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In reply: Pharmacokinectic analysis in anesthesia certainly has captured the interest of anesthesiologists as judged by the volume of correspondence arising from two recent thiopental pharmacokinetic publications,[1,2] and an accompanying editorial.[3] A goal of pharmacokinetic data analysis is to use the drug plasma concentration *vs.* time curve to characterize the rate of drug elimination from the body (clearance) and the extent of drug distribution (volume of distribution). These are often the most important parameters with physiologic meaning that can be obtained from plasma concentration *vs.* time data. As Dr. Feingold indicates, there are many mathematical techniques available to characterize the plasma concentration *vs.* time curve and derive the pharmacokinetic parameters of clearance and volume of distribution. Polyexponential equations have the advantages of being mathematically simple, not requiring complicated analytical techniques for fitting, and are used easily to calculate clearance and volume of distribution. There is a large body of experience in their application to pharmacokinetic data analysis.

Drs. Feingold and Mertens are bothered by the large intersubject variability in the thiopental pharmacokinetic parameters. This large variability may be due to the quality of data collection and analysis. It may, however, reflect the true large variability that exists in human populations. Large variability has been shown to be true for theophylline clearance in patients.[4] Large intersubject variability decreases the utility of the population mean as a predictor for any one individual, requires that group sizes be larger to demonstrate statistical differences between different populations, and emphasizes the need for individualization of drug dosage.

I would like to correct a graphical oversight in the editorial figure.[3] The intercept of the distribution phase (A) line should be below the predicted drug plasma concentration at time zero. This correction is shown in figure 1.

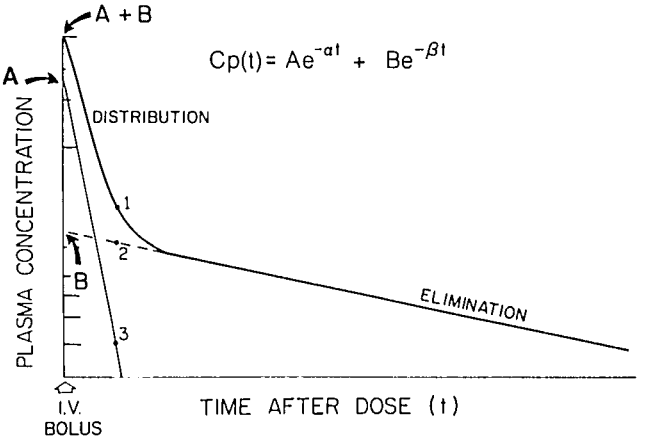

FIG. 1. To characterize the distribution phase it is necessary to subtract the concurrent and slower component of drug elimination. This is done by subtracting point 1 (plasma concentration observed on the distribution phase) from point 2 (corresponding plasma concentration on the extrapolated elimination phase line). The difference is plotted as a separate value, point 3. This feathering or residuals technique is done at several time intervals and a straight line drawn to characterize the residuals. The slope of this line represents the rate constant of the distribution phase (α).

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Another Warning Concerning the Hazards of Selector Shunt Values

To the Editor:—Hypoxic and barotrauma problems relating to the improper use of selector valves connecting ventilators to anesthesia gas machines continue to occur. Several reports of recent occurrences have been directed

to the attention of the ASA Committee on Mechanical Equipment. This problem was reported by Sears and Bocar[1] and additional comments were made by Cooper[2] and Parker.[3]

Since selector shunt valves of this type are currently available in the market place, users must be cautioned to be extremely careful to ascertain that the valves are properly connected and are used only in accord with manufacturers' instructions.

T. C. DEAS, M.D.
Chairman

American Society of Anesthesiologists
Committee on Mechanical Equipment

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Methohexital is Not Contraindicated in Epileptics

To the Editor:—We must contend several statements in the discussion of two case reports by Drs. Rockoff and Goudsouzian of seizures induced by methohexital.[1]

Failure to recognize different effects of barbiturates on the brain at different ages has misled the authors to extrapolate observations on one infant and another young child to recommending the "avoidance of methohexital in patients with psychomotor, temporal or complex seizure disorder" of all ages. The excitatory effects of barbiturates in children are exemplified by restlessness following use for premedication. The selection of methohexital for anaesthesia in their first case after another barbiturate, phenobarbitone, has increased the frequency of the seizures seems questionable.

Methohexital sodium has been administered intravenously to many millions of patients without documented seizures. The few reported have occurred in known or crypto-epileptics with abnormal EEG recordings.[2–7] In our study[8] of 48 epileptics deprived of anticonvulsant medication prior to activated EEG recording, two patients developed grand mal seizures after 30 mg and 20 mg, methohexital 1 per cent respectively. Both patients had a history of grand mal seizures for 9 years and 9 months respectively. The seizure resolved spontaneously in the 25 year old female patient, but airway obstruction necessitated i.v. suxamethonium, laryngoscopy and intubation in the 12-year-old boy. Further iv injections of methohexitone 1 per cent were administered uneventfully in both cases. Goldie *et al.*[9] reported the use of i.v. bolus injection then infusion of methohexital for activated EEG recording in subnormal and mentally ill children. The only reported seizure developed in a normal intelligent boy with idiopathic epilepsy after discontinuation of the 0.1% methohexital infusion. These reports contradict the statement that "the epileptogenic effects of methohexital appear to be limited to individuals with psychomotor seizures".[1]

The significance of the route of administration has not been related to the incidence of seizures. The variable absorption following rectal administration of methohexital is illustrated by the failure of their second patient to go to sleep after two doses of 20-25 mg/kg body weight. We have observed that even incremental intravenous injections of 1.0% methohexital are more likely to precipitate grand mal seizures in starved epileptics from whom anticonvulsant medication has been withdrawn that an i.v. infusion of methohexital 0.09%. However, the later technique did precipitate status petit mal on two occasions and myoclonic jerks on one occasion during 43 administrations. During activated EEG recording, the attending anaesthetist can ensure a patent airway. The same cannot be said for computerised axial tomography of the head. It is difficult to justify the choice of the unreliable route of rectal administration when overdosage and airway obstruction in the supine position is just as likely as underdosage. The intramuscular route allows more reliable absorption of methohexital than given rectally, but the injection of such a large volume as 3 ml into the buttock of a 3½ year old child is hardly the height of compassion!

We would agree with Drs. Rockoff and Goudsouzian that methohexital should be used with care in known or suspected epileptics of all types, particularly in those from whom anticonvulsant medication has been withheld or in whom control is poor. However we agree with Whitwam[10] and Moreland, et al[11] that methohexital is