not been reported previously. Earlier reports dealing with secondary fentanyl peaks occurring postoperatively have dealt with the dangers associated with respiratory depression in the spontaneously ventilating patient. We have described the occurrence of another side effect of fentanyl that could seriously compromise the mechanically ventilated patient, particularly when hypothermia is superimposed. Treatment with naloxone or neuromuscular blockers was effective attenuating the rigidity.

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Estimating Allowable Blood Loss: Corrected for Dilution

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Several formulas have been derived for estimating allowable pre-transfusion blood loss.[1,2] One such formula is:

$$V_L = EBV \times \frac{H_O - H_F}{H_O} \qquad (1)$$

where V_L = allowable blood loss; EBV = patient's estimated blood volume; H_O = patient's initial hematocrit (or hemoglobin concentration); and H_F = patient's minimum allowable hematocrit (or hemoglobin concentration). This "linear" formula implies that the fractional decrease in hemoglobin or hematocrit is equal to the fraction of the total blood volume that has been lost. This would be true if all of the shed blood had the initial hematocrit. However, intravascular volume usually is maintained prior to blood transfusion by administration of crystalloids; hematocrit therefore should decrease gradually. Because each milliliter of shed blood contains progressively less hemoglobin, the above formula overestimates the hemoglobin loss. Inconsistencies may result. For example, formula 1 predicts that if blood losses exceed the total blood volume, the resulting hemoglobin concentration will be negative!

Bourke and Smith discussed this problem in 1975,[1] and described the problem of isovolemic hemodilution in terms of the differential equation:

$$\frac{dH}{dV_L} = -\frac{H}{EBV}$$

The solution of this equation with initial H = H_O and initial V_L = O is:

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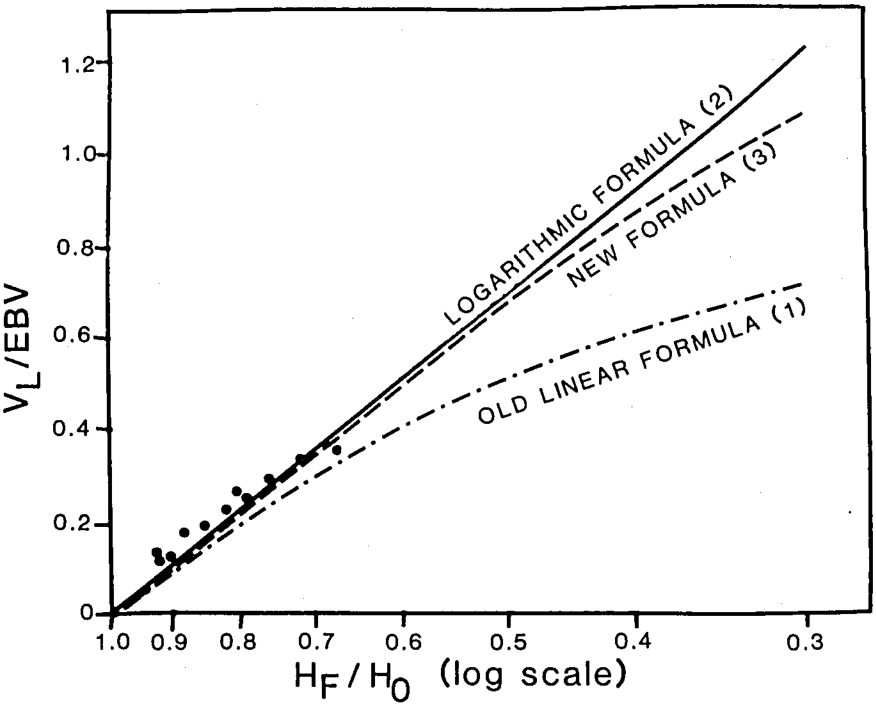

FIG. 1. Blood loss (as a fraction of estimated blood volume: V_L/EBV) *vs.* resulting hematocrit (as a fraction of initial hematocrit: H_F/H_O). Patient measurements appear as circles; lines represent the relationship predicted by the indicated formula. The new formula 3 approximates the logarithmic formula 2 throughout the range of clinical applicability, and closely correlates with the observed data.

$$V_L = EBV \times \ln\left(\frac{H_O}{H_F}\right) \qquad (2)$$

This formula, also described by Ward *et al.*[2] has been shown to correspond accurately to measured blood losses in both humans[1] and dogs.[2] However, because it requires the use of the natural logarithm function, it is not suited to routine use. Bourke and Smith[1] attempted to overcome this problem by using an approximation to the logarithm, but their formula was cumbersome and difficult to remember.†

METHODS

As shown in the Appendix, a new formula, approximating the logarithm of equation 2, was derived:

$$V_L = EBV \times \left(\frac{H_O - H_F}{H_{AV}}\right) \qquad (3)$$

where H_{AV} is the average of the initial and minimum allowable hemoglobin concentrations or hematocrits. Verbally, this formula states that the allowable blood loss is equal to the estimated blood volume multiplied by a fraction whose numerator is the difference between the initial and minimum allowable hemoglobin concentration (or hematocrit) and whose denominator is the average of the initial and minimum allowable hemoglobin concentrations (or hematocrits). As seen in figure 1, formula 3 closely approximates the logarithmic formula for allowable blood loss. In fact, provided blood loss is less than the estimated blood volume, the maximum discrepancy between the new formula 3 and the logarithmic formula 2 is only 7.5%.

To test this formula, eight adult patients undergoing surgical procedures with the potential for significant blood loss participated in this phase of our investigation, which had the approval of our institutional review board. After induction of anesthesia, each patient received adequate intravenous "crystalloid" solutions to maintain hemodynamic stability. Just prior to incision, we measured the hematocrit and estimated the blood volumes as indicated in table 1.[3]

During surgery, we measured suctioned blood (subtracting irrigation volumes), weighed sponges, and carefully estimated losses onto the drapes and floor. Circulating volume was maintained using crystalloids or colloids. As blood losses increased, we redetermined the hematocrit and recorded the measured blood loss at the time the sample was taken. If the hematocrit was greater than 27%, we delayed the start of erythrocyte transfusion until additional blood losses occurred; we then repeated the hematocrit determination.

For each patient, we obtained one or two simultaneous measurements of blood loss and hematocrit. For each measured hematocrit, the allowable blood loss (to reach this hematocrit) was computed using the linear

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† $V_L = EBV \times (H_O - H_F) \times \left(3 - \frac{(H_O + H_F)}{2}\right)$ (H_O and H_F must be *hematocrits* expressed as decimal fractions: *e.g.*, a hematocrit of 45% is 0.45.).

TABLE 1. Estimated Blood Volume as a Function of Body Habitus (ml per Kg Body Weight)[3]

	Male	Female
Obese	60	55
Thin	65	60
Normal	70	65
Muscular	75	70

formula 1 and the new formula 3. Each of these estimates of allowable blood loss was compared with the measured blood loss to determine which estimate was more accurate. Wilcoxon's test was used for paired observations[4] to determine if either of the formulas was consistently more accurate. A value of $P < 0.05$ was taken as indicating statistical significance.

RESULTS

Demographic data for our subjects are shown in table 2. The ratio of blood lost to estimated blood volume (V_L/EBV) is plotted against the ratio of post-loss hematocrit to initial hematocrit (H_F/H_O) in figure 1. Figure 1 also shows the values of (V_L/EBV) which would be predicted by the old, linear formula 1, the new logarithmic approximation 3, and the true logarithmic formula 2. The new formula very closely approximates the logarithmic formula 2, while the linear formula 1 becomes increasingly inaccurate when blood losses exceed 20% of the EBV. In all but one of the paired blood loss and hematocrit measurements, the new formula provided a closer approximation to the allowable blood loss for a given target hematocrit than did the old, linear formula ($P < 0.05$).

DISCUSSION

To insure an adequate hematocrit for oxygen transport while minimizing unnecessary blood transfusions, a scheme for deciding when erythrocytes should be transfused is desirable. The linear formula 1 has the advantage of mathematical simplicity, but may underestimate the blood loss required to achieve a given hematocrit by up to 500 ml in a patient with an initial hematocrit of 45%. While maintaining the mathematical simplicity of the linear formula, my new formula 3 may help to reduce the number of unnecessary intraoperative blood transfusions.

Because the initial hematocrits of most of the patients I studied were relatively low, differences between the allowable blood loss predicted by the linear formula and the new formula were relatively small (average of 100 ml). Thus, use of the new formula did not alter the management of these patients. However, since the new formula consistently predicted blood loss more accurately than the linear formula, its application in patients with higher starting hematocrits could reduce unnecessary intraoperative blood replacement.

Any formula will have certain limitations. Both the logarithmic formula and the new logarithmic approximation described here assume relatively slow, steady blood loss with maintenance of intravascular volume with erythrocyte-free solutions. If blood loss is acute and not simultaneously replaced, these formulas will overestimate the allowable blood loss. However, under these circumstances it is unlikely that any formula can accurately account for many of the circulatory changes accompanying the hypovolemic state.

Because of its accuracy and ease of use, the new formula should be considered for calculation of allowable pre-transfusion blood loss during surgical procedures when intravascular volume is maintained.

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APPENDIX

The function ln (x) appears as the curved line in figure 2. Our goal is to find an approximation to this function when

TABLE 2. Demographic Data of Study Patients

Patient Number	Sex	Age (yr)	Build	Weight (kg)	Estimated Blood Volume (ml)	Initial Hct. H_O (%)	Surgical Procedure
1	M	59	Normal	66	4620	34.0	Radical neck dissection
2	M	64	Normal	64	4480	34.0	Aortic bifurcation graft
3	M	62	Normal	79	5530	33.5	Declotting of aortic bifurcation graft
4	M	59	Normal	76	5320	39.0	Repeat total hip arthroplasty
5	M	64	Normal	73	5110	46.0	Total hip arthroplasty
6	M	65	Obese	102	6120	32.0	Repeat total hip arthroplasty
7	F	55	Normal	71	4615	34.0	Radical neck dissection
8	M	53	Normal	57	3990	33.0	Radical neck dissection

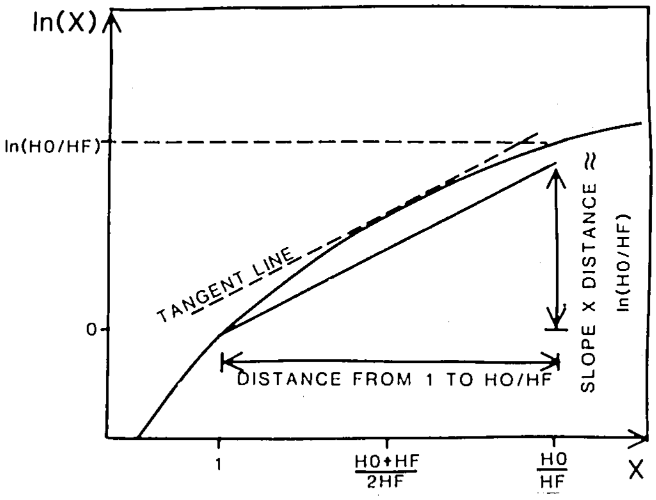

FIG. 2. Derivation of the approximation to ln (H_O/H_F). The slope of the curve ln(x) at the midpoint between 1 and H_O/H_F (slope of tangent line) multiplied by the distance between 1 and H_O/H_F approximates ln (H_O/H_F).

$x = H_O/H_F$. As shown in the figure, one such approximation can be made by multiplying the distance from 1 to H_O/H_F by the slope of the line which is tangent to the curve at the midpoint between 1 and H_O/H_F. Since the coordinate of the midpoint between 1 and H_O/H_F is

$$\frac{(H_O + H_F)}{2H_F},$$

the slope of the tangent to ln (x) at this point is:

$$\frac{2H_F}{(H_O + H_F)}.$$

The distance from 1 to H_O/H_F is

$$\frac{(H_O - H_F)}{H_F}.$$

Thus, the product of the slope and distance is:

$$\frac{2H_F}{(H_O + H_F)} \times \frac{(H_O - H_F)}{H_F} = \frac{(H_O - H_F)}{\left(\frac{(H_O + H_F)}{2}\right)},$$

which approximates ln H_O/H_F. Recognizing that the denominator of this fraction is merely the average of the initial and final hemoglobin concentrations or hematocrits, and substituting in formula 2 gives:

$$V_L = \text{EBV} \times \frac{H_O - H_F}{H_{AV}} \qquad (3)$$