Improving on the Adrogué–Madias Formula

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Abstract

The Adrogué–Madias (A-M) formula is correct as written, but technically, it only works when adding 1 L of an intravenous (IV) fluid. For all other volumes, the A-M algorithm gives an approximate answer, one that diverges further from the truth as the IV volume is increased. If 1 L of an IV fluid is calculated to change the serum sodium by some amount, then it was long assumed that giving a fraction of the liter would change the serum sodium by a proportional amount. We challenged that assumption and now prove that the A-M change in [sodium] ([Na]) is not scalable in a linear way. Rather, the Δ[Na] needs to be scaled in a way that accounts for the actual volume of IV fluid being given. This is accomplished by our improved version of the A-M formula in a mathematically rigorous way. Our equation accepts any IV fluid volume, eliminates the illogical infinities, and most importantly, incorporates the scaling step so that it cannot be forgotten. However, the nonlinear scaling makes it harder to obtain a desired Δ[Na]. Therefore, we reversed the equation so that clinicians can enter the desired Δ[Na], keeping the rate of sodium correction safe, and then get an answer in terms of the volume of IV fluid to infuse. The improved equation can also unify the A-M formula with the corollary A-M loss equation wherein 1 L of urine is lost. The method is to treat loss as a negative volume. Because the new equation is just as straightforward as the original formula, we believe that the improved form of A-M is ready for immediate use, alongside frequent [Na] monitoring.

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Introduction

"They don't tell you this, but all you have to do is add 500 cc's instead of a liter." This is what I (S.C.) overheard my renal fellow (M.S.) telling an internal medicine resident on our nephrology consult service. The resident had seen a patient with hyponatremia, and the primary team was going to give 500 mL of hypertonic saline. She wanted to know how the intravenous (IV) fluid would alter the patient's serum sodium by applying the Adrogué–Madias (A-M) formula that calculates the expected change in [sodium] (Δ[Na]) (1,2). For reference, the formula is $\Delta[\mathrm{Na}] = \frac{[\mathrm{Na+K}]_{\mathrm{IVF}} - [\mathrm{Na}]}{\mathrm{TBW}+1}$, where $[\mathrm{Na+K}]_{\mathrm{IVF}}$ is the sodium plus potassium concentration of the IV fluid, [Na] is the patient's serum sodium, and TBW is the total body water. At the time, she was confused by the 500 mL because it conflicted with the 1 L that is supposed to be added to the TBW in the denominator. She turned to her supervising renal fellow, and after some quick thinking, he told her to substitute in the 500. As their attending, I did not immediately correct the mistake, as it dawned on me how the A-M formula is ripe for misuse. The following two scenarios may not be common mistakes, but they are potential mistakes, as the formula gets interpreted by millions of health care providers. To minimize the risk of misinterpretation, we suggest ways to improve the A-M formula to be more exact and comprehensive.

Potential Mistake 1: Dose-Response Reversed

Even the users who know that the denominator's "1" refers to 1 L may be tempted to substitute in the actual volume of IV fluid if it differs from 1 L. In our case, that meant changing the 1 to 0.5. However, thinking through the numerical logic, we see that TBW + 0.5 yields a smaller denominator that makes the entire fraction larger in value, implying that the Δ[Na] is greater when less IV fluid is infused. This violates the normal dose-response relationship, but doctors may not pause long enough to realize the mistake. If 500 mL gave too high a Δ[Na], they may try to lower the Δ[Na] by increasing the one to two, still thinking that the one is adjustable. After the Δ[Na] is acceptably small, the doctor orders a larger volume of hypertonic saline to be infused. Such an error in treating chronic hyponatremia could result in osmotic demyelination.

Potential Mistake 2: Forgetting to Scale

Users may keep the "1" as is, but the properly calculated Δ[Na] may be too big or too small. The next step of the A-M algorithm is to scale the Δ[Na] to the desired value, assuming that the dose-response relationship is linear (1,3). For example, if a liter of hypertonic saline gave a Δ[Na] of + 12 mEq/L, but you only wanted to raise the patient's [Na] by 6, then you would infuse half a liter of 3% NaCl. However, this scaling step of the A-M algorithm is not embedded in the formula and could be forgotten. Instead, to attenuate the Δ[Na], the doctor may change the only variable under our control and plug in a less concentrated IV fluid like normal saline (NS). Unfortunately, the drop-off between 3% at 513 mEq/L and NS at 154 mEq/L is

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steep, and then, the Δ[Na] becomes much too small. Will the doctor go with 1.5% saline, thinking that half the concentration should give half the Δ[Na]? (It does not.) Mistakes can also be made in formulating and mixing a noncommercial IV fluid, not to mention the possible breaks in sterility.

Seemingly Mismatched Units

At first glance, it may seem that the units on either side of the A-M equation do not match. The numerator is a difference between an IV fluid's cationic solute concentration and the patient's serum sodium. Hence, the numerator's unit is in milliequivalents per liter. That is divided by TBW + 1, which has a unit of liter. Thus, the overall unit seems to be milliequivalents per liter squared. On the other side of the equation, Δ[Na] has a unit of milliequivalents per liter. Such a mismatch would normally invalidate an equation, but the A-M formula is saved by a single phrase in their papers: $[\mathrm{Na}^+]_{\mathrm{inf}} - [\mathrm{Na}^+]_{\mathrm{s}}$ is a simplification of the expression $\left([\mathrm{Na}^+]_{\mathrm{inf}} - \text{initial } [\mathrm{Na}^+]_{\mathrm{s}}\right) \times 1\ \mathrm{L}$ (1,3). In other words, the numerator is shorthand for a hidden multiplication. Multiplying by one can be omitted, but that one carries a unit of volume (*i.e.*, liter) that is needed to restore the numerator's unit back to milliequivalents (and thus, self-consistency). Most users are unaware of this fact. Not seeing the "×1 L," they may forget that the IV fluid volume is fixed at 1 L, leading some to tinker with the "1" in the denominator.

To Infinity and Beyond

Many of the A-M clinical examples use hypertonic saline because the Δ[Na] is large and it is less objectionable to scale the effect downward, meaning that <1 L of IV fluid is infused. What if the Δ[Na] is to be scaled up? Let us say that giving 1 L of NS results in a Δ[Na] of +1 because in a hypothetical patient, the A-M formula yields $\frac{154-111}{42+1} = 1$. If we want to correct the serum sodium from 111 all the way to 140, the A-M algorithm (1,3) implies that 29 L of NS should be infused. Adrogué and Madias (1) would reject this plan, judging by a similar example in their paper, but their reason has more to do with clinical futility rather than a scaling flaw. Using the A-M scaling paradigm, we could in theory raise the serum sodium from 111 to 181. However, is it even possible to reach 181 with NS? The serum sodium would plateau at NS's [Na] of 154. Our thought experiments raise concerns about the A-M methodology.

Adrogué and Madias derived their formula from the principles of sodium physiology as deduced by Edelman *et al.* (4). The A-M mathematical proof of the first step involving 1 L of fluid is valid and enduring. However, in the second step of applying the math to patient care (in their example cases), they assume that the effect of 1 L on the Δ[Na] can be scaled proportionally (1,3). This dose-response relationship may seem logical, but can the Δ[Na] be scaled in a linear way? If so, could the scaling continue all the way to infinity? We hint above that the answer is no, but mathematics can answer the preceding two questions definitively.

Proof Strategy

If the A-M volume must be 1 L (as in TBW + 1) and the non–1-L volumes do not scale linearly, then the A-M algorithm is technically only correct when 1 L of IV fluid is being given. We wanted to generalize A-M so that it could accommodate the entire range of volumes that are going to be administered in the real world. We can allow any volume to be infused by representing it as the generic variable V. Plug V, instead of one, back into the Edelman equation and solve for the Δ[Na] as Adrogué and Madias did long ago. Fortuitously, many terms cancel that simplify the more versatile equation into a final form that is almost as elegantly simple as the A-M formula.

Savory Math

The Edelman equation states that the serum sodium is a function of the sum of exchangeable sodium and exchangeable potassium divided by the total body water: $[\mathrm{Na}] = \frac{\mathrm{Na_e} + \mathrm{K_e}}{\mathrm{TBW}}$ (4). There are also a slope and a y-intercept that make this linear relationship more precise, but for simplicity, we (and Adrogué and Madias) used a slope of one and a y-intercept of zero (5,6). Define the initial serum sodium as $[\mathrm{Na}]_1 = \frac{\mathrm{Na_e} + \mathrm{K_e}}{\mathrm{TBW}}$. Allow an IV fluid to be added. Its effect on the serum sodium will depend on the fluid's sodium + potassium concentration and its total volume. After the IV fluid is infused, the serum sodium becomes $[\mathrm{Na}]_2 = \frac{\mathrm{Na_e} + \mathrm{K_e} + [\mathrm{Na+K}]_{\mathrm{IVF}} \cdot V}{\mathrm{TBW} + V}$, where $[\mathrm{Na+K}]_{\mathrm{IVF}}$ is the sodium plus potassium concentration of the IV fluid (in milliequivalents per liter) and V is the volume of IV fluid given (in liters). $[\mathrm{Na}]_2$ minus $[\mathrm{Na}]_1$ is the Δ[Na]:

$$\Delta[\mathrm{Na}] = [\mathrm{Na}]_2 - [\mathrm{Na}]_1 = \frac{\mathrm{Na_e} + \mathrm{K_e} + [\mathrm{Na+K}]_{\mathrm{IVF}} \cdot V}{\mathrm{TBW} + V} - \frac{\mathrm{Na_e} + \mathrm{K_e}}{\mathrm{TBW}}. \tag{1}$$

Use algebra to simplify Equation 1 into: (Supplemental Appendix)

$$\Delta[\mathrm{Na}] = \frac{[\mathrm{Na+K}]_{IVF} - [\mathrm{Na}]}{TBW + \underbrace{V}_{\substack{any\\ vol.}}} \underbrace{\cdot V}_{\substack{scaling\\ step}}. \tag{2}$$

Form Factor

The final equation above follows the template of the A-M formula. In fact, their numerators look identical. As expected, their denominators are similar but different. Adrogué and Madias chose to add 1 L; hence, the TBW + 1. We allowed for any volume of IV fluid, reflected in the TBW + V. The scaling step in the A-M algorithm that was on the basis of "common sense" was added *post hoc* manually. It is a separate step that does not appear in the original A-M equation. However, the scaling step in Equation 2 was generated by the math automatically. It is a built-in step and cannot be overlooked. Sensibly, multiplying the main fraction by a V that is less than one (liter) scales the Δ[Na] downward (in accordance with dose-response), and multiplying by a V that is greater than one scales the Δ[Na] upward. In the case of multiplying by a $V = 1$, Equation 2 reduces exactly to the original A-M formula, as it must.

Objections Overruled

This improved A-M formula resolves all of the previously mentioned shortcomings. It does not force us to add 1 L but allows us to add any volume of IV fluid. The A-M scaling step was implicit and retrofitted onto the formula. However, the improved equation's scaling step is overt and integrated into the formula. Also, the scaling is now done correctly. Although it seems rational, the $\Delta[\mathrm{Na}]$ of the A-M formula does not scale up or down in a linear way. If A-M calculates the $\Delta[\mathrm{Na}]$ to be $+1$ mEq/L, but we want to increase the serum sodium by 6, then it is not as simple as giving 6 L of IV fluid. However, the correct volume is more difficult to calculate because of the nonlinearity. At least, the scaling to infinity that was possible with A-M has been mathematically prohibited. No matter how big the V term gets, the serum sodium cannot rise or fall beyond that IV fluid's $[\mathrm{Na+K}]$. Even if our prior hypothetical patient with a serum sodium of 111 is flooded with NS, the highest the serum sodium can go is 154, capping the $\Delta[\mathrm{Na}]$ in this case at 43. This limit is corroborated by letting V go to infinity (Supplemental Appendix).

Clinical Teaching

A few patient cases can illustrate the right and wrong ways to use the A-M equation. In the case from the introduction that the resident and fellow were consulted on, the man weighed 95 kg so the TBW was calculated at 57 L. His initial sodium was 110 mEq/L, and 500 mL of 3% NaCl was going to be given. What would the $\Delta[\mathrm{Na}]$ be? Mistake 1 from before: If the TBW + 1 was changed to TBW + 0.5, then the computation would be

$$\Delta[\mathrm{Na}] = \frac{[\mathrm{Na+K}]_{\mathrm{IVF}} - [\mathrm{Na}]}{\mathrm{TBW} + 0.5} = \frac{513 - 110}{57 + 0.5} = 7.$$

(The correct A-M would be $\Delta[\mathrm{Na}] = \frac{513-110}{57+1} = 6.95$, which is not too far off.) An increase of 7 mEq/L in the serum sodium sounded reasonable. What if they stopped there? Then, they would be committing mistake 2. The $\Delta[\mathrm{Na}]$ of seven is per liter of IV fluid, an easily forgettable fact. Because the actual volume was 500 mL, the (invisible) scaling step of the A-M algorithm would attenuate the $\Delta[\mathrm{Na}]$ by one-half. If the primary team wanted to raise the sodium by seven, then they would be undertreating the patient by giving only 500 mL. The two mistakes would have been averted by using the improved A-M formula:

$$\Delta[\mathrm{Na}] = \frac{[\mathrm{Na+K}]_{\mathrm{IVF}} - [\mathrm{Na}]}{\mathrm{TBW} + V} \cdot V = \frac{513 - 110}{57 + 0.5} \cdot 0.5 =$$

$$3.504347826086\bar{6}95652173913.$$

Another way to arrive at the same answer is to go back to basics. The principle of total body cationic osmoles (TBCO) interprets the initial sodium as being $110 = \frac{6270}{57}$. The 500 mL of 3% NaCl would deliver $513\ \frac{\mathrm{mEq}}{\mathrm{L}} \cdot 0.5\ \mathrm{L} = 256.5$ mEq of sodium. This gets added to the numerator, whereas 0.5 L is added to the TBW in the denominator to get a new sodium of $\frac{6270 + 256.5}{57 + 0.5} \cong 113.5$. This gives a $\Delta[\mathrm{Na}]$ of $113.5 - 110 = 3.5\cdots$, and this is exactly the value—down to the last decimal place (extra repeating digits not shown)—obtained by the improved A-M equation.

Next, a 28-year-old woman who abuses alcohol was found to have a sodium of 105. She weighed 63.5 kg, so her TBW was estimated at 31.75 L. When she is given 2 L of NS, the A-M formula would predict that the $\Delta[\mathrm{Na}] = \frac{154-105}{31.75+1} = 1.5$. A misused A-M formula would give $\Delta[\mathrm{Na}] = \frac{154-105}{31.75+2} = 1.45$. After getting the NS, she had a sodium of 109, so the actual $\Delta[\mathrm{Na}]$ was 4, which differs noticeably from the 1.5 calculated above. Trainees might be confused at this point, until they realize that they omitted the scaling step. Multiply 1.5 by 2 to get 3 for the $\Delta[\mathrm{Na}]$. If the improved A-M equation were to be used, trainees would get $\Delta[\mathrm{Na}] = \frac{154-105}{31.75+2} \cdot 2 = 2.90\bar{3}7$. This is actually the correct $\Delta[\mathrm{Na}]$, not the three according to the scaled A-M. The approximately 2.9 value is corroborated by the TBCO method: $\frac{3333.75 + 154 \cdot 2}{31.75+2} - 105 = 2.90\bar{3}7$. TBCO is good for teaching purposes. After trainees truly understand TBCO, they can use the improved A-M as a shortcut.

Metamorphosis

Alluded to above, the reality that scaling is nonlinear makes it more difficult to titrate the V to achieve a desired $\Delta[\mathrm{Na}]$. Plug in a guess for V. Was the calculated $\Delta[\mathrm{Na}]$ too large or too small? Oh well, refine the guess for V and recalculate. Such trial and error is not going to be indulged by clinicians. They have a $\Delta[\mathrm{Na}]$ goal in mind and would prefer that the equation produce the required V. Then, they can divide that V by the time it takes to correct the serum sodium at a safe rate (7–11). Of course, V divided by time is the IV fluid rate. Pragmatically, this is what the clinician really wants to know in order to prescribe therapy for a dysnatremia. We can rearrange the improved A-M equation to solve for V directly (Supplemental Appendix):

$$V = \frac{\Delta[\mathrm{Na}] \cdot \mathrm{TBW}}{[\mathrm{Na+K}]_{\mathrm{IVF}} - [\mathrm{Na}]_2}, \tag{3}$$

where $[\mathrm{Na}]_2$ is the target sodium that the clinician is aiming for in a patient. Getting a V that is infinite or negative means that a desired $\Delta[\mathrm{Na}]$ is not achievable with that particular IV fluid. A different IV fluid should be tried.

Flattening the Curve

Comparing the graphs of the original versus improved A-M formulas is instructive. Vary the scaling on the x-axis, which is basically the IV fluid volume, and observe the effect on $\Delta[\mathrm{Na}]$ on the y-axis. For graphing purposes, the A-M equation is $y = \frac{[\mathrm{Na+K}]_{\mathrm{IVF}} - [\mathrm{Na}]}{\mathrm{TBW}+1} \cdot x$, and the result is a straight line (Figure 1A). Its slope is $\frac{[\mathrm{Na+K}]_{\mathrm{IVF}} - [\mathrm{Na}]}{\mathrm{TBW}+1}$, a constant determined by whatever values are entered for $[\mathrm{Na+K}]_{\mathrm{IVF}}$, $[\mathrm{Na}]$, and TBW. The y-intercept is zero. As seen on the y-axis, any $\Delta[\mathrm{Na}]$ is attainable from $-\infty$ to $+\infty$ (more on negative volumes later). Obviously, this scaling is unrealistic, as IV fluids are limited in the $\Delta[\mathrm{Na}]$ that they can effect.

For graphing purposes, the improved equation is $y = \frac{[\mathrm{Na+K}]_{\mathrm{IVF}} - [\mathrm{Na}]}{\mathrm{TBW}+x} \cdot x$, and its resulting curve is shaped like a reciprocal function (Figure 1A). Between scaling volumes

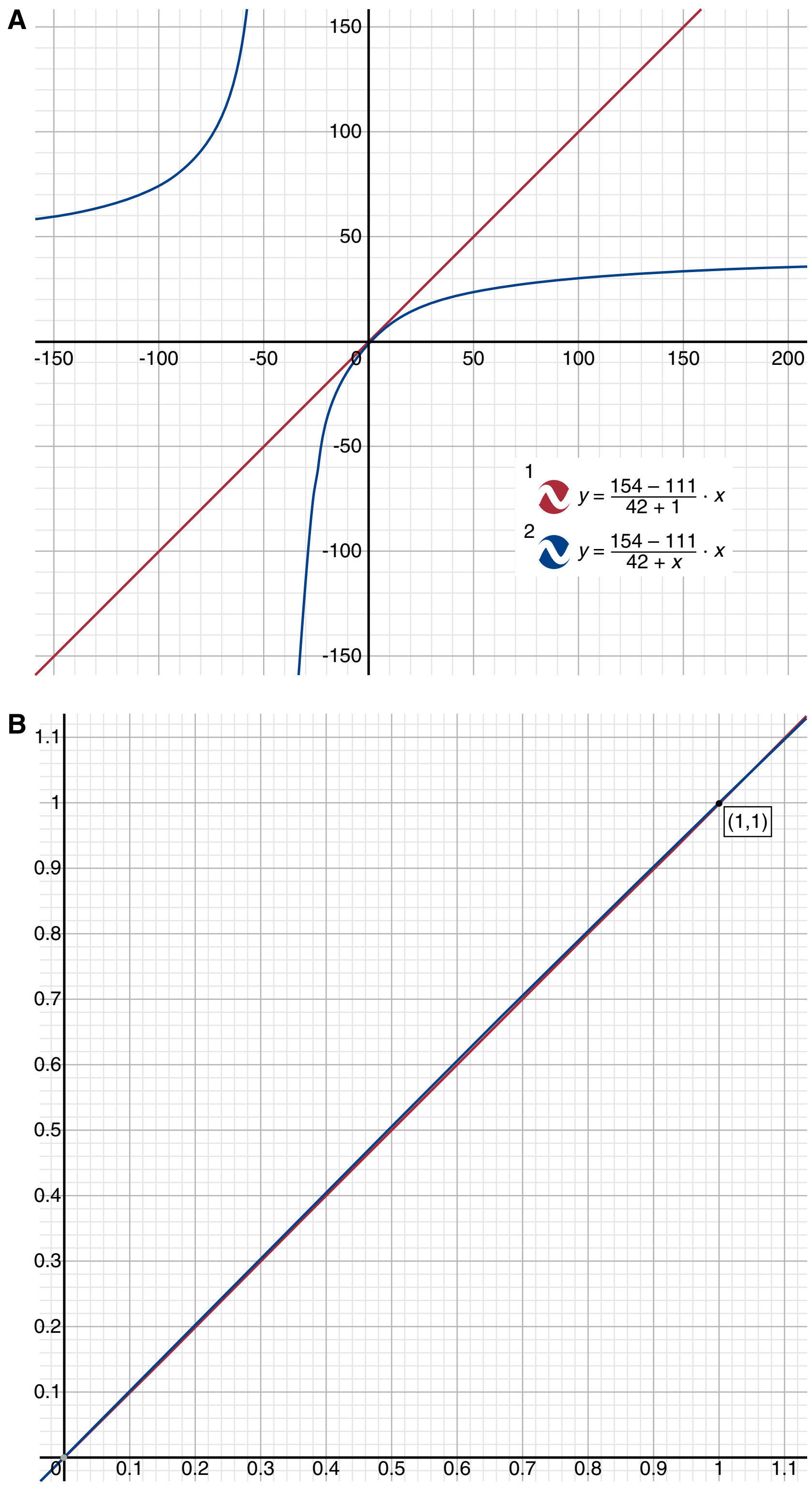

Figure 1. | Graph shows how a scaled Adrogué–Madias (A-M) formula diverges from the improved version of A-M. (A) Suppose a patient with a total body water of 42 L and a serum sodium of 111 mEq/L is going to be treated with normal saline (NS). The A-M formula yields a Δ[sodium] (Δ[Na]) of +1 mEq/L per liter of NS that is infused $\left(\frac{154-111}{42+1} = 1\right)$. Scale this Δ[Na] as desired by multiplying by any volume of NS. The result is a straight line with a slope of one (in red). To graph the improved equation, keep the baseline parameters the same for a fair comparison with A-M. Because it can accommodate any volume of NS, not just 1 L, the improved equation appears as a curve (in blue). (B) A close-up view is shown of the A-M formula and of the improved equation for scaling volumes between 0 and 1 L. The A-M formula's line (red) almost overlaps with the improved equation's curve (blue). The two intersect at $x = 1$ L, as expected, and then deviate farther apart.

of 0 and 1 L, the curve approximates the linear A-M graph quite closely (Figure 1B), and the correct Δ[Na] differs only slightly from that of the original A-M. Thus, A-M works fairly well if the calculated Δ[Na] should be scaled down to a smaller desired Δ[Na]. However, if the A-M Δ[Na] needs to be scaled up to a larger value (*i.e.*, $x > 1$), then the line (original A-M) starts to deviate from the curve (improved A-M) (Figure 1A). For increasing values of x, the deviation becomes more and more pronounced. The asymptotes of the improved equation are located at $x = -\text{TBW}$ and $y = [\text{Na}+\text{K}]_{\text{IVF}} - [\text{Na}]$.

Negative Volume and the A-M Loss Formula

Negative quantities may seem nonsensical at first, but on further scrutiny, they often have a real physical counterpart. A negative volume in human physiology implies a loss of fluid from the body. The lost fluid creates a negative space, so to speak, that needs to be filled in order to get back to zero (or net even). The most familiar example of a negative volume is urinary output. Appropriately, urine is recorded in the negative column of the input/output section of the chart, and clinicians are comfortable with the notion of a net negative input/output. To ascertain the effect of urinary loss on serum sodium, Adrogué and Madias derived a "fluid-loss formula" to calculate the Δ[Na] if 1 L of urine removed a known amount of sodium and potassium (2). The A-M loss equation can be derived from scratch, but a shortcut can be taken from our improved equation to the loss equation by treating urine fluid (fl) volume as a negative quantity. Plug $V = -1$ into Equation 2, and the result is $\Delta[\text{Na}] = \frac{[\text{Na}+\text{K}]_{\text{fl}} - [\text{Na}]}{\text{TBW}+V} \cdot V \Rightarrow \Delta[\text{Na}] = \frac{[\text{Na}] - [\text{Na}+\text{K}]_{\text{fl}}}{\text{TBW}-1}$. One step of algebra was all it took to recreate the loss equation. Thus, the original A-M and the A-M loss formula are intimately related as two sides of an overarching equation, the improved A-M.

Point Counterpoint: Playing Diablo's Advocate

The A-M formula is one of the first "descendants" of the Edelman equation. The A-M applicability is perhaps limited because it assumes there are no inputs or outputs except for the IV fluid that is being used to treat the dysnatremia. That is unrealistic, of course. To handle the realities of patient care, others later derived more capable sodium equations, also on the basis of Edelman, that account for any ongoing gains and losses of Na, K, and H_2O. Can any of the newer equations accurately predict the change in serum sodium in real life? The challenges seem daunting. TBW itself is difficult to estimate. It is a struggle to get complete and reliable information on all of the inputs/outputs (like insensible losses) and their [Na + K]. These measurements are not reported instantly, and the lag time may be sufficient for the data to become obsolete. Even if we could plug in the most up-to-date data, they are likely to change in the near future, sometimes quite rapidly and drastically (12), making it problematic to use any sodium equation prospectively. What about the Edelman equation? There could be hidden variables that significantly affect the correlation with [Na], including (*1*) slope ≠1, (*2*) *y*-intercept ≠0 (Supplemental Appendix), (*3*) hyperglycemia, and (*4*) osmotically inactive stores of sodium (6,13–16). With all of these hurdles, it may not be surprising that the sodium equations were found to be wanting in accuracy by at least two studies (17–19).

On the other hand, the Edelman equation does form the basis of our understanding of [Na] physiology. It must work some of the time, even if it needs refining. Because of how math works, the sodium equations derived from Edelman are just as valid as Edelman itself. One study found that A-M and three other sodium equations could predict Δ[Na] fairly well in critically ill patients (20). Another study focused exclusively on A-M and found that its calculated Δ[Na] nearly matched the actual Δ[Na] in patients with either hypo- or hypernatremia (21,22). A group that previously showed poor reliability of the sodium equations over a 12- to 30-hour period later retested them but over a 2- to 4-hour period and found a much better accuracy (23). We (S.C. and J.S.) applied our own Edelman-based equation to prescribe IV fluid therapy to five patients with dysnatremia and came close to reaching our therapeutic targets for their serum sodium (24).

If the predicted strays too far from the actual serum sodium, midcourse corrections can be made by recalculating the predictions with fresh laboratory data. Thus, the sodium equations work hand in hand with the safe practice of frequent [Na] monitoring. To act rationally on each new set of laboratory data, we are encouraged to have "a sound understanding of the pathophysiology of salt and water balance" (1). What better way is there to express our understanding than to use the quantitative tools rooted in the Edelman equation to inform our therapeutic decisions?

Final Thoughts

The A-M formula was published in 1997. In the >20 years since its debut, A-M has probably been used on the wards more than any other sodium equation (25). How many of those countless times has the formula been misused? The potential mistakes we pointed out can be avoided by the improved equation because it uses the actual volume of IV fluid and it embodies the scaling step in its very formula. It may not be completely foolproof, but the general equation is worth adopting now. Lastly, more capable sodium equations exist (20,24,26–30), but the A-M formula has the enviable advantage of simplicity. Our improved equation is barely more complex than A-M, so maybe this "version 2.0" will enjoy the same widespread use and longevity.

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The graphs were generated by a free online program at desmos.com/calculator.

Author Contributions

S. Chen conceptualized the study; S. Chen, R. Chiaramonte, and J. Shey were responsible for methodology and validation; S. Chen was responsible for visualization; M. Shieh was responsible for formal analysis; S. Chen wrote the original draft; and S. Chen, R.

Chiaramonte, J. Shey, and M. Shieh reviewed and edited the manuscript.

Supplmental Material

Supplemental Appendix. Derivation of the improved Adrogué-Madias (A-M) equation.

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Supplemental Appendix

Derivation of the improved Adrogué-Madias (A-M) equation

See main text under the heading "Savory Math" for details on the variables. The general strategy uses an accounting of the total body cationic osmoles (TBCO), the relevant ones being Na^+ and K^+ for dysnatremia. When an IV fluid is infused, its sodium and potassium amounts are added to the numerator of the Edelman fraction, and its volume is added to the denominator. This gives the theoretical new serum sodium, or $[\mathrm{Na}]_2$. Subtract the initial serum sodium, or $[\mathrm{Na}]_1$, to get:

$$\Delta[\mathrm{Na}] = [\mathrm{Na}]_2 - [\mathrm{Na}]_1 = \frac{\mathrm{Na_e} + \mathrm{K_e} + [\mathrm{Na{+}K}]_{\mathrm{IVF}} \cdot V}{\mathrm{TBW} + V} - \frac{\mathrm{Na_e} + \mathrm{K_e}}{\mathrm{TBW}} \tag{4}$$

Then manipulate equation (4), following the rules of algebra:

$$\Delta[\mathrm{Na}] = \frac{(\mathrm{Na_e} + \mathrm{K_e} + [\mathrm{Na{+}K}]_{\mathrm{IVF}} \cdot V) \cdot \mathrm{TBW}}{(\mathrm{TBW} + V) \cdot \mathrm{TBW}} - \frac{(\mathrm{Na_e} + \mathrm{K_e}) \cdot (\mathrm{TBW} + V)}{(\mathrm{TBW} + V) \cdot \mathrm{TBW}}$$

$$\Delta[\mathrm{Na}] = \frac{\mathrm{Na_e} \cdot \mathrm{TBW} + \mathrm{K_e} \cdot \mathrm{TBW} + [\mathrm{Na{+}K}]_{\mathrm{IVF}} \cdot V \cdot \mathrm{TBW}}{(\mathrm{TBW} + V) \cdot \mathrm{TBW}} - \frac{\mathrm{Na_e} \cdot \mathrm{TBW} + \mathrm{Na_e} \cdot V + \mathrm{K_e} \cdot \mathrm{TBW} + \mathrm{K_e} \cdot V}{(\mathrm{TBW} + V) \cdot \mathrm{TBW}}$$

$$\Delta[\mathrm{Na}] = \frac{\mathrm{Na_e} \cdot \mathrm{TBW} - \mathrm{Na_e} \cdot \mathrm{TBW} + \mathrm{K_e} \cdot \mathrm{TBW} - \mathrm{K_e} \cdot \mathrm{TBW} + [\mathrm{Na{+}K}]_{\mathrm{IVF}} \cdot V \cdot \mathrm{TBW} - \mathrm{Na_e} \cdot V - \mathrm{K_e} \cdot V}{(\mathrm{TBW} + V) \cdot \mathrm{TBW}}$$

$$\Delta[\mathrm{Na}] = \frac{[\mathrm{Na{+}K}]_{\mathrm{IVF}} \cdot V \cdot \mathrm{TBW} - \mathrm{Na_e} \cdot V - \mathrm{K_e} \cdot V}{(\mathrm{TBW} + V) \cdot \mathrm{TBW}}$$

$$\Delta[\mathrm{Na}] = \frac{[\mathrm{Na{+}K}]_{\mathrm{IVF}} \cdot V \cdot \mathrm{TBW}}{(\mathrm{TBW} + V) \cdot \mathrm{TBW}} - \frac{\mathrm{Na_e} \cdot V + \mathrm{K_e} \cdot V}{(\mathrm{TBW} + V) \cdot \mathrm{TBW}}$$

$$\Delta[\mathrm{Na}] = \frac{[\mathrm{Na{+}K}]_{\mathrm{IVF}} \cdot V}{\mathrm{TBW} + V} - \underbrace{\frac{\mathrm{Na_e} + \mathrm{K_e}}{\mathrm{TBW}}}_{\text{Edelman}} \cdot \frac{V}{\mathrm{TBW} + V}$$

Abridge $[\mathrm{Na}]_1$ to $[\mathrm{Na}]$, i.e., the patient's initial serum sodium, and substitute in $[\mathrm{Na}] = \frac{\mathrm{Na_e}+\mathrm{K_e}}{\mathrm{TBW}}$:

$$\Delta[\mathrm{Na}] = \frac{[\mathrm{Na{+}K}]_{\mathrm{IVF}} \cdot V}{\mathrm{TBW} + V} - [\mathrm{Na}] \cdot \frac{V}{\mathrm{TBW} + V}$$

$$\Delta[\mathrm{Na}] = \frac{[\mathrm{Na{+}K}]_{\mathrm{IVF}} \cdot V - [\mathrm{Na}] \cdot V}{\mathrm{TBW} + V}$$

$$\Delta[\text{Na}] = \frac{[\text{Na+K}]_{\text{IVF}} - [\text{Na}]}{\text{TBW} + \underbrace{V}_{\substack{\text{any}\\\text{vol.}}}} \underbrace{\cdot V}_{\substack{\text{scaling}\\\text{step}}} \tag{5}$$

Equation (5) is the improved version of the A-M formula. It accommodates any volume of infusate (V), not just one liter, and includes the scaling step (multiply by V).

Limit calculation proves that the correct scaling prohibits $\Delta[\text{Na}]$ from going to infinity:

Using just the right-hand side of the improved A-M equation (5), which is the delta [Na], we can ask how the serum sodium will change if an extremely large volume of IV fluid is infused. That is mathematically equivalent to letting the V go to infinity:

$$\lim_{V\to\infty} \frac{[\text{Na+K}]_{\text{IVF}} - [\text{Na}]}{\text{TBW} + V} \cdot V$$

$$\lim_{V\to\infty} \frac{[\text{Na+K}]_{\text{IVF}} - [\text{Na}]}{\cancel{\text{TBW} + V}^{\,\infty}} \cdot \cancel{V}^{\,\infty}$$

$$\lim_{V\to\infty} [\text{Na+K}]_{\text{IVF}} - [\text{Na}]$$

$$\lim_{V\to\infty} 154 - 111 = 43$$

The last line using example values for $[\text{Na+K}]_{\text{IVF}}$ and [Na] comes from the hypothetical in the main text about infusing normal saline (NS) into a patient whose serum sodium is 111 mEq/L. No matter how much NS is given, the delta [Na] will max out at 43 mEq/L.

Flip the equation: enter a desired delta [Na] and get the IV fluid volume to infuse

Rearrange equation (5) to solve not for delta [Na] but for V:

$$\Delta\,[\mathrm{Na}] = \frac{[\mathrm{Na{+}K}]_{\mathrm{IVF}} - [\mathrm{Na}]}{\mathrm{TBW} + V} \cdot V$$

$$\begin{aligned}
\Delta\,[\mathrm{Na}] \cdot \mathrm{TBW} + \Delta\,[\mathrm{Na}] \cdot V &= [\mathrm{Na{+}K}]_{\mathrm{IVF}} \cdot V - [\mathrm{Na}] \cdot V \\
\Delta\,[\mathrm{Na}] \cdot \mathrm{TBW} &= [\mathrm{Na{+}K}]_{\mathrm{IVF}} \cdot V - ([\mathrm{Na}] \cdot V + \Delta\,[\mathrm{Na}] \cdot V) \\
\Delta\,[\mathrm{Na}] \cdot \mathrm{TBW} &= [\mathrm{Na{+}K}]_{\mathrm{IVF}} \cdot V - ([\mathrm{Na}] + \Delta\,[\mathrm{Na}]) \cdot V
\end{aligned}$$

Substitute in $[\mathrm{Na}] + \Delta[\mathrm{Na}] = [\mathrm{Na}]_2$, where $[\mathrm{Na}]_2$ is the target serum sodium:

$$\begin{aligned}
\Delta\,[\mathrm{Na}] \cdot \mathrm{TBW} &= [\mathrm{Na{+}K}]_{\mathrm{IVF}} \cdot V - [\mathrm{Na}]_2 \cdot V \\
\Delta\,[\mathrm{Na}] \cdot \mathrm{TBW} &= ([\mathrm{Na{+}K}]_{\mathrm{IVF}} - [\mathrm{Na}]_2) \cdot V
\end{aligned}$$

$$V = \frac{\Delta\,[\mathrm{Na}] \cdot \mathrm{TBW}}{[\mathrm{Na{+}K}]_{\mathrm{IVF}} - [\mathrm{Na}]_2} \tag{6}$$

Equation (6) is more useful to the clinician who often has a desired delta [Na] in mind and wants to know how to achieve it in terms of an IV fluid volume to prescribe.

Slope and y-intercept

Edelman et al.'s scatter plot (their Figure 7) suggested that the relationship between [Na] and $\frac{\mathrm{Na_e{+}K_e}}{\mathrm{TBW}}$ was a diagonal line. However, that best-fit line did not have a slope of 1 (rather, 1.11) and did not have a y-intercept of 0 (rather, -25.6). This skewing and displacement of the line are believed to be caused by a Gibbs-Donnan equilibrium. Thus, the Edelman equation without simplification is:

$$[\mathrm{Na}] = m \cdot \frac{\mathrm{Na_e} + \mathrm{K_e}}{\mathrm{TBW}} + b$$

where m is the slope (that is close to but not exactly 1) and b is the y-intercept (that is close to but not exactly 0). Using the full Edelman equation above to re-derive the delta [Na] equations may improve their accuracy. First, we re-derived the Nguyen-Kurtz equation because it is the most comprehensive and versatile; it includes a generic input, a generic output, and a therapeutic

IV fluid. Then the simpler sodium equations, which are just special cases, flow directly from Nguyen-Kurtz in its slope/y-intercept format. For example, A-M uses only the therapeutic IV fluid, so zeroing out the generic input and generic output in Nguyen-Kurtz will yield the A-M equation in *its* own slope/y-intercept format. The same principle applies to Barsoum-Levine.

By the full Edelman equation, the starting sodium is $[\mathrm{Na}]_1 = m \cdot \frac{\mathrm{Na_e+K_e}}{\mathrm{TBW}} + b$. As before, the therapeutic IV fluid's relevant parameters can be denoted as $[\mathrm{Na{+}K}]_{\mathrm{IVF}}$ and V_{IVF}. The generic input variables can be called $[\mathrm{Na{+}K}]_{\mathrm{In}}$ and V_{In}, and the generic output variables can be called $[\mathrm{Na{+}K}]_{\mathrm{Out}}$ and V_{Out}. When the effects of all these gains/losses are entered into the full Edelman equation, the ending sodium is:

$$[\mathrm{Na}]_2 = m \cdot \frac{\mathrm{Na_e} + \mathrm{K_e} + [\mathrm{Na{+}K}]_{\mathrm{IVF}} \cdot V_{\mathrm{IVF}} + [\mathrm{Na{+}K}]_{\mathrm{In}} \cdot V_{\mathrm{In}} - [\mathrm{Na{+}K}]_{\mathrm{Out}} \cdot V_{\mathrm{Out}}}{\mathrm{TBW} + V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}}} + b$$

Then the delta [Na] is calculated by:

$$\Delta[\mathrm{Na}] = [\mathrm{Na}]_2 - [\mathrm{Na}]_1 = m \cdot \frac{\mathrm{Na_e} + \mathrm{K_e} + [\mathrm{Na{+}K}]_{\mathrm{IVF}} \cdot V_{\mathrm{IVF}} + [\mathrm{Na{+}K}]_{\mathrm{In}} \cdot V_{\mathrm{In}} - [\mathrm{Na{+}K}]_{\mathrm{Out}} \cdot V_{\mathrm{Out}}}{\mathrm{TBW} + V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}}} + b - \left(m \cdot \frac{\mathrm{Na_e} + \mathrm{K_e}}{\mathrm{TBW}} + b\right)$$

First, the b's are subtracted out. Next, factor out the m's:

$$\Delta[\mathrm{Na}] = m \cdot \left[\frac{\mathrm{Na_e} + \mathrm{K_e} + [\mathrm{Na{+}K}]_{\mathrm{IVF}} \cdot V_{\mathrm{IVF}} + [\mathrm{Na{+}K}]_{\mathrm{In}} \cdot V_{\mathrm{In}} - [\mathrm{Na{+}K}]_{\mathrm{Out}} \cdot V_{\mathrm{Out}}}{\mathrm{TBW} + V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}}} - \frac{\mathrm{Na_e} + \mathrm{K_e}}{\mathrm{TBW}}\right]$$

Put what is inside the brackets over a common denominator:

$$\Delta[\mathrm{Na}] = m \cdot \left[\frac{(\mathrm{Na_e} + \mathrm{K_e}) \cdot \mathrm{TBW} + [\mathrm{Na{+}K}]_{\mathrm{IVF}} \cdot V_{\mathrm{IVF}} \cdot \mathrm{TBW} + [\mathrm{Na{+}K}]_{\mathrm{In}} \cdot V_{\mathrm{In}} \cdot \mathrm{TBW} - [\mathrm{Na{+}K}]_{\mathrm{Out}} \cdot V_{\mathrm{Out}} \cdot \mathrm{TBW}}{(\mathrm{TBW} + V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}}) \cdot \mathrm{TBW}} - \frac{(\mathrm{Na_e} + \mathrm{K_e}) \cdot (\mathrm{TBW} + V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}})}{(\mathrm{TBW} + V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}}) \cdot \mathrm{TBW}}\right]$$

The $(\mathrm{Na_e} + \mathrm{K_e}) \cdot \mathrm{TBW}$ terms are subtracted out, leaving:

$$\Delta[\mathrm{Na}] = m \cdot \left[\frac{[\mathrm{Na{+}K}]_{\mathrm{IVF}} \cdot V_{\mathrm{IVF}} \cdot \mathrm{TBW} + [\mathrm{Na{+}K}]_{\mathrm{In}} \cdot V_{\mathrm{In}} \cdot \mathrm{TBW} - [\mathrm{Na{+}K}]_{\mathrm{Out}} \cdot V_{\mathrm{Out}} \cdot \mathrm{TBW}}{(\mathrm{TBW} + V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}}) \cdot \mathrm{TBW}} - \frac{(\mathrm{Na_e} + \mathrm{K_e}) \cdot (V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}})}{(\mathrm{TBW} + V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}}) \cdot \mathrm{TBW}}\right]$$

Above, in the first fraction, the TBW's cancel out, leaving:

$$\Delta[\mathrm{Na}] = m \cdot \left[\frac{[\mathrm{Na{+}K}]_{\mathrm{IVF}} \cdot V_{\mathrm{IVF}} + [\mathrm{Na{+}K}]_{\mathrm{In}} \cdot V_{\mathrm{In}} - [\mathrm{Na{+}K}]_{\mathrm{Out}} \cdot V_{\mathrm{Out}}}{\mathrm{TBW} + V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}}} - \frac{(\mathrm{Na_e} + \mathrm{K_e}) \cdot (V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}})}{(\mathrm{TBW} + V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}}) \cdot \mathrm{TBW}}\right]$$

Above, in the second fraction, isolate the $\frac{\mathrm{Na_e}+\mathrm{K_e}}{\mathrm{TBW}}$ into a separate multiplier:

$$\Delta[\mathrm{Na}] = m \cdot \left[\frac{[\mathrm{Na{+}K}]_{\mathrm{IVF}} \cdot V_{\mathrm{IVF}} + [\mathrm{Na{+}K}]_{\mathrm{In}} \cdot V_{\mathrm{In}} - [\mathrm{Na{+}K}]_{\mathrm{Out}} \cdot V_{\mathrm{Out}}}{\mathrm{TBW} + V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}}} - \frac{V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}}}{\mathrm{TBW} + V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}}} \cdot \frac{\mathrm{Na_e} + \mathrm{K_e}}{\mathrm{TBW}}\right]$$

The $\frac{\mathrm{Na_e}+\mathrm{K_e}}{\mathrm{TBW}}$ is equal to $\frac{[\mathrm{Na}]_1 - b}{m}$, seen by rearranging $[\mathrm{Na}]_1 = m \cdot \frac{\mathrm{Na_e}+\mathrm{K_e}}{\mathrm{TBW}} + b$. Substituting in:

$$\Delta[\mathrm{Na}] = m \cdot \left[\frac{[\mathrm{Na{+}K}]_{\mathrm{IVF}} \cdot V_{\mathrm{IVF}} + [\mathrm{Na{+}K}]_{\mathrm{In}} \cdot V_{\mathrm{In}} - [\mathrm{Na{+}K}]_{\mathrm{Out}} \cdot V_{\mathrm{Out}}}{\mathrm{TBW} + V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}}} - \frac{V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}}}{\mathrm{TBW} + V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}}} \cdot \frac{[\mathrm{Na}]_1 - b}{m}\right]$$

Distribute the m and combine the fractions over a common denominator:

$$\Delta[\mathrm{Na}] = \frac{m \cdot [\mathrm{Na{+}K}]_{\mathrm{IVF}} \cdot V_{\mathrm{IVF}} + m \cdot [\mathrm{Na{+}K}]_{\mathrm{In}} \cdot V_{\mathrm{In}} - m \cdot [\mathrm{Na{+}K}]_{\mathrm{Out}} \cdot V_{\mathrm{Out}} - (V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}}) \cdot ([\mathrm{Na}]_1 - b)}{\mathrm{TBW} + V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}}}$$

Group the similar terms according to their volume multipliers:

$$\Delta[\mathrm{Na}] = \frac{m \cdot [\mathrm{Na{+}K}]_{\mathrm{IVF}} \cdot V_{\mathrm{IVF}} + b \cdot V_{\mathrm{IVF}} - [\mathrm{Na}]_1 \cdot V_{\mathrm{IVF}} + m \cdot [\mathrm{Na{+}K}]_{\mathrm{In}} \cdot V_{\mathrm{In}} + b \cdot V_{\mathrm{In}} - [\mathrm{Na}]_1 \cdot V_{\mathrm{In}} - m \cdot [\mathrm{Na{+}K}]_{\mathrm{Out}} \cdot V_{\mathrm{Out}} - b \cdot V_{\mathrm{Out}} + [\mathrm{Na}]_1 \cdot V_{\mathrm{Out}}}{\mathrm{TBW} + V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}}}$$

Factor out the volume multipliers:

$$\Delta[\mathrm{Na}] = \frac{(m \cdot [\mathrm{Na{+}K}]_{\mathrm{IVF}} + b - [\mathrm{Na}]_1) \cdot V_{\mathrm{IVF}} + (m \cdot [\mathrm{Na{+}K}]_{\mathrm{In}} + b - [\mathrm{Na}]_1) \cdot V_{\mathrm{In}} - (m \cdot [\mathrm{Na{+}K}]_{\mathrm{Out}} + b - [\mathrm{Na}]_1) \cdot V_{\mathrm{Out}}}{\mathrm{TBW} + V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}}}$$

Break up the one big fraction into three smaller fractions:

$$\Delta[\mathrm{Na}] = \underbrace{\frac{m \cdot [\mathrm{Na{+}K}]_{\mathrm{IVF}} + b - [\mathrm{Na}]_1}{\mathrm{TBW} + V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}}} \cdot V_{\mathrm{IVF}}}_{\text{Module for therapeutic IV fluid}} + \underbrace{\frac{m \cdot [\mathrm{Na{+}K}]_{\mathrm{In}} + b - [\mathrm{Na}]_1}{\mathrm{TBW} + V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}}} \cdot V_{\mathrm{In}}}_{\text{Module for generic input}} - \underbrace{\frac{m \cdot [\mathrm{Na{+}K}]_{\mathrm{Out}} + b - [\mathrm{Na}]_1}{\mathrm{TBW} + V_{\mathrm{IVF}} + V_{\mathrm{In}} - V_{\mathrm{Out}}} \cdot V_{\mathrm{Out}}}_{\text{Module for generic output}} \tag{7}$$

Each of the smaller fractions is seen to function like a module for a particular input/output. The pattern is consistently repeated and can be generalized into a rubric for incorporating any number of gains and losses:

1) Sign: Inputs (including the therapeutic IV fluid) are added, and outputs are subtracted.

2) Each input or output fluid's [Na+K] is modified by the slope and y-intercept, as in $m \cdot [\text{Na+K}]_{\text{IVF}} + b$ for example, similar to the way that the $\frac{\text{Na}_\text{e}+\text{K}_\text{e}}{\text{TBW}}$ is modified by the slope and y-intercept in the full Edelman equation.

3) From part 2), subtract the patient's starting sodium, $[\text{Na}]_1$. This forms the numerator.

4) Divide by a denominator that is basically the new body volume after all gains and losses: $\text{TBW} + V_{\text{IVF}} + V_{\text{In}} - V_{\text{Out}}$.

5) Multiply the whole fraction by the volume of the input or output, V_{IVF} for example.

6) Sum up all of the modules to calculate the delta [Na].

Knowing the rubric, one can fathom the complexity of the equation and even reconstruct it.

Equation (7) is the delta [Na] version of the Nguyen-Kurtz sodium formula with a slope and y-intercept. From this all-inclusive version, modules can be omitted to quickly arrive at the other eponymous sodium equations in their slope and y-intercept forms. For example, the Adrogué-Madias formula considers only the IV fluid, so removing the generic input and generic output reduces equation (7) to:

$$\Delta[\text{Na}] = \frac{m \cdot [\text{Na+K}]_{\text{IVF}} + b - [\text{Na}]_1}{\text{TBW} + V_{\text{IVF}}} \cdot V_{\text{IVF}} \tag{8}$$

This A-M formula with a slope and y-intercept is reminiscent of equation (5), reproduced here:

$$\Delta[\text{Na}] = \frac{[\text{Na+K}]_{\text{IVF}} - [\text{Na}]}{\text{TBW} + V} \cdot V$$

If $m = 1$ and $b = 0$, as A-M assumes, then equation (8) turns into equation (5) *exactly*, as it should. This internal consistency also serves as a check on all of the preceding algebra.

Flip the equation again: slope and y-intercept edition

As with flipping equation (5)—delta [Na]—into equation (6)—volume of IVF—, equation (7) can also be rearranged to solve for the volume of therapeutic IV fluid to infuse. Arguably, this is the more useful information to know when treating a dysnatremia. Without delving into the algebraic details, we present the formula for the IVF volume:

$$V_{\text{IVF}} = \frac{\Delta[\text{Na}] \cdot \text{TBW} - \overbrace{(m \cdot [\text{Na+K}]_{\text{In}} + b - [\text{Na}]_2) \cdot V_{\text{In}}}^{\text{Module for generic input}} + \overbrace{(m \cdot [\text{Na+K}]_{\text{Out}} + b - [\text{Na}]_2) \cdot V_{\text{Out}}}^{\text{Module for generic output}} \mp \cdots}{m \cdot [\text{Na+K}]_{\text{IVF}} + b - [\text{Na}]_2} \tag{9}$$

Equation (9) is a little harder to remember, but a few rules will help in reconstructing it:

1) Sign: Contrarily, inputs are subtracted, and outputs are added. The $\mp$ indicates the opposite of the expected sign, and the ellipsis indicates the modular, expandable nature of the equation.
2) The numerator starts off with the $\Delta[\text{Na}] \cdot \text{TBW}$, like in equation (6). This gives a sense of how much cationic solute should be gained or lost to achieve a desired change in serum sodium.
3) From there, the numerator accommodates as many modules as there are inputs and outputs.
4) Each module is stereotypically an I/O fluid's [Na+K], modified by the slope and y-intercept, minus the *ending* serum sodium, $[\text{Na}]_2$. Multiply that difference by the volume of the I/O.
5) Divide the entire numerator by a denominator consisting of the therapeutic IV fluid's [Na+K], modified by the slope and y-intercept, minus the $[\text{Na}]_2$.

Check: If generic I's/O's are zeroed out, equation (9) turns into equation (6) for $m = 1, b = 0$:

$$V = \frac{\Delta[\text{Na}] \cdot \text{TBW}}{[\text{Na+K}]_{\text{IVF}} - [\text{Na}]_2}$$

Amazingly, our equation (9) is mathematically identical to the Nguyen-Kurtz equation (6) from their article (*Clin Exp Nephrol* 7: 125-137, 2003). Written in our nomenclature, their (6) was:

$$V_{\text{IVF}} = \frac{([\text{Na}]_1 - b) \cdot \text{TBW} - ([\text{Na}]_2 - b) \cdot (\text{TBW} + V_{\text{In}} - V_{\text{Out}}) + m \cdot ([\text{Na+K}]_{\text{In}} \cdot V_{\text{In}} - [\text{Na+K}]_{\text{Out}} \cdot V_{\text{Out}})}{[\text{Na}]_2 - b - m \cdot [\text{Na+K}]_{\text{IVF}}}$$

That can be massaged into our equation (9), which has a more memorable pattern and grouping.