The Mathematics of Resuscitation: 1980 Presidential Address, American Burn Association

ARTHUR D. MASON, JR., M.D.

This morning, we again reach that moment when custom dictates that the President, in one of his last official acts, address the organization. Presidents approach this address in many ways. Some dwell on history, others on philosophy; some rail against the ill-liturgical bonds which inhibit us all, but most, in one way or another, exhort the membership to greater effort. These addresses often stem from the day-to-day activities of their authors. If the daily occupation of the President is administrative, his address usually reflects administrative concern; the practicing surgeon may speak of care and complications, the educator of teaching and its problems. For many years, playing Merlin in a Camelot of my own choosing, I have had the unique opportunity to work with ideas which is granted to the Chief Sorcerer and so, this morning, I invite you to explore an idea with me. Like most ideas, it is neither all new nor all old, and at this time it is incomplete. I present it now for two reasons; first, because I believe there is a greater dearth of ideas than of any other resource in our search for better care, and that our success or failure will ultimately be measured by our ability to develop them, and second, in the hope that my thoughts about this topic may lead one of you to a better solution.

Most hypotheses, great or small, begin with some simple and usually inaccurate speculation. This morning's theme begins with the simple notion that volume loss in burns may be constant; that each square centimeter of a burn may remove as much edema fluid and exudate from the body as any other, and that this may be true not only from area to area in one patient, but from patient to patient as well. There are many things wrong with this notion—we know that edema varies with burn depth, with anatomic site, with time after injury, and with the state of the circulation. What is false in particular, however, is often true in the aggregate—much of what is known of chemistry and physics rests on this peculiar fact. Perhaps this is also true in this instance.

If we were to assemble measurements of edema and exudate volume from a large number of patients with small burns, each so small that it had little impact on the general circulation, during the first 24 hours after injury, we might calculate a mean volume loss per unit area and then make an estimate of the error of this mean, realizing that anatomic site, burn depth, and other variables have contributed specific increments to that error. Experiments might be designed to assess the magnitude of these increments; for the moment, however, let us assume the error to be small in relation to the size of the mean, permitting us a useful statement of the average volume loss per unit area of burn in the first 24 hours after injury. We will call this value $\bar{K}$ and give it dimensions of milliliters per square meter of burn surface.

Not much is known of the value of $\bar{K}$ in the human. In burned animals, most measurements suggest that the injured area doubles in volume. In the human, this suggests a range of 2,000 to 4,000 milliliters per square meter of burn. Moyer (5) has shown that gradual losses of extracellular fluid amounting to 21% of body weight produce symptoms in healthy volunteers which might be expected to occur in adults with burns of 20 to 25% of the total body surface—calculation from this base suggests that $\bar{K}$ is of the order of 4,000 milliliters per square meter. It seems improbable that volume loss in a 50% burn exceeds 1 plasma volume, and this, too, suggests a value approximating 4,000 milliliters per square meter. For the moment, then, let us accept 4,000 milliliters per square meter as an estimate of the mean volume loss constant, $\bar{K}$.

Now, if we think of a large burn as a collection of smaller burns of varying depth, we may speculate that the volume demand of such an injury may be estimated from its surface area and $\bar{K}$. For this to be true, the large burn must have reached dynamic equilibrium with a normal or near normal circulation, and we will assume this to be true when resuscitation is satisfactory.

Using Meeh's equation

$$S = k \cdot W^{2/3}$$

$S =$ surface area, $m^2$

$W =$ body weight, kg

$k = 0.1$

as a basis for estimating total body surface area, we may estimate the volume loss in any burn by applying an equation which summarizes the discussion to this point.

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From the United States Army Institute of Surgical Research, Brooke Army Medical Center, Fort Sam Houston, TX 78234 (address for reprints).

\[ V = \frac{\% \text{ burn}}{100} \times R \times S \]\n
\[ V = \text{volume loss, } 0-24^\circ, \text{ ml} \]
\[ S = \text{surface area, m}^2 \]
\[ R = 4,000. \]

Next, let us consider the nature of this volume loss. The fluid which pours into the interstitium of a burn is similar to plasma. It is often discussed as though it were sequestered in the burn site, but everything we know of burn edema and of its accumulation suggests that it should, at least in most respects, be considered to be in dynamic equilibrium with and virtually a part of the plasma volume (Fig. 1). The volume shift following a major burn behaves as though a large, new unfulfilled plasma space had been created by the injury; resuscitation can be viewed as an effort to expand the plasma volume enough to permit the coexistence of this new space with a normal plasma volume. If this is true, we should be able to find direct reflections of the estimation of mean volume loss in clinical resuscitation. In animal skins, which do not blister, exudate loss at the burn surface is not large and the edema mass tends to be confined to the area underlying the burn wound. In the human, however, burns of any consequence are uniformly accompanied by physical loss of the epidermal barrier; with the edema pouring into a leaky sac, exudate loss is sufficiently large to be of consequence and may continue for some time. Cope and Moore (3), in 1947, estimated this loss at 25 ml/% burn/day in adults, a little more than one third our estimate of \( R \). This, too, should be reflected in clinical experience.

As you know, resuscitation is accomplished in a number of ways, using electrolyte solutions with or without colloid according to several formulae. We will consider three widely used formulae, the Parkland, the Brooke, and the Evans, along with an experimental series reported by Barton and Laing (1) using plasma alone. The volumes of solution recommended by these formulae in the first 24 hours range from 4 ml/kg/% burn down to approximately 1 ml/kg/% burn, and their recommended salt loads vary similarly. All these formulae are more or less empirical; all effectively prevent burn shock; all were developed for and clinically validated in adults. In some sense, despite their divergence, each must be correct. The important differences among them must be sought outside their ability to forestall burn shock.

In discussing these formulae, we must examine the behavior in the body of their component solutions. It will simplify this discussion to confine our attention to two idealized solutions, one, normal plasma, and the other, an isotonic balanced salt solution equivalent to an ultrafilterate of this plasma. In studies of hemorrhage, Moyer (5) has shown that in hypovolemic states, plasma volume expansion by an isotonic salt solution amounts to approximately one fourth the administered volume, the remaining three fourths being distributed to the interstitial fluid. In isovolemic subjects, plasma distributes in the same manner, but with decreased blood volume, administered plasma remains wholly in the plasma volume. Studies of this sort are not available in burns, but it seems fair to assume that similar distributions occur, the exception being that the colloid solutions also freely enter the interstitium in the area of the burn. In essence, until isovolemia is established, we will assume that the whole volume of plasma administered is available to expand the combined plasma/burn edema space while only one fourth of the administered volume of electrolyte solution serves a similar purpose, the remainder producing edema in the uninjured portion of the body (Fig. 2).

Now, we can write an equation for the amount of
10 PRINT "ENTER NORMAL WT. (LBS.)";
20 INPUT W
30 W=W/2.2
40 H=0
50 PRINT "ENTER % BURN";
60 INPUT B
70 PRINT
80 K=4000
90 S=1*W^(2/3)
100 V=INT(B/100*S*K)
110 PRINT "DOSE
INTERSTITIAL"
120 PRINT "COLL ELEC ML/KG ML/KG/% BURN EDEMA EDEMA/KG COST"
130 PRINT "F"
140 FOR F=0 TO 1 STEP .25
150 D=INT((4*F*V)/(1+(3*F)))
160 E=INT(V-D)*4
170 M=(D+E)/W
180 N=M/B
190 D=D+E-V
200 G=D/W
210 P=2000*(D/1000)+E/1000
220 PRINT USING "#.#
130 PRINT "ENTER SELECTED COLLOID DOSE (-1 TO EXIT, -2 FOR NEW RUN)";
230 IF H>0 THEN PRINT \ GO TO 270
240 NEXT F
250 PRINT
260 PRINT
270 PRINT "DOSE MUST BE LESS THAN":V+1:"ML."
280 IF D>5 THEN PRINT \ GO TO 270
290 IF D=1 GO TO 370
300 IF D=2 THEN PRINT \ GO TO 10
310 IF D=2 THEN PRINT \ GO TO 10
320 E=INT(V-D)*4
330 F=D/(D+E)
340 H=H+1
350 PRINT
360 GO TO 170
370 END

Fig. 3. BASIC computer program RESTEMP.
TABLE I
Output of program RESTEMP in two instances of 50% burn

<table>
<thead>
<tr>
<th>Normal Wt (kg)</th>
<th>f</th>
<th>Colloid (ml)</th>
<th>Electrolyte (ml)</th>
<th>Mil/kg</th>
<th>Mil/kg/% burn</th>
<th>Burn Edema (ml)</th>
<th>Interstitial Edema (ml)</th>
<th>Interstitial Edema (ml/kg)</th>
<th>Cost ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>70</td>
<td>0.00</td>
<td>0</td>
<td>13,584</td>
<td>194</td>
<td>3.88</td>
<td>3,396</td>
<td>10,188</td>
<td>146</td>
<td>13.58</td>
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<td></td>
<td>0.25</td>
<td>1,940</td>
<td>5,824</td>
<td>111</td>
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<td>3,396</td>
<td>4,366</td>
<td>62</td>
<td>392.82</td>
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<td>0.50</td>
<td>2,716</td>
<td>2,720</td>
<td>78</td>
<td>1.55</td>
<td>3,396</td>
<td>2,040</td>
<td>29</td>
<td>545.92</td>
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<td>0.75</td>
<td>3,334</td>
<td>1,048</td>
<td>60</td>
<td>1.19</td>
<td>3,396</td>
<td>785</td>
<td>11</td>
<td>662.54</td>
</tr>
<tr>
<td></td>
<td>1.00</td>
<td>3,396</td>
<td>0</td>
<td>49</td>
<td>0.97</td>
<td>3,396</td>
<td>0</td>
<td>0</td>
<td>679.20</td>
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<tr>
<td>10</td>
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<td>0</td>
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<td>371</td>
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<td>2,784</td>
<td>278</td>
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<td>0.25</td>
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<td>928</td>
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<td>119</td>
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<td>744</td>
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<td>56</td>
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<tr>
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<td>0.75</td>
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<td>788</td>
<td>114</td>
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<td>928</td>
<td>216</td>
<td>22</td>
<td>171.49</td>
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<td></td>
<td>1.00</td>
<td>928</td>
<td>0</td>
<td>93</td>
<td>1.86</td>
<td>928</td>
<td>0</td>
<td>0</td>
<td>186.60</td>
</tr>
</tbody>
</table>

TABLE II
Comparison of resuscitative volumes predicted by burn formulae with RESTEMP estimation

<table>
<thead>
<tr>
<th>f</th>
<th>Burn Formula</th>
<th>Formulas Volume (ml/kg/% burn)</th>
<th>Computer Estimation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00</td>
<td>Parkland</td>
<td>4</td>
<td>3.88</td>
</tr>
<tr>
<td>0.25</td>
<td>Brooke</td>
<td>2</td>
<td>2.22</td>
</tr>
<tr>
<td>0.50</td>
<td>Evans</td>
<td>2</td>
<td>1.55</td>
</tr>
<tr>
<td>0.75</td>
<td></td>
<td></td>
<td>1.19</td>
</tr>
<tr>
<td>1.00</td>
<td>Barton/Laing</td>
<td>1</td>
<td>0.97</td>
</tr>
</tbody>
</table>

Resuscitative fluid required to restore plasma volume, using either of the two idealized solutions or any combination thereof. For this purpose, it will be convenient to define f, the ratio of the administered volume of plasma (P) to total resuscitative volume (Q):

\[ f = \frac{P}{Q} = \frac{P}{P + 4(V - P)} \]

\[ Q = \frac{4V}{1 + 3f} \]

\[ E = 4(V - P). \]

E, of course, is the administered volume of balanced electrolyte solution.

These equations may be used to examine the selected burn formulae. The examination is facilitated by using a computer program (Fig. 3) which, when provided with appropriate values for body weight and burn size, uses the equations we have developed to generate a series of estimates. The algorithms are very simple and can be implemented on a hand-held calculator.

Since each of the selected resuscitation formulae has been validated by clinical experience in adults, and the classic Brooke formula, in particular, is known to underestimate the requirement in children, we will first examine the application of this program in an adult weighing 70 kg and having a 50% burn (Table I). Body weight and burn size are entered, and the program responds with estimates of the resuscitative volumes required to restore plasma volume to normal at increasing fractional levels of plasma administration. Estimates of volume loss in the burn, edema accumulation in the normal, uninjured interstitium, and cost are also produced. The estimated volumes, in terms of ml/kg/% burn, agree reasonably well with the zero to 24-hour predictions of each of the classic formulae and with the volume approximations used by Barton and Laing in their experimental group (Table II). It thus appears reasonable that all these formulae should perform adequately in adults despite the considerable differences among them. Indeed, by simply varying f, we might write any number of such formulae for the adult burned patient. Note, however, that if our assumptions are valid, each would be precisely correct at only one body weight.

If we next examine the estimates in a child weighing 10 kg and having a 50% burn (Table I), several features emerge. First, the requirement, in ml/kg/% burn, increases sharply, a consequence of the proportionally larger surface area in the child and a result consistent with clinical experience. More important, resuscitation with electrolyte alone now imposes a rather large edema burden, approaching 30% of body weight, on the uninjured part of the body, a burden which is sharply diminished by the use of even a modest fractional volume of plasma.

In a larger burn, this volume of edema following electrolyte resuscitation appears potentially troublesome even in the adult and in the child becomes very large (Table III). The alternatives to imposing this burden appear to be either the use of colloid or less than ideal resuscitation.

Figure 4 summarizes the relationship of the calculated resuscitative volume to body weight over a range of values for fractional plasma administration. The upper curve depicts resuscitation with electrolyte alone; it intersects the Parkland formula volume at 64 kg and hovers near it across the adult weight range. The predicted requirement in children approaches twice that in adults and considerably exceeds 4 ml/kg/% burn. The other curves behave similarly, approximating the individual burn formulae in the adult and rising sharply as body...
TABLE III
Output of program RESTEMP in two instances of 80% burn

<table>
<thead>
<tr>
<th>Normal Wt</th>
<th>f</th>
<th>Colloid (ml)</th>
<th>Electrolyte (ml)</th>
<th>MI/kg</th>
<th>MI/kg/% burn</th>
<th>Burn Edema (ml)</th>
<th>Interstitial Edema (ml)</th>
<th>Interstitial Edema (ml/kg)</th>
<th>Cost ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>70</td>
<td>0.00</td>
<td>0</td>
<td>21,740</td>
<td>311</td>
<td>3.88</td>
<td>5,435</td>
<td>16,305</td>
<td>233</td>
<td>21.74</td>
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<td>0.25</td>
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<td>178</td>
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<td>5,435</td>
<td>6,990</td>
<td>100</td>
<td>630.32</td>
</tr>
<tr>
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<td>4,348</td>
<td>124</td>
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<td>5,435</td>
<td>3,261</td>
<td>47</td>
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<td>1,004.88</td>
</tr>
<tr>
<td></td>
<td>1.00</td>
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<td>4,455</td>
<td>446</td>
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<tr>
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<td>848</td>
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<td>340</td>
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<td>1,485</td>
<td>1,911</td>
<td>191</td>
<td>172.15</td>
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<tr>
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<td>1,188</td>
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<td>89</td>
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<td>183</td>
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<td>1,485</td>
<td>346</td>
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<td>149</td>
<td>1.86</td>
<td>1,485</td>
<td>0</td>
<td>0</td>
<td>297.00</td>
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</tbody>
</table>

Fig. 4. Relation of estimated resuscitative volume to body weight at levels of colloid administration utilized in selected burn formulae.

Fig. 5. Relation of estimated edema volume in uninjured interstitium to administered colloid fraction.

administered. At present, we do not know what burden of edema to consider dangerous. Urinary excretion of sodium tends to alleviate this burden, but is not usually large in the 48 hours after injury. Most of us suspect, as did Cope and Moore (3), and Evans (4), many years ago, that excessive volume and salt loads risk either immediate or delayed pulmonary edema, and volume loading experiments in animals invariably produce massive intestinal edema, a possible factor in postburn ileus. Only experience will disclose the merit, if any, of deliberately restricting edema load in the normal interstitium, but if such restriction is desirable, this set of equations will provide a guide to flexible control of resuscitation, using electrolyte solutions alone in smaller burns and larger patients and high fractions of plasma in the resuscitation of larger burns, children, and those in whom any excessive volume load is an unwarranted risk.

Humans, unlike burned animals, usually require additional resuscitation during the second 24 hours after injury. Edema itself, other than that which we impose, is usually maximal within 24 hours of injury and does not seem likely to account for this additional need. Two factors may play a part. The first, and probably the smaller, is erythrocyte loss by hemolysis. Although significant in other respects, this loss can hardly exceed 300 ml/square meter/24 hours in the adult (6). The greater loss is probably the exudate which, in the human, continues to weep through the denuded, leaky edema space and whose volume may be, as noted above, on the order of 1,200 to 1,500 ml/square meter/24 hours. Between them, these losses approach half the loss during the first 24 hours after injury, a volume quantitatively consistent with the continuing need for administered volume expressed by most burn resuscitation formulae. Beyond 48 hours, leakage is presumed to become less prominent.

To summarize, then, we have begun with a rather fragile speculation about the burn wound, borrowed a fact here and a fact there, added an educated guess or two, and arrived at what appears to be a reasonably comprehensive theory of resuscitation which is supported
at a number of points by clinical experience. This theory accounts for the clinical success of divergent resuscitation formulae and suggests that certain risks may vary considerably and in nonlinear manner with patient size, burn size and the particular fluids used.

As I have said, the idea is by no means complete, nor, certainly, is it entirely new. Some of the illustrations I have used this morning were published in 1951 by Oliver Cope (2) and most of the facts used to develop the idea are 25 years old and attributable to studies by him, by Francis Moore, and by Carl Moyer. Newton, borrowing from Lucan, pointed out in a letter to Descartes that if we see further it is because we stand on the shoulders of giants. He failed to point out how long it might take us to climb to that vantage point.

Yet, in its present form, the hypothesis is new, and I hope you will find it useful. Its value, if any, resides more in what it suggests than in what it is—it is an outline, a skeleton in need of flesh, a theory in need of testing. Perhaps one of you will choose to fill in its blanks. And if so, we will have come full circle and arrived again at the beginning, for this is my way, as I bid you farewell as President, to exhort you to greater effort.

REFERENCES