References

1. Younker D, Rodriguez V, Kavanagh J: Massive air embolism during cesarean section. ANESTHESIOLOGY 65:77–79, 1986
2. Albin MS, Babinski MF, Gilbert J, Smith SL: Venous air embolism is not restricted to neurosurgery (Letter). ANESTHESIOLOGY 59:151, 1983
3. Albin MS, Carroll RG, Maroon JC: Clinical considerations concerning detection of venous air embolism. Neurosurgery 3: 380–384, 1978
4. Amussat JZ: Recherches sur l'introduction accidentelle de l'air dans less veins. Paris, Germer Bailliere, 1839, p 255
5. Bunegin L, Albin MS, Helsel PE, Hoffman A, Hung TK: Positioning the right atrial catheter: A model for reappraisal. ANESTHESIOLOGY 55:343–348, 1981
6. Smith SL, Albin MS, Ritter RR, Bunegin L: CVP catheter placement from antecubital veins using a J-wire catheter guide. ANESTHESIOLOGY 60:238–240, 1984

(Accepted for publication September 11, 1986.)

Anesthesiology
66:94, 1987

In reply:—We appreciate very much the comments offered by Dr. Robinson and Dr. Albin. Their welcome discussion of both precordial Doppler monitoring and appropriately positioned multi-orificed central venous catheters in the management of parturients undergoing cesarean section with regional anesthesia significantly broadens the scope and intent of our original article.

DIRK YOUNKER, M.D.
VICTOR RODRIGUEZ, M.D.
JAMES KAVANAGH, M.D.
Department of Anesthesiology
Baylor College of Medicine
One Baylor Plaza
Houston, Texas 77030

(Accepted for publication September 11, 1986.)

Anesthesiology
66:94, 1987

Safety of Continuous Epidural Infusions

To the Editor:—We read with interest the case report by Lin *et al.*[1] regarding neurologic sequelae after accidental injection of toxic substances into the epidural space. We recognized the potential for this disaster prior to our initiating continuous epidural opiate infusions, and have taken steps to minimize the potential for such an occurrence.

We agree with the authors' recommendations for decreasing such accidents, and offer further suggestions:

1. We use a special solution administration set (#2C1503 Travenol Laboratories Inc., Deerfield, Illinois) which has no injection ports and makes a Leur lock connection with the epidural catheter. In addition, we securely tape this connection.

2. All patients treated with epidural morphine postoperatively are sent to one of two hospital wards where the nursing staff is familiar with epidural opiate analgesia and the equipment involved.

3. Any manipulations of the tubing or catheter are performed by a member of our department.

GLENN A. FROMME, M.D.
Assistant Professor of Anesthesiology

SCOTT R. ATCHISON, M.D.
Instructor in Anesthesiology

Department of Anesthesiology
Mayo Medical School
Rochester, Minnesota 55905

Reference

1. Lin D, Becker K, Shapiro HM: Neurologic changes following epidural injection of potassium chloride and diazepam: A case report with laboratory correlations. ANESTHESIOLOGY 65:210–212, 1986

(Accepted for publication September 15, 1986.)

Anesthesiology
66:94–95, 1987

Safe, Continuous Epidural Infusions

To the Editor:—Drs. Lin, Becker, and Shapiro[1] present a timely report on neurologic changes following accidental drug injection through continuous epidural catheters.

One way that accidental injection of a continuous epidural catheter can be prevented is by the use of rigid tubing without any ports designed for continuous pressure

monitoring. This is manufactured in a variety of lengths. Another very satisfactory tubing that is more flexible and of lower volume is the 60-inch Microbore Extension Set made by Bruce Medical (product code ET-60M). These products have the additional advantages of having Luer lock ends, low volume, and excellent transparency. It is probably a good idea to also color code any connection sites, or to identify this tubing in some other way to further prevent accidental addition of medications into the epidural line.

PHILLIPA L. ZYLANOFF, M.D.
Department of Anesthesiology
University of South Alabama
Mobile, Alabama 36617

REFERENCE

1. Lin D, Becker K, Shapiro HM: Neurologic changes following epidural injection of potassium chloride and diazepam: A case report with laboratory correlations. ANESTHESIOLOGY 65:210–212, 1986

(Accepted for publication September 25, 1986.)

Anesthesiology
66:95–96, 1987

Elimination of Atracurium in Humans

To the Editor:—Fisher and colleagues propose a two-compartment model for atracurium and report that "more than one-half of the clearance of atracurium occurs via pathways other than Hofmann elimination and ester hydrolysis."[1] In the following, a different yet simpler and model-independent pharmacokinetic analysis of their data is offered.

1) The authors make an *a priori* assumption that the pharmacokinetic properties of atracurium can be described using a two-compartment model, and propose that atracurium leaves the central compartment (Fig. 1b) *via* three processes characterized by the rate constants k_{organ}, $k_{in\ vitro}$, and k_{12}. Since the authors did not determine either the amount of atracurium eliminated from the body (hepatic or renal excretion) or the arterio-venous concentration difference for atracurium across the excretory organs, k_{organ} (*i.e.*, the rate constant for hepatic and/or renal elimination) was not amenable to independent estimation. Therefore, k_{organ} becomes pharmacokinetically indistinguishable from, and merges with, k_{12}. This consideration leads to a simplified pharmacokinetic model represented by a *single* compartment out of which atracurium disappears *via* processes controlled by two rate constants: $k_{in\ vitro}$ and a composite rate constant k_x.

2) The data presented in figures 2, 3, and 5 convincingly document a monoexponential degradation of atracurium starting approximately 30 min after its addition to blood *in vitro*. (The derived rate constants $K_{nonorgan}$ presented in Table 1 display incorrect units, *viz.*, min/kg instead of reciprocal time.)

3) Allowing for a lag period identical to that found necessary in the *in vitro* experiments, plasma concentration of atracurium *in vivo* (Fig. 4) also decays monoexponentially.

4) The analysis presented in 2) and 3) demonstrates that the degradation of atracurium in human plasma proceeds monoexponentially *in vitro* as well as *in vivo;* the decay is faster *in vivo* than *in vitro*. Therefore, the simplest and the most plausible descriptions of how atracurium disappears from *plasma* are (using the authors' abbreviations)

$$\textit{in vitro}: \quad C = A \cdot e^{-(k_{in\ vitro}) \cdot t} \tag{a}$$

$$\textit{in vivo}: \quad C = A \cdot e^{-(k_{in\ vivo}) \cdot t} \tag{b}$$

where

$$k_{in\ vivo} = k_{in\ vitro} + k_x \tag{c}$$

The rate constant k_x characterizes the additional disappearance for atracurium *in vivo*. In agreement with the theoretical considerations outlined in 1), the data of Fisher *et al.* may be interpreted as follows: intravenous administration of atracurium leads to its distribution into a *single* volume, approximately equal to between 2 and 3 times the plasma volume (an amazingly small volume of distribution). From here, atracurium disappears by the known processes of Hofmann elimination and ester hydrolysis (represented by $k_{in\ vitro}$ in equations (a) and (c)), as well as by one or more unknown processes (characterized by the rate constant k_x in equation (c)). These postulated, but unknown, decay processes could be: (1) a chemical degradation of atracurium not evident *in vitro*, (2) tissue uptake, and/or (3) elimination of atracurium from the body by the excretory organs. Data on plasma concentrations of atracurium alone cannot differentiate among them. Equation (c) permits partitioning the *in vivo* decay rate constant into two parts of which the unknown part (k_x) contributes about 60% of the total (from Table 1, the average $k_{in\ vitro} = 0.0214\ min^{-1}$ and the average $k_{in\ vivo} = 0.0584\ min^{-1}$; hence, $k_x = 0.0370\ min^{-1}$. The contribution of the rate constant k_x to the total rate constant $k_{in\ vivo}$ is thus about 63%).

In summary, the *a priori* assumption by Fisher *et al.*[1] of a two-compartment pharmacokinetic model for atracurium is not necessary to interpret their experimental data, nor is it supported by these data. Similarly, since no ex-