oxidative stress but also to HIV replication and disease progression. Although animal studies are exciting, results from these studies cannot be used as claims of efficacy in the treatment of human diseases unless proper clinical trials are performed. For example, vitamin E may slow cancer development in murine AIDS (5), but in human smokers (6), another oxidatively stressed population with antioxidant deficiencies, supplementation with vitamin E and β-carotene actually increased risk for lung cancer. What about the HIV population? Observational studies (7, 8) suggest that over-the-counter multivitamin and antioxidant vitamin supplements may have some benefits and slow the progression to AIDS. On the basis of our study (4), I agree with Watson that such supplements may be used in an attempt to overcome antioxidant deficiencies. However, it is not yet proven that these supplements given to humans infected with HIV will result in the same efficacy as reported in in vitro or animal studies. So far, few trials have addressed this issue. In HIV-infected patients, a trial investigating the effect of β-carotene supplementation on immune function was negative (9) and another with selenium and β-carotene produced mixed results (10).

Therefore, from our point of view, although antioxidant supplementation has been proven to be of benefit in animal models, the data on supplementation in humans are unfortunately lacking. We hope to be able to remedy this in the near future; we have now documented increased oxidative stress and antioxidant micronutrient deficiencies in humans infected with HIV. As for "the mechanisms underlying the increased oxidative stress but also to HIV replication and disease progression..." we agree with Watson that it is likely these are related mostly to activated polymorphonuclear leukocytes and cytokine production, as mentioned in the introduction of our article (4).

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Bioimpedance: 50 kHz parallel reactance and the prediction of body cell mass

Dear Sir:

Several important comments need to be made concerning the paper by Kotler et al (1). Although a rhetorical case was made for body cell mass (BCM) predicted by 50-kHz parallel reactance (Xp), no theoretical basis was provided. Kotler et al stated that a major uncertainty in the theory underlying bioelectrical impedance analysis is whether the body's ionic conductivity is arranged as a series or parallel circuit. We can find no rigorous study in the literature supporting this statement or any single-frequency (SF) prediction of cell volume. It was suggested that the improved prediction of total body potassium (TBK) by Xp compared with series reactance (Xs) was proof that Xp was superior for predicting BCM. Impedance measured at any SF can be interpreted as a series or parallel circuit, with both resulting in 2 final elements, resistance (R) and reactance (X). The problem is that biological tissue consists of >2 elements (2, 3). A 3-element model, consisting of resistance extracellular water (Re) in parallel with a series cell membrane capacitance (Cm) and resistance intracellular water (Ri), has been used since 1925 to interpret impedance measurements on individual biological cells (2). Cole added an important fourth term to the model (exponent α) in 1940 to represent the effect of the infinite number of series Cm and Ri values (cells) in a cell suspension (tissue) (3). The improved correlation in predicting TBK-BCM with Xp compared with Xs means nothing because Xs is not used for anything and neither Xp nor Xs has any scientific basis.

It should be noted that the Xp equation has R in it. The correlation and SEE values for the predicted BCM by Xp were only 0.04 and 1.1% better, respectively, than when series R alone was used (Kotler et al’s Table 5). The same R was also used to predict total body water (TBW). Lulaski (4), who is now a proponent of an Xp-predicted BCM, previously promoted X as a measure of extracellular water (ECW). Confusingly, this was dismissed several years later by the same authors in Kotler et al’s paper because X was contributing virtually nothing to the prediction (5). Resistance predicts ECW, intracellular water (ICW), and TBW with
almost equal accuracy at any SF (6). How well did R alone at 50 kHz predict ECW? Reference measures of both TBW and ICW had been measured.

The prediction of TBW with use of R is dependent on a high intercorrelation between ECW and TBW (6) because only a portion of ICW is measured (2). Furthermore, the proportion of ICW measured at 50 kHz varies with characteristic frequency, which changes when the ECW, ICW, or cell membranes change (2, 7). The ECW and ICW resistivities differ by a factor of 3–4 (2). To predict TBW with an SF resistance requires that TBW resistivity be known and remain constant. How can it remain constant when a simple change in the ratio of ECW to ICW will change it (2, 7)?

Kotler et al made the statement that a "logarithmic transformation" was more representative of the body's complex shape (1). Kotler's group discovered randomly what we have been reporting since 1992, that the relation between impedance and body water is nonlinear because of mixture effects (that is, conductor-nonconductor interactions) (2). The exponent Kotler et al discovered statistically for height (Ht) was close to the 1.5 exponent we reported in 1992 by using Hanai mixture theory (2). We found that Ht\(^{1.5}\) provided a simple form of mixture theory but relied on differences in body composition being purely due to differences in fluid rather than differences in both conductor and nonconductor. By developing a new equation that incorporated total object volume, we found that both conductor and nonconductor effects were accounted for (2).

Kotler et al used TBK and BCM interchangeably throughout their paper, reported no absolute values for TBK or BCM predicted by X\(_p\), and did not report exactly how BCM was determined (1). The relation between TBK and BCM is derived only from the ICW-BCM relation. Without a report of how BCM was determined, this study cannot be replicated. Kotler et al assumed that if the regression coefficients, SEEs, means, and SDs for the model and validation groups were not different statistically, the derived model was valid. Final results were reported by using equations derived from the entire group. Although correlation and SEE values for the model and validation groups were reported, the regression coefficients and mean offsets were not. Thus, the cross-validation reported could not be fully evaluated. If the parameters of an equation vary randomly and are sample dependent, the scientific basis of the equation can be challenged and it would be poor at detecting change. It is curious that the scaling coefficients (statistically derived ICW resistivity) reported for the entire group were 59.06 for males and 1.30 for females (1). Such a difference between males and females is not realistic. The predictions across the board were significantly improved when the sexes were combined. That there was significant random error is supported by Kotler et al's Figure 1 (1), in which there were many outliers, some out by as much as 50%. Possibly this explains why only correlations and SEE percentages were reported.

Impedance is frequency dependent, so how well did X\(_p\) at different frequencies predict BCM? Was the best prediction provided by 50 kHz? If the Cole model (3) and basic alternating circuit theory have any validity, X at any SF, either parallel or series, will be affected by all of the elements in the tissue (that is, \(R_{EF}, R_p, C_m, \text{ and } \alpha\)). What is the effect of a change in each of these variables on X\(_p\)? If X\(_p\) does not physically relate to TBK or is reliant on the elements in the tissue having relative uniformity between individuals, its ability to measure change will be poor. Because of high intercorrelation between variables, only data that conform to a plausible physical model (eg, Cole's model) should be considered (2). An investigation to answer many of these questions was conducted recently (7).

In closing, why is there such a need to make an SF measurement work? Whatever the reason, it does not appear to be based on science. Granted, when impedance was first proposed, neither microprocessors nor multifrequency measurements were available, but this is no longer the case.

Human tissue is an electronic network consisting of multiple elements. Only in the body-composition field is an SF analysis of a multiple-component network considered. Although a multifrequency-modeling approach introduces new questions, an SF method is fraught with inherent error.

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Antenatal iron supplementation as a child survival strategy

Dear Sir:

A recent double-masked, placebo-controlled clinical trial examined the effect of daily supplementation with 100 mg elemental Fe during the third trimester of pregnancy on iron status of women and newborns in Niger (1). This study found that supplementation 1) decreased the prevalence of maternal iron deficiency anemia at delivery and 3 mo postpartum, 2) improved the iron status of infants at 3 mo, and 3) increased birth length and