To the Editor:

We read with interest the letter by Dr. Hildebrandt which raises three issues. The first is the interpretation of Figure 4. The data and regression coefficients in Figure 4 are correctly plotted. The labeling of the x and y axis is apparently potentially confusing. In Figure 4A and B, the y axis is Δ lung-thorax elastance (ΔELT), and for Figure 4C and D, the y axis is Δ lung-thorax compliance (ΔCLT). The regression coefficient for the data in Figure 4C is y = 0.5x + 0.33. Thus changes in ΔCLT (y) are indeed one-half those in lung compliance (x).

The second issue is the relative contribution of changes in lung (EL) or chest-wall elastance (Ecw) to changes in ΔELT. Dr. Hildebrandt notes that when one excludes data in which ΔELT was ± 5 cmH2O/L, changes in Ecw contributed nearly half of the total change. We noted this in the Results section of our manuscript (i.e. in some patients changes in ELT were due primarily to changes in Ecw). In fact, changes in Ecw accounted for at least half the observed change in ELT in nine of 30 observations. For these nine step changes in PEEP the average |ΔELT| was 2.3 and |ΔEcw| was 2.1 cmH2O/L. From a clinical point of view this magnitude of change is relatively insignificant. In contrast, the majority of step changes in which ΔELT changed by ± 5 cmH2O/L were reflective of changes in EL and not Ecw. Most but not all were at higher PEEP steps. Changes of this magnitude are clinically important and related to changes in lung status.

The third issue is whether elastance (E) is a more sensitive index of changing lung status than compliance (C). Dr. Hildebrandt is, of course, correct in that the relative changes in magnitude must be equal. If changes in E and C are indeed interpreted relatively, then of course both will yield the same information.

Our point relates to what we believe to be the common intuitive response of the bedside clinician. For example, consider a constant tidal volume of 1 L; lung status deteriorates sequentially and airway pressure progressively increases from 10 to 20 cmH2O and, later, from 40 to 50 cmH2O. The two changes in elastance are identical at 10 cmH2O/L. The comparable changes in compliance are 50 ml/cmH2O and 5 ml/cmH2O respectively. We believe these differences in incremental values can lead to inappropriate clinical conclusions as to the magnitude of deterioration. “Discrimination” might have been a better term than “sensitivity.”

Jeffrey A. Katz, M.D.; H. Barrie Fairley, M.B., B.S.; Gerard M. Ozanne, M.D.; and Steven E. Zinn, M.D., Department of Anesthesia, University of California, San Francisco General Hospital, San Francisco

Reprint requests: Dr. Katz, 1001 Potrero Avenue, Department of Anesthesia, San Francisco 94110

Erythromycin-Induced Digoxin Toxicity

To the Editor:

Lindenbaum et al1 have described the tendency of some people to develop cardioactive, reduced metabolites of digoxin. After antibiotic administration, this process may be reversed resulting in elevation of serum digoxin levels.

The purpose of this communication is to report what we believe to be the first recognized case of erythromycin-induced digoxin toxicity.

CASE REPORT

A 71-year-old retired nurse was admitted to The Brooklyn Hospital with severe back pain. Ten months before, she had aortic valve replacement with a prosthetic aneurysm for aortic stenosis and insufficiency. This operation was complicated by a myocardial infarction that resulted in severe left ventricular dysfunction. With vasodilator therapy (hydralazine and isosorbide dinitrate), furosemide, digoxin, 0.25 mg per day, and warfarin, she was subsequently able to work as a volunteer at the hospital. Steady state digoxin levels obtained periodically ranged between 1.4 and 1.7 ng/ml and prothrombin time ranged between 25 and 32 sec. Serum creatinine, measured one month before admission, was 0.9 mg/dl. Four days before admission, she developed cough and wheezing. Chest x-ray film showed no change in heart size or lung field. Erythromycin, 250 mg, and theophylline were prescribed. Because of nausea, which occurred only after she ingested the medication, she took only four erythromycin tablets and stopped the theophylline. Two days later, after paroxysmal coughing, she developed back pain which subsequently resulted in her hospitalization. Shortly after admission, which was four days after taking 1 g of erythromycin, she developed severe nausea and vomiting. Electrocardiogram at that time showed an A-V junctional rhythm; digoxin level was 2.6 ng/ml. Prothrombin time was 47 sec. Serum creatinine was 1.4 mg/dl at time of admission and was subsequently found to be 1.0 and 0.9 mg/dl while in the hospital. After stopping digoxin, nausea abated and sinus rhythm returned. Subsequently, both digoxin and warfarin were resumed at lower doses. One month later, digoxin, 0.25 mg per day, was resumed and steady state digoxin was 1.3 ng/ml. Serum creatinine was 1.2 ng/dl at this time.

This woman developed marked prolongation of prothrombin time and elevation of digoxin levels associated with ECG and gastrointestinal toxicity four days after receiving 1 g of erythromycin. These changes occurred even though she had been taking the same dosages of digoxin and coumadin. Also, toxicity did not recur when the same dosages of these drugs were resumed one month later. She did not demonstrate any changes in renal or hepatic function that could explain what, until that time, had been stable blood values. This report therefore would appear to illustrate the clinical significance of the findings of Lindenbaum et al.1 It also suggests that a small dose of orally administered erythromycin (1 g) can alter gut flora substantially, resulting in concomitant increased prothrombin time and serum digoxin level concentrations to toxic levels.

Howard S. Friedman, M.D., F.C.C.P., Chief of Cardiology; and Martin V. Bonencontre, M.D., Director of Medicine, The Brooklyn Hospital, Brooklyn

Reprint requests: Dr. Friedman, Chief of Cardiology, The Brooklyn Hospital, Brooklyn 11201

REFERENCE

1 Lindenbaum J; Rund CG; Butler VP, Jr; Tse-Eng D; Saha JR. Inactivation of digoxin by the gut flora. N Engl J Med 1981; 305:789-94.