特別講演 II

Fluid Therapy in Shock and Critical Illness

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The fluid management of shock depends upon numerous associated medical conditions including: the primary illness, age, medical history, amount of physical injury, the amount of blood and fluid losses, time delay in instituting therapy, the choice of fluids used and the amount and rate of their administration. Irrespective of the mixture of these clinical influences, the major precipitating physiologic event in shock, trauma, dehydration states, and other surgical emergencies is almost always hypovolemia, and the most important immediate therapeutic priority is restoration of blood volume. This paper will center on evaluation of fluid problems, monitoring of physiologic alterations, severity of illness, prediction of outcome, and fluid therapy of the critically ill surgical patient.

The most frequent identifiable fluid problems in acute illness are: (a) dehydration from fluid losses; (b) shock due to plasma volume losses directly from hemorrhage or secondary to fluid shifts precipitated by trauma; and (c) intracellular losses associated with malnutrition, chronic wasting diseases, inadequate food intake, hypercatabolic states, or other forms of energy depletion. A major controversy concerns the relative efficacy of crystalloids and colloids; i.e., whether crystalloids are better than colloids or vice versa. However, the real issues are: (a) What is the specific deficiency that the patient really has, reduced plasma volume or reduced interstitial water? (b) What are the specific indications for each available therapy? and (c) What is the most efficacious approach to these problems.

Evaluation of Clinical Problems due to Fluid Abnormalities

Clinical Criteria for Fluid Therapy

Blood volume restoration have been accepted as the most important goal in the treatment of shock and its sequelae, but criteria for achieving this goal have not been well defined. Clinical studies are often incompletely controlled with poor documentation either for the degree of hypovolemia or for early complete correction of hypovolemia. The common clinical criteria most often used are arterial pressure, heart rate, hematocrit, urine output, central venous pressure, and pulmonary arterial wedge pressures. In critically ill postoperative patients, most of these variables have been shown to be unreliable when compared with careful measurements of blood volume^{1)~3)}.

The normal values of these commonly monitored variables arterial pressure, heart rate, central venous

Table 1 Number and percent of patients with two or more values in the normal range

	Nonsurvivors		Survivors	
	Number	%	Number	%
Mean arterial pressure	29	78	68	89
Heart rate	30	81	66	87
Central venous pressure	35	95	72	95
Pulmonary wedge pressure	11	30	21	28
Cardiac index	35	95	64	84
Mean of these variables		76		75

pressure, wedge pressure and cardiac output, provide rather poor criteria for monitoring; normal values were restored in an average of 75 percent of the survivors as compared with 76 percent of the nonsurvivors (Table 1).

As an alternative to measuring blood volume, the fluid challenge or volume load may be used to assess the capacity of the circulatory system to accept an added volume without exceeding venous pressure limits that produce pulmonary overload. Although the immediate changes in central venous pressure and pulmonary arterial wedge pressures are directly correlated with volume changes produced by rapid infusions,

Table 2

Cardiorespiratory variables: abbreviations, units, calculations, normal values, preferred values, and predictive capacity

Volume-Related Variables	Abbreviations	Units	Measurements or Calculations	Normal Values	Preferred Values	Percent Correct
Mean arterial pressure	MAP	mmHg	Direct measurement	82—102	>84	75
Central ven. pressure	CVP	cmH ₂ O	Direct measurement	1—9	<5	62
Central blood volume	CBV	ml/M ²	$CBV = MTT \times CI \times 16.7$	660—1000	>925	61
Stroke index	SI	ml/M ²	$SI = CI \div HR$	30—50	>48	67
Hemoglobin	Hgb	g/dl	Direct measurement	12—16	>12	66
Mean pulmon. art. press.	MPAP	mmHg	Direct measurement	11—15	<19	68
Wedge pressure	WP	mmHg	Direct measurement	0—12	>9.5	70
Blood volume	BV	ml/M ²	$BV = PV \div (I-Hct)^a \times SA$	men 2.74 women 2.37	>3.0 >2.7	76
Red cell mass	RCM	ml/M ²	$RCM = BV - PV$	men 1.1 women 0.95	>1.1 >0.95	85
Flow-Related Variables						
Cardiac index	CI	liter/min·M ²	Direct measurement	2.8—3.6	>4.5	70
Left vent. stroke work	LVSF	g·M/M ²	$LVSF = SI \times MAP \times .0144$	44—68	>55	74
Left cardiac work	LCW	kg·M/M ²	$LCW = CI \times MAP \times .0144$	3—4.6	>5	76
Right vent. stroke work	RVSF	g·M/M ²	$RVSF = SI \times MPAP \times .0144$	4—8	>13	70
Right cardiac work	RCW	kg·M/M ²	$RCW = CI \times MPAP \times .0144$	0.4—0.6	>1.1	69
Stress-Related Variables						
System. vasc. resist.	SVR	dyne·sec/cm ⁵ ·M ²	$SVR = 79.92(MAP-CVP)^b \div CI$	1760—2600	<1450	62
Pulmon. vasc. resist.	PVR	dyne·sec/cm ⁵ ·M ²	$PVR = 79.92(MPAP-WP)^b \div CI$	45—225	<226	77
Heart rate	HR	beat/min	Direct measurement	72—88	<100	60
Rectal temperature	temp	°F	Direct measurement	97.8—98.6	>100.4	64
Oxygen-Related Variables						
Hgb saturation	SaO ₂	%	Direct measurement	95—99	>95	67
Arterial CO ₂ tension	PaCO ₂	torr	Direct measurement	36—44	>30	69
Arterial pH	pH	...	Direct measurement	7.36—7.44	>7.47	74
Mixed venous O ₂ tension	PvO ₂	torr	Direct measurement	33—53	>36	68
Arterial-mixed venous O ₂ content difference	C(a-v)O ₂	ml/dl	$C(a-v)O_2 = CaO_2 - CVO_2$	4—5.5	<3.5	68
O ₂ delivery	DO ₂	ml/min·M ²	$DO_2 = CaO_2 \times CI \times 10$	520—720	>550	76
O ₂ consumption	VO ₂	ml/min·M ²	$VO_2 = C(a-v)O_2 \times CI \times 10$	100—180	>167	69
O ₂ extraction rate	O ₂ ext	%	$O_2 \text{ ext} = (CaO_2 - CvO_2) \div CaO_2$	22—30	<31	69
Perfusion-Related Variables						
Red cell flow rate	RCFR	...	$RCFR = CI \times Hct$	0.6—1.8	>1.3	72
Blood flow/volume ratio	BFVR	...	$BFVR = CI \div BV$	0.6—1.8	>1.7	75
O ₂ transport/red cell mass	OTRM	...	$OTRM = VO_2 \div RCM$	0.06—0.18	>0.25	79
Tissue O ₂ extraction	TOE	...	$TOE = C(a-v)O_2 \div RCFR$	1.8—6.6	>5.7	75
Efficiency of tissue O ₂ ext	ETOE	...	$ETOE = C(a-v)O_2 \div RCM$	0.06—0.18	>1.3	91
O ₂ transport/red cell flow	OTRF	...	$OTRF = VO_2 \div RCFR$	1—7	<3	71

^a Hct corrected for packing fraction and large vessel hematocrit/total body hematocrit ratio.

^b Venous pressures expressed in mmHg.

the long-term measurements of venous pressures are not well correlated with volume because of compliance changes in the venous tree that occur with time.

Hemodynamic and Oxygen Transport Variables

Physiologic monitored variables may now be readily and repeatedly obtained using a systemic arterial and a pulmonary arterial catheter (Table 2)^{4)~6)}. This type of invasive monitoring provides frequent measurements of arterial and venous pressures of systemic and pulmonary circulations, cardiac output, arterial and mixed venous gases, and hemoglobin or hematocrit. From these directly measured variables, an array of hemodynamic values may be derived including cardiac index (CI), systemic and pulmonary vascular resistance (SVR and PVR), left and right ventricular stroke work, and cardiac work. More importantly, it is easy to determine the bulk movement of oxygen: O_2 delivery ($\dot{V}\text{O}_2$), O_2 consumption ($\dot{V}\text{O}_2$), O_2 extraction, the pulmonary venous admixture or shunting ($\dot{Q}_{sp}/\dot{Q}_t$), and the alveolar-arterial O_2 gradient ($P(A-a)\text{O}_2$). These variables are readily calculated by a computer or a hand-held programmable calculator⁷⁾.

Biologic Relevance of Monitored Physiologic Variables

We evaluated the biologic importance of each cardiorespiratory variable based on its ability to predict outcome by a nonparametric predictive index; i.e., the capacity each variable to predict outcome was considered to be a measure of its biologic relevance (Table 2)⁵⁾⁶⁾. The predictive index was determined in- perically from the frequency distributions of the survivor's and nonsurvivors' values.

As the relevance of a given variable to survival or death is the ultimate criterion of its usefulness to clinical decision-making, it is appropriate to select those monitored variables that provide the most crucial information to therapeutic management. Variables reflecting oxygen transport importance⁵⁾⁶⁾.

Goals of Therapy

Fluid therapy in acute catastrophies should at least involve correction of the specific underlying physiologic defects. More particularly, therapy should be directed not just to restoring physiologic parameters to the normal values but to optimal values that lead to the best possible outcome. The most rigorous criterion for evaluation of the relative effectiveness of each agent is its capacity to restore circulatory function and tissue perfusion. This is best evaluated by measured changes in flow, volume, oxygen delivery and oxygen consumption during and after administration of each agent according to a well-defined prospective protocol^{8)~10)}. In essence those variables most related to outcome may be used as "proxy outcome measures" i.e., criteria to evaluate the patient cardiorespiratory status throughout the period of critical illness.

Criteria for Fluid Therapy in Critically Ill Surgical Patients

Criteria for fluid therapy were defined by the median values of survivors of life-threatening surgical conditions; they include: (a) blood volume 500 ml in excess of the norm, i.e., 3.2 L/M^2 for males, 2.8 L/M^2 for females, (b) blood flow 50% greater than the norm ($4.5 \text{ L/min}\cdot\text{M}^2$), and (c) $\dot{V}\text{O}_2$ about 25% greater than normal ($167 \text{ ml/min}\cdot\text{M}^2$). These increments are needed to supply the increased metabolism associated with fever, sepsis, and the need for tissue repair of the critically ill postoperative patient⁹⁾¹⁰⁾.

Tissue Perfusion and Oxygen Transport as Criteria for Therapy

Tissue perfusion, which reflects overall circulatory function, may be evaluated in terms of oxygen delivery and oxygen consumption. There is abundant evidence that oxygen transport is: (a) the major function of the circulation; (b) oxygen is the most flow-dependent blood constituent, because oxygen has the greatest extraction ratio; and (c) oxygen transport is strongly related to survival or death. The changes in the values of these variables after various therapeutic interventions provide more sensitive and specific criteria of circulatory performance than the gross overall mortality rates.

Oxygen consumption represents the sum of all oxidative metabolic reactions and is, therefore, a measure of the body's total overall metabolism. It may be rate-limited by the circulatory alterations of trauma, surgical operations, anesthetic agents, postoperative states and other forms of stress. As such, it represents an exquisitely sensitive method for evaluating both the overall metabolic status and the circulatory (delivery) system needed to supply the required substances. As such, the $\dot{V}\text{O}_2$ produces a useful means to assess

Table 3 Results of predictors after surgical operations

		Last Available Predicted Value			
		Survival	Death	Total	%Correct
Actual Outcome	Survived	206	13	219	94*
	Died	8	73	81	90**
Total		214	86	300	93
%Correct		96***	85***		

*Sensitivity, percentage of survivors with correctly predicted outcome
**Specificity, percentage of nonsurvivors with correctly predicted outcome
***Predictive accuracy, percentage of survivors among patients predicted to live
****Predictive precision, percentage of nonsurvivors among patients predicted to die

the adequacy of both metabolic and circulatory systems.

Clinical Use of a Predictive (Severity) Index

A predictive index was developed for critically ill postoperative general surgical patients; it was based on a computerized algorithm that compares a given observed value of a patient with the frequency distributions of previously observed survivors' and nonsurvivors' values; this is done for each monitored variable at each postoperative stage. The difference in the mean values of this index for survivors and nonsurvivors was statistically significant ($p<0.001$) during each stage of shock. Sensitivity of the index in prediction of survival ranged from 70–93% depending upon stage; the specificity of the index ranged from 76–92%; and the predictive accuracy ranged from 87–96%. The overall percentage of accuracy in a large series of critically ill patients was remarkably high^(9)~10) (Table 3).

A major use of the predictive index is that of a measure of the severity of illness; i.e., to evaluate the cardiorespiratory status at intervals in order to track the course of critically ill patients; in this sense it is used as a measure of the process of care. Secondly, the severity index is used to evaluate the relative efficacy of alternative therapies given to critically ill patients in prospective clinical trials¹⁰⁾¹¹⁾.

This approach was found to provide a reasonably accurate method to predict outcome in a prospective series of patients. The advantage of predictors is that they analyze the complex physiologic problems with no preconceptions and an absolute minimum number of assumptions. The criteria are heuristically determined solely by observed values of critically ill trauma and postoperative patients who survived and those who subsequently died.

Prospective Evaluation of Survivors' Values as Therapeutic Goals

The hypothesis was tested that the median values of survivors of lifethreatening postoperative conditions rather than the norms of unstressed healthy volunteers are the appropriate therapeutic goals for critically ill postoperative patients⁹⁾. We prospectively studied a series of 300 patients as a test of the validity of the predictor and 232 patients who were prospectively allocated to a control group that had normal values as therapeutic goals (mortality 35%) and a protocol group that used the empirical derived median values of survivors and therapeutic goals (mortality 12.5%)¹⁰⁾.

These prospective clinical trials suggest that at least half and possibly as much as 2/3 of postoperative deaths may be due to physiologic problems that can be identified, described, predicted, and prevented. It follows that therapy for the critically ill patient should be defined by physiologic criteria, and administration of therapy should be monitored to attain prophylactically optimal physiologic goals rather than giving therapy to attain normal values after the deficiency has occurred⁹⁾¹⁰⁾.

Fluid Therapy

Dehydration States

As a general rule, it is often expedient to begin by: (a) replacing water and electrolyte losses with crystalloid solutions, (b) red cell deficits with blood, packed red cells, and (c) blood volume deficits with

Fig. 1 Body composition measured by $^{35}\text{SO}_4$ (shown in the left column) is compared with measurements using $^{82}\text{Br}^-$ (shown in the right column). Note that in the control period the intracellular water (ICW), which is the interstitial water (ISW) plus plasma volume (PV), is smaller for $^{35}\text{SO}_4$ measurement and that the PV may be reduced despite increases in ISW.

plasma proteins or their colloid substitutes. After 1/3 of the estimated acute fluid losses are given rapidly and 1/3 are given slowly over 4–8 hours, fluids are continued until blood pressure and urine output are restored, provided CVP does not rise above 15 cmH₂O. Because of the complex physiologic compensations, the simple cc for cc fluid replacement is a useful “rule of thumb” to start fluid therapy, but it is not a reliable end-point. The appropriate therapeutic approach is to titrate therapy until arterial pressure, urine output, Hct, HR, and CVP return to the normal range. Then re-evaluate to determine if the patient would benefit from invasive monitoring with a pulmonary arterial (Swan-Ganz) catheter.

Resuscitation of Emergency Victims

A recent prospective study evaluated a branch chain decision tree protocol which used about 1/3 colloids, depending on age, cardiac history and response to therapy (Fig. 2). In a prospective study, the outcomes of 603 successive hypotensive emergency victims were evaluated. The data were stratified according to identifiable clinical determinants, including: lowest mean arterial pressure (MAP), age, sex, severity of illness, primary illness or injury, estimated blood loss, volume of fluids given, use of the protocol, and satisfactory compliance with the protocol. The resuscitation times were significantly shorter, and the number of resuscitation-related complications was significantly less, with the regimen of about one-fourth colloids compared with a regimen of crystalloids only¹².

Fig. 2 Clinical algorithm for initial (first hour) resuscitation emergency admissions. This protocol or clinical algorithm was Designed for resuscitation of the acute emergency patient to restore circulatory integrity as rapidly as possible without producing fluid overload.

Step 1 If the MAP is zero or nearly zero, determine that there is a cardiac arrest and begin cardiopulmonary resuscitation (see below). If the patient has an MAP<20 mmHg, alert personnel for a possible cardiac arrest.

Step 2 If the MAP<60 mmHg, immediately start D5RL 1000 ml and run as rapidly as possible, especially if the MAP<50 mmHg.

Step 3 If the patient is less than 45 years of age and does not have a cardiac history, place a central venous pressure line and start another D5RL 1000 ml, plus 500 ml of plasma protein fraction or artificial colloid through a third iv line.

Step 4 Monitor the CVP at frequent intervals during the rapid infusion of these three solutions so as not to exceed values greater than 15 cmH₂O. If the CVP>15 cmH₂O, go directly to the ICU protocol below.

Step 5 If the hematocrit<25%, give 2 units of type-specific blood. Later, when cross-matched blood becomes available, transfusions of whole blood or packed red cells should be given to maintain Hct>33%.

Step 6 Rapid restoration of the MAP to 60 mmHg is the titration endpoint for fluids in this section; if the MAP<60 mmHg, recycle from Steps 2 through 6. If an MAP>60 mmHg has been achieved, proceed to step 7.

Step 7 If the MAP<80 mmHg, go to step 8; if not, proceed to step 13.

Step 8 If the MAP<80 mmHg, inquire from the patient, the patient's family, or a precious hospital record to evaluate the patient's "normal" preillness control MAP. If the MAP<80 mmHg and the heart rate>80 beat/min, measure orthostatic blood pressure (step 12).

Step 9 As in step 3, the cardiac patient requires less salt and water but more colloid. If the age of the patient>45 yr or there is a cardiac history, give 500 ml of colloid; if the age<45 yr and there is no cardiac history, give 1000 ml of D5RL plus 500 ml of colloid.

Step 10 Fluids may be given safely if the CVP<15 cmH₂O; if the latter is exceeded, go to the ICU protocol (below) and continue to give fluids as needed to restore circulatory integrity provided wedge pressures of 18 mmHg are not exceeded.

Step 11 If the MAP<80 mmHg without exceeding a CVP>15 cmH₂O, the objective of this cycle has been achieved; if the MAP<80 mmHg, recycle steps 7 through 11.

Step 12 Orthostatic blood pressure is measured; if there is a change in the MAP less than 10 mmHg on sitting or standing, this is presumptive evidence of at least 1000 ml of blood volume deficit.

Step 13 After the MAP has been restored to the normal value (>80 mmHg), it is still necessary to be sure that the pre-illness blood pressure was normal. If a prior hypertension was observed, the patient should be recycled from steps 7 through 13 using 80% of the pre-illness value as the criterion for the adequacy of resuscitation.

Step 14 Examine the patient for evidence of CNS depression, drug poisoning, or drug abuse.

Step 15 Examine the patient for evidence of head injury or other trauma. If positive, the patient should be treated in accordance with a coma-head injury protocol.

Fluid Therapy of Shock

In fluid therapy, the most important, as well as the most controversial, questions are the physiologic criteria for therapeutic goals. Unfortunately, however, the medical literature has few adequately designed, well controlled studies in this important area. The efficacy of alternative fluid therapies is best evaluated by physiologic responses that are related to survival, rather than commonly monitored variables that are routinely used because of their convenience. If the effects of sodium, which are to increase blood pressure and urine output are selected as the criteria of efficacy, then sodium-rich solutions are likely to be judged efficacious, but if cardiac output, blood volume, O₂ transport, and O₂ consumption are the appropriate out-

come measures, then colloids and blood are clearly the most effective agents¹²⁾¹³⁾¹⁴⁾. In our view, the therapeutic goals are best defined by values of survivors of life-threatening shock and trauma conditions in their recovery stage⁹⁾¹⁰⁾. We believe that the high risk critically ill postoperative patient requiring fluid resuscitation should have a pulmonary artery (Swan-Ganz) catheter to define physiologic problems and to titrate fluid therapy to the optimal goals defined by the pattern of the survivors of life-threatening operations. The therapeutic agent that is used is less important than the achievement of these goals.

Indications for Various Fluids

Whole Blood and Red Cells

Whole blood transfusions have long been regarded as the ideal fluid therapy, but transfusions are limited by high cost, limited availability, allergic reactions, hepatitis, autoimmune diseases and the delay required for crossmatching and processing. Some of these problems have been partially answered by antigen screening and the use of washed or frozen red cells. In critically ill postoperative patients, whole blood of red cells are indicated. When blood volume measurements are available, for red cell mass less than 1.2 L/M² and less than 1.0 N/M² for women, or when hematocrits are less than 32 percent in critically ill postoperative patients. Although whole blood or packed red cell transfusions are often needed, reliance must be placed on other fluids for resuscitation and subsequent management of hypovolemic critically ill patients.

Crystalloids

Ringer's lactate, saline, glucose solutions, and other crystalloids are currently the most widely used fluid therapy in patients with shock and trauma because they are inexpensive, readily available, and free of reactions. Ringer's lactate is most effective in correcting dehydration, restoring sodium deficits, increasing urine output, and expanding the interstitial water. Because only 1/5 of the infused Ringer's lactate transiently stays in the plasma volume, it is a poor plasma volume expander for critically ill patients, but it may be adequate for the routine postoperative patient who is not very ill. When given in excess, it may lead to pulmonary complications.

Colloids

Colloids are an alternative to massive infusions of saline solutions in patients in shock and with acute illness to restore plasma volume and to minimize excessive salt and water which may overexpand the interstitial water. Albumin, 5% plasma protein fraction (PPF), and synthetic colloids (dextran-40, dextran-60, and hydroxyethyl starch) primarily expand the plasma volume. The underlying hypotheses of this concept are that: (a) Starling's law of the capillary circulation governs the distribution of water between plasma volume and interstitial fluid volume at least during the early stages of shock; (b) in states of traumatic and septic shock there is a maldistribution of extracellular water that results in relative expansion of interstitial water and contraction of plasma volume; (c) overexpansion of the interstitial water predisposes the patient to pulmonary edema and shock lung; and (d) the capillary leak occurs rather late in postoperative and post-traumatic ARDS¹⁴⁾. When it does occur, albumin as well as crystalloids leak into both the peripheral and pulmonary interstitium.

Comparison of Physiologic Effects of Crystalloids and Colloids in Prospective Clinical Trials

Recent prospectively randomized studies comparing crystalloids and colloids were conducted by Boutros et al.¹⁵⁾ in critically ill postoperative patients and by Jelenko et al.¹⁶⁾ in burn patients and by Rackow et al.¹⁷⁾¹⁸⁾ in hypotensive shock patients; these studies showed statistically significant advantages in colloid administration.

We have explored an approach that compares the relative effectiveness of alternative therapies using the patient as his own control¹³⁾¹⁹⁾²⁰⁾. As an example, a series of burn patients were given various colloids and lactated Ringer's solution alternately during the period of their critical illness (Fig. 3). Increases in cardiac output, oxygen delivery (availability), and oxygen consumption were significantly greater after colloids than twice or four times the volume of the crystalloids²⁰⁾.

Recently, Hauser et al.¹⁵⁾ compared the changes after one liter of lactated Ringer's solution with those of 25 g of 25% albumin (100 ml) given in random order to a prospective series of critically ill surgical patients with early shock lung (Fig. 4). Albumin increased plasma volume 465 ± 47 (SE) ml by shifting over 350 ml of

Fig: 3 Clinical algorithm for critically ill postoperative patient.

Fig. 4 Cardiorespiratory values during resuscitation of a patient with severe burns are shown.

Fig. 5 Changes in plasma volume, cardiac index, colloid osmotic pressure, oxygen consumption, alveolar-arterial oxygen gradient, and pulmonary venous admixture are compared after intervention with 1000 ml of lactated Ringer's solution (RL) and 100 ml of 25 percent albumin (SPA) in a crossover study. Note the greater increase in plasma volume, cardiac index, colloidal osmotic pressure and oxygen consumption after SPA. Alveolar-arterial oxygen gradient as well as pulmonary venous admixture were unaffected by SPA whereas after infusion of RL, alveolar-arterial gradient increased. (From Hauser CJ, Shoemaker WC, turpin I, et al: Hemodynamic and oxygen transport responses to body water shifts produced by colloids and crystalloids in critically ill patients. Surg Gynecol Obstet 1980; 150: 811.)

water from the interstitial water to the intravascular water. Simultaneously, albumin increased cardiac index, mean arterial pressure, left ventricular stroke work, oxygen delivery and oxygen consumption; lung function variables were not worsened but in many instances actually improved. By contrast, one liter of Ringer's lactate expanded plasma volume only 194 ± 18 ml at its maxima which was at the end of infusion, i.e., over 80% of the infused crystalloid almost immediately equilibrated or "leaked" into the interstitial water and the small proportion of fluid remaining in the plasma, then decreased exponentially. After Ringer's lactate administration, oxygen consumption decreased despite the slightly increased oxygen availability, and pulmonary oxygen transport deteriorated slightly. The hemodynamic responses to the administered fluid

Fig. 6 Cardiac index responses to various agents are shown in patients with adult respiratory distress syndrome (ARDS) during the episode of respiratory distress (left section), patients with ARDS not during the episode of respiratory distress (center section), and patients without ARDS (right section). The data represent changes in cardiac index ± 1 SEM during and after the administration of each agent. (From Appel PL and Shoemaker WC: Fluid therapy in adult respiratory failure. *Crit Care Med* 1981; 9: 862.)

were directly proportional to volume expansion. Thus, colloids improve hemodynamics and oxygen transport by plasma expansion, while crystalloids principally expand interstitial volume; when tolerated, they may restore plasma volume if given in great excess¹³.

Recently this series was expanded to include 300 fluid therapy interventions in early ARDS occurring in postoperative and septic patients¹⁴. Fig. 5–7 illustrate the flow and oxygen transport variables in: (a) patients during respiratory failure, (b) these same patients not during (before or after) the ARDS episode, and (c) a concurrent group of critically ill patients who did not develop ARDS. These data show significant increases in hemodynamic and oxygen transport after infusion of colloids but no essential changes except increased arterial pressure and systemic (peripheral) vascular resistance after infusion of Ringer's lactate (Table 4). Table 5 shows changes in hemodynamic and oxygen transport variables after 500 ml of colloids given during periods of ARDS compared with changes after 500 ml of colloids given to patients without ARDS. These therapeutic interventions were made an average of 40 ± 48 hours after onset of ARDS. Table 6, by contrast, shows no significant differences in cardiac output after infusion of colloids, whole blood, or crystalloids in patients in the preterminal stage of ARDS defined as the last 24–48 hours of life. These data indicate that the capillary leak syndrome occurs rather late in ARDS; it appears to be the result, not the pathogenic cause of ARDS^{13,14,19}. Colloids may improve physiologic variables that determine survival after ARDS until there is evidence that they significantly increase $\dot{Q}_{sp}/\dot{Q}_t$ and $P(A-a)O_2$.

Criteria for Fluid Overload: Pulmonary Edema

Pulmonary edema is produced by acute congestive failure with or without fluid overload and with or without reduced oncotic pressure; it is also produced by acute noncardiac pulmonary failure with leaking of the capillary-alveolar membrane. When pulmonary congestion occurs, it is necessary to evaluate the etiologic influences as well as the implications of each potential therapy. These etiologic influences are most revealed by measurements after the fact, but they may be elucidated by measurements of physiologic events which

Fig. 7 Changes in oxygen delivery and oxygen consumption during and after the administration of various agents are shown, as described in Fig. 6. (From Appel PL and Shoemaker WC: Fluid therapy in adult respiratory failure. Crit Care Med 1981; 9: 862.)

Fig. 8 Cardiac index responses to the administration of various agents in patients with postoperative adult respiratory distress syndrome and in patients with adult respiratory distress syndrome caused by sepsis are compared. (From Appel PL and Shoemaker WC: fluid therapy in adult respiratory failure. Crit Care Med 1981; 9: 862.)

Table 4 cardiorespiratory responses to fluid therapy
lactated ringer's solution(n=19) albumin 5 %(N=39)

Variable	Units	Control	Mid-point	After Infusion	Control	Mid-point	After Infusion
			(500ml)	(1000ml)		(250ml)	(500ml)
Mean Arterial Pressure	mmHg	90±16*	95±18	99±16**	85±20	90±19**	89±22**
Cardiac Index	L/min•M ²	3.97±0.94	4.19±0.85	4.22±1.16	3.04±0.99	3.57±1.1**	3.68±1.1**
CVP	cmH ₂ O	6.1±5.2	7.3±4.3	8.2±5	4.7±5.9	6.4±6.6	7.5±7.3**
Heart Rate	beat/min	108±29	108±27	110±24	103±28	103±19	103±26
Mean Pulmonary Arterial Pressure	mmHg	15.2±6.5	17.3±10.9	17.1±6.1	16.5±7.1	18.2±6.3	20.2±7**
Pulmonary Wedge Pressure	mmHg	8.5±2.6	9.9±3.3	9.7±2.7	7.5±6.1	9.0±4.9	11.1±6.5**
Systemic Vasc. Resistance	dyne•sec/cm ⁵ •M ²	1647±397	1589±410	1458±343**	2307±941	1969±959**	1912±8.8***
Pulmonary Vasc. Resistance	dyne•sec/cm ⁵ •M ²	163±76	167±56	157±117	246±133	211±90**	216±111**
Left cardiac work	kg•M/M ²	4.9±1.7	5.3±2.2	5.4±1.8	3.5±1.5	4.3±1.5**	4.5±1.8**
Right cardiac work	kg•m/M ²	0.84±0.41	0.96±0.45	1.03±0.45	0.69±0.43	0.91±0.37**	1.0±0.45**
Hematocrit	%	30.2±6.1	28.7±6.5	29.2±6.2	34.7±4.7	33.2±4	31.3±4.1**
O ₂ delivery	ml/min•M ²	565±176	580±204	585±208	458±164	504±149**	512±157**
O ₂ consumption	ml/min•M ²	145±31	149±23	146±34	128±36	131±33	129±31
O ₂ extraction	%	24±3	24±5	27±8	29±8	28±4	29±9

*Mean±SD **p<0.5 ***p<0.01

Table 5 changes in cardiorespiratory variable after administration of all colloids in ards patients during and not during their ards

	During ARDS	Not During ARDS
Number	134	117
Mean arterial pressure, mmHg	5.3±0.9**	2.9±1.0**
Mean pulmonary arterial pressure, mmHg	2.6±0.4**	3.8±0.6**
Cardiac index, L/min•M ²	0.66±0.98**	0.78±0.09**
Central venous pressure, cmH ₂ O	2.5±0.4**	2.1±0.4**
Wedge pressure, mmHg	2.6±0.4**	3.3±0.5**
Systemic vascular resistance, dyne•sec/cm ⁵ •M ²	-247±39**	-378±50**
Pulmonary vascular resistance, dyne•sec/cm ⁵ •M ²	-31±10**	-22±13*
Left ventricular stroke work, g•m/M ²	9.3±1.0**	9.6±1.2**
O ₂ delivery, ml/min•M ²	42±11**	45±12**
O ₂ consumption, ml/min•M ²	7.9±4.2*	7±4.8*
Pulmonary shut,%	1.4±0.6	1.4±1.0

*p<0.05 **p<0.01

Values represent Mean±1 SEM changes from control measurements after all colloids(albumin, PPF, and Dextran-40). Positive numbers represent increases, and negative values represent decreases from the control values. From Appel and Shoemaker(33).

Table 6 cardiac index responses to various agents in terminal ards

Infusion	Control Values	After
Colloids, 500ml(N= 6)	4.27±0.71*	4.36±0.67
Whole Blood or Packed Cell Transfusion(N= 7)	3.23±0.74	3.22±0.68
Crystalloids, 100ml(N= 4)	3.38±0.45	3.24±0.61

*Mean±1 SEM ; values are expressed in L/min•M². From Appel and Shoemaker(33).

occur prior to the development of ARDS²¹⁾.

Cardiogenic pulmonary edema is characterized by low cardiac output, high pulmonary arterial wedge pressures (greater than 20 mmHg), appearance on X-ray film of soft fluffy "butterfly" radio-opacities, bilateral basilar rales, and frothy pink sputum.

Noncardiogenic pulmonary edema, often called ARDS, is comprised of a wide variety of pulmonary problems including postoperative and post-traumatic respiratory failure or shock lung, inhalation of smoke or industrial poisons (chlorine, phosgene, hydrogen sulfide), viral pneumonia, status asthmaticus, sepsis, cerebral trauma, high altitude sickness, interstitial pneumonitis, disseminated intravascular coagulation, uremia, radiation therapy, and heroin overdose. It is characterized by progressively falling PaO_2 in the face of increasing FIO_2 , relatively normal wedge pressures (5 to 12 mmHg), bilateral rales and evidence on X-ray film of pulmonary congestion. Combinations of cardiogenic and noncardiogenic respiratory failure may occur.

Peripheral and pulmonary edema may develop after prolonged fluid infusions that do not exceed the "safe" venous pressure limits; when large volumes of sodium-rich solutions are used this is particularly true in patients with limited myocardial performance.

Criteria for optimal therapy strongly depend on these clinical and physiologic distinctions. Controversies frequently occur when these subsets of pulmonary problems are not clearly differentiated.

Summary of Recommendations for Fluid Therapy

Based on these findings, the following recommendations for therapy may be proposed. In general, loss of red cells should be replaced with red cells, water loss from dehydration should be replaced with crystalloids, and plasma volume losses should be replaced with plasma or its colloidal equivalent (that is, plasma protein fraction and 5 or 25 percent albumin, or artificial colloids such as dextran or hydroxyethyl starch, if cost is a problem).

Saline, glucose, and lactated Ringer's solution in various combinations are commonly used for initial resuscitation in mild degrees of shock and subsequent fluid replacement of daily losses. In general, 3 liters of fluid usually replace acute losses in mild to moderately ill patients who do not have extrarenal fluid losses and who are tolerating nothing by mouth. However, patients with enteric fistulae, diarrhea, vomiting, large volumes of nasogastric suction, and other extrarenal fluid losses may require several times this volume to replace the estimated fluid losses. After the estimated fluid losses are replaced, the optimal volume is best determined by fluid balance studies which collect, measure, and record urinary, nasogastric suction, fecal, and enteric fistula losses; estimated insensible losses are added to this. The 5 to 10 percent glucose solutions, Ringer's lactate, or Ringer's lactated in 5 percent glucose (D5RL) may be given through peripheral veins, but more hyperosmotic solutions such as hyperalimentation fluids must be given through central lines as they produce a high incidence of thrombophlebitis.

In shock, at least one-third of the fluids given should be colloids in order to maintain the administered fluids in the blood volume compartment. Whole blood or packed red cells should be given in sufficient quantities to maintain DO_2 , VO_2 , and other perfusion variables at their optimal values.

Nutritional Support

In high risk critically ill patients, hypercatabolic states associated with sepsis, chronic wasting diseases, malnutrition, carcinomatosis, gastrointestinal fistulae, diarrheas, malabsorption states, ulcerative colitis, regional enteritis, and other depletion syndromes require total parenteral nutrition or at least parenteral supplementation. This must be considered in any assessment of fluid therapy. Many available fluid preparations contain about 1 calorie/ml together with electrolytes; this allows up to about 3,000–4,000 calories/dat.

The various types of fluid regimens may be supplemented with 25% albumin or 5% Plasma Protein fraction (PPF) to correct deficiencies in plasma, albumin, or plasma protein concentrations. Low plasma albumin concentration and oncotic pressure may reflect increased nitrogen metabolism in the hypercatabolic critically ill patient. These defects should be treated just as other deficits need to be restored.

Therapy of Shock Lung

Excess salt and water is thought to be the most common cause of respiratory complications in the immediate postoperative stage. Most respiratory care physicians believe that postoperative patients with ARDS should be kept "on the dry side" by fluid restriction and diuretics. However, if hypovolemia occurs in the face of expanded interstitial water as commonly occurs in post-operative patients, fluid restriction and diuretics may further reduce plasma volume, worsen the circulatory shock, and exacerbate the shock lung. This problem is resolved by keeping the interstitial water, not the plasma volume, "on the dry side", since further reduction of plasma volume in the barely compensated hypovolemic patient may precipitate the return of shock.

It has been argued theoretically that even though albumin gives an immediate improvement in hemodynamics, eventually the administered albumin will leak into the lung and drag additional water with it. however, there is no evidence that exogenous administered albumin (or any other substance) is handled differently than the same endogenously produced substance. In critically ill patients, it would seem reasonable to correct low plasma albumin concentrations (less than 3 g/dl) and plasma oncotic pressures (less than 20 mmHg) with appropriate amounts of 25 percent albumin, since it has been clearly demonstrated that pulmonary edema is produced by excess salt and water with low left atrial pressures in the face of hypoalbuminemia²⁹). Moreover, shock lung is clearly a complication of shock. Significant degrees of hypovolemia, increased pulmonary vascular resistance, and inadequate cardiac output, oxygen delivery and oxygen consumption were documented in patients prior to the development of ARDS after hemorrhage and trauma²¹). When these defects were prevented in prospective controlled studies, both mortality and morbidity were significantly reduced⁹)¹⁰).

Summary

When only pressures and flow are examined, but not oxygen transport and oxygen consumption, crystalloids may appear to be satisfactory, particularly in the elective patient who is not in shock. Body water shifts after hemorrhage, trauma and various combinations of these; proponents of the crystalloid school of thought believe reduced interstitial water (ISW) is the major problem in both hemorrhage and trauma, while others, who question the validity of $^{35}\text{SO}_4$ as a measure of ISW, believe that the primary circulatory problem is hypovolemia. Sodium is known to increase arterial pressure and urine output; if these effects are used to test therapeutic efficacy; then sodium-rich solutions will be found to be effective even though they do not correct the essential defect of shock and trauma states.

Fluid shifts have been described as either a "leak" or "equilibration" of the administered fluids according to the viewpoint of the observer. Irrespective of these interpretations, the net water shift in or out of the plasma volume has been measured before and after fluid therapy. In essence, crystalloids expand the ISW, as over 80% leaves the plasma before the end of the infusion; by contrast, albumin increases plasma volume particularly in the early postoperative course of critically ill surgical patients. Blood volume expansion with massive volumes of crystalloids by virtue of the associated massive interstitial water expansion, may improve plasma volume, but this may also impede peripheral oxygen diffusion and worsen tissue oxygenation. In the postoperative shock patient, and the patient in early ARDS, blood volume and oxygen delivery are more effectively provided by colloids.

Pulmonary edema may result from cardiogenic factors, noncardiac (ARDS) factors and excessive fluid administration. Salt and water restriction, diuretics and other supportive measures are usually indicated. When pulmonary edema is associated with hypovolemia, concentrated (25%) albumin may restore body water distribution by shifting fluid from the interstitium into the plasma volume. However, when pulmonary edema is due to interstitial pneumonitis, viral pneumonia and other medical causes of respiratory failure, the pulmonary capillary-alveolar membrane leak which usually occurs in the late stage of ARDS may be worsened by colloid therapy.

Irrespective of philosophical considerations of protagonists of a "partyline", the critically ill, high risk patient should be monitored with sophisticated hemodynamic and O_2 transport measurements in order to

optimize the values of these variables to achieve maximum chances of survival.

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