Calculation of Blood O₂

To the Editor:—Prompted by the excellent paper by Dr. Theye, "Calculation of Blood O₂ content from optically determined Hb and HbO₂" (ANESTHESIOLOGY 33:653, 1970), we would like to draw your readers' attention to our similar findings, presented to the Anaesthetic Research Society in July 1970, and published in abstract (Foëx, Prys-Roberts, Hahn and Fenton, Brit J Anaesth 42:803, 1970). Our intention is to clarify a situation which has become distorted over the past few years.

Although Hüfner's factor of 1.34[1] was widely accepted for many years, this acceptance was by no means universal, and a number of other values for the O₂ combining capacity of hemoglobin were suggested before the latest value of 1.39 was established[2] as a result of the now-accepted recalculation of the molecular weight of hemoglobin.[3] We compared direct measurements of blood O₂ content[4] with derived estimates based on measurements of P_{O_2}, P_{CO_2} and pH and hemoglobin concentration[5] of the same blood, utilizing a standard oxyhemoglobin dissociation curve,[6] and employing either 1.34 or 1.39 as the O₂-combining factor. Our results showed not only that estimates based on a factor of 1.39 were consistently higher than values measured directly but also that comparison of blood samples tonometered to high or low pH (either respiratory or non-respiratory) yielded values which were about 1.0 ml/100 ml higher than the content measured directly, even using a factor of 1.34, which gave a good correlation at normal acid–base conditions. We concluded, therefore, that the results could be interpreted in two ways. If the O₂-combining factor were assumed to be both correct and constant (whichever value one chose), then the established correction factors for the oxyhemoglobin dissociation curve[7, 8] seriously overestimate the magnitude of the Bohr effect, in both acidotic and alkalotic conditions. If, however, these established correction factors are assumed to be correct, then the observed differences could only indicate that the O₂-combining factor was not a constant value. We have tested the latter hypothesis by estimating the whole-blood O₂-combining capacity of blood tonometered at high O₂ partial pressures and at various pH values, but could not

detect any significant alteration in total O₂-combining capacity with changes in pH, although the calculated O₂-combining factor was significantly lower than 1.39. Even if we accept that errors in the established correction factors for the Bohr effect merely reflect the inevitable scatter of values distributed around a mean, we are still faced with a problem in estimating the O₂ content of whole blood. We cannot yet identify whether the discrepancy between the observed (1.34) and theoretical (1.39) values for O₂-combining capacity of hemoglobin is due to inactive hemoglobins (carboxyhemoglobin and methemoglobin) present in small quantities in normal human blood, or due to reduced O₂ affinity of the hemoglobin at a molecular level. Like Dr. Theye, we have been unable to detect by spectrophotometric means more than 1 per cent of all abnormal hemoglobins.

The main purpose of this letter is to draw attention to a paradox arising from the natural temptation to abandon derived measurements of blood O₂ content and to accept only values measured directly, either by the traditional Van Slyke method or by one of the more recent polarographic modifications. Most anesthetists and respiratory physiologists measure blood O₂ content for the purpose of deriving the arteriovenous O₂ content difference (Ca_{O_2}–$C\bar{v}_{O_2}$), or for substitution in Berggren's equation[9] for pulmonary venous admixture. The latter poses a problem, since if one uses directly-measured values of O₂ content in arterial and mixed venous blood, what factor should be used for the calculation of the end-pulmonary capillary O₂ content (Cc'_{O_2}) from estimated alveolar P_{O_2}? We have established that when a factor of 1.34 is used for estimates on whole blood from normal non-smoking humans, the relation between estimated and directly-measured O₂ content has a slope of 1.006 (SE slope 0.0109), although the mean intercept may deviate by as much as 1.2 ml/100 ml. Under these conditions, if we subtract two values of O₂ content from each other, the resulting value will not be in error by more than 0.2 ml/100 ml over a wide range of differences, *i.e.*, as much as a 15 ml/100 ml arteriovenous difference, even though the individual estimated values may differ significantly

from the directly measured value. We therefore commend the practice of deriving O_2 content from measurements of P_{O_2} for the purposes mentioned above, simply because of the consistency of the error in each estimate, which then cancels out on subtraction. This, of course, is possible only if the values being subtracted lie on an estimated/measured O_2 content relation having a slope of 1.00. Theye's results and ours clearly show that 1.39 overestimates the O_2-combining capacity of hemoglobin in practice, and we have found that the "traditional" factor of 1.34 is arbitrarily correct.

It is indeed paradoxical, in a world of progressive quest for greater accuracy in measurement, that we are forced to accept errors deliberately because of the intangibility of end-pulmonary capillary blood!

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To the Editor:—The letter from Dr. Prys-Roberts and associates stresses several uncertainties involved in calculating blood O_2 content from P_{O_2}, Hb, and HbO_2. My remarks will be confined to the point common to their previous [1] and our recent publication.[2]

In their and our laboratories, calculation of blood O_2 content using existing standard methods for the determination of P_{O_2}, Hb, and HbO_2 and the O_2-combining factor for Hb of 1.39 yields values for O_2 content which are significantly larger than those obtained by the Van Slyke procedure. There is little reason to question the absolute accuracy of the Van Slyke procedure, since it is direct, relies on no assumptions outside the realm of basic chemistry and physics, and has been validated by comparison with an independent standard.[3] Also, in more recent times, O_2 content by the Van Slyke procedure has been shown to agree with O_2 content determined by other, independent methods based upon measurement of P_{O_2} after release of the O_2 chemically combined with the Hb.[4,5] Accordingly, it has been concluded that the error resides in the method for calculation of blood O_2 content. This is customarily accomplished by appropriate substitution in the equation:

$$\text{Blood } O_2 \text{ content} = P_{O_2} \times S + Hb \times F \times HbO_2,$$

where P_{O_2} is the tension of O_2 in the whole-blood sample, S is the O_2 solubility factor for the temperature at which P_{O_2} was measured, Hb is the concentration of hemoglobin available for combination with O_2, F is the O_2-combining factor of Hb, and HbO_2 is the fractional amount of hemoglobin chemically combined with O_2.

There is little reason to believe that the error resides in the calculation of the physically dissolved component $(P_{O_2} \times S)$, since this is ordinarily less than 1 per cent of the total O_2 content and none of the possibilities considered would be of sufficient magnitude to eliminate the discrepancy. It is more likely that the problem resides in the calculation of the chemically combined component (Hb $\times$ F $\times HbO_2$), as suggested by Prys-Roberts and ourselves. Possibilities include an erroneously high international standard for Hb relative to the actual amount of Hb available for combination with O_2, a theoretical value for F which