

Dennis M. Fisher, M.D.

Contact Information:

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1997-Present: Principal

The “P Less Than” Company, San Francisco, CA

Working with numerous pharmaceutical companies (AGY Technologies, Abbott, Acura, Adolor, Alavita, Alexza, Altea Therapeutics, Anthera, Astellas, Baxter, Biocryst, Brookwood, Burroughs Wellcome, Cara Therapeutics, Cardiome, Cogentus, Cognition, DepoMed, DURECT, DynPort Vaccines, Endo Pharmaceuticals, Epiphany, Exelixis, GeoMed, Glaxo Wellcome, GSK, iMedd, Intermune, Jazz, Johnson & Johnson, MAP Pharmaceuticals, Medtronic, Neurogen, NeuroMed Technologies, Nippon Organon, NovoNordisk, NPS Pharma, Organon, Pharmacofore, Prestwick Pharmaceuticals, Protein Design Labs, Sciele, Sention, SNDC, Telik, Vanda, Valeant, Yamanouchi, YM Biosciences [Delex]) in a variety of roles. This includes pharmacokinetic analysis (including population techniques) and simulation of preclinical and phase 1-4 clinical trials, development of pharmacodynamic models, various pharmacometric analyses, and evaluation of failed clinical trials (including identification of the causes of failure and development of revised trial designs). Assisted these companies in the development of clinical investigation plans and protocols, focussing particular on optimizing dosing regimens. Advised some of these companies regarding NDAs and ex-US regulatory packages prior to submission. Assisted companies in preparation for and/or at FDA and ex-US regulatory meetings. Assisted companies in the review of safety events prior to NDA submission.

2003-Present: Principal and Founder

NDA Partners

NDA Partners is a unique international consultancy with a single focus—to dramatically improve the success rate and development speed of our clients’ biopharmaceutical and medical device discoveries. Working primarily with investor-driven emerging companies, we help our clients make the critical decisions with respect to their product development investments, recognize and understand the scientific and regulatory issues that will impact their programs, avoid the common pitfalls that have derailed other companies and drug development programs, and design and implement optimal product development and regulatory programs. Clients have included Care Capital, DPharm, Inotek, M Pharma, Orqis, Vion, and Warburg Pincus.

2001-2003: Vice President of Medical Affairs

2000-2002: Medical Director

DURECT Corporation, Cupertino, CA

Sole physician in startup pharmaceutical company. Responsible for development, implementation, evaluation, and reporting of clinical investigation plan for lead product, Chronogesic Sufentanil Pain Therapy System. Three trials (a critical phase 2 trial, a pharmacokinetics trial, and a pilot phase 3 trial) were completely successfully and the phase 3 program was initiated. Also responsible for identification, evaluation, and implementation of other compounds for development using DURECT's depot technologies. An IND was filed for one of these programs. A second program completed "proof of concept". For these programs and others, I led or participated actively in regulatory meetings including FDA (CDER, CDRH, Office of the Ombudsman), MPA (Sweden), MCA (UK), and CPMP (EU). Worked with DURECT's business development group to partner the lead product; this included initiating contact with numerous pharmaceutical companies, presenting the development plan to these companies, and participating in their diligence process. Through DURECT's finance group, met with numerous investors to assist in their diligence.

1998-2000: Consultant

Pharsight Corporation, Mountain View, CA

Performed clinical trial simulation for three clients, Protein Design Labs, DURECT, and Anesta. In one instance, advised a client that, based on simulations, a clinical trial design was likely to fail. The client decided to proceed with the trial, it failed, the development program was placed on "clinical hold" by FDA. Subsequently, the client asked for simulation of additional trial designs in order to permit resumption of the clinical program.

1981-2000: Faculty Member

Department of Anesthesia, University of California, San Francisco, CA

Joined the faculty as an Assistant Professor of Anesthesia and Pediatrics in 1981, promoted to Associate Professor in 1987, then to Professor (tenured) in 1991. Performed numerous clinical studies and pharmacokinetic analyses, supported either by funds from a series of NIH Research Awards, grants or awards from pharmaceutical companies, or grants from UCSF. Became an Associate Editor of Anesthesiology in 1988, joined the Editorial Board from 1992-2000 including six years as Editor of the Medical Intelligence/Review Article section of the journal. Employed on a part-time basis by FDA (Special Government Employee) as a Primary Reviewer of several NDAs, including the critical safety review of a potent opioid.

EDUCATION:

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| Bachelor of Science, Massachusetts Institute of Technology, Cambridge, Massachusetts | 1968-72 |
| Master's in City Planning, Massachusetts Institute of Technology | 1971-72 |
| Doctor of Medicine, Yale University, New Haven, Connecticut | 1972-76 |
| Internship (pediatrics), The Children's Hospital of Philadelphia | 1976-77 |
| Residency (pediatrics), The Children's Hospital of Philadelphia | 1977-78 |
| Residency (anesthesia), Hospital of the University of Pennsylvania, Philadelphia | 1978-80 |
| Fellow (pediatric anesthesia and critical care medicine), The Children's Hospital of Philadelphia | 1980 |
| Research fellow (anesthesia), University of California, San Francisco | 1981 |
| <i>In vitro</i> drug metabolism, Laboratory of Hepatic Pathophysiology, INSERM, Clichy, France, Director: Dr. Dominique Pessayre (sabbatical) | 1988-89 |

POSITIONS HELD:

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| DURECT Corporation | |
| Medical Director | 2000-03 |
| Vice President for Medical Affairs | 2001-03 |
| Consultant | 2003- |
| University of California, San Francisco: | |
| Assistant Professor of Anesthesia and Pediatrics in Residence | 1981-87 |
| Associate Professor of Anesthesia and Pediatrics | 1987-91 |
| Professor of Anesthesia and Pediatrics | 1991-2000 |
| Moffitt-Long Hospitals: | |
| Attending Physician, Pediatric Intensive Care Unit | 1981-88 |
| Acting Director, Pediatric Anesthesia | 1986-88 |
| Director, Remote Anesthesia | 1990-92 |
| Cardiovascular Research Institute: | |
| Scientific Staff | 1986-2000 |

SPECIALTY MEDICAL CERTIFICATIONS:

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| American Board of Pediatrics | 1981 |
| American Board of Anesthesiology | 1982 |

MEDICAL LICENSURE:

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| California | 1980 |
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UNIVERSITY AND PUBLIC SERVICE:

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| UCSF Departmental Committees: | |
| Resident Selection Committee | 1981-84,89-91,95-96 |
| Saturday Morning Conference Committee | 1984 |
| Mandatory Fourth Year Committee | 1984 |
| Committee for the Evaluation of Non-clinical Time | 1984 |
| Computer Committee | 1984-2000 |
| Chairman | 1991-2000 |
| Research Committee | 1984- |
| Departmental Meeting Committee | 1985-87 |
| Fellowship Selection Committee | 1985-90 |
| Finance Committee | 1989-98 |
| Long Range Planning Committee | 1993-94 |
| UCSF Extramural Committees: | |
| Scientific Advisory Board, Association of University Anesthesiologists | 1990-93 |
| Chairman, Subcommittee on Pediatric Anesthesia, American Society of Anesthesiologists | 1992-95 |
| Committee on Scientific Papers, American Society of Anesthesiologists | 1992-94 |
| Educational Advisory Committee, Society for Pediatric Anesthesia | 1992-95 |
| Subcommittee of Neuromuscular Transmission, American Society of Anesthesiologists | 1998-2000 |

Subcommittee of Anesthetic Action, American Society of Anesthesiologists 1998-2000

Editorial Boards:

Anesthesiology (Associate Editor) 1989-91

Anesthesiology (Editor) 1991-2000

Anesthesiology (Editor for Medical Intelligence/Review Articles) 1995-2000

Consulting Editorial Services:

Acta Anaesth Scand 1998

American Journal of Physiology 1993

Anesthesia and Analgesia 1984,1991-

Anesthesiology 1981-

Canadian Journal of Anesthesia 1987

Clinical Pharmacology and Therapeutics 1999

Critical Care Medicine (abstracts) 1984-90

Journal of Clinical Anesthesia 1992

Journal of Pediatric Gastroenterology and Nutrition 1992

Journal of Pharmacokinetics and Biopharmaceutics 1983,1989

Journal of Pharmacology and Experimental Therapeutics 1997-98

New England Journal of Medicine 1993-95, 1997-

Pharmacy and Therapeutics Forum 1983

Radiology 1992-

Consulting Services:

Food and Drug Administration, Committee on Anesthetics, Subcommittee to Establish Guidelines, 1990-1991

Anesthesia for Pediatric Patients for Painful Procedures, Oncology Department, Children's Hospital of Los Angeles, 1988-1992

Food and Drug Administration Center for Drug Evaluation and Research, Expert Specialist (Consultant), 1993-1994

Food and Drug Administration Committee on Anesthesia and Life Support, Subcommittee on Pediatric Sedation/Premedication, 1994

Food and Drug Administration Committee on Anesthesia and Life Support, Consultant Reviewer, 1995-1996

Grant Reviews:

Program Project Site Visitor, National Cancer Institute, Seattle, 1994

Grant Reviewer, Veteran's Administration, 1997

Multicenter Trial Grant Reviewer, National Institutes of Health, 1999

Grant Reviewer, Frontiers in Anesthesia, International Anesthesia Research Society, 1999

Grant Reviewer, Veteran's Administration, 2002

Visiting Professorships:

Sophia Children's Hospital, Rotterdam, Holland 1983

Hahnemann University 1984

The Pennsylvania State University, Hershey, Pa.

Loyola University 1986

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| University of Wisconsin Medical School | |
| The Medical College of Wisconsin | |
| Massachusetts General Hospital | |
| Children's Hospital Medical Center, Boston | |
| George Washington University | 1987 |
| Children's Hospital National Medical Center, Washington, D.C. | |
| State University of New York, Brooklyn | 1988 |
| Yale University | 1989 |
| Lund University, Sweden | |
| University of Chicago | |
| McGill University, Montreal | 1990 |
| Children's Hospital of Pittsburgh | 1991 |
| Northwestern University, Chicago | |
| New York University Medical Center | |
| West Virginia University | 1992 |
| Duke University | |
| Emory University | 1994 |
| University of Washington | |
| Oregon Health Sciences University | |
| Washington University | 1995 |
| Texas Children's Hospital | 1996 |
| Bowman Gray | |
| Northwestern University | |
| University of New Mexico | 1997 |
| Columbia University | |
| New York Hospital, Cornell University | 1998 |
| University of California, San Diego | 1999 |

PROFESSIONAL SOCIETIES:

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| California Society of Anesthesiologists | 1981- |
| American Society of Anesthesiologists | 1978- |
| Society of Critical Care Medicine | 1980- |
| American Academy of Pediatrics | 1981- |
| Association of University Anesthesiologists | 1984- |
| Association of Paediatric Anaesthetists of Great Britain and Ireland | 1986- |
| International Anesthesia Research Society | 1979- |

TEACHING:

Supervision and instruction of research fellows:

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|-------------------------|---------|
| Barbara Palmisano, M.D. | 1982-83 |
| Mark Singleton, M.D. | 1984 |
| Robert Hertzka, M.D. | 1985-86 |
| Jane Henderson, M.D. | 1986 |
| Drew Brodsky, M.D. | 1987 |
| Ian Gauntlett, M.D. | 1987-88 |

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| Eckhart Kuhls, M.D. | 1987-88 |
| Paul Bragg, M.D. | 1990-91 |
| Peter Wright, M.D. | 1992-94 |
| Paul Hart, M.D. | 1993-94 |
| Andrew Luks | 1995-96 |
| James Hsu, M.D. | 1997-98 |
| Matthias Paul, M.D. | 1999-2001 |

Supervision and instruction of students:

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| Alice Yeh, Medical Student, Northwestern University | 1990 |
| George Lee, Undergraduate Student, Harvard University | 1996 |
| Shuba Iyengar, Undergraduate Student, University of California, Berkeley | 1996 |

Miscellaneous:

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| Instructor, Basic Life Support | |
| Instructor, Pediatric Advanced Life Support | |
| Tutor, Workshop on Advanced Methods in Pharmacokinetics/ Pharmacodynamics, San Francisco, 1992, 1995, 1997, 1999, 2001; Sils-Maria, Switzerland, 1994, 1996, 1998, 2000, 2002; (Lecturers: Lewis Sheiner, M.D., Malcolm Rowland, Ph.D.) | |
| Course Director, Workshop on Advanced Methods in Pharmacokinetics/ Pharmacodynamics, San Francisco, 2004 | |
| Lecturer, Workshop on Advanced Methods in Pharmacokinetics/ Pharmacodynamics, Sils-Maria, Switzerland, 2006 | |
| Course Director, Workshop on Advanced Methods in Pharmacokinetics/ Pharmacodynamics, San Francisco, 1999, 2001; | |
| Tutor, NONMEM Short Course, Bethesda, 1992; San Francisco, 1994, 1995, 1996, 1997, Rockville, 1998 (Directed by Lewis Sheiner, M.D., and Stuart Beal, Ph.D.) | |
| Lecturer, Co-Director, Fisher / Shafer NONMEM Workshop, Newark, 2005; San Francisco, 2006 | |

AWARDS, HONORS AND GRANT SUPPORT:

Honors

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| Third prize, Residents Essay Contest, American Society of Anesthesiologists | 1981 |
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Funding: UCSF Intramural

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| Academic Senate Multi-User Equipment Grant (Principal Investigator, \$17,000) | 1984 |
| Academic Senate Committee on Research Opportunity Fund Award (Principal Investigator, \$7500) | 1986 |
| Academic Senate Committee on Research (Principal Investigator, \$3000) | 1987 |
| Research Evaluation and Allocation Committee (Coinvestigator, \$8000) | 1989-90 |
| Academic Senate Committee on Research (Coinvestigator, \$12,801) | 1990 |
| Academic Senate Committee on Research (Principal Investigator, shared equipment, \$9630) | 1991 |

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| Funding, Extramural: National Institutes of Health | |
| National Service Research Award (\$43,276) | 1980-82 |
| Paralysis — Its antagonism during anesthesia and surgery, (Coinvestigator, 30%) | 1983-85 |
| Muscle Relaxants and Antagonists in Pediatric Anesthesia, New Investigator's Award (\$107,000) | 1983-86 |
| Paralysis — its antagonism during anesthesia and surgery (Coinvestigator, 10%) | 1985-90 |
| Maturational Changes in Response to IV Anesthetic Drugs (RO1, principal investigator, \$327,559) | 1989-92 |
| Kinetics and dynamics of fentanyl anesthesia in neonates (RO1, principal investigator, \$769,188) | 1992-96 |

ORIGINAL ARTICLES

1. Fisher DM, O'Keeffe C, Stanski DR, Cronnelly R, Miller RD, Gregory GA: Pharmacokinetics and pharmacodynamics of *d*-tubocurarine in infants, children and adults. *Anesthesiology* 57:203-208, 1982
2. Fisher DM, Fahey MR, Cronnelly R, Miller RD: Potency determination for vecuronium (ORG NC45): Comparison of cumulative and single-dose techniques. *Anesthesiology* 57:309-310, 1982
3. Fisher DM, Frewen T, Swedlow DB: Increase in intracranial pressure during suctioning — Stimulation vs. rise in PaCO₂. *Anesthesiology* 57:416-417, 1982
4. Cronnelly R, Fisher DM, Miller RD, Gencarelli P, Nguyen-Gruenke L, Castagnoli N Jr: Pharmacokinetics and pharmacodynamics of vecuronium (ORG NC45) and pancuronium in anesthetized man. *Anesthesiology* 58:405-408, 1983
5. Rupp SM, Shinohara Y, Fisher DM, Miller RD, Castagnoli N: Pharmacokinetics and pharmacodynamics of 4-aminopyridine in anesthetized dogs. *J Pharmacol Exp Ther* 225:351-354, 1983
6. Fisher DM, Miller RD: Neuromuscular effects of vecuronium (ORG NC45) in infants and children during N₂O, halothane anesthesia. *Anesthesiology* 58:519-523, 1983
7. Fisher DM, Cronnelly R, Miller RD, Sharma M: Neuromuscular pharmacology of neostigmine in infants and children. *Anesthesiology* 59:220-225, 1983
8. Dailey P, Fisher DM, Shnider SM, Baysinger CL, Shinohara Y, Miller RD, Abboud TK, Kim KC: Pharmacokinetics, placental transfer, and neonatal effects of vecuronium and pancuronium administered during cesarean section. *Anesthesiology* 60:569-574, 1984
9. Fisher DM, Cronnelly R, Sharma M, Miller RD: Clinical pharmacology of edrophonium in infants and children. *Anesthesiology* 61:428-433, 1984
10. Miller RD, Rupp SM, Fisher DM, Cronnelly R, Fahey MR, Sohn YJ: Clinical pharmacology of vecuronium and atracurium. *Anesthesiology* 61:444-453, 1984

11. Palmisano BW, Fisher DM, Willis M, Gregory GA, Ebert PA: The effect of paralysis on oxygen consumption in normoxic children after cardiac surgery. *Anesthesiology* 61:518-522, 1984
12. Hennis PJ, Cronnelly R, Sharma M, Fisher DM, Miller RD: Metabolites of neostigmine and pyridostigmine do not contribute to antagonism of neuromuscular blockade in the dog. *Anesthesiology* 61:534-539, 1984
13. Fahey MR, Rupp SM, Fisher DM, Miller RD, Sharma M, Canfell C, Castagnoli K, Hennis PJ: The pharmacokinetics and pharmacodynamics of atracurium in patients with and without renal failure. *Anesthesiology* 61:699-702, 1984
14. Fisher DM, Castagnoli K, Miller RD: Vecuronium kinetics and dynamics in anesthetized infants and children. *Clin Pharmacol Ther* 37:402-406, 1985
15. Adzick NS, deLorimier AA, Harrison MR, Glick PL, Fisher DM: Major childhood tumor resection using normovolemic hemodilution anesthesia and hetastarch. *J Pediatr Surg* 20:372-375, 1985
16. Fahey MR, Rupp SM, Canfell C, Fisher DM, Miller RD, Sharma M, Castagnoli K, Hennis PJ: Effect of renal failure on laudanosine excretion in man. *Br J Anaesth* 57:1049-1051, 1985
17. Shi W-Z, Fahey MR, Fisher DM, Miller RD, Canfell C, Eger EI II: Laudanosine (a metabolite of atracurium) increases the minimum alveolar concentration of halothane in rabbits. *Anesthesiology* 63:584-588, 1985
18. Fisher DM, Robinson S, Brett CM, Perin G, Gregory GA: Comparison of enflurane, halothane and isoflurane for diagnostic and therapeutic procedures in children with malignancies. *Anesthesiology* 63:647-650, 1985
19. Fisher DM, Canfell PC, Fahey MR, Rosen JI, Rupp SM, Sheiner LB, Miller RD: Elimination of atracurium in humans: Contribution of Hofmann elimination and ester hydrolysis vs. organ-based elimination. *Anesthesiology* 65:6-12, 1986
20. Fisher DM, Rosen JI: A pharmacokinetic explanation for increasing recovery time following larger or repeated doses of nondepolarizing muscle relaxants. *Anesthesiology* 65:286-291, 1986
21. Singleton MA, Rosen JI, Fisher DM: Plasma concentrations of fentanyl in infants, children and adults. *Can J Anaesth* 34:152-155, 1987
22. Gambee AM, Hertzka RE, Fisher DM: Preoxygenation techniques: Comparison of 3-minutes and 4-breaths. *Anesth Analg* 66:468-470, 1987
23. Rupp SM, Castagnoli KP, Fisher DM, Miller RD: Pancuronium and vecuronium pharmacokinetics and pharmacodynamics in younger and elderly adults. *Anesthesiology* 67:45-49, 1987
24. Brett CM, Fisher DM: Thiopental dose-response relations in unpremedicated infants, children, and adults. *Anesth Analg* 66:1024-1027, 1987
25. Weiskopf RB, Reid IA, Fisher DM, Holmes MA, Rosen JI, Keil LC: Effects of fentanyl on vasopressin secretion in human subjects. *J Pharmacol Exp Ther* 242:970-973, 1987

26. Henderson JM, Brodsky DA, Fisher DM, Brett CM, Hertzka RE: Preinduction of anesthesia in pediatric patients with nasally-administered sufentanil. *Anesthesiology* 68:671-675, 1988 (accompanied by an editorial)
27. Singleton MA, Rosen JI, Fisher DM: Pharmacokinetics of fentanyl in the elderly. *Br J Anaesth* 60:619-622, 1988
28. Nussmeier NA, Moskowitz GJ, Weiskopf RB, Cohen NH, Fisher DM, Eger EI II: *In vitro* anesthetic washin and washout via bubble oxygenators: Influence of anesthetic, and gas and pump flows. *Anesth Analg* 67:982-987, 1988
29. London MJ, Sybert PE, Mangano DT, Fisher DM, Bainton CR, Hickey RF: Surface-induced hypothermia: Effects on coronary blood flow autoregulation and vascular reserve. *J Surg Research* 45:481-495, 1988
30. Caldwell JE, Castagnoli KP, Canfell PC, Fahey MR, Lynam DP, Fisher DM, Miller RD: Pipecuronium and pancuronium: A comparison of their pharmacokinetics and durations of action. *Br J Anaesth* 61:693-697, 1988
31. Fisher DM, Caldwell JE, Sharma M, Wirén J-E: The influence of bambuterol (carbamylylated terbutaline) on the duration of action of succinylcholine-induced paralysis in humans. *Anesthesiology* 69:757-759, 1988
32. Gauntlett IS, Fisher DM, Hertzka RE, Kuhls E, Spellman MJ, Rudolph C: Pharmacokinetics of fentanyl in neonatal humans and lambs: Effects of age. *Anesthesiology* 69:683-687, 1988
33. Hertzka RE, Gauntlett IS, Fisher DM, Spellman MJ: Fentanyl-induced ventilatory depression: Effects of age. *Anesthesiology* 70:213-218, 1989
34. Caldwell JE, Canfell PC, Castagnoli KP, Lynam DP, Fahey MR, Fisher DM, Miller RD: The influence of renal failure on the pharmacokinetics and duration of action of pipecuronium bromide in patients anesthetized with halothane and nitrous oxide. *Anesthesiology* 70:7-12, 1989
35. Nussmeier NA, Lambert ML, Moskowitz GJ, Cohen NH, Weiskopf RB, Fisher DM, Eger EI II: Washin and washout of isoflurane administered via bubble oxygenators during hypothermic cardiopulmonary bypass. *Anesthesiology* 71:519-525, 1989
36. Shi W-Z, Fahey MR, Fisher DM, Miller RD: Modification of central nervous system effects of laudanoline by inhaled anaesthetics. *Br J Anaesth* 63:598-600, 1989
37. Zeltzer LK, Jay SM, Fisher DM: The management of pain associated with pediatric procedures: Pharmacologic intervention for medical/surgical procedures. *Pediatr Clin N Amer* 36:941-964, 1989
38. Kitts JB, Fisher DM, Canfell PC, Spellman MJ, Caldwell JE, Heier T, Fahey MR, Miller RD: Pharmacokinetics and pharmacodynamics of atracurium in the elderly. *Anesthesiology* 72:272-275, 1990
39. Fisher DM, Canfell PC, Spellman M, Rosen JI, Miller RD: Pharmacokinetics and pharmacodynamics of atracurium in infants and children during N₂O-halothane anesthesia. *Anesthesiology* 73:33-37, 1990

40. Fisher D, Labbe G, Berson A, Tinel M, Loeper J, Larrey D, Pessayre D: Inhibition of rat liver estrogen 2/4-hydroxylase activity by troleandomycin. Comparison with erythromycin and roxithromycin. *J Pharmacol Exper Ther* 254:1120-1127, 1990
41. Spears RS, Yeh A, Fisher DM, Zwass MS: The "educated hand": Can anesthesiologists assess changes in neonatal pulmonary compliance manually? *Anesthesiology* 75:693-696, 1991 (accompanied by an editorial)
42. Fisher DM, Zwass MS: MAC of desflurane in 60% nitrous oxide in infants and children. *Anesthesiology* 76:354-356, 1992
43. Zwass MS, Fisher DM, Welborn LG, Coté CJ, Davis PJ, Dinner M, Hannallah RS, Liu LMP, Sarner J, McGill WA, Alifimoff JK, Embree PA, Cook DR: Induction and maintenance characteristics of anesthesia with desflurane and nitrous oxide in infants and children. *Anesthesiology* 76:373-378, 1992
44. Szenohradzky J, Fisher DM, Segredo V, Caldwell JE, Bragg P, Sharma M, Gruenke L, Miller RD: Pharmacokinetics and neuromuscular blocking effects of rocuronium bromide (ORG 9426) in patients with normal renal function or with renal failure. *Anesthesiology* 77:899-904, 1992
45. Bragg P, Fisher DM, Donati F, Meistelman C, Lau M, Sheiner LB: Comparison of twitch depression of the adductor pollicis and the respiratory muscles: Pharmacodynamic modeling without plasma concentrations. *Anesthesiology* 80:310-319, 1994
46. Cauldwell C, Lau M, Fisher DM: Is intramuscular mivacurium an alternative to intramuscular succinylcholine? *Anesthesiology* 80:320-325, 1994
47. Wright PMC, Hart P, Lau M, Sharma M, Gruenke L, Fisher DM: Cumulative characteristics of atracurium and vecuronium: A simultaneous clinical and pharmacokinetic study. *Anesthesiology* 81:59-68, 1994
48. Caldwell JE, Szenohradzky J, Segredo V, Wright PMC, McLoughlin C, Sharma ML, Gruenke LD, Fisher DM, Miller RD. The pharmacodynamics and pharmacokinetics of the metabolite 3-desacetylvecuronium (ORG 7268) and its parent compound, vecuronium, in human volunteers. *J Pharmacol Exp Ther* 270:1216-1222, 1994
49. Kelley S, Cauldwell C, Fisher DM, Lau, M, Sharma M, Weisiger R: Recovery of hepatic drug metabolic function following hypothermic preservation. *Anesthesiology* 82:251-258, 1995
50. Larijani GE, Gratz I, Afshar M, McDonald PA, Fisher DM. The effect of isoflurane vs. balanced anesthesia on rocuronium's pharmacokinetics and infusion requirement. *Pharmacotherapy* 15:36-41, 1995
51. Wright PMC, Hart P, Lau M, Brown R, Sharma ML, Gruenke L, Fisher DM. The magnitude and time course of vecuronium potentiation by desflurane versus isoflurane. *Anesthesiology* 82:404-411, 1995
52. Magorian T, Wood P, Caldwell JE, Fisher DM, Segredo V, Szenohradzky J, Sharma ML, Gruenke LD, Miller RD. The pharmacokinetics and neuromuscular effects of rocuronium in patients with liver disease. *Anesth Analg* 80:754-759, 1995

53. Hart PS, McCarthy GJ, Brown R, Lau M, Fisher DM: The effect of plasma cholinesterase activity on mivacurium infusion rates. *Anesth Analg* 80:760-763, 1995
54. Hart PS, Wright PMC, Lau M, Brown R, Sharma M, Miller RD, Gruenke L, Fisher DM: Edrophonium increases mivacurium concentrations during constant mivacurium infusion and large doses minimally antagonize paralysis. *Anesthesiology* 82:912-918, 1995
55. Vuksanaj D, Fisher DM: Pharmacokinetics of rocuronium in children aged 4-11 years. *Anesthesiology* 82:1104-1110, 1995
56. Kuhls E, Gauntlett I, Lau M, Brown R, Rudolph C, Teitel D, Fisher DM: Effect of increased intraabdominal pressure on hepatic extraction and clearance of fentanyl in neonatal lambs. *J Pharmacol Exp Ther* 274:115-119, 1995
57. Szenohradzky J, Lau M, Brown R, Sharma ML, Fisher DM: The effect of neostigmine on twitch tension and muscle relaxant concentration during infusion of mivacurium or vecuronium. *Anesthesiology* 83:83-87, 1995
58. Bragg P, Zwass MS, Lau M, Fisher DM: Opioid pharmacodynamics in neonatal dogs: Differences between morphine and fentanyl. *J Appl Physiol* 79:1519-1524, 1995
59. Caldwell JE, Lau M, Fisher DM: Atracurium vs. vecuronium in asthmatics: a blinded randomized comparison. *Anesthesiology* 83:986-989, 1995
60. Markakis DA, Hart PS, Lau M, Brown R, Fisher DM: Does age or pseudocholinesterase activity predict mivacurium infusion rate in children? *Anesth Analg* 82:39-43, 1995
61. Shangraw RE, Fisher DM: Pharmacokinetics of dichloroacetate in patients undergoing liver transplantation. *Anesthesiology* 84: 851-858, 1996
62. Reynolds LM, Lau M, Brown R, Fisher DM: Intramuscular rocuronium in infants and children: Dose ranging and tracheal intubating conditions. *Anesthesiology* 85:231-239, 1996 (accompanied by an editorial)
63. Lee GC, Iyengar S, Szenohradzky J, Caldwell JE, Wright PMC, Brown R, Lau M, Luks A, Fisher DM: Optimizing design of neuromuscular studies: Stabilization period and tetanic recruitment. *Anesthesiology* 86:48-54, 1997
64. Fisher DM, Szenohradzky J, Wright PMC, Lau M, Brown R, Sharma M: Pharmacodynamic modeling of vecuronium-induced twitch depression: Rapid plasma-effect site equilibration explains faster onset at resistant laryngeal muscles than at the adductor pollicis. *Anesthesiology* 86:558-566, 1997
65. Fisher DM, Wright PMC: Are plasma concentration values necessary for pharmacodynamic modeling of muscle relaxants? *Anesthesiology* 86:567-575, 1997
66. Viele MK, Weiskopf RB, Fisher DM: Renal effects and pharmacokinetics of recombinant human hemoglobin in humans. *Anesthesiology* 86:848-858, 1997
67. Fisher DM, Ramsay MAE, Hein HAT, Marcel RJ, Sharma M, Ramsay KJ, Miller RD: Pharmacokinetics of rocuronium during the three stages of liver transplantation. *Anesthesiology* 86:1306-1316, 1997

68. Birmingham PK, Tobin MJ, Henthorn TK, Fisher DM, Berkelhamer MC, Smith FA, Fanta KB, Coté CJ: Twenty-four hour pharmacokinetics of rectal acetaminophen in children: An old drug with new recommendations. *Anesthesiology* 87:244-252, 1997
69. Reynolds LM, Lau M, Brown R, Luks A, Sharma M, Fisher DM: Bioavailability of intramuscular rocuronium in infants and children. *Anesthesiology* 87:1096-1105, 1997
70. Talke P, Richardson CA, Scheinin M, Fisher DM: Postoperative pharmacokinetics and sympatholytic effects of dexmedetomidine. *Anesth Analg* 85:1136-1142, 1997
71. Luks AM, Zwass MS, Brown RC, Lau M, Chari G, Fisher DM: Opioid-induced analgesia in neonatal dogs: Pharmacodynamic differences between morphine and fentanyl. *J Pharmacol Exp Ther* 284:136-141, 1998
72. Weiskopf RB, Viele MK, Feiner J, Kelley S, Lieberman J, Noorani M, Leung JM, Fisher DM, Murray WR, Toy P, Moore MA: Human cardiovascular and metabolic response to acute, severe isovolemic anemia. *JAMA* 279:217-221, 1998
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