

## Chapter 43

### REFERENCES

1. Savege TM, Ramsay MAE, Curran JPJ, et al. Intravenous anaesthesia by infusion. A technique using alphaxalone/alphadolone (Althesin). *Anaesthesia*. 1975;30:757-764.
2. Goodchild CS, Robinson A, Nadeson R. Antinociceptive properties of neurosteroids. IV pilot study demonstrating the analgesic effects of alphadolone administered orally to humans. *Br J Anaesth*. 2001;86:528-534.
3. Lowenstein E, Hallowell P, Levine FH, et al. Cardiovascular response to large doses of intravenous morphine in man. *N Engl J Med*. 1969;281:1389-1393.
4. Leslie K, Clavisi O, Hargrove J. Target-controlled infusion versus manually-controlled infusion of propofol for general anaesthesia or sedation in adults. *Cochrane Database Syst Rev*. 2008;3:CD006059.
5. Alvis JM, Reves JG, Govier AV, et al. Computer assisted continuous infusions of fentanyl during cardiac anesthesia: comparison with a manual method. *Anesthesiology*. 1985;63:41-49.
6. Ausems ME, Vuyk J, Hug CC, Stanski DR. Comparison of a computer-assisted infusion versus intermittent bolus administration of alfentanil as a supplement to nitrous oxide for lower abdominal surgery. *Anesthesiology*. 1988;68:851-861.
7. Reves J, Glass PSA, Jacobs J. Midazolam and alfentanil: new anesthetic drugs for continuous infusion and an automated method of administration. *Mt Sinai J Med*. 1989;56:99-107.
8. White PF. Use of continuous infusion versus intermittent bolus administration of fentanyl or ketamine during outpatient anesthesia. *Anesthesiology*. 1983;59:294-300.
9. White PF, Dworsky WA, Horai Y, Trevor AJ. Comparison of continuous infusion of fentanyl or ketamine versus thiopental—determining the mean effective serum concentration for outpatient surgery. *Anesthesiology*. 1983;59:564-569.
10. Prys-Roberts C, Sear JW. Nonbarbiturate intravenous anaesthetics and continuous infusion anaesthesia. In: Prys-Roberts C, Hug CC, eds. *Pharmacokinetics of Anaesthetic Drugs*. Oxford, UK: Blackwell Scientific; 1984:128-156.
11. Prys-Roberts C. Cardiovascular effects of continuous intravenous anaesthesia compared with those of inhalational anaesthesia. *Acta Anaesthesiol Scand*. 1982;26(Suppl 75):10-17.
12. Sear JW. Pharmacokinetics and pharmacodynamic aspects of continuous infusion anaesthesia: concept of minimum infusion rate as index of equipotency for IV agents. *Clin Anaesth*. 1984;2(1):223-242.
13. Sear JW. Intravenous anaesthesia in the 1990s: a view from Europe. In: Dundee JW, Sear JW, eds. *Intravenous Anaesthesia—What Is New? Clinical Anaesthesiology: International Practice and Research*. London, UK Balliere Tindall; 1991:399-424.
14. Roberts FL, Dixon J, Lewis GTR, et al. Induction and maintenance of anaesthesia. A manual infusion scheme. *Anaesthesia*. 1988;43(Suppl):14-17.
15. Persson P, Nilsson A, Hartvig P, et al. Pharmacokinetics of midazolam in total I.V. anaesthesia. *Br J Anaesth*. 1987;59:548-556.
16. Persson MP, Nilsson A, Hartvig P, Tamsen A. Pharmacokinetics of midazolam in total intravenous anaesthesia. *Br J Anaesth*. 1987;59:548-556.
17. Thiel DR, Stanley TE, White W, et al. Midazolam and fentanyl continuous infusion anesthesia for cardiac surgery: a comparison of computer-assisted versus manual infusion systems. *J Cardiothorac Vasc Anesth*. 1993;7:300-306.
18. Scott JC, Ponganis KV, Stanski DR. EEG quantitation of narcotic effect: the comparative pharmacodynamics of fentanyl and alfentanil. *Anesthesiology*. 1985;62:234-241.
19. Mertens MJ, Engbers FH, Burm AG, Vuyk J. Predictive performance of computer-controlled infusion of remifentanyl during propofol-remifentanyl anaesthesia. *Br J Anaesth*. 2003;90:132-141.
20. Marsh BJ, White M, Morton N, Kenny GN. Pharmacokinetic model driven infusion of propofol in children. *Br J Anaesth*. 1991;67:41-48.
21. Schnider TW, Minto CF, Gambus PL, et al. The influence of method of administration and covariates on the pharmacokinetics of propofol in adult volunteers. *Anesthesiology*. 1998;88:1170-1182.
22. Minto CF, Schnider TW, Shafer SL. Pharmacokinetics and pharmacodynamics of remifentanyl. II. Model application. *Anesthesiology*. 1997;86:24-33.
23. Kruger-Thiemer E. Continuous intravenous infusion and multicompartment accumulation. *Eur J Pharmacol*. 1968;4:317-324.
24. Schwillden H. A general method for calculating the dosage scheme in linear pharmacokinetics. *Eur J Clin Pharmacol*. 1981;20:379-386.
25. Vaughan DP, Tucker GT. General theory for rapidly establishing steady state drug concentrations using consecutive constant rate intravenous infusions. *Eur J Clin Pharmacol*. 1975;9:235-238.
26. Vaughan DP, Tucker GT. General derivation of the ideal intravenous drug input required to achieve and maintain a

- constant plasma drug concentration. Theoretical application to lignocaine therapy. *Eur J Clin Pharmacol.* 1976;10:433-440.
27. Crankshaw DP, Boyd MD, Bjorksten AR. Plasma drug efflux: a new approach to optimization of drug infusion for constant blood concentration of thiopental or methohexital. *Anesthesiology.* 1987;67:32-41.
  28. Jacobs JR. Algorithm for optimal linear model-based control with application to pharmacokinetic model-driven drug delivery. *IEEE Trans Biomed Eng.* 1990;37:107-109.
  29. Tavernier A, Coussaert E, D'Hollander A, Cantraine E. Model-based pharmacokinetic regulation in computer-assisted anesthesia. An interactive model: CARIN. *Acta Anaesthesiol Belg.* 1987;38:63-68.
  30. Jacobs JR, Williams EA. Algorithm to control "effect compartment" drug concentrations in pharmacokinetic model-driven drug delivery. *IEEE Trans Biomed Eng.* 1993;40:993-999.
  31. Shafer SL, Gregg KM. Algorithm to rapidly achieve and maintain stable drug concentrations at the site of drug effect with computer-controlled infusion pump. *J Pharmacokinetic Biopharm.* 1992;20:147-169.
  32. Schwilden H, Schuttler J, Stoekel H. Pharmacokinetics as applied to total intravenous anaesthesia. Theoretical considerations. *Anaesthesia.* 1983;38(Suppl):51-52.
  33. Coetzee JF, Glen JB, Wium CA, Boshoff L. Pharmacokinetic model selection for target controlled infusions of propofol. Assessment of three parameter sets. *Anesthesiology.* 1995; 82:1328-1345.
  34. Schuttler J, Schwilden H, Stoekel H. Pharmacokinetics as applied to total intravenous anaesthesia. Practical implications. *Anaesthesia.* 1983;38(Suppl):53-56.
  35. Glen JB. The development of "Diprifusor": a TCI system for propofol. *Anaesthesia.* 1998;1982;53(Suppl 1):13-21.
  36. Bailey JM, Schwieger IM, Hug CC Jr. Evaluation of sufentanil anesthesia obtained by a computer-controlled infusion for cardiac surgery. *Anesth Analg.* 1993;76:247-252.
  37. Barvais L, Heitz D, Schmartz D, et al. Pharmacokinetic model-driven infusion of sufentanil and midazolam during cardiac surgery: assessment of the prospective predictive accuracy and the quality of anesthesia. *J Cardiothorac Vasc Anesth.* 2000;14:402-408.
  38. Hudson RJ, Henderson BT, Thomson IR, Moon M, Peterson MD. Pharmacokinetics of sufentanil in patients undergoing coronary artery bypass graft surgery. *J Cardiothorac Vasc Anesth.* 2001;15:693-699.
  39. Pandin PC, Cantraine F, Ewalenko P, et al. Predictive accuracy of target-controlled propofol and sufentanil coinfusion in long-lasting surgery. *Anesthesiology.* 2000;93:653-661.
  40. Schraag S, Kenny GN, Mohl U, Georgieff M. Patient-maintained remifentanil target-controlled infusion for the transition to early postoperative analgesia. *Br J Anaesth.* 1998;81: 365-368.
  41. Slepchenko G, Simon G, Goubaux B, et al. Performance of target-controlled sufentanil infusion in obese patients. *Anesthesiology.* 2003;98:65-73.
  42. Drover DR, Lemmens H. Population pharmacodynamics and pharmacokinetics of remifentanil as a supplement to nitrous oxide anesthesia for elective abdominal surgery. *Anesthesiology.* 1998;89:869-877.
  43. Hoymork SC, Raeder J, Grimsmo B, Steen PA. Bispectral index, predicted and measured drug levels of target-controlled infusions of remifentanil and propofol during laparoscopic cholecystectomy and emergence. *Acta Anaesthesiol Scand.* 2000;44:1138-1144.
  44. Lang E, Kapila A, Shlugman D, et al. Reduction of isoflurane minimal alveolar concentration by remifentanil. *Anesthesiology.* 1996;85:721-728.
  45. Jacobs JR. Analytical solution to the three compartment pharmacokinetic model. *IEEE Trans Biomed Eng.* 1988;35:763-765.
  46. Struys MM, De Smet T, Depoorter B, et al. Comparison of plasma compartment versus two methods for effect compartment-controlled target-controlled infusion for propofol. *Anesthesiology.* 2000;92:399-406.
  47. Wakeling H, Zimmerman J, Howell S, Glass P. Targeting effect compartment or central compartment of propofol. What predicts loss of consciousness? *Anesthesiology.* 1999;90:92-97.
  48. Gepts E, Camu F, Cockshott ID, Douglas EJ. Disposition of propofol administered as a constant rate intravenous infusion in humans. *Anesth Analg.* 1987;66:1256-1263.
  49. Smith C, McEwan AL, Jhaveri R, et al. The interaction of fentanyl on the Cp50 of propofol for loss of consciousness and skin incision. *Anesthesiology.* 1994;81:820-828.
  50. Vuyk J, Engbers F, Lemmens H, et al. Pharmacodynamics of propofol in female patients. *Anesthesiology.* 1992;77:3-9.
  51. Passot S, Servin F, Allary R, et al. Target-controlled versus manually-controlled infusion of propofol for direct laryngoscopy and bronchoscopy. *Anesth Analg.* 2002;94:1212-1216.
  52. White M, Schenkels MJ, Engbers F, et al. Effect-site modelling of propofol using auditory evoked potentials. *Br J Anaesth.* 1999;82:333-339.
  53. Leslie K, Absalom A, Kenny GN. Closed-loop control of sedation for colonoscopy using the bispectral index. *Anaesthesia.* 2002;57:693-697.
  54. Kazama T, Ikeda K, Morita K, et al. Comparison of the effect-site  $k(e)0s$  of propofol for blood pressure and EEG bispectral index in elderly and younger patients. *Anesthesiology.* 1999;90:1517-1527.
  55. Van Poucke GE, Bravo LJ, Shafer SL. Target controlled infusions: targeting the effect site while limiting peak plasma concentration. *IEEE Trans Biomed Eng.* 2004;51:1869-1875.
  56. Jacobs JR, Reves JG. Effect site equilibration time is a determinant of induction dose requirement. *Anesth Analg.* 1993;76:1-6.
  57. Vinik HR, Bradley EL, Kissin I. Triple anesthetic combination: propofol-midazolam-alfentanil. *Anesth Analg.* 1994;78: 354-358.
  58. Stanski DR, Maitre PO. Population pharmacokinetics and pharmacodynamics of thiopental: the effect of age revisited. *Anesthesiology.* 1990;72:412-422.
  59. Sanders DJ, Jewkes CF, Sear JW, Verhoeff F, Foex P. Thoracic electrical bioimpedance measurement of cardiac output and cardiovascular responses to the induction of anaesthesia and to laryngoscopy and intubation. *Anaesthesia.* 1992;47:736-740.
  60. Mehta D, Bradley EL, Kissin I. Effect of alfentanil on hypnotic and antinociceptive components of thiopental sodium anesthesia. *J Clin Anesth.* 1991;3:280-284.
  61. Tomlin SL, Jenkins A, Lieb WR, et al. Stereoselective effects of etomidate optical isomers on gamma-aminobutyric acid type A receptors and animals. *Anesthesiology.* 1998;88:708-717.
  62. Harris CE, Murray A, Anderson JM, et al. Effects of thiopentone, etomidate and propofol on the haemodynamic response to tracheal intubation. *Anaesthesia.* 1988;43(Suppl):32-36.

63. Absalom A, Pledger D, Kong A. Adrenocortical function in critically ill patients 24 hours after a single dose of etomidate. *Anaesthesia*. 1999;54:861-867.
64. Hildreth AN, Mejia VA, Maxwell RA, et al. Adrenal suppression following a single dose of etomidate for rapid sequence induction: a prospective randomized study. *J Trauma*. 2008;65:573-579.
65. Moore RA, Allen MC, Wood PJ, Rees LH, Sear JW. Perioperative endocrine effects of etomidate. *Anaesthesia*. 1985;40:124-130.
66. Ledingham IM, Watt I. Influence of sedation on mortality in critically ill multiple trauma patients. *Lancet*. 1983;i:1270.
67. Morris C, McAlister C. Etomidate for emergency anaesthesia: mad, bad and dangerous to know? *Anaesthesia*. 2005;60:737-740.
68. Ray DC, Haw AW, McKeown DW. Induction drug and outcome of patients admitted to the intensive care unit after emergency laparotomy. *Eur J Anaesthesiol*. 2010;27:481-485.
69. Jabre P, Combes X, Lapostolle F, et al. Etomidate versus ketamine for rapid sequence intubation in acutely ill patients: a multicentre randomised controlled trial. *Lancet*. 2009;374:293-300.
70. Cuthbertson BH, Sprung CL, Annane D, et al. The effects of etomidate on adrenal responsiveness and mortality in patients with septic shock. *Intensive Care Med*. 2009;35:1868-1876.
71. Jackson WJ. Should we use etomidate as an induction agent for endotracheal intubation in patients with septic shock? A critical appraisal. *Chest*. 2005;127:1031-1038.
72. Kulka PJ, Bremer F, Schuttler J. Narkoseeinleitung mit etomidat in lipidemulsion. *Anaesthesist*. 1993;42:205-209.
73. Vanacker B, Wiebalck A, Van Aken H, et al. Induktionsqualität und Nebennierenrindenfunktion: Ein klinischer Vergleich von Etomidat-lipuro und hypnomidate. *Anaesthesist*. 1993;42:81-89.
74. Doenicke AW, Roizen MF, Hoernecke R, Lorenz W, Ostwald P. Solvent for etomidate may cause pain and adverse effects. *Br J Anaesth*. 1999;83:464-466.
75. Nebauer AE, Doenicke A, Hoernecke R, Angster R, Maker M. Does etomidate cause haemolysis? *Br J Anaesth*. 1992;69:58-60.
76. Doenicke A, Roizen MF, Nebauer AE, et al. Comparison of two formulations of etomidate, 2-hydroxypropyl-cyclodextrin (HPCD) and propylene glycol. *Anesth Analg*. 1994;79:933-939.
77. St Pierre M, Dunkel M, Rutherford A, Hering W. Does etomidate increase postoperative nausea? A double-blind controlled comparison of etomidate in lipid emulsion with propofol for balanced anaesthesia. *Eur J Anaesthesiol*. 2000;17:634-641.
78. Nilsson A, Tamsen A, Persson P. Midazolam/fentanyl anaesthesia for major surgery. Plasma levels of midazolam during prolonged total intravenous anaesthesia. *Acta Anaesthesiol Scand*. 1986;30:66-69.
79. Dawson D, Sear JW. Influence of induction of anaesthesia with midazolam on the neuro-endocrine response to surgery. *Anaesthesia*. 1986;41:268-271.
80. Crozier TA, Beck D, Schlaeger M, Wuttke W, Kettler D. Endocrinological changes following etomidate, midazolam or methohexital for minor surgery. *Anesthesiology*. 1987;66:628-635.
81. Desborough JP, Hall GM, Hart GR, Burrin JL. Midazolam modifies pancreatic and anterior pituitary hormone secretion during upper abdominal surgery. *Br J Anaesth*. 1991;67:390-396.
82. Nilsson A, Persson MP, Hartvig P. Effects of the benzodiazepine antagonist flumazenil on postoperative performance following total intravenous anaesthesia with midazolam and alfentanil. *Acta Anaesthesiol Scand*. 1988;32:441-446.
83. Dawidowicz AI, Fornal E, Mardarowicz M, Fijalkowska A. The role of human lungs in the biotransformation of propofol. *Anesthesiology*. 2000;93:992-997.
84. He YL, Ueyama H, Tashiro C, Mashimo T, Yoshiya I. Pulmonary disposition of propofol in surgical patients. *Anesthesiology*. 2000;93:986-991.
85. Court MH, Duan SX, Hesse LM, Venkatakrishnan K, Greenblatt DJ. Cytochrome P450 2B6 is responsible for inter-individual variability of propofol hydroxylation by human liver microsomes. *Anesthesiology*. 2001;94:110-119.
86. Oda Y, Hamaoka N, Hiroi T, et al. Involvement of human liver cytochrome P450 2B6 in the metabolism of propofol. *Br J Clin Pharmacol*. 2001;51:281-285.
87. Schuttler J, Ihmsen H. Population pharmacokinetics of propofol: a multicenter study. *Anesthesiology*. 2000;92:727-738.
88. Stokes DN, Hutton P. Rate-dependent induction phenomena with propofol: implications for the relative potency of intravenous anaesthetics. *Anesth Analg*. 1991;72:578-583.
89. Kazama T, Ikeda K, Morita K, et al. Relation between initial blood distribution volume and propofol induction dose requirement. *Anesthesiology*. 2001;94:205-210.
90. Schnider TW, Minto CF, Shafer SL, et al. The influence of age on propofol pharmacodynamics. *Anesthesiology*. 1999;90:1502-1516.
91. Bryson HM, Fulton BR, Faulds D. Propofol: an update of its use in anaesthesia and conscious sedation. *Drugs*. 1995;50:513-559.
92. Spens HJ, Drummond GB. Ventilatory effects of etanalone during induction of anaesthesia: comparison with propofol and thiopentone. *Br J Anaesth*. 1996;77:194-199.
93. Pfenninger E, Himmelseher S. Neuroprotektion durch ketamin auf zellularer ebene. *Anaesthesist*. 1997;46(Suppl 1):s47-s54.
94. Schuttler J. S-(+) ketamine: the beginning of a new ketamine era. *Anaesthesist*. 1992;41:585-587.
95. Schuttler J, Stanski DR, White PF, et al. Pharmacodynamic modeling of the EEG effects of ketamine and its enantiomers in man. *J Pharmacokinet Biopharm*. 1987;15:241-253.
96. White PF, Schuttler J, Shafer A, et al. Comparative pharmacology of the ketamine isomers. *Br J Anaesth*. 1985;57:197-203.
97. Cordata DJ, Herkes GK, Mather LE, et al. Prolonged thiopentone infusion for neurosurgical emergencies: usefulness of therapeutic drug monitoring. *Anesth Intensive Care*. 2001;29:339-348.
98. Christensen JH, Andreasen F, Kristoffersen MB. Comparison of the anaesthetic and haemodynamic effects of chlormethiazole and thiopentone. *Br J Anaesth*. 1983;55:391-397.
99. Cordato DJ, Gross AS, Herkes GK, Mather LE. Pharmacokinetics of thiopentone enantiomers following intravenous injection or prolonged infusion of rac-thiopentone. *Br J Clin Pharmacol*. 1997;43:355-362.
100. Crankshaw DP, Edwards NE, Blackman GL, et al. Evaluation of infusion regimens for thiopentone as a primary anaesthetic agent. *Eur J Clin Pharmacol*. 1985;28:543-552.



101. Prys-Roberts C, Sear JW, Low JM, Phillips KC, Dagnino J. Hemodynamic and hepatic effects of methohexital infusion during nitrous oxide anesthesia in humans. *Anesth Analg.* 1983;62:317-323.
102. Sear JW, Phillips KC, Andrews CJH, Prys-Roberts C. Dose response relationships for infusions of Althesin or methohexitone. *Anaesthesia.* 1983;38:931-936.
103. Sear JW, Prys-Roberts C, Phillips KC. Age influences the minimum infusion rate ( $ED_{50}$ ) for continuous infusions of Althesin and methohexitone. *Eur J Anaesthesiol.* 1984;1:319-325.
104. Carter JA, Clarke TN, Prys-Roberts C, Spelina KR. Restoration of baroreflex control of heart rate during recovery from anaesthesia. *Br J Anaesth.* 1986;58:415-421.
105. Vuyk J, Hennis PJ, Burm AG, de Voogt JW, Spierdijk J. Comparison of midazolam and propofol in combination with alfentanil for total intravenous anesthesia. *Anesth Analg.* 1990;71:645-660.
106. Persson MP, Nilsson A, Hartvig P. Relation of sedation and amnesia to plasma concentrations of midazolam in surgical patients. *Clin Pharmacol Ther.* 1988;43:324-331.
107. Albrecht S, Ihmsen H, Hering W, et al. The effect of age on the pharmacokinetics and pharmacodynamics of midazolam. *Clin Pharmacol Ther.* 1999;65:630-639.
108. Greenblatt DJ, Ehrenberg BL, Culm KE, et al. Kinetics and EEG effects of midazolam during and after 1-minute, 1-hour and 3-hour intravenous infusions. *J Clin Pharmacol.* 2004;44:605-611.
109. Hudson RJ. Midazolam pharmacokinetics in patients undergoing abdominal aortic surgery. *Anesth Analg.* 1994;79:219-225.
110. Short TG, Tam YH, Tan P, Oh TE. Pharmacokinetic model-controlled infusion of midazolam. A prospective evaluation during general anaesthesia. *Anaesthesia.* 1993;48:187-191.
111. Nilsson A, Persson MP, Hartvig P, Wide L. Effects of total intravenous anaesthesia using midazolam/alfentanil on the adrenocortical and hyperglycaemic response to abdominal surgery. *Acta Anaesthesiol Scand.* 1988;32:379-384.
112. Bowdle TA, Radant AD, Cowley DS, et al. Psychedelic effects of ketamine in healthy volunteers: relationship to steady-state plasma concentrations. *Anesthesiology.* 1998;88:82-88.
113. Gray C, Swinhoe CF, Myint Y, Mason D. Target controlled infusion of ketamine as analgesia for TIVA with propofol. *Can J Anesth.* 1999;46:957-961.
114. Domino EF, Domino SE, Smith RE, et al. Ketamine kinetics in unmedicated and diazepam-premedicated subjects. *Clin Pharmacol Ther.* 1984;36:645-653.
115. Wieber J, Gugler R, Hengstmann JH, Dengler HJ. Pharmacokinetics of ketamine in man. *Anaesthesist.* 1975;24:260-263.
116. Schuttler J, Schuttler M, Kloos S, Nadstawek J, Schwilden H. Optimal dosage strategies in total intravenous anesthesia using propofol and ketamine. *Anaesthesist.* 1991;40:199-204.
117. Kharasch ED, Labroo R. Metabolism of ketamine stereoisomers by human liver microsomes. *Anesthesiology.* 1992;7:1201-1207.
118. Clements JA, Nimmo WS. Pharmacokinetics and analgesic effect of ketamine in man. *Br J Anaesth.* 1981;53:27-30.
119. Idvall J, Ahlgren I, Aronsen KR, Stenberg P. Ketamine infusions: pharmacokinetics and clinical effects. *Br J Anaesth.* 1979;51:1167-1173.
120. Ihmsen H, Geisslinger G, Schuttler J. Stereoselective pharmacokinetics of ketamine: R(-)-ketamine inhibits the elimination of S(+)-ketamine. *Clin Pharmacol Ther.* 2001;70:431-438.
121. Persson J, Hasselstrom J, Maurset A, et al. Pharmacokinetics and non-analgesic effects of S- and R-ketamines in healthy volunteers with normal and reduced metabolic capacity. *Eur J Clin Pharmacol.* 2002;57:869-875.
122. White M, de Graaff P, Renshof B, van KAM E, Dzoljic M. Pharmacokinetics of S (+) ketamine derived from target controlled infusion. *Br J Anaesth.* 2006;96:330-334.
123. White PF, Ham J, Way WL, Trevor AJ. Pharmacology of ketamine isomers in surgical patients. *Anesthesiology.* 1980;52:231-239.
124. Morgan DJ, Campbell GA, Crankshaw DP. Pharmacokinetics of propofol when given by intravenous infusion. *Br J Clin Pharmacol.* 1990;30:144-148.
125. Servin F, Cockshott ID, Farinotti R, Haberer JP, Winckler C, Desmonts JM. Pharmacokinetics of propofol infusions in patients with cirrhosis. *Br J Anaesth.* 1990;65:177-183.
126. Wessen A, Persson PM, Nilsson A, Hartvig P. Clinical pharmacokinetics of propofol given as a constant-rate infusion and in combination with epidural blockade. *J Clin Anesth.* 1994;6:193-198.
127. Soltesz S, Silomon M, Graf G, Mencke T, Boulaadass S, Molter GP. Effect of a 0.5% dilution of propofol on pain on injection during induction of anesthesia in children. *Anesthesiology.* 2007;106:80-84.
128. Ward DS, Norton JR, Guivarc'h PH, Litman RS, Bailey PL. Pharmacodynamics and pharmacokinetics of propofol in a medium-chain triglyceride emulsion. *Anesthesiology.* 2002;97:1401-1408.
129. Doenicke AW, Roizen MF, Rau J, et al. Pharmacokinetics and pharmacodynamics of propofol in a new solvent. *Anesth Analg.* 1997;85:1399-1403.
130. Kim KM, Choi BM, Park SW, et al. Pharmacokinetics and pharmacodynamics of propofol microemulsion and lipid emulsion after an intravenous bolus and variable rate infusions. *Anesthesiology.* 2007;106:924-934.
131. Jung JA, Choi BM, Cho SH, et al. Effectiveness, safety and pharmacokinetic and pharmacodynamic characteristics of microemulsion propofol in patients undergoing elective surgery under total intravenous anaesthesia. *Br J Anaesth.* 2010;104:563-576.
132. Baker MT, Naguib M. Propofol: the challenges of formulation. *Anesthesiology.* 2005;103:860-876.
133. Trapani A, Laquintana V, Lopodota A, et al. Evaluation of new propofol aqueous solutions for intravenous anesthesia. *Int J Pharm.* 2004;278:91-98.
134. Egan TD, Kern SE, Johnson KB, Pace NL. The pharmacodynamics and pharmacodynamics of propofol in a modified cyclodextrin formulation (captisol) versus propofol on a lipid formulation (Diprivan): an encephalographic and hemodynamic study in a porcine model. *Anesth Analg.* 2003;97:72-79.
135. Ravenelle F, Vachon P, Rigby-Jones AE, et al. Anaesthetic properties of propofol polymeric micelle: a novel water soluble propofol formulation. *Br J Anaesth.* 2008;101:186-193.
136. Altomare C, Trapani G, Latrofa A, et al. Highly water-soluble derivatives of the anaesthetic agent propofol: in vitro and in vivo evaluation of cyclic amino acid esters. *Eur J Pharm Sci.* 2003;20:17-26.

137. Banaszczyk MG, Carlo AT, Millan V et al. Propofol phosphate. A water-soluble propofol prodrug: in vivo evaluation. *Anesth Analg.* 2002;95:1285-1292.
138. Cullen PM, Turtle M, Prys-Roberts C, Way WL, Dye J. Effect of propofol anesthesia on baroreflex activity in humans. *Anesth Analg.* 1987;66:1115-1120.
139. Nagyova B, Dorrington KL, Gill EW, et al. Comparison of the effects of sub-hypnotic concentrations of propofol and halothane on the acute ventilatory response to hypoxia. *Br J Anaesth.* 1995;75:713-718.
140. Nieuwenhuijs D, Sarton E, Teppema L, et al. Propofol for monitored anesthesia care: implications on hypoxic control of cardiorespiratory responses. *Anesthesiology.* 2000;92:46-54.
141. Sear JW, Diedericks J, Foex P. Continuous infusions of propofol administered to dogs: effects on ICG and propofol disposition. *Br J Anaesth.* 1994;72:451-455.
142. Murray JM, Trinick TR. Hepatic function and indocyanine green clearance during and after prolonged anaesthesia with propofol. *Br J Anaesth.* 1992;69:643-644.
143. Baker MT, Chadam MV, Ronnenberg WC Jr. Inhibitory effects of propofol on cytochrome P450 activity in rat hepatic microsomes. *Anesth Analg.* 1993;76:817-821.
144. Chen TL, Ueng TH, Chen SH, et al. Human cytochrome P450 mono-oxygenase system is suppressed by propofol. *Br J Anaesth.* 1995;74:558-562.
145. Janicki PK, James MFM, Erskine WAR. Propofol inhibits enzymatic degradation of alfentanil and sufentanil by isolated liver microsomes in vitro. *Br J Anaesth.* 1992;68:311-312.
146. Chen TL, Chen TG, Tai YT, et al. Propofol inhibits renal cytochrome P450 activity and enflurane defluorination in vitro in hamsters. *Can J Anaesth.* 2000;47:680-686.
147. Mertens MJ, Vuyk J, Olofson E, Bovill JG, Burm AG. Propofol alters the pharmacokinetics of alfentanil in healthy male volunteers. *Anesthesiology.* 2001;94:949-957.
148. Pavlin DJ, Arends RH, Gunn HC, et al. Optimal propofol-alfentanil combination for supplementing nitrous oxide for outpatient surgery. *Anesthesiology.* 1999;91:97-108.
149. Bouillon T, Bruhn J, Radu-Radulescu L, et al. Non-steady state analysis of the pharmacokinetic interaction between propofol and remifentanil. *Anesthesiology.* 2002;97:1350-1362.
150. Vuyk J. Pharmacokinetic and pharmacodynamic interactions between opioids and propofol. *J Clin Anesth.* 1997;9(Suppl 1):23s-26s.
151. Vuyk J, Lim T, Engbers F, et al. The pharmacodynamic interaction of propofol and alfentanil during lower abdominal surgery in women. *Anesthesiology.* 1995;83:8-22.
152. Mertens MJ, Olofson E, Engbers FHM, et al. Propofol reduces perioperative remifentanil requirements in a synergistic manner. Response surface modeling of perioperative remifentanil-propofol interactions. *Anesthesiology.* 2003;99:347-359.
153. Rudkin GE, Osborne GA, Curtis NJ. Intra-operative patient-controlled sedation. *Anaesthesia.* 1991;46:90-92.
154. Borgeat A, Wilder-Smith O, Forni M, Suter PM. Adjuvant propofol enables better control of nausea and emesis secondary to chemotherapy for breast cancer. *Can J Anaesth.* 1994;41:1117-1119.
155. Borgeat A, Wilder-Smith OHG, Salah M, et al. Subhypnotic doses of propofol relieve pruritus induced by epidural and intrathecal morphine. *Anesthesiology.* 1992;76:510-512.
156. Salah M, Borgeat A, Wilder-Smith OH, et al. Epidural morphine-induced pruritus: propofol versus naloxone. *Anesth Analg.* 1994;78:1110-1113.
157. Newman MF, Murkin JM, Roach G, et al. Cerebral physiologic effects of burst suppression doses of propofol during non-pulsatile cardiopulmonary bypass. *Anesth Analg.* 1995;81:452-457.
158. Stone JG, Young WL, Marans ZS, et al. Consequences of electroencephalographic suppressive doses of propofol in conjunction with deep hypothermic circulatory arrest. *Anesthesiology.* 1996;85:497-501.
159. Peden CJ, Cloote AH, Stafford N, Prys-Roberts C. The effect of intravenous dexmedetomidine premedication on the dose requirement of propofol to induce loss of consciousness in patients receiving alfentanil. *Anaesthesia.* 2001;56:408-413.
160. Dutta S, Karol MD, Cohen T, Jones RM, Mant T. Effect of dexmedetomidine on propofol requirements in healthy subjects. *J Pharm Sci.* 2001;90:172-181.
161. Ramsay MAE, Luteran DL. Dexmedetomidine as a total intravenous anesthetic agent. *Anesthesiology.* 2004;101:787-790.
162. Mather LE, Cousins MJ. Low dose chlormethiazole infusion as a supplement to central neural blockade: blood concentrations and clinical effects. *Anaesth Intensive Care.* 1980;8:421-425.
163. Lentschener C, Ghimouz A, Bonnichon P, et al. Remifentanil-propofol vs. sufentanil-propofol: optimal combinations in clinical anesthesia. *Acta Anaesthesiol Scand.* 2003;47:84-89.
164. Hansen EG, Duedahl TH, Rousing J, Hilsted KL, Dahl JB. Intra-operative remifentanil might influence pain levels in the immediate post-operative period after major abdominal surgery. *Acta Anaesthesiol Scand.* 2005;49:1464-1470.
165. Hughes MA, Glass PSA, Jacobs JR. Context-sensitive half-time in multicompartment pharmacokinetic models for intravenous drugs. *Anesthesiology.* 1992;76:334-341.
166. Kapila A, Glass PSA, Jacobs JR, et al. Measured context-sensitive half-times of remifentanil and alfentanil. *Anesthesiology.* 1995;83:968-975.
167. Youngs EJ, Shafer SL. Pharmacokinetic parameters relevant to recovery from opioids. *Anesthesiology.* 1994;81:833-841.
168. Bailey JM. Technique for quantifying the duration of intravenous anesthetic effect. *Anesthesiology.* 1995;83:1095-1103.
169. Jacobs JR, Reves JG, Glass P. Rationale and technique for continuous infusion anesthesia. *Int Anesthesiol Clin.* 1991;29:23-38.
170. Shafer SL, Varvel JR. Pharmacokinetics, pharmacodynamics and rational opioid selection. *Anesthesiology.* 1990;74:53-63.
171. Joly V, Richebe P, Guignaud B, et al. Remifentanil-induced postoperative hyperalgesia and its prevention with small-dose ketamine. *Anesthesiology.* 2005;103:147-155.
172. Absalom AR, Amutike D, Lal A, White M, Kenny G. Accuracy of the "Paedfusor" in children undergoing cardiac surgery or catheterization. *Br J Anaesth.* 2003;91:507-513.
173. Sear JW. Development of pharmacophoric maps for cardiovascular depression by intravenous anaesthetic agents: comparison with maps for immobilizing activity. *Br J Anaesth.* 2010;104:684-690.
174. Doenicke AW, Roizen MF, Rau J, Kellermann W, Babl J. Reducing pain during propofol injection: the role of the solvent. *Anesth Analg.* 1996;82:472-474.
175. Champion ME, Gan TJ. Fospropofol disodium for sedation. *Drugs Today (Barc).* 2009;45:567-576.

176. Garnock-Jones KP, Scott LJ. Fospropofol. *Drugs*. 2010;70:469-477.
177. Siegel LC, Konstantatos A. PF0713 produced rapid infusion of general anesthesia without injection pain in a phase 1 study. *Anesthesiology*. 2009;ASA abstracts:A463.
178. Kanamitsu N, Osaki T, Itsuji Y, Yoshimura M, Tsujimoto H, Soga M. Novel water-soluble sedative-hypnotic agents: isoindolin-1-one derivatives. *Chem Pharm Bull (Tokyo)*. 2007;55:1682-1688.
179. Rigby-Jones A, Ohkura T, Shimizu S, Cross M, Sneyd J. First human administration of JM1232, a novel isoindoline derivative benzodiazepine agonist. *Eur J Anaesthesiol*. 2008;25 (Suppl 44):129 (abstract 9AP2-6).
180. Rigby-Jones AE, Sneyd JR, Okhura T, Tominaga H, Cross M. MR04A3 (aqueous 1.0% JM-1232 (-)) pharmacokinetics and pharmacodynamics in man. *Anesthesiology*. 2009;ASA abstracts:A464.
181. Kilpatrick GJ, McIntyre MS, Cox RF, et al. CNS 7056: a novel ultra-short acting benzodiazepine. *Anesthesiology*. 2007;107:60-66.
182. Mutter C, Rudolf G, Diemunsch PA, Tilbrook GS, Borgeat A. CNS 7056X an ultra-short acting benzodiazepine: pharmacokinetic and pharmacodynamic study in pig. *Anesthesiology*. 2006;105:A1610 (abstract).
183. Antonik LJ, Goldwater DR, Kilpatrick GJ, et al. A phase I SAD study evaluating the safety, pharmacokinetics and pharmacodynamics of CNS 7056. *Anesthesiology*. 2009;ASA abstracts:A1603.
184. Beattie D, Jenkins T, McCullough J, et al. The in vivo activity of THRX-918661, a novel, pharmacokinetically responsive sedative/hypnotic agent. *Anaesthesia*. 2004;59:101 (abstract).
185. Egan TD, Shafer SL, Jenkins TE, Beattie DT, Jaw-Tsai SS. The pharmacokinetics and pharmacodynamics of THRX-918661, a novel sedative/hypnotic agent. *Anesthesiology*. 2003;99:A516 (abstract).
186. Cotten JF, Forman SA, Laha JK, et al. Carboetomidate: a pyrrole analog of etomidate designed not to suppress adrenocortical function. *Anesthesiology*. 2010;112:637-644.
187. Cotten JF, Husain SS, Forman SA, et al. Methoxycarbonyl-etomidate: a novel rapidly metabolized and ultra-short-acting etomidate analogue that does not produce prolonged adrenocortical suppression. *Anesthesiology*. 2009;111:240-249.
188. Forman SA, Stewart D, Husain S, et al. MTS-etomidate selectively reacts with cysteines in the GABA A receptor etomidate binding site. *Anesthesiology*. 2009;ASA abstracts:A1382.
189. Stewart DS, Husain SS, Miller KW, Forman SA. MTS-etomidate selectively reacts within the GABA A receptor etomidate binding site. *Biophys J*. 2009;96:487a-488a.
190. Absalom AR, Kenny GN. Closed-loop control of propofol anaesthesia using bispectral index performance assessment in patients receiving computer-controlled and manually-controlled remifentanyl infusions for minor surgery. *Br J Anaesth*. 2003;90:737-741.
191. Absalom A, Sutcliffe N, Kenny GN. Closed-loop control of anaesthesia using Bispectral Index performance assessment in patients undergoing major orthopaedic surgery under combined general and regional anaesthesia. *Anesthesiology*. 2002;96:67-73.
192. Leslie JB, Cohen LB, Silvestri G, Gan T-J. Clinical safety of fospropofol sodium sedation during diagnostic and therapeutic procedures. *Anesthesiology*. 2008;109:A190 (abstract).
193. Mortier E, Struys M, De Swet T, Versichelen L, Rolly G. Closed-loop controlled administration of propofol using bispectral analysis. *Anaesthesia*. 1998;53:749-754.
194. Struys MM, De Smet T, Versichelen L, et al. Comparison of closed-loop controlled administration of propofol using Bispectral Index as the controlled variable versus "standard practice" controlled administration. *Anesthesiology*. 2001;95:6-17.