Correspondence

Acid-Base Debate

To the Editor:—The debate concerning acid-base problems in general and the interpretation of acid-base data in particular has been complicated by misunderstanding and misinterpretation. In the Editorial entitled, "The Great Transatlantic Acid-Base Debate" (ANESTHESIOLOGY, Sept.–Oct., 1965), Dr. Bunker writes (in reference to the terms buffer base and base excess): "These calculated parameters do not apply to the whole organism; *and they do not apply to the whole blood as it circulates within the patient.*" The first statement is obviously true and it also applies to *p*H, P_{CO_2}, potassium, and all other blood parameters. However, we are completely unable to understand the second statement. It would be the same as stating that chloride titrated in a sample of drawn blood does not apply to the blood as it circulates within the patient; or, that titratable acid measured in the voided urine does not apply to the urine in the bladder.

Dr. Bunker draws attention to the difference between the *in vitro* CO_2 titration curve for whole blood and the *in vivo* CO_2 titration curve. However, he omits a reference to Shaw and Messer,[1] who demonstrated and explained this difference in 1932. More recent experimental studies by Cohen, Bracket and Schwartz [2, 3] accurately defined the *in vivo* CO_2 titration curves for dog and man. Dr. Bunker rightfully gives Schwartz and co-workers credit for these careful studies. He emphasizes correctly that ignorance of the difference between the *in vivo* and *in vitro* CO_2 titration curves leads to the erroneous conclusion that acute respiratory acidosis (CO_2-inhalation) causes a simultaneous accumulation of non-volatile acid in the organism.

"The defenders from Copenhagen" (*i.e.*, Astrup, Engel, Jørgensen & Siggaard-Andersen) are represented in the editorial as part of a reactionary group that does not take the mentioned differences into account. It might be of interest to point out that this group, far from misinterpreting the *in vivo* CO_2 titration curve, redetermined this curve experimentally in dogs in 1962 [4] and clearly explained that the base deficit measured in the blood during CO_2-inhalation is not due to a metabolic production of acid in the *organism,* but is caused by an altered distribution of hydrogen ions (or bicarbonate ions) between the blood and the extravascular itssue.

The editorial claims that the *in vivo* CO_2 titration curve allows a ready separation of the metabolic and the respiratory components of acid-base disturbances. Thus, if the values for *p*H and HCO_3^- fall outside the *in vivo* curve, this should indicate the presence of a metabolic acid-base disturbance (*i.e.*, accumulation in the *whole organism* of non-volatile acid or base). However, this could also indicate an altered distribution of hydrogen ion (or bicarbonate ion) between the body phases. Such an altered distribution might be caused by dehydration, overhydration, or potassium-depletion.

The slope of the *in vivo* CO_2 titration curve has thus far been defined only in dogs and in healthy young adults, but it must undoubtedly vary considerably with, for example, hemoglobin concentration, and the relative sizes of blood volume and extracellular fluid volume. It appears that values obtained for the acid base status of the blood, when plotted in existing diagrams, apply only to the blood and do not necessarily represent the acid base status of the whole organism.

A report from the New York Academy of Sciences on acid-base terminology and interpretation has recently been published. It clarifies many issues which have been under debate. [See ANESTHESIOLOGY 27: 6, 1966.]

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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.)