possible adverse effects of atracurium. No atracurium-related effects on these parameters were found. As indicated in our Tracrium® package insert, adverse reactions in these clinical studies were minimal and largely confined to histamine-related events that occurred predominantly at dosages beyond the recommended dosage range.

Tracrium® has been on the market since December 1982 in England and since December 1983 in the United States. An estimated 1,000,000 patients have received the drug. Continuing product surveillance has revealed an extremely low incidence of adverse reactions, none of which suggest any tissue toxicity associated with atracurium administration.

In summary, we feel that the preclinical testing and clinical experience to date have demonstrated that Tracrium® is a safe and effective neuromuscular blocking agent.

Allen E. Cato, M.D., Ph.D.
Director
Department of Clinical Research

Charles G. Lineberry, Ph.D.
Head
Anesthesia/Analgesia Section
Department of Clinical Research

A. W. Macklin, D.V.M., Ph.D.
Associate Head
Department of Toxicology and Experimental Pathology

References

( Accepted for publication August 9, 1984.)

Further Comments Regarding Drug Disposition in the Surgical Patient

To the Editor: — Discussions with colleagues concerning our recent editorial, “New Approaches to Assessment of Drug Disposition in the Surgical Patient,”1 prompt us to clarify a fundamental point which is of educational interest.

In our editorial we stated, “Collectively, these studies suggest that anesthesiologists should consider that the doses of many drugs given to surgical patients may need to be changed on commencement of total parenteral nutrition. Drugs eliminated primarily by hepatic metabolism especially require dosage adjustment.” On the basis of the study of Pantuck et al.,2 a uniform change should not be made in the dose of all drugs eliminated primarily by hepatic metabolism. Our editorial emphasized that a uniform change in drug dosage could not be made because of large interindividual pharmacokinetic variations in surgical patients. Nevertheless, intraindividual variations are often small, generally an order of magnitude less than interindividual variations, thereby permitting in a given patient extremely sensitive application of either the antipyrine test or of sequential comparisons of elimination rates of other drugs. This approach enabled Pantuck et al.2 to identify nutritional factors as one potential cause of the previously recognized3 perioperative induction of drug metabolism. While one cannot characterize as changed or unchanged the rate of elimination of a drug added to therapy in a particular patient during or after surgery, Pantuck et al.2 have alerted us to the possibility of altered disposition of certain drugs in some patients following commencement of parenteral nutrition. This should increase the vigilance of anesthesiologists under such conditions. While the antipyrine test was the method used to make this discovery, the antipyrine test has several limitations.4 For example, there is the well-recognized inability to extrapolate closely from results with the antipyrine test to other drugs.4 One important contribution of the test is the demonstration that a given condition often produces large interindividual differences in this inductive effect, as illustrated by the results of Pantuck et al.2 and Duvaldestin et al.3 Therefore, at the present time we recommend a highly individualized approach to drug dosage in all surgical patients. The study of Pantuck et al.2 should alert us to
the possibility of a special subset of patients on parenteral nutrition, i.e., those receiving drugs with low therapeutic indices and drugs subject to extensive hepatic metabolism. Based on their clinical responses, these patients may require adjustment in drug dosages.

ELLiot S. VeseLL, M.D.
Evan Pugh Professor and Chairman
Department of Pharmacology
The Pennsylvania State University
College of Medicine
Hershey, Pennsylvania 17033

JUlien F. Biebuyck, M.B., D. PHIL.
University Professor of Anesthesia and Chairman
Department of Anesthesia

The Pennsylvania State University
College of Medicine
Hershey, Pennsylvania 17033

REFERENCES
(Accepted for publication August 10, 1984.)

New Problem Leaks Out

To the Editor: — The complications and problems associated with the use of the Swan–Ganz catheter are numerous and well documented. 1–5 Recently, however, we encountered a problem not previously described in the literature. A dog was cannulated via the femoral approach for a routine high-frequency jet ventilation study. A #7 Fr. Edwards flow-directed thermodilution catheter was inserted following cutdown and positioned in the pulmonary artery according to waveform. Cardiovascular data were collected repeatedly without difficulty until 2 h later, when there was difficulty obtaining the pulmonary artery occlusion pressure. On two occasions, 1 ml of air was injected into the inflation port but not returned. Because it was suspected that the balloon had ruptured, it was immediately replaced. However, when the catheter was examined, no apparent rupture of the balloon could be seen. Next, the balloon was tested by rapid inflation with 1.5 ml of air, resulting in uniform and sustained inflation; whereas slow inflation confirmed the presence of a small leak. To localize this site, the catheter slowly was inflated under water, and bubbles were seen escaping from the distal weld between balloon and catheter surface. Rapid inflation had resulted in tamponade of the faulty joint with no appreciable leak.

It is recommended that Swan–Ganz catheters be inflated slowly and with the minimum of air to avoid possible rupture. 6,7 This case serves to illustrate one inherent problem associated with Swan–Ganz catheter placement, even when following recommended procedures. Rapid inflation of balloon-tipped catheters cannot be justified, because of increased risk of balloon rupture with resultant air embolism, pulmonary artery damage, or failure to detect preexisting balloon rupture.

RICHard RILEY, M.B., B.S.
Research Fellow
Department of Anesthesia
Montefiore Hospital
3459 Fifth Avenue
Pittsburgh, Pennsylvania 15213

REFERENCES