action, Davide Verotta, Ph.D. (University of California, San Francisco), described the mathematical development of a generalized conceptual model for pharmacokinetic/pharmacodynamic data. This generic model incorporates both the direct and indirect effect models of action and allows effect data to be described as a combination of both mechanisms. For drugs best described by one method or the other, the model reduces to a pure direct or a pure indirect effect model. Hybrid effect models may be best suited for describing the effects of prolonged administration of drugs that have a direct initial effect and a secondary/delayed indirect effect, including tolerance. Thus, this model may give more accurate insight into the true physiologic action of drugs.

Physiologic/Pharmacokinetic Models. The third session, moderated by Arthur J. Atkinson, Jr., M.D. (Northwestern University), was dedicated to the physiologic interpretation of pharmacokinetic models and the development of physiologic models that describe the concentration profiles of drugs. Sven Björkman, Ph.D. (Malmö and Stanford University), presented a physiologic model that described the arterial and tissue disposition of fentanyl and alfentanil.

Physiologic interpretation of pharmacokinetic models is facilitated if the structure of the model is identified anatomically *via* tissue blood flow and tissue drug concentration measurements. Because it is difficult to independently manipulate one type of tissue within a whole animal, it is necessary to construct a hybrid model of each tissue and relate it to the arterial drug concentration. A hybrid physiologic model with a parallel architecture similar to the anatomy of the cardiovascular system can be constructed by sampling various tissues and the corresponding local arterial inflow. Each tissue can be represented as a superficial tissue compartment with a local blood compartment in contact with systemic arterial blood. Occasionally, the addition of a deep parenchymal compartment is required to explain the observed tissue concentration profiles. In the hybrid model for fentanyl and alfentanil described by Björkman *et al.*, the calculated extraction ratio was similar to the extraction ratio in the literature for all organ beds except the heart and brain. In the heart, which has a high extraction ratio, it is possible that the nonstationarity due to active control of coronary blood flow affects the extraction ratio of injectable anesthetics. The brain was found to have an extraction ratio for injectable anesthetics that varied with time. The development of hybrid physiologic models has clinical applications in determining the impact of physiologic parameters on arterial and brain tissue concentrations. These models may help predict changes in effect that result from physiologic perturbations.

The lung is in a unique position as a tissue compartment in that it is exposed to 100% of the cardiac output. Besides being responsible for gas exchange, the lung is a metabolically active tissue. The system controlling the distribution of blood flow throughout the lung and the exchange of fluid and micro- and macromolecules between the lung's vascular and interstitial compartments is complex. Thomas R. Harris, M.D., Ph.D. (Vanderbilt University), explained the mathematical models of the exchange of molecules in both the normal and abnormal pulmonary capillary beds. Basic chemical engineering theory of mass and momentum balance combined with the use of tracers of known size and characterized physical properties has helped elucidate pulmonary microvasculature transport processes. Experiments in animal models, *in vitro* preparations, and clinical subjects revealed that urea may be useful as a marker in characterizing the lung microcirculation during various physiologic and pathologic perturbations. Future studies with urea not only may give greater insight into the physiology of mass exchange in the pulmonary capillary beds but also may lead to development of potential modes of therapy that may help to prevent lung sequestration of water (pulmonary edema) and endogenous and exogenous substances.

The closing presentation by Michael J. Avram, Ph.D. (Northwestern University), was an overview of circulatory-based pharmacokinetic models. Based on the early work of investigators including Price, Jacquez, Dedrick and Bischoff, and Atkinson, Avram and colleagues developed compartmental models to describe the intravascular mixing of drugs and markers from the moment of injection, thus characterizing the pharmacokinetics during the timeframe of drug action of many of the intravenous drugs used in anesthesia. First developed using Indocyanine Green (ICG), an inert marker of intravascular space, their model is a parallel circuit compartmental model of lumped blood circuits based on the concentration profile obtained from rapidly sampling a single arterial site. The intravascular space model is physiologically interpretable in that it accounts for the recirculation of ICG and describes the distribution of cardiac output between a low-capacitance circuit and a large-capacitance circuit. Models for markers of extracellular fluid space (inulin) and total body water (antipyrine) have been developed by assuming that the intravascular mixing of these markers, administered concomitantly with ICG, are described by the ICG model. By superposition, any differences between the drug profile and the ICG profile are modeled as distribution of drug out of the intravascular space. These compartmental recirculatory pharmacokinetic models can be used to describe alterations in the pharmacokinetics of these markers and various intravenous anesthetics during physiologic perturbations, define the pharmacokinetic basis of interindividual differences in drug response, and reveal the interrelationship between physiology and drug disposition.

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Society for Obstetric Anesthesia and Perinatology: Twenty-sixth Annual Meeting. Philadelphia, Pennsylvania, May 11–14, 1994.

At the opening session, Mark C. Norris, M.D., the 1994 Society for Obstetric Anesthesia and Perinatology (SOAP) meeting host, along with the incoming president, Barbara L. Leighton, M.D., and their Philadelphia cohorts, greeted the attendees with warm words of welcome. After a moving eulogy by Mark A. Rosen, M.D., and Samuel C. Hughes, M.D., in memory of the late Sol Shnider, the scientific program commenced.

The first scientific session was the Gertie Marx Resident Research Competition. Five well prepared and diverse oral presentations set the tone for a meeting of excellence in obstetric anesthesia research.

In collaboration with one of our British colleagues, a simple clinical test to identify women at high risk for experiencing severe hypotension during induction of spinal anesthesia was the topic of the first presentation, "Advance Prediction of Hypotension Risk at Cesarean Delivery under Spinal Anesthesia." More aggressive treatment of hypotension in the perioperative period and closer monitoring was emphasized by the authors Kinsella and Norris. However, in contrast with earlier studies, the sitting tilt test was found to be of no valid predictive value.

"The Relation of Cerebral Blood Flow to Post Dural Puncture Headache" was the topic of the second investigation by Alvarado *et al.,* from Baylor College of Medicine in Houston. Parturients who developed postdural puncture headache were shown to have different cerebral blood flow characteristics that were highly suggestive of cerebral vasodilation when compared with a control group who had accidental dural puncture with no subsequent headache. This finding may have important therapeutic implications.

The third study was "Inhibition of Enkephalin Metabolizing Enzymes by a New Prodrug, RB101, Enhances Pregnancy Induced Analgesia in Mice." Singh *et al.* from the Oregon Health Sciences University used this novel agent to elucidate the role of endogenous enkephalins in producing analgesia in pregnant animals. It was postulated that drugs such as RB101 may portend the development of future analgesics that will produce analgesia without the side effects of exogenously administered opioids.

The fourth presentation, "The Depth of the Lumbar Epidural Space by Magnetic Resonance Imaging," challenged the results of previous dye injection studies suggesting the lower epidural space is sawtooth-shaped. These researchers, Roark and Harris, from John Hopkins University, determined that, in the lumbar epidural space, the greatest distance from the ligamentum flavum to the dura mater is found in the middle of the intervertebral, interlaminar space and not in the more caudal aspect. The latter was suggested as a possible explanation for accidental dural puncture during placement of lumbar epidural catheters.

"Intrathecal Sufentanil: Relationships between Diluent Volume, Sensory and Blood Pressure Changes, and Duration of Analgesia" was the final presentation in the Resident Research Competition by Riley *et al.*, from Stanford University. The intent of the study was to determine whether sensory and hemodynamic changes relate to the concentration of the solution of sufentanil used for intrathecal administration and whether sensory changes are predictive of hemodynamic perturbations or the duration of pain relief. The results of this study suggest that diluent volume does not influence analgesia or sensory changes with intrathecal sufentanil and, furthermore, that sensory changes are not predictive of the duration of analgesia or the degree of hemodynamic alterations. The data indicate that the effects of intrathecal sufentanil are predominantly mediated *via* spinal opioid receptors rather than by local anesthetic action.

Felicity Reynolds, M.B., B.S., M.D., Professor of Obstetric Anaesthesia at St. Thomas' Hospital in London, was the invited guest speaker. She presented the 1994 Fred Hehre Memorial Lecture and honored the attendees with a brilliant discussion, "In Defence of Bupivacaine." Reynolds led us from the development and initial use of bupivacaine in the early 1960s through its use today in obstetric anesthesia. She stated that, when bupivacaine was first released in 1963, it appeared free from tachyphylaxis and exhibited less accumulation when given in appropriate doses throughout a prolonged labor. Additionally, she traced her personal interests from those days as an occasional obstetric anesthetist to now as a pharmacokineticist.

Other highlights of the scientific program were the three "What's New" lectures in obstetrics, neonatology, and obstetric anesthesia. An outstanding summary, "HIV and Other Blood-borne Pathogens in Obstetrics: *Keeping It Safe for All Involved,*" was presented by Neil S. Silverman, M.D. He discussed the topic under the headings "HIV in Pregnancy" and "Hepatitis in Pregnancy" and concluded with "Blood-borne Agents and the Invasivist, or *What if I Get Stuck?*" He emphasized that hepatitis B virus is a preventable illness and urged that immunization against hepatitis B virus be made mandatory for all health-care providers at risk.

"Medicolegal Aspects of Teratology," presented by Robert L. Brent, M.D., Ph.D., D.Sc., provided an informative description of the "irresponsible expert witness" and the effects of litigation-produced pain, disease, and suffering. His statement, "There is no area of our legal system with such a high percentage of innocent defendants," was followed by an eloquent discussion of the malpractice crisis. Brent also discussed the effects on family, who may lose their objectivity, and the expert witnesses, who may abandon their veracity and ethics in testimony. He concluded by recommending changes in the medical, legal, and lay sectors of our society and volunteered that the contingency fee system provokes and promotes "negligence litigation," which frequently develops into a "disease" all its own.

An extraordinary in-depth survey of the literature from 1993 relative to obstetric anesthesia was contributed by Valerie A. Arkoosh, M.D. A comprehensive review of topics, from here and overseas, in the fields of obstetrics, anesthesia, and perinatology, covered outcome studies, maternal and fetal physiology, pharmacokinetics/pharmacodynamics, and new anesthesia techniques and medications and was superbly presented with insight and humor. More importantly, Arkoosh pointed out and analyzed the interrelationships between studies published in the different specialty fields.

The excellent judgment and high standards of the reviewers were tested by the numerous abstracts of outstanding quality submitted for presentation at the scientific sessions. Because it is beyond the scope of this forum to mention all of the presentations, discussion will be limited to a select few.

Hawkins and colleagues, from the University of Colorado, characterized the changing nature of obstetric anesthesia practice in their study, "Obstetric Anesthesia Manpower Survey: 1992 vs 1981." They demonstrated a significant increase in the use of regional anesthesia for cesarean section, with a concomitant decrease in the use of general anesthesia, from 41% in 1981 to 16% in 1992. In hospitals performing fewer than 500 deliveries per year, 68% of anesthetics for cesarean section were performed by a nurse anesthetist, either supervised by an obstetrician or practicing independently.

The effects of epidural analgesia on the progress of labor have long been a source of concern for obstetricians and anesthesiologists. Chestnut and colleagues at the University of Iowa performed a study titled, "Does Early Administration of Epidural Analgesia Affect Obstetric Outcome in Nulliparous Women Who Are in Spontaneous Labor?" They could not detect an increase in the incidence of forceps delivery, use of oxytocin augmentation, or duration of labor in nulliparous women receiving early epidural analgesia compared with a group given epidural anesthesia later in labor. Neither was there a significant increase in the incidence of cesarean section in those patients who received early epidural anesthesia.

From Boston, Groves and colleagues at the Beth Israel Hospital, Harvard Medical School, continued their earlier investigation of back pain after epidural analgesia. In their study, "Incidence of Long Term Postpartum Back Pain and Its Relationship with Epidural Anesthesia,"

they could not demonstrate an increase in the incidence of back pain 12–18 months postpartum in women who received epidural anesthesia compared with women who did not.

Based on preliminary data suggesting that intrathecal neostigmine potentiates the analgesic effects of intrathecal clonidine, Hood and Eisenach, from Wake Forest, performed a study, "The Hemodynamic and Spinal Cord Blood Flow Effects of Intrathecal Neostigmine in Sheep." Using colored microspheres, they demonstrated that intrathecal neostigmine has no effect on spinal cord blood flow. Further, they demonstrated that intrathecal neostigmine partially reverses the hemodynamic depression produced by intrathecal clonidine alone. They recommended that further toxicologic studies be performed in preparation for performing controlled human studies.

The high lipophilicity of sufentanil has led to the widespread belief that it has little effect on respiratory function when administered intrathecally. This assumption was questioned in a study by Arkoosh and colleagues, "Does Intrathecal Sufentanil Depress the Ventilatory Response to CO_2 in the Parturient?" They demonstrated that central respiratory drive, as measured by the ventilatory response to carbon dioxide, decreased within 20 min of intrathecal sufentanil administration and lasted for as long as 120 min.

Palmer and coworkers, of the University of Arizona, attempted to answer the question, "What Is the Optimal Dose of Subarachnoid Morphine for Post-cesarean Analgesia?" By comparing the total amount of opioid administered *via* intravenous patient-controlled analgesia in patients receiving between 0.1 and 0.5 mg intrathecal morphine, they were unable to demonstrate additional patient-controlled morphine-sparing effects in patients given more than 0.1 mg intrathecally. At the same time, they demonstrated a greater incidence of nausea and pruritus at doses greater than 0.1 mg intrathecally. They suggested that even 0.1 mg may be too large a dose.

Birnbach and colleagues, from St. Luke's-Roosevelt Medical Center in New York, contributed a poster presentation, "Thrombocytopenia in the Cocaine Abusing Parturient." Of parturients with a positive urine screen for cocaine, 4.6% had an admission platelet count less than 100,000 K/mm^3 compared with 0% in patients with a negative urine cocaine screen (preeclamptic patients were excluded from the study). The investigators therefore recommended that parturients suspected of cocaine abuse have a platelet count determined before the initiation of regional anesthesia.

M. Joanne Douglas, M.D., F.R.C.P., reviewed the 40 poster presentations, which were very well displayed in an area adjacent to the technical exhibits and led to many spirited discussions along with very succinct challenges to the presenters.

An innovative theme for Thursday's lunch-time sessions proved to be a success, whereby small groups ate together while discussing research planning or challenging clinical cases. For the early risers, a continuation of the customary breakfast panels included current clinically applicable topics. With views presented from across the Atlantic as well as locally, the Friday morning panel addressed "Ambulation and Labor Analgesia: Are They Compatible?" The Saturday morning breakfast panel had as its topic "Failed Intubation: Preventing the Unthinkable," which also provided recommendations for preventing and salvaging a failed intubation.

To conclude the meeting on Saturday afternoon, optional refresher course lectures were offered by noted authorities from the Philadelphia area, including H. Jane Huffnagle, D.O., Brett B. Gutsche, M.D., and J. Stephen Naulty, M.D. Their topics included "Spinal Opioid Labor Analgesia," "Epidural Block, How to Make It Safe and Effective," and "Epidural Analgesia for Labor—What Can We Do to Improve Outcome?"

These are exciting times in our field for scientific research and expanding clinical practice, and it is with much enthusiasm that members await the 27th annual SOAP meeting, to be held in Montreal, Quebec, Canada.

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