

a separate anesthesia gas machine leak test should be performed with each vaporizer individually dialed to a concentration setting of 0%. A dialed setting of 0% is required because the self-sealing valve ports on the manifold are not open unless the vaporizer is dialed to a concentration (ON). If a significant leak is discovered, the vaporizer should be checked for proper positioning.

Procedures for anesthesia gas machine leak tests that help ensure Ohmeda TEC 4[®] vaporizer mounting integrity appear in both the Ohmeda 8000[®] and Modulus II[™] Operation and Maintenance manuals. They do not, however, appear in the earlier Fraser Harlake Boyle System[®] instruction manuals.

Anesthesiology
62:843, 1985

In summary, it is always important, when mounting an Ohmeda TEC 4[®] vaporizer to ensure correct positioning. Proper positioning is essential for a properly functioning vaporizer. For additional information, contact Ohmeda at (608)221-1551.

RAYMOND T. RIDDLE
Product Compliance Administrator
Ohmeda
P.O. Box 7550
Madison, Wisconsin 53707

(Accepted for publication January 16, 1985.)

Beta-adrenergic Blocking Drugs and Apnea

To the Editor:—With interest I read the report on "Timolol and Postoperative Apnea in Neonates and Young Infants" by Bailey.¹

Recent research concerning overdoses of beta-adrenergic blocking drugs (propranolol, timolol, and sotalol) in experimental animals was performed in the National Institute of Public Health and Environmental Hygiene, Bilthoven, The Netherlands. These experiments showed the primary cause of death to be respiratory arrest. When death from respiratory arrest was prevented by artificial ventilation the survival time, using the same doses of the drugs, was significantly prolonged.* When much larger doses of the drugs were used in ventilated animals, death occurred from hemodynamic and cardiac failure.

Some beta-adrenergic blocking drugs are rapidly absorbed when applied topically to the eye, which might easily lead to overdose, especially in children. In

addition, there may be an increased susceptibility in the neonate to this type of drug or immaturity of the blood brain barrier. Any or all of these factors may have been responsible for the apnea reported by Dr. Bailey, which would seem to confirm our finding that overdose of certain beta blockers produces respiratory arrest. It would be interesting to know whether there were other observed signs that can be ascribed to beta-adrenergic blockade such as a decrease in heart rate and blood pressure.

J. J. M. LANGEMEIJER, M.D.
Department of Anesthesiology
University Hospital
Catharijnesingel 101
Utrecht
The Netherlands

REFERENCE

1. Bailey PL: Timolol and postoperative apnea in neonates and young infants. ANESTHESIOLOGY 61:622, 1984

(Accepted for publication January 16, 1985.)

* Langemeijer JJM, De Wildt DJ, De Groot G, Sangster B: Respiratory failure as main determinant of toxicity due to overdose with different beta-blocking drugs in rats, unpublished data.

Anesthesiology
62:843-844, 1985

Cortisol Following Etomidate Administration: Should We Give It the Time of Day?

To the Editor:—The excellent studies by Wagner and White¹ and by Fragen *et al.*² document that etomidate decreases adrenocortical response to surgery. However, neither group of investigators considered the possible effect of the circadian rhythm in plasma concentration

of cortisol. During a normal circadian rhythm, plasma concentrations of cortisol may vary by a factor of five or more (*e.g.*, typically from a nadir of 3 $\mu\text{g}/\text{dl}$ at midnight to a peak of 15 $\mu\text{g}/\text{dl}$ at 6:00 A.M.).³ These circadian-related alterations in cortisol levels are similar

in magnitude to the changes in cortisol following etomidate administration. For instance, plasma concentrations of cortisol decreased significantly from a baseline value of 11.4 $\mu\text{g}/\text{dl}$ to an average of 5.5 $\mu\text{g}/\text{dl}$ in the first and second hours after induction of anesthesia with etomidate.² Some or all of this decrease may be related to the circadian variation in plasma concentrations of cortisol.

Any contribution of the circadian rhythm would tend to increase the variability of plasma concentrations of cortisol measured following etomidate administration. These circadian-related changes may explain, at least in part, the conflicting results obtained by different investigators in this area of research.

DONALD D. KOBLIN, PH.D., M.D.
Resident in Anesthesia

Anesthesiology
62:844, 1985

*Department of Anesthesia
The Milton S. Hershey Medical Center
College of Medicine
The Pennsylvania State University
P.O. Box 850
Hershey, Pennsylvania 17033*

REFERENCES

1. Wagner RL, White PF: Etomidate inhibits adrenocortical function in surgical patients. *ANESTHESIOLOGY* 61:647-651, 1984
2. Fragen RJ, Shanks CA, Molteni A, Avram MJ: Effects of etomidate on hormonal response to surgical stress. *ANESTHESIOLOGY* 61:652-656, 1984.
3. Moore-Ede MC, Czeisler CA, Richardson GS: Circadian time-keeping in health and disease. Part 1. Basic properties of circadian pacemakers. *N Engl J Med* 309:469-476, 1983

(Accepted for publication January 16, 1985.)

The Renal Effects of Dopamine

To the Editor:—By using dobutamine to control for the effects of dopamine on systemic blood pressure and flow, renal plasma flow, and glomerular filtration rate (GFR), Hilberman *et al.*¹ quite elegantly show that the diuretic and natriuretic effects of dopamine are independent of these variables. They go on to suggest, however, that dopamine inhibits tubular solute reabsorption directly. As pointed out by Miller² in his editorial, the control of tubular function is complex and may depend on multiple variables in addition to global renal plasma flow and GFR, including changes in the regional distribution of blood flow within the kidney and stimulation of many different types of adrenergic receptors or sympathetic nerve terminals located in both proximal and distal tubules.

An alternative, and more readily verifiable explanation for the observations of Hilberman *et al.* is that the dopamine infusion may have suppressed the adrenal secretion of aldosterone. Tonic dopaminergic suppression of plasma aldosterone, perhaps maximal even at endogenous levels of dopamine in normal individuals, has been demonstrated by the use of dopamine antagonists and infusions by Noth *et al.*³ There is also *in vitro* evidence to suggest that this effect may occur in the adrenal glomerulosa cells, independent of the effect of dopamine on renal blood flow and the resultant suppression of the renin-angiotensin-aldosterone system.^{3,4}

Hilberman *et al.* state that elevation of plasma angiotensin-II was likely in their post-cardiac surgical patients, but they do not comment on the stimulation of aldoste-

rone release that would result, and they did not measure plasma aldosterone levels before and after the infusions of dopamine and dobutamine. Suppression of aldosterone secretion might account for at least part of the diuresis and natriuresis seen in the dopamine group. Studies attempting to demonstrate a direct natriuretic and diuretic effect of dopamine on the renal tubule will need control for this important variable.

G. MARK CRAMOLINI, M.D.
*Instructor in Anesthesia
Harvard Medical School,
Assistant in Anesthesia,
The Children's Hospital
300 Longwood Avenue
Boston, Massachusetts 02115*

REFERENCES

1. Hilberman M, Maseda J, Stinson EB, Derby GC, Spencer RJ, Miller DC, Oyer PE, Myers BD: The diuretic properties of dopamine in patients after open-heart operation. *ANESTHESIOLOGY* 61:489-494, 1984
2. Miller ED Jr: Renal effects of dopamine (editorial). *ANESTHESIOLOGY* 61:487-488, 1984
3. Noth RH, McCallum RW, Contino C, Havelick J: Tonic dopaminergic suppression of plasma aldosterone: *J Clin Endocrinol Metab* 51:64-69, 1980
4. McKenna TJ, Island DP, Nicholoso WE, Liddle GW: Dopamine inhibits angiotensin-stimulated aldosterone biosynthesis in bovine adrenal cells. *J Clin Invest* 64:287-293, 1979

(Accepted for publication January 16, 1985.)