisol—An Apoptosis Inhibitor

Preclinical Studies of a Kidney Safe Iodinated Contrast Agent

Elizabeth S. Rowe, Vernon D. Rowe, Sangita Biswas, Gerold Mosher, Lovella Insisienmay, Marlies K. Ozias, Michael R. Gralinski, John Hunter, James S. Barnett

From the Rowe Neurology Institute, Lenexa, KS (VDR, SB, LI, MKO, JH, JSB); Verrow Pharmaceuticals, Inc, Lenexa, KS (ESR, GM); and CorDynamics, Inc, Chicago, IL (MRG).

ABSTRACT

BACKGROUND AND PURPOSE: Contrast-induced acute kidney injury (CI-AKI) is a serious complication of the use of iodinated contrast agents. This problem is particularly acute in interventional neurology and interventional cardiology, probably due to the intra-arterial route of injection, high contrast volumes, and preexisting risk factors of these patients. In an attempt to develop a contrast agent that is less damaging to the kidneys, we have studied the effects of adding a small amount of the substituted cyclodextrin, sulfobutyl-ether-β-cyclodextrin (SBECD), to iohexol in rodent models of renal toxicity.

METHODS: Renally compromised mice and rats were injected with iohexol and iohexol-SBECD via the tail vein. The renal pathology, creatinine clearance, and survival benefits of iohexol-SBECD were studied. The safety of direct intra-arterial injection of the iohexol-SBECD formulation was studied in a dog heart model system. Mechanism of action studies in cell culture model using a human kidney cell line was performed using flow cytometry.

RESULTS: Nephrotoxicity was significantly reduced using iohexol-SBECD compared to iohexol alone, at mole ratios of iohexol:SBECD of 1:0.025. SBECD increased survival from 50% to 88% in a rat survival study. In the dog heart model, iohexol-SBECD

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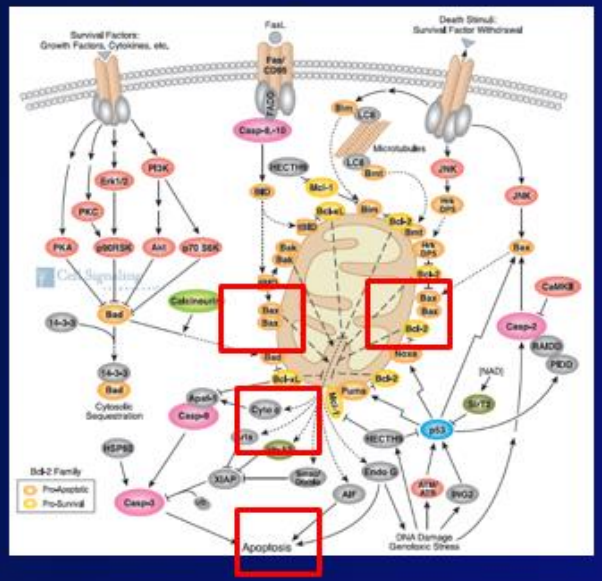
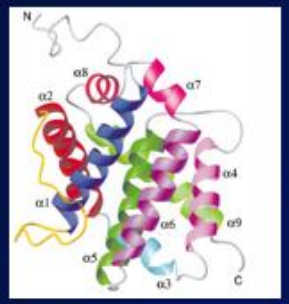
Mitochondrial Control of Apoptosis: Signaling protein BAX





BAX

Conformational Change, Insertion into Mitochondrial Membrane, Creating Pores

Release of Cytochrome C into cytoplasm Which begins apoptotic cascade

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Verrow Team at the FDA for Pre--IND Meeting on Veropaque

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Contrast-Induced Acute Kidney Injury Still a Major Problem

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Outcomes after Angiography with Sodium Bicarbonate and Acetylcysteine

S.D. Weisbord, M. Gallagher, H. Jneid, S. Garcia, A. Cass, S.-S. Thwin, T.A. Conner, G.M. Chertow, D.L. Bhatt, K. Shunk, C.R. Parikh, E.O. McFalls, M. Brophy, R. Fergus... H. Wu, M. Andrzejczyk, J. Myles, J. Kaufman and P.M. P...

BACKGROUND

Intravenous sodium bicarb... acute kidney injury and as... definitive evidence of their...

METHODS

...

Table 3. Primary and Secondary End Points.

Outcome	Sodium Bicarbonate (N=2511)	Sodium Chloride (N=2482)	Odds Ratio (95% CI)	P Value	Acetylcysteine (N=2495)	Placebo (N=2498)	Odds Ratio (95% CI)	P Value
	no. of patients (%)				*no. of patients (%)*			
Primary end point*	110 (4.4)	116 (4.7)	0.93 (0.72–1.22)	0.62	114 (4.6)	112 (4.5)	1.02 (0.78–1.33)	0.88
Secondary end points								
Contrast-associated acute kidney injury†	239 (9.5)	206 (8.3)	1.16 (0.96–1.41)	0.13	228 (9.1)	217 (8.7)	1.05 (0.87–1.28)	0.58
Death by 90 days	60 (2.4)	68 (2.7)	0.87 (0.61–1.24)	0.43	67 (2.7)	61 (2.4)	1.10 (0.78–1.57)	0.59
Need for dialysis by 90 days	32 (1.3)	29 (1.2)	1.09 (0.65–1.81)	0.73	30 (1.2)	31 (1.2)	0.97 (0.58–1.60)	0.90
Persistent kidney impairment by 90 days	28 (1.1)	25 (1.0)	1.10 (0.64–1.91)	0.71	26 (1.0)	27 (1.1)	0.96 (0.56–1.66)	0.89
Hospitalization with acute coronary syndrome, heart failure, or stroke by 90 days	272 (10.8)	251 (10.1)	1.08 (0.90–1.29)	0.40	244 (9.8)	279 (11.2)	0.86 (0.71–1.04)	0.11
All-cause hospitalization by 90 days	1071 (42.7)	1052 (42.4)	1.01 (0.90–1.13)	0.85	1069 (42.8)	1054 (42.2)	1.03 (0.91–1.15)	0.64

* The primary end point was a composite of death, the need for dialysis, or a persistent increase of at least 50% from baseline in the serum creatinine level at 90 days. Data regarding 90-day creatinine levels were missing in 119 patients (4.7%) in the sodium bicarbonate group, 103 (4.1%) in the sodium chloride group, 105 (4.2%) in the acetylcysteine group, and 117 (4.7%) in the placebo group.

† Contrast-associated acute kidney injury was defined as an increase in serum creatinine of at least 25% or at least 0.5 mg per deciliter (44 μmol per liter) from baseline at 3 to 5 days after angiography. Data regarding serum creatinine levels on days 3 to 5 were missing in 212 patients (8.4%) in the sodium bicarbonate group, 229 (9.2%) in the sodium chloride group, 210 (8.4%) in the acetylcysteine group, and 231 (9.2%) in the placebo group.

The NEW ENGLAND JOURNAL of MEDICINE

Verrow Pharmaceuticals

The Verrow Story—Summary

- Verrow applies for **patents**
- Verrow becomes a **C-corporation**, Verrow Pharmaceuticals, Inc., acquires angel investors in Series A round
- Meets with **FDA on three drugs**, seeks further capital in a difficult environment
- **Patents granted or abandoned** according to development costs and market potential, and additional patents prosecuted
- **Captisol-Enabled Iohexol** focus of development
- **Continued research** and discovery on Mechanism of Action
- **Note--**Verrow received three unfavorable licensing offers over the years, which were rejected (Kenny Rogers), and Mike Hird (the pain of a bad deal lasts a lot longer than no deal at all)
- **2018--Verrow M&A by Ligand Pharmaceuticals, Inc.**

Verrow Pharmaceuticals

January 18, 2018

Ligand Establishes Program to Develop Captisol-Enabled, Next-Generation Contrast Agents for Diagnostic Imaging

Focus will be on hospital-based products that could benefit from reduced renal toxicity

Leverages Captisol® and new intellectual property from Verrow Pharmaceuticals acquisition

SAN DIEGO--(BUSINESS WIRE)-- **Ligand Pharmaceuticals Incorporated (NASDAQ: LGND)** announces initiation of a program to develop contrast agents with reduced renal toxicity. Contrast agents are injectable solutions used during diagnostic imaging

The Verrow Team

- Vernon Rowe, M.D., President, CEO, physician scientist, inventor
- Elizabeth Rowe, Ph.D., MBA, COO
- John Hunter, Psy.D., Chief clinical officer
- Jerry Mosher, Ph.D., Chief Scientific Officer (previous)
- Sangita Biswas, Ph.D., Research Scientist (previous)
- Lovella Issisienmay, Laboratory Technician
- James Barnett, lab assistant (previous), premedical student
- John Burke, patent attorney, Akerman-Senterfit
- Mike Hird, business attorney, Pillsbury
- Randy Schultz, health care attorney, Lathrop
- Larry Swain, business attorney, Polsinelli

Verrow Pharmaceuticals

MD-PhD Cooperation, Mentorship, and Teamwork Is Crucial in the Verrow Story

Verrow Pharmaceuticals

What's Next for the Verrow Team?
Neurrow Pharmaceuticals, Inc.

- *Novel approaches to neurodegenerative disease*

Neurrow
Pharmaceuticals Inc

Or Maybe "Connecting the Dots" in a Clinical Syndrome

- Headache, Dysautonomia, Sleep Disordered Breathing, Hypermobility
- Frequently associated with autoimmune disorders (Hashimoto's Thyroiditis, Lupus, Sjogren's, GI disorders, ?psychiatric disorders)
- Poor vagal tone (vagal afferents from the gut control the immune system and other cardiovascular functions—POTS)
- Variably elevated Beighton hypermobility scores
- ? hEDS (Type 5, hypermobile Ehlers-Danlos)
- ?Hypermobility Spectrum Disorder
- A new syndrome?
- The central question: How do we improve the quality of life for these patients **before** a "cure" is found?

A Progressive Disorder—Nature *and* Nurture…

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Dermal fibroblast-to-myofibroblast transition sustained by αvß3 integrin-ILK-Snail1/Slug signaling is a common feature for hypermobile Ehlers-Danlos syndrome and hypermobility spectrum disorders

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Hypermobility Spectrum Disorders
Fibroblast-to-myofibroblast transition
αvβ3 integrin
Snail1/Slug
Chronic generalized inflammation

ABSTRACT

Hypermobile Ehlers-Danlos syndrome (hEDS) is a heritable connective tissue disorder with unknown molecular basis mainly characterized by generalized joint hypermobility, joint instability complications, and minor skin changes. The phenotypic spectrum is broad and includes multiple associated symptoms shared with chronic inflammatory systemic diseases. The stricter criteria defined in the 2017 EDS nosology leave without an identity many individuals with symptomatic joint hypermobility and/or features of hEDS; for these patients, the term Hypermobility Spectrum Disorders (HSD) was introduced. We previously reported that *in vitro* cultured hEDS and HSD patients' skin fibroblasts show a disarray of several extracellular matrix (ECM) components and dysregulated expression of genes involved in connective tissue homeostasis and inflammatory/pain/immune responses. Herein, we report that hEDS and HSD skin fibroblasts exhibit *in vitro* a similar myofibroblast-like phenotype characterized by the organization of α-smooth muscle actin cytoskeleton, expression of OB-cadherin/cadherin-11, enhanced migratory capability associated with augmented levels of the ECM-degrading metalloproteinase-9, and altered expression of the inflammation mediators CCN1/CYR61 and CCN2/CTGF. We demonstrate that in hEDS and HSD cells this fibroblast-to-myofibroblast transition is triggered by a signal transduction pathway that involves αvß3 integrin-ILK complexes, organized in focal adhesions, and the Snail1/Slug

The Journal of Clinical Investigation

Rescuing the physician-scientist workforce: the time for action is now

Dianna M. Milewicz,[1] Robin G. Lorenz,[2] Terence S. Dermody,[3] Lawrence F. Brass,[4] and the National Association of MD-PhD Programs Executive Committee[5]

[1]Department of Internal Medicine, University of Texas Health Science Center at Houston, Houston, Texas, USA. [2]Department of Pathology, University of Alabama at Birmingham, Birmingham, Alabama, USA. [3]Departments of Pediatrics and Pathology, Microbiology, and Immunology, Vanderbilt University School of Medicine, Nashville, Tennessee, USA. [4]Departments of Medicine and Pharmacology, University of Pennsylvania, Philadelphia, Pennsylvania, USA. [5]The National Association of MD-PhD Programs Executive Committee is detailed in the Supplemental Acknowledgments.

The 2014 NIH Physician-Scientist Workforce (PSW) Working Group report identified distressing trends among the small proportion of physicians who consider research to be their primary occupation. If unchecked, these trends will lead to a steep decline in the size of the workforce. They include high rates of attrition among young investigators, failure to maintain a robust and diverse pipeline, and a marked increase in the average age of physician-scientists, as older investigators have chosen to continue working and too few younger investigators have entered the workforce to replace them when they eventually retire. While the policy debates continue, here we propose four actions that can be implemented now. These include applying lessons from the MD-PhD training experience to postgraduate training, shortening the time to independence by at least 5 years, achieving greater diversity and numbers in training programs, and establishing Physician-Scientist Career Development offices at medical centers and universities. Rather than waiting for the federal government to solve our problems, we urge the academic community to address these goals by partnering with the NIH and national clinical specialty and medical organizations.

In June 2014, the NIH Physician-Scientist Workforce (PSW) Working Group completed a year of data collection and deliberation, and released a report about the status of the PSW (1). The report is a combination of good news and bad news. The good news is that, despite the decline in the NIH budget, the size of the PSW has remained relatively stable. The bad news is that the current demographics, diversity, and career progression of this workforce raise concerns about the future. For a start, although apparently stable in size, the PSW is even smaller than many of us realized, and the apparent stability has hidden important demographic trends. In

At the same time that the PSW has remained stable in size, data in the report show that the average age of the workforce is rising, as older investigators remain employed and younger investigators have not emerged in sufficient numbers. The average age at which a physician-scientist received his or her first NIH R01 grant in 2011 was 44 years for MD-PhDs and 45 years for MDs: approximately 10 years older than in 1980 (2). R01-funded investigators (physicians and non-physicians) younger than 37 years have all but disappeared, and the time from graduating medical school to obtaining a first faculty position has increased to over 10 years for MD-PhDs and even longer for

J Clin Invest. 2015;125(10):3742–3747. doi:10.1172/JCI84170.

Recommendations of the NIH Physician-Scientist Workforce Working Group—Some Good, Some Unrealistic

- Continue MSTP programs (8 yrs) and share results
- Shorten time to independence by 5 years (?)
  - Exposure during fellowship, residency, and others (+)
  - Improve transition to independence--restructure grants using K99/R00 grants (+)
- Improve demographic diversity in Physician Scientist Training Programs (increase women and minorities) (?)
- Centralize mentorship of trainees at all levels—institutionally and nationally (?)

Milewicz et al, J Clin Invest. 2015

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Physician Scientist Training in the United States: A Survey of the Current Literature

R. O. Kosik[1], D. T. Tran[2], Angela Pei-Chen Fan[3], G. A. Mandell[1], D. C. Tarng[3], H. S. Hsu[3], Y. S. Chen[3], T. P. Su[3], S. J. Wang[3], A. W. Chiu[3], C. H. Lee[3], M. C. Hou[3], F. Y. Lee[3], W. S. Chen[1], and Q. Chen[4]

Abstract

The declining number of physician scientists is an alarming issue. A systematic revi... performed, so as... for the training o...

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Angela Pei-Chen Fan,...

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Table 2. Sample, Methods, and Outcomes.

Programs	Sample size	Time to follow-up (years)	Academic employment (%)	Graduates with research grants (%)	Publications (M ± SD)
Medical Scientist Training Program (MSTP)	410	5–25	83 (64; 65; 79; 67)	NIH: 78 (60; 76; 65; 61) Other federal: 19 (15%; 37; 19; 20) Private industry: 33 (40; 15; 24; 41) Private foundation: 74 (46; 58; 62; 48) Other: 53 (46; 56; 58; 52)	1975 Cohort: 51.2 ± 38.3 1980 Cohort: 46.8 ± 38.9 1985 Cohort: 25 ± 20.1 1990 Cohort: 13.5 ± 12.5
Duke MD-PhD Program	107	5–25	62	NIH: 68 1970–1974 Cohort: 100 1985–1990 Cohort: 40	N/A
Mayo Clinic MD-PhD Program	32	5–17	60	Any source: 38* NIH: 31	First author: 7.2 ± 6.3** (8.3)# Any author: 18.2 ± 20.1*** (24.1)
Clinician Investigator Training Program (CI)	64	5–15	77	Any source: 67* NIH: 27	First author: 9.7 ± 7.8** (9.5) Any author: 26.5 ± 24.5*** (25.7)
Mayo Clinic National Research Service Award—T32 Fellowship Training Grants (NRSA-T32)	78	5–15	62	Any source: 41* NIH: 15	First author: 6.7 ± 8.0** (6.4) Any author: 17.9 ± 26.3*** (16.1)

(continued)

Rowe: Suggestions for Sustaining and Increasing the Physician Scientist "Workforce"--**Grants**

- Continue **MSTP** Programs, but **create other programs** based on institutional capabilities, as in Kosik et al.
- **NIH** should **maximize** spending on needs-driven research by **incentivizing** grant submissions with both MD and PhD Co-Principle Investigators, and MD physician scientists alone
- **Study section** adjustments
- **Priority score weighting** of study sections in favor of MD and PhD teams
- **Weigh patents more than publications** in the granting process

Rowe: Suggestions for Sustaining and Increasing the Physician Scientist "Workforce"--**Training**

- **Weight medical school admission policies** towards students interested in science
- Institute **debt forgiveness** programs for trainees year for year for postgraduate scientific education
- Expose **residents and fellows**, as well as **premedical and medical students**, to the **tools of basic science**
- **Intersperse basic science and clinical exposure** in a **flexible** paradigm
- Make **PhD investigators** a part of every **rounding team**
- Apply a **modular startup model**, like RNI and Verrow, to drug and device development
- **Facilitate interaction** between those **startups** and **academics**
- **Technology Transfer** policies may need to be **changed**

Verrow Pharmaceuticals

Advice to Young Physician Scientists
Seven Principles: An Approach To the Practice of Medicine

- The **problem** is the **problem**, so pick an important one to solve
- **Look** where the **light isn't**
- **Seek out mentors** to show the way
- **Believe** your **data**
- **Beware** of **animal models**—they rarely reflect human disease, though they're easy to study
- **Survey** modern **basic science methods** as **tools to solve a clinical puzzle**
- **Never, ever give up**

Thank you!

Call me if you have questions.
I'd be happy to talk with you!

Verrow Pharmaceuticals