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The Two-Digit Rule and Winter's Formula

To the Editor,

I recently wondered, "How does the "Two-digit rule" for determining the adequacy of respiratory compensation for metabolic acidosis relate to Winter's formula?" Many clinicians were taught this rule-of-thumb: the last two digits of the pH (those visible if you hold your thumb over the "7") should provide an approximation of pCO_2 (in mm Hg) in the presence of normal respiratory compensation. Although Winter's formula is easy to remember and perform, the Two-digit rule is even easier. Winter's formula and the Two-digit rule have both been derived empirically from clinical data (1,2). But the reason the Two-digit rule should work has never, to our knowledge, been adequately explained. We wondered how the two rules were related.

We began with serum HCO_3 values ranging from 4 -18 mmol/L and used them to calculate the corresponding predicted pCO_2 values using Winter's formula (3). Next, we used the Henderson-Hasselbalch equation to calculate the corresponding pH for each $[HCO_3^-]/pCO_2$ pair and used the Two-digit rule to re-calculate the corresponding predicted pCO_2. The predicted compensatory pCO2 calculated by the Two-digit rule and Winter's formula were then compared.

Table 1. Comparison of predicted compensatory respiratory response to metabolic acidosis by Winter's formula and the Two-digit rule. Results of the Two-digit rule in red font fall outside the 95% standard error range of Winter's formula. (Click here to view Table 1 in a separate, enlarged window)

[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
18	35 (33-37)	47	7.33	33 (33-37)
16	32 (30-34)	49	7.31	31 (30-34)
14	29 (27-31)	50	7.30	30 (27-31)
12	26 (24-28)	52	7.28	28 (24-28)
10	23 (21-25)	55	7.26	26 (21-25)
8	20 (18-22)	60	7.22	22 (18-22)
6	17 (15-19)	68	7.17	17 (15-19)
5	16 (14-18)	75	7.13	13 (14-18)
4	14 (12-16)	84	7.08	8 (12-16)

Estimates of pCO_2 by the Two-digit rule were then superimposed over Winter's original graphical data, from which the Winter's formula was derived (1). See below.

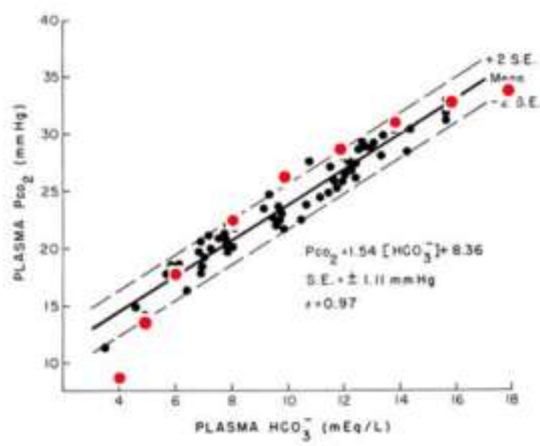

Figure 1. Predicted pCO2 by the Two-digit rule (in red font) superimposed over the original graphic used to derive Winter's formula (1). (Click here to view Figure 1 in a separate, enlarged window)

Note that the Two-digit rule provides pCO_2 estimates within two standard errors (+/- 2 mm Hg) of Winter's formula, for most $[HCO_3^-]$ values ranging from 5-18 mmol/L. At a HCO_3 of 10 mmol/L, the Two-digit rule overestimates pCO_2 by 1mmHg compared to Winter's formula. At HCO_3 above 18 mmol/L and below 5 mmol/L, the Two-digit rule underestimates pCO_2 compared to Winter's.

The apparently linear relationship between pH (the negative base-ten logarithm of [H+]) and related partial pressure of pCO2 in mm Hg is explained by the three relationships that link their association.
1) pH has a negative logarithmic association with $[H^+]$. As most who have used the simplified form of the Henderson-Hasselbalch equation ($[H+] = 24 * pCO_2/HCO_3$) will remember, this relationship is conveniently approximately linear over the narrow range of physiological pH values, such that [H+] values of 30, 40, 50 and 60 nmol/L approximately correspond to pHs of 7.50, 7.40, 7.30 and 7.20 respectively. 2) Central chemoreceptors in the ventral medulla (and other locations) respond to increasing brain interstitial [H+] by increasing ventilatory drive in a fashion that is also approximately linear in the physiological range of pH values (3). See figure below. 3) Ventilatory drive is inversely linearly related to pCO_2.
(More precisely, $Pa_{CO2} = V_{CO2} * K/V_{ALV}$, where V_{CO2}=the rate of CO_2 production, K, is a proportionality constant, and V_{ALV}=alveolar minute ventilation (total ventilation – dead space ventilation.)

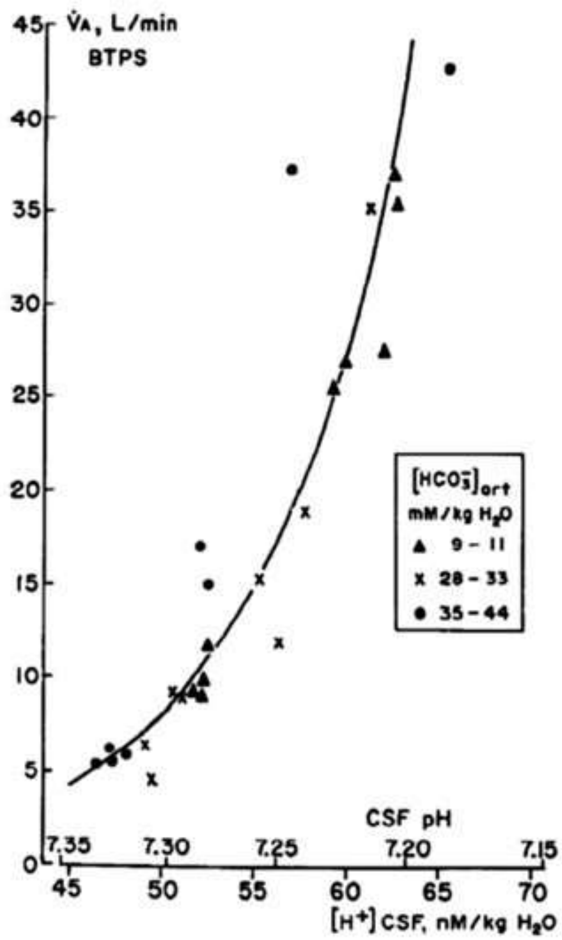

Figure 2. The ventilatory response to changes in brain interstitial fluid pH as studied in conscious goats (3). (Click here to view Figure 2 in a separate, enlarged window)

Therefore, It's not surprising that the last two digits of the pH should have a positive, approximately linear correlation with pCO_2. However, the *convenience* of the correlation (two digits of the pH *equaling* the pCO_2) is purely fortuitous. The Two-digit rule provides a good approximation of the expected compensatory pCO_2 as calculated by Winter's formula for $[HCO_3^-]$ ranging from 5-18 mmol/L.

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2. Fulop M. A guide for predicting arterial CO2 tension in metabolic acidosis. Am J Nephrol. 1997;17(5):421-4. [CrossRef] [PubMed] (This shows empirical derivation of two-digit rule.)
3. Fencl V, Miller TB, Pappenheimer JR. Studies on the respiratory response to disturbances of acid-base balance, with deductions concerning the ionic composition of cerebral interstitial fluid. Am J Physiol. 1966 Mar;210(3):459-72. [CrossRef][PubMed] (This shows relationship between resp drive and [H].)