

## CORRESPONDENCE

failure. Thus, he argues that such an analyzer is essential and would not rely on the setting of the vaporizer to indicate effective concentration. However, we remember that anesthesia was given successfully 20 yr ago, when analyzers were not in common use and the danger of overdose was far greater with the more soluble anesthetics. Two additional observations come to mind. First, any failure that might occur almost certainly would lead to an underdose rather than an overdose, because the vaporizer would shut off. Second, warning signs of overdosing should emanate from not only the analyzer (a signal, presuming limits had been set to detect such an event) but also from the patient (increased pulse rate and decreased blood pressure).

We accept Szocik's suggestion that we include the cost of loading the anesthetic circuit and patient's lungs, a cost that favors isoflurane. Even the small additional amount of \$0.25 for the first 30 min of desflurane probably should not be ignored.

Johnstone correctly notes that both desflurane and isoflurane are considerably more expensive than halothane. Similarly, Abajian and Viscomi ask why we did not include halothane and enflurane in our discussion. Given the current medicolegal concerns regarding the administration of halothane to adults, is halothane a viable alternative? We compared only desflurane and isoflurane because the use of halothane for adults has virtually disappeared in the United States. Also, the use of enflurane has decreased so markedly that it, too, is of limited interest.

Johnstone, Abajian and Viscomi, Macario, and Meyer believe that marketing issues, such as the pricing of a drug before *versus* after expiration of its patent, would limit our analysis. Generic competition might further lower the price of isoflurane, and patent protection may allow an increase in the price of desflurane. Either change would increase the relative cost of adopting desflurane as part of one's practice. However, figure 2 in our report can be used to compare cost at

any new price that might be set. The concern regarding future price changes implies that there is a danger to the acceptance of desflurane—that one might become “addicted” to its use. This concern ignores the modular nature of modern anesthetic machines and underestimates the assertiveness of most anesthetists. Ohmeda has made a “revolutionary” vaporizer that can be substituted for other Tec-type vaporizers. However, such a substitution can be immediately reversed by the anesthetist who does not become “addicted” to the use of desflurane and who concludes that the benefit does not justify the cost.

Thus, we are not as pessimistic as some of the correspondents appear to be concerning the cost of desflurane *versus* the cost of isoflurane. Desflurane can be *more or less* costly to use than isoflurane. Reducing the cost of desflurane requires an understanding of pharmacokinetic principles. Applying those principles may be slightly more complicated than the approach suggested, for example, by Johnstone. It is, however, more rational.

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(Accepted for publication March 9, 1994.)

Anesthesiology  
80:1408-1409, 1994  
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## Digoxinlike Immunoreactive Substance in Critically Ill Patients

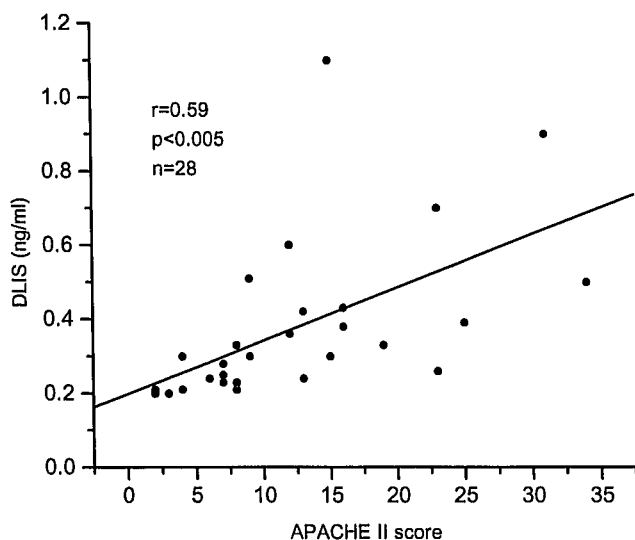
*To the Editor:*—A digoxinlike immunoreactive substance (DLIS) has been detected in the absence of treatment with cardiac glycosides in the serum of patients with renal or liver failure, in newborn infants, and in third-trimester pregnant women.<sup>1,2</sup> The structure and physiologic function of DLIS are unknown. DLIS is produced principally by the adrenal gland.<sup>3</sup> It inhibits Na<sup>+</sup>/K<sup>+</sup>-adenosine triphosphatase and may produce natriuresis. For this reason it has been proposed that DLIS is produced in conditions of volume overloading.<sup>4</sup> We therefore have examined the occurrence of DLIS in patients of an intensive care unit.

The sera of 135 randomly selected patients were analyzed on the day of admission by fluorescence polarization immunoassay (FPIA). This method is used most widely for digoxin monitoring but also has a high sensitivity to DLIS.<sup>5</sup> All digoxin determinations were done in the Abbott TDx<sup>®</sup> autoanalyzer with FPIA reagents (Digoxin II reagent pack, Abbott Diagnostics, North Chicago, IL). The digoxin antiserum (rabbit) does not cross-react with other drugs except dig-

itoxin. FPIA digoxin immunoreactivity was extrapolated from fluorescence polarization data stored in the autoanalyzer and consisting of analytic digoxin standards (Abbott Diagnostics). Before digoxin measurement by FPIA, the serum protein was precipitated, in accordance with the manufacturer's recommendations. None of the patients had been treated with a cardiac glycoside. We also determined the patients' Acute Physiology and Chronic Health Evaluation II (APACHE II) score, which has been found to correlate with the subsequent risk of hospital death.<sup>6</sup>

Of the 135 patients tested, 101 had nonmeasurable DLIS concentrations; 6 had DLIS concentrations less than the lower detection limit of 0.2 ng/ml (for a total of 107 DLIS-negative patients); and 28 (21%) had DLIS concentrations greater than 0.2 ng/ml (28 DLIS-positive patients). Of the 28 DLIS-positive patients, only 6 showed signs of liver or renal impairment. The DLIS-positive group consisted of patients with head injury (4), liver failure (3), rupturing abdominal aneurysm (1), coronary bypass surgery (2), acute heart transplant

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**Fig. 1.** Relation between the concentration of digoxinlike immunoreactive substance (DLIS) and the Acute Physiology and Chronic Health Evaluation II score in DLIS-positive patients. The DLIS concentration is positively correlated with the APACHE II score. DLIS and APACHE II evaluations were performed on the day of admission.

rejection (1), multiple stab wounds (1), renal insufficiency (3), eclampsia (1), respiratory insufficiency (4), esophageal neoplasm (1), sepsis with peritonitis (4), necrotizing fasciitis (1), epidural abscess (1) and meningitis (1). The hospital mortality of the DLIS-positive patients was significantly greater than that of the DLIS-negative patients (14 of 28 vs. 9 of 107;  $P < 0.001$ ), with a predictive value of  $14/28 = 50\%$  (sensitivity  $14/23 = 61\%$ ; specificity  $98/112 = 88\%$ ). Only 1 of 8 patients with DLIS concentrations greater than 0.4 ng/ml survived. We also demonstrated a positive correlation between the APACHE II score and the DLIS concentration in the DLIS-positive group (fig. 1). DLIS concentrations did not, however, correlate with any of the factors making up the APACHE II score.

These data suggest that DLIS is produced in critically ill patients without liver or renal failure. Drug monitoring in these patients could therefore detect falsely high glycoside levels. Moreover, the data suggest that DLIS is an effective marker of increased mortality risk. Further studies are necessary to evaluate the physiologic and therapeutic factors influencing DLIS production in critically ill patients.

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(Accepted for publication March 9, 1994.)