food should interfere with nitrate effects.\(^1\)

Recent hemodynamic studies in coronary patients indicate increased cardiac and stroke index without changes in mean arterial or pulmonary wedge pressures, which is consistent with the effect of food on STI in our study.\(^2\) Previous studies of normal conscious dogs were also in agreement, indicating an enhanced inotropic state during the postprandial period.\(^3\) These findings could have had a bearing on the altered thallium myocardial kinetics reported by Wilson and colleagues, perhaps through alterations in flow, and as the authors suggest, myocardial metabolism.

**To the Editor:**

Dr. Spodick's comments concerning the effect of eating on cardiac hemodynamics are greatly appreciated. With specific reference to our study, they point out the possibility that the increased clearance of thallium-201 from the myocardium may have been due in part to a decrease in coronary resistance and, therefore, an increase in coronary blood flow (since arterial pressure also increased), as observed by Vatner et al.\(^1\) However, previous studies by us failed to show an increase in coronary blood flow during intravenous infusion of glucose-insulin-potassium solution, even though thallium-201 myocardial clearance increased.\(^2\) We cannot exclude an increase in coronary blood flow in the patients who ate, but suspect that an independent effect of insulin on the myocardial handling of **K**\(^+\) is also involved. Future studies are needed to elucidate the relative importance of flow and metabolism in **K**\(^+\) kinetics.

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**Effects of Beta-Adrenergic Agents on Hypokalemia**

**To the Editor:**

We read with interest the paper of Rohr et al entitled, "Efficacy of parenteral albuterol in the treatment of asthma" (Chest 1986; 89;348). The authors discuss different metabolic effects of adrenergic agents parenterally administered. They note that these drugs could produce hypokalemia, potentially dangerous especially in patients with previous borderline or low serum K\(^+\) levels. This effect was previously described with different \(\beta\_2\)-adrenergic agents administered either by inhalation or per os.\(^4\) In this context, it is interesting to note our findings in a group of 12 patients with COPD to whom we administered a \(\beta\_2\)-adrenergic agent (pirbuterol, 15 mg p.o.).\(^4\) None was on steroid or digitalis therapy. Aminophylline and diuretic therapies were withdrawn 24 hr before study. In these patients, we measured plasma K\(^+\) and systolic blood pressures for gas analysis obtained through an indwelling catheter placed in the humeral artery. The samples were obtained before and at 60, 120 and 150 min after pirbuterol administration. Control plasma K\(^+\) (mean±SEM) was 4.25±0.14 and 3.76±0.07, 3.71±0.07 and 3.78±0.11 mEq/L at 60, 120 and 150 min after pirbuterol administration, respectively. These values were significantly different as compared with control values (p<0.001).

Maximal decrease of plasma K\(^+\) \((\Delta \text{max } K^+)\) was 0.58±0.10, range 0.10-1.20 mEq/L, and occurred in nine of the patients at 60 or 120 min. No significant changes were found in PaCO\(_2\) or pH control values when compared with those at the moment of \(\Delta \text{max } K^+\) (PaCO\(_2\) 47.8±2.4 vs 49.1±2.3 mmHg; pH 7.39±0.01 vs 7.36±0.01). A significant correlation was found between control plasma K\(^+\) values vs \(\Delta \text{max } K^+\) after pirbuterol administration (Fig.1).

That signifies that the patients with higher control plasma K\(^+\) levels would respond strongly to \(\beta\_2\)-adrenergic stimulation, while those who have lower plasma K\(^+\) levels this response is less evident.

As far as we know, this response has not been previously described. We believe that this finding has clinical implications suggesting that previously hypokalemic patients respond to \(\beta\_2\)-adrenergic stimulation with a lesser decrease in plasma K\(^+\) levels. The mechanisms involved could be attributed to the decrease in the activity of the Na\(^+\)-K\(^+\) pump ATPase activated and the modification of the cellular membrane permeability to ions as the concentration of extracellular K\(^+\) diminishes.\(^5\)\(^6\)

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**References**


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**Figure 1.** Correlation between control plasma K\(^+\) values vs \(\Delta \text{max } K^+\) after pirbuterol administration.
To the Editor:

We were interested by the possible association between the control serum K⁺ levels and maximum decrease in serum K⁺ after β₂-adrenergic drug administration described by Raimondi et al. When we re-examined our data in this light there was no linear correlation found in the group that received IM albuterol (r = .10), a weak correlation in the IV albuterol group (r = .50) and a good linear correlation in the SC albuterol group (r = .79). Overall our data may suggest a linear correlation between serum K⁺ and the maximum decrease in serum K⁺, but certainly not as strongly as the data shown by Raimondi et al. (r = .87). Unfortunately, the authors do not mention whether or not their subjects had recently received any β₂-adrenergic agents prior to the evaluation day.

Even if this correlation is borne out by future work in this area, it must be kept in mind that we observed significant EKG abnormalities in subjects with a relatively low control serum K⁺, but not in subjects with the largest decrease in serum K⁺.

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Erratum

To the Editor:

Our published abstract entitled "Impact of Diagnosis-related Groups' Prospective Payment on Utilization of Medical Intensive Care" contains an error due to a previously-overlooked miscalculation. (Chest 1986; 89:445s.)

The middle of the abstract states, "In the first six months of 1985, 113 Medicare patients treated in MICU showed an average loss per discharge of $9,807, which rose to $18,360 among those who expired (35 percent)." The corrected statement should read, "In the first six months of 1985, 113 Medicare patients treated in MICU showed an average loss per discharge of $11,875, which rose to $30,304 among those who expired (35 percent)."

This correction does not in any way change the message or the conclusions of the abstract.

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Steroids in COPD

The Scripture According to Albert

To the Editor:

The controversy of corticosteroid use in stable chronic obstructive pulmonary disease rages on (Chest 1986; 89:494-90). However, the apparent efficacy of steroid treatment in acute exacerbations of COPD has been resoundingly established forever with a single well-designed trial by Albert. This study has been referenced in nearly every article on the topic of steroids in COPD since it was reported in 1980. Sahn, Hudson, Mendelsta and even Eliasson (a staunch opponent of steroids in COPD) proselytize a role for corticosteroid therapy in patients with chronic bronchitis and acute respiratory failure.

Because it is a "landmark" case and the sole study quoted to justify steroid use in acute exacerbations of COPD, I believe Albert's study deserves special scrutiny. When analyzed correctly, his trial does not support the use of steroids, but rather clearly demonstrates the lack of efficacy in this situation.

Albert et al designed an excellent study. They conducted a double-blind, randomized, placebo controlled trial of patients with acute exacerbations of COPD. Both groups received therapy with intravenous aminophylline, inhaled isoproterenol and ampicillin. The steroid group received 0.5mg/kg of methylprednisolone every 6 hrs intravenously. At the initiation of the study, the steroid and placebo groups were felt to be statistically similar with respect to a number of variables including age, arterial blood gases, FEV and FVC. The only flaw in this protocol was the failure to report and compare presenting theophylline levels or evidence of pulmonary infection such as sputum cultures or chest x-ray findings. Differences in these data between the two groups would influence an apparent response to treatment. If at presentation the patients in the methylprednisolone group had significantly lower theophylline levels, a clinical response (as compared to placebo) may have been falsely attributed to corticosteroid therapy when in fact instituting adequate theophylline levels made the difference.

Unfortunately, despite a good study design, Albert used unsound statistical methods to analyze the data. He consequently erroneously rejected the null hypothesis and claimed a statistically significant difference between the control and steroid groups. His major mistake was to compare the percent change in FEV₁ and FVC relative to the presenting values. Any two measurements over time from the same individual are not independent but correlated. Therefore, the difference or percent change in these measurements are not solely a function of the subjects' experience or treatment in the time interval. Albert should have simply used the Student's unpaired t-test to compare the absolute FEV₁ and FVC of the placebo and steroid groups at the end of the trial as he did at the beginning.

Albert states that the admitting FEV₁ levels for the placebo group (675 ± 267 ml) and the steroid group (602 ± 240 ml) were not statistically different (p<0.1). However, the degree of obstruction is important because of the effect of regression to the mean. The lower the initial pulmonary function (further from the mean), the greater the likelihood for a subsequent measurement to show improvement (movement towards the mean). Albert amplifies this tendency by using the initial FEV₁, as the denominator to calculate the percent change in subsequent FEV₁ measurements. Regardless of treatment, the methylprednisolone group has a greater probability of showing a significant improvement because of its greater initial obstruction.

Albert did not report his raw data, but I was able to estimate the prebronchodilator FEV₁ for the placebo and methylprednisolone groups from the graph of mean percent changes he presented. At the end of the trial, the mean placebo and steroid FEV₁ were approximately 796 ml and 801 ml respectively. I doubt they are statistically different.

When the data from Albert's study is analyzed as it should be (using absolute volumes rather than percent changes) there appears to be no significant differences between the control and methylprednisolone groups. The calculated probability of a type 2 error is less than 0.2 in this study. The null hypothesis must therefore be accepted and I conclude that steroid therapy does not play a