Anesthesiology
60:526, 1984

Is the Application of an Esmarch Bandage Justified?

To the Editor:—In the recent literature there were reported three cases[1-3] of massive pulmonary embolism (two of them fatal[2,3] following the application of an Esmarch bandage. In two patients[1,2] this event was preceded by 2 weeks of immobilization without anticoagulation. The third patient, however, was anticoagulated and not immobilized for a week before her fatal embolism. Dislodgement of a venous thrombus during application of the Esmarch bandage was most probably the direct cause of embolism in all three cases.

The necessity of a bloodless operative field in limb surgery is indisputable. There are two common means to achieve this goal: 1) exsanguination through an Esmarch bandage and application of tourniquet ischemia; and 2) drainage through vertical positioning of the limb for a few minutes and application of tourniquet ischemia.

There is no doubt that in the second case some blood still remains in the extremity. However, this is manifested only by slight oozing during the incision. Later, there is no bleeding.

Seeing no important differences between these two methods, I do not think the application of an Esmarch bandage prior to tourniquet ischemia is necessary. Especially, not if the possibility of thrombus dislodgement is obviously present. Three reported cases of pulmonary embolism within 2 years should be a serious warning for our surgeons.

DR. MED. DRAZEN N. MIHIC
Privatklinik Linde
CH-2503 Biel
Switzerland

REFERENCES

1. Estrera AS, King RP, Platt MR: Massive pulmonary embolism: A complication of the technique of tourniquet ischemia. J Trauma 22:60–62, 1982
2. Pollard BJ, Pharm B, Lovelock HA, Jones RM: Fatal pulmonary embolism secondary to limb exsanguination. ANESTHESIOLOGY 58:373–374, 1983
3. Mihic DN, Binkert E: Tödliche Lungenembolie nach Blutleere und Periduralanaesthesie. Reg Anaesth 6:83–85, 1983

(Accepted for publication December 1, 1983.)

Anesthesiology
60:526–528, 1984

Acute Tolerance to Thiopental is Alive and Well

To the Editor:—Hudson *et al.*,[1] using power spectral analysis of the electroencephalogram (EEG) to measure the effects of thiopental on the brain, were unable to demonstrate the development of acute tolerance during three sequential infusions of thiopental, 9.6 ± 2.0, 5.6 ± 0.9, and 5.2 ± 1.2 $mg \cdot kg^{-1}$, respectively. But does this disprove the existence of acute tolerance to thiopental? I think not.

We[2,3] first encountered acute tolerance to thiopental in humans more than 30 years ago. Plasma thiopental concentrations at awakening in subjects receiving large doses (43–67 $mg \cdot kg^{-1}$) of thiopental were considerably greater than those at awakening in the same subject after smaller doses (22–40 $mg \cdot kg^{-1}$) (fig. 1, table 1). Indeed, extrapolation of point 4, "orientation," from curve BB ("3.25 grams") to curve AA ("2.0 grams") in figure 1 shows that awakening after the larger dose occurred at a plasma drug level corresponding to deep anesthesia following the smaller dose in the same subject. Dundee *et al.*[4] later reported analogous findings in surgical patients receiving smaller doses (2–15 $mg \cdot kg^{-1}$): the larger the dose, the higher the plasma thiopental level at awakening.

Earlier studies in dogs by Shideman *et al.*[5] demonstrated a related form of acute tolerance to thiopental: when doses of 10 $mg \cdot kg^{-1}$ were repeated at short intervals after apparently complete recovery from the depressant effects of the previous dose, the plasma levels at which the righting reflex returned were successively higher with each additional dose. Altenburg *et al.*[6] also found another form of acute tolerance to thiopental in dogs, using CMR_{O_2} rather than awakening as the parameter of interest: pretreatment with thiopental decreased sharply the rate of decline of CMR_{O_2} produced by subsequent infusion of the drug.

All of the above studies validate the concept of acute tolerance to thiopental by comparing the effects of two

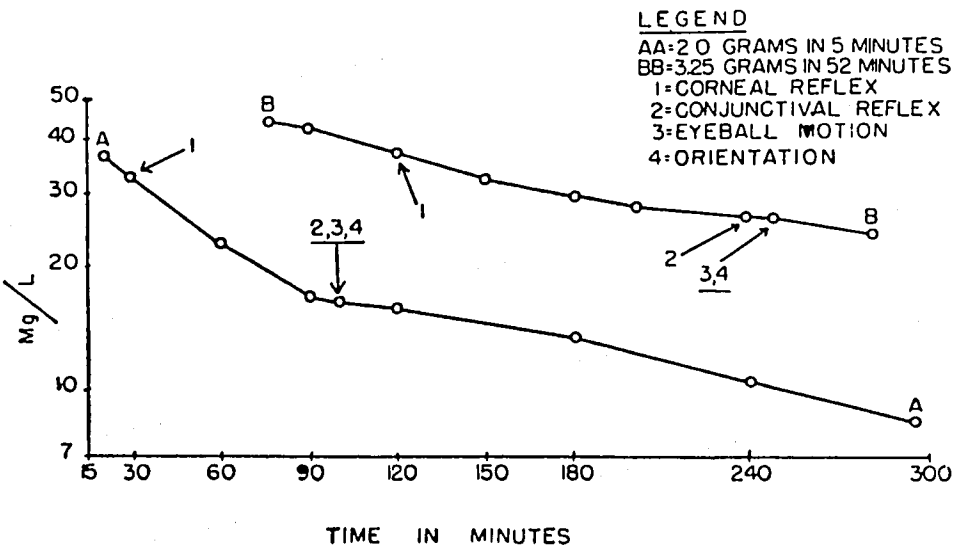

FIG. 1. Plasma levels and clinical signs after two different dosages of thiopental in the same subject.[2]

or more different dosages in the same or different individuals. The phenomenon cannot be recognized by strict adherence to a single dosing regimen, as illustrated with subject N in table 1, whose three large doses of thiopental (50, 54, and 65 $mg \cdot kg^{-1}$) administered at weekly intervals were associated with identical plasma levels at awakening. To the unwary this too would negate the concept of acute tolerance.

Note in passing the clinical corollary: to avoid invoking acute tolerance, keep the doses and increments of thiopental small.

Why did Hudson *et al.* fail to demonstrate the phenomenon in their elegant study? For two reasons—1) while their first dose was not small, they did follow the clinical corollary to a degree by decreasing the dosage of thiopental in their second and third infusions, thereby avoiding further development of acute tolerance (their protocol thus differed from that of Shideman *et al.*,[5] who repeated the full dose each time their dogs awoke and did show acute tolerance with each successive dose); 2) they used a deep stage of thiopental anesthesia (a flaw that they recognized but chose to accept), rather than the lighter levels (awakening) examined by us and others. Consider point 1, "corneal reflex" in figure 1: extrapolation of this point from curve BB to curve AA shows very little difference, *i.e.*, minimal tolerance, for this sign of deep anesthesia, in contrast to the marked difference, *i.e.*, obvious tolerance, with point 4, "orientation," permitting awakening at relatively high plasma drug levels.

TABLE 1. Acute Tolerance to Thiopental.[3] Awakening was Defined as the Subject's Ability to Protrude His* Tongue upon Spoken Command. Doses Administered at Weekly Intervals

Subject	Dose ($mg \cdot kg^{-1}$)	Plasma Level at Awakening ($mg \cdot l^{-1}$)
V	59	32.6
	36	22.6
M	67	27.8
	40	19.3
G	43	19.8
	22	13.2
N	50	26.0
	54	26.0
	65	27.0
	33	16.8

* All subjects were male.

How might Hudson *et al.* utilize their sophisticated technology to demonstrate acute tolerance to thiopental? They might modify their protocol to start with a larger priming dose of thiopental, deliberately overreaching their present EEG end point and following the subsiding plasma levels as the spectral edge receded to its previously chosen position (acute tolerance would predict this to occur at a higher plasma level). Alternatively, although I am less certain of this, they might extend their present protocol for (say) another six or seven repetitions of thiopental dosage to the same EEG end point to determine whether or not the plasma levels remain the same. (Brand *et al.*[7] showed duration of sustained exposure to thiopental could be a factor: using an early EEG-controlled servo apparatus to administer thiopental, they found in many subjects gradually increasing plasma drug concentrations in the face of constant EEG patterns and clinical signs, again validating acute tolerance.)

In sum, with their excellent model and a little extra effort, Hudson *et al.* probably could demonstrate acute

tolerance to thiopental in humans. In any case, the phenomenon *does* exist.

LESTER C. MARK, M.D.
Department of Anesthesiology
Columbia University
New York, New York 10032

REFERENCES

1. Hudson RJ, Stanski DR, Saidman LJ, Meathe E: A model for studying depth of anesthesia and acute tolerance to thiopental. ANESTHESIOLOGY 59:301–308, 1983
2. Mark LC, Papper EM, Brodie BB, Rovenstine EA: Quantitative pharmacologic studies with Pentothal. NY State J Med 49:1546–1549, 1949
3. Brodie BB, Mark LC, Lief PA, Bernstein E, Papper EM: Acute tolerance to thiopental. J Pharmacol Exp Ther 102:215–218, 1951
4. Dundee JW, Price HL, Dripps RD: Acute tolerance to thiopentone in man. Br J Anaesth 28:344–352, 1956
5. Shideman FE, Kelly AR, Adams BJ: Blood levels of thiopental (Pentothal) following repeated administration to the dog. Fed Proc 7:255, 1948
6. Altenburg BM, Michenfelder JD, Theye RA: Acute tolerance to thiopental in canine cerebral oxygen consumption studies. ANESTHESIOLOGY 31:443–448, 1969
7. Brand L, Mazzia VDB, Van Poznak A, Burns JJ, Mark LC: Lack of correlation between electroencephalographic effects and plasma concentrations of thiopentone. Br J Anaesth 33:92–96, 1961

(Accepted for publication December 1, 1983.)