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To the Editor.—The central issue in the current acid-base debate, as Drs. Siggaard-Andersen and Engel are clearly aware, is the difference between what happens in a patient and what happens in a test tube. As a practicing physician who has accepted the responsibility for patient care, I am grateful to Schwartz, Relman, and their colleagues who have tried to interpret disturbances in acid-base balance in terms of what happens to human beings. By the same token I believe that the test tube school has, by its narrow interpretations, failed to meet the needs of physiology and of medicine. More seriously, consciously * or unconsciously, they have encouraged the application of the *in vitro* scheme to the interpretation of clinical problems, which application they now apparently acknowledge would be in error.

I should like to reply to Drs. Siggaard-Andersen and Engel in two somewhat different ways: in the first I suggest that the calculation of base excess (or deficit) is hardly comparable to the measurement of the concentration of chloride in whole blood, the objective validity of which is easily subject to direct experimental confirmation. Base excess (or deficit) is a derived and hypothetical quantity which presumably reflects the magnitude of a change in one direction or the other from some "normal" starting point. The starting point is, or should be, "normal" acid-base balance in the patient. If carbon dioxide tension and bicarbonate have risen in the patient (which can be considered to be "*in vivo* titration"), blood drawn from the patient at the elevated P_{CO_2} cannot be back-titrated *in the test tube* to give a value of bicarbonate (*i.e.*, base) which has any meaning. Thus, my comment that "these calculated parameters . . . do not apply to the whole blood as it circulates within the patient."

The reply offered in the previous paragraph, is not apt to help Drs. Siggaard-Andersen or Engel, for it is only a rewording of what Schwartz and his associates have already said, and what Drs. Siggaard-Andersen and Engel have rejected on many occasions. Nor is it apt to help those less involved in the fray who wonder how two groups of "experts" apparently can be so much at odds. We have all been aware that "semantic" difficulties are involved. Therefore I should like to focus attention on a specific semantic consideration that I believe may represent the crux of the disagreement. I present this as the second answer which I believe is facilitated within the context of a specific example: If P_{CO_2} rises *in vivo* from 40 mm. of mercury to 100 mm. of mercury and bicarbonate rises from 24 mEq./liter to 28 mEq./liter—rather than to the (approximate) 32 mEq./liter which would occur during *in vitro* titration in normal blood, it is clear that half the bicarbonate generated by the buffering of carbonic acid has leaked out of the vascular compartment. In that there is a loss of 4 mEq./liter bicarbonate (base) from the blood, it could be argued that this represents a base deficit (or "negative base excess") of 4 mEq./liter in the blood. This is a most devious way of expressing the bicarbonate translocation which, it is agreed by all, occurs during alterations in P_{CO_2}. It is certainly in conflict with the widely held understanding of what base excess is intended to mean. Base excess (or deficit) is almost universally considered synonomous with metabolic alkalosis or acidosis, and the report from the New York Academy of Sciences seems to endorse this interpretation. However, it is encouraging to note from their letter that this is not the current interpretation of Drs. Siggaard-Andersen and Engel.

* Certainly the recommendation for the use of calculation of the base excess as the basis for acid or alkali therapy must be considered as explicit encouragement. (See page 1037, The Acid-Base Metabolism, Astrup, Jørgensen, Siggaard-Andersen, and Engel: The Lancet 1, 1035, 1960.)

It is, in fact, apparent that Schwartz and his colleagues on the one hand, and Astrup and his associates on the other, agree on the physicochemical events which occur during alterations in carbon dioxide tension. The difference is related to how to describe these events. The Astrup school has adopted a nomenclature including something called base excess (or deficit) which reflects (1) alterations in the distribution of bicarbonate across cell membranes, and which may be entirely independent of any alterations in non-volatile acids or base and, (2) alterations in the concentrations in blood of non-volatile acids or bases. The measurement of base excess, accordingly, does *not* tell which is going on. It certainly does *not* justify the therapeutic implications which have been commonly adopted. It *has* served as a source of widespread confusion, in short, a cruel hoax on the physician and student who have tried to understand acid-base balance in physiologic terms. Schwartz and his associates have presented a readily understood physiologic approach which should form the basis for a much wider understanding of the nature of acid-base disturbances.

Drs. Siggaard-Andersen and Engel correctly state that Shaw and Messer were aware that an elevation in P_{CO_2} is accompanied by a shift in bicarbonate from blood to tissue. Siggaard-Andersen also reported, in 1962, a small difference between *in vivo* and *in vitro* titration curves, to which he attributed little importance. Schwartz claimed no priority for the idea, although he has, of course, provided to date by far the most complete data. The issue is rather the importance of the difference between acid-base as studied in blood and that of intact man, which remained for Schwartz and Relman to put forward.

The report of the conference on acid-base terminology and interpretation from the New York Academy of Medicine does not, in my opinion, clarify the issues, but rather solidifies the conflicting interpretations. Likewise further debate, which I myself have encouraged, is less apt to resolve the issues than are new data. The current report by E. B. Brown, Jr. and R. L. Clancy (J. Appl. Physiol. 20, 885, 1965) confirms the *in vivo* titration curves of Schwartz and his colleagues and supports their interpretations.

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Oxygen Tension Temperature Factor

To the Editor.—Dr. Hedley-Whyte and his co-workers [1] believe that, to measure arterial oxygen tension when hemoglobin is not fully saturated, the oxygen electrode must be kept at the temperature of the patient. Few would deny the desirability of this approach but our experience of maintaining a 24-hour service for measurement of blood P_{O_2} suggests that this is frequently impracticable. We believe, furthermore, that a satisfactory correction factor may now be applied for partially desaturated blood.[2] At full saturation our measurements of the thermal coefficient of P_{O_2} agree precisely with those of Hedley-Whyte and Laver,[3] and in partially desaturated blood, the coefficient rises towards the value calculated for desaturated blood by Bradley *et al.*[4] Our measured value approached the calculated value at a saturation of about 90 per cent, at which level the change in dissolved oxygen is of little importance.

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Percentage Saturation of Hemoglobin	Exponential Factor for Thermal Coefficient	Percentage Change for 1°C
100	0.005	1.2
99	0.013	2.9
97	0.021	4.8
90	0.028	6.3