Effects of increased red cell mass on subclinical tissue acidosis in hyaline membrane disease

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Abstract

Aim—To determine whether there are subclinical deficits in oxygen delivery in ventilated premature neonates.

Method—Ventilated premature neonates weighing less than 1500 g, who were transfused for anaemia or who were given colloids for clotting abnormalities (or oedema), were haemodynamically monitored during the first week of life. Calf muscle surface pH (tpH) was measured in conjunction with peripheral limb blood flow by occlusion plethysmography.

Results—Packed red blood cell transfusions corrected a subclinical regional tissue acidosis (low tpH) without affecting arterial pH or limb blood flow. This observation also correlated with an increase in regional oxygen delivery. The data were also suggestive of a pattern of pathological, supply dependent, oxygen delivery and are similar to other observations made in adults with adult respiratory distress syndrome.

Conclusions—Packed red blood cells increase regional oxygen delivery and tissue surface pH. In contrast, colloid infusion provided no substantial cardiovascular or metabolic benefit to these patients and should be avoided when oxygen delivery is at issue and when there may be leaky pulmonary capillaries.

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In acutely ill very low birthweight preterm neonates (< 1500 g) blood volume falls soon after birth as a result of frequent blood sampling and large evaporative water losses.[1][2] Under these circumstances, haemoglobin and haematocrit concentrations will not reliably depict the total body capacity to deliver oxygen as secondary shifts in body fluid compartments and a change in the size of capacitance vessels may result in "normal" values even after substantial losses of red cell numbers.[3-5] In this regard, the absolute red cell mass (RCM) (a quantity; haematocrit x blood volume) is thought to reflect better the actual diminished oxygen carrying capacity. In fact, when the value for RCM is multiplied by cardiac output, total body oxygen delivery can be determined and used as a predictor of survival.[5-7]

The clinical impact of the difference between RCM and haematocrit is of concern because a compensatory redistribution of regional blood flow will also ensue if systemic oxygen delivery is inadequate.[8-10] Any maldistribution of peripheral blood flow will further exaggerate subclinical organ deficits in oxygen delivery which may still go unrecognised in the presence of normal systemic haemodynamics.[9-11] Fortunately, this maladaptive redistribution of regional blood flow can be identified in adults by measuring intramucosal gut pH (gut tonometry),[12][13] or by determining muscle surface pH (tissue pH electrodes).[14-18]

Knowledge of low intramucosal tpH and deficits in regional O_2 delivery have been correlated with survival in adults.[19-21] Whether similar information will prove therapeutically or prognostically useful in sick preterm neonates is yet to be determined. Furthermore, as none of the current recommendations for assessing the need for red blood cell transfusion in very low birthweight neonates is based on actually measuring oxygen delivery to *any* particular vascular bed,[22-25] we examined this issue in 33 of our ventilated VLBW patients.

Methods

During July 1978 through June 1980, VLBW neonates (< 1500 g at birth) were selected for study from the general population of patients admitted to the Perinatology Center of the New York Hospital-Cornell Medical Center if their principal diagnosis was hyaline membrane disease (HMD) and if they required oxygen and mechanical ventilation. Parents of those patients meeting these criteria were approached to obtain consent for placement of a tissue pH electrode (tpH; equivalent "muscle surface" pH electrode)[14-18] and for measurement of peripheral blood flow by occlusion plethysmography. The study protocol was approved by the New York Hospital Institutional Review Board concerning human investigation. The procedure was performed solely for research purposes on the assumption that tpH would reflect arterial blood pH and would thus avoid some blood sampling when used in conjunction with transcutaneous oxygen and carbon dioxide electrodes.

All patients were managed under radiant warmers for the duration of this study. Endotracheal tubes were placed on admission if FIO_2 > 0.40 was necessary to keep the PaO_2 > 50 mm Hg, or for a $PaCO_2$ > 45-50 mm Hg. Ventilator settings were then adjusted to keep the arterial blood pH between 7.30 and 7.45, the $PaCO_2$ between 30 and 45 mm Hg,

and the PaO_2 between 50 and 70 mm Hg. Antibiotics (ampicillin and gentamicin) were administered for at least 72 hours after birth in all patients or until sampled body fluid cultures showed no growth. Parenteral fluid intake was adjusted to maintain the urine output at 1 to 2 ml/kg/hour and electrolytes were added to it to maintain serum concentrations in the normal physiological range. Umbilical catheters were placed on postnatal day 1 to permit monitoring of blood pressure, for blood sampling every 2 to 4 hours, and for infusion of fluids. All patients were maintained on a nil by mouth regimen throughout the duration of study.

During the course of this study, routine neonatal intensive care interventions were monitored for their impact on tpH during the first seven days after birth. Decisions to transfuse blood products were made by the neonatologist who was directly responsible for the overall medical management of the patient independently of the monitoring protocol used during transfusions. When transfusions were administered, monitored data included observations on the effects of administration of either packed red blood cells (10 to 15 ml/kg; 10 to 20% of estimated blood volume of 80-90 ml/kg[1][2] for a haematocrit below 35 to 40 (customary clinical practice at the time of study) or for colloid infusion using fresh frozen plasma (FFP, 10 ml/kg) or albumin (5 ml/kg for 25% or 15 ml/kg for 5% product). Colloid solutions were given for evidence of clotting abnormalities (FFP), to replace chest tube drainage (FFP or 5% albumin), or to assist in fluid mobilisation in the presence of peripheral oedema (25% albumin). These interventions remain within currently accepted therapeutic guidelines today.[8][22-25]

For 1 hour before, and for 1 hour after, transfusion, heart rate, blood pressure (umbilical arterial catheter, Hewlett-Packard transducers plus the HP Clinical Monitoring System), respiratory rate (thoracic impedance), and tissue surface pH were each recorded on a paper strip chart recorder (Electronics for Medicine, Indianapolis, USA). The continuous clinical data were sampled for 5 minutes every quarter of an hour and averaged to represent the entire hour for each individual transfusion in each patient. An arterial and venous (inferior vena cava) blood gas and a peripheral haematocrit were simultaneously sampled immediately before starting a transfusion and at the conclusion of the hour following the transfusion. Peripheral blood flow was measured every 15 minutes for 1 hour before and immediately following transfusions; values were averaged for each monitored variable before and after transfusion.

Sterile, glass tipped, flexible lead tissue surface pH electrodes were inserted and calibrated in vivo using the method of La Gamma *et al*[18] to measure muscle surface pH. In brief, a small skin puncture (2 to 3 mm in length using a No 11 scalpel) was made midway down on the medial aspect of the skin of the calf with the use of a local anaesthetic.

The 21 gauge tpH electrode (Microelectrodes Incorporated, Massachutsetts, USA) was inserted between the skin and the muscle surface after forming a subcutaneous pocket by blunt dissection with a sterile probe. Calibration of the pH meter (Corning Analytical pH Meter, Corning, New York, USA) and electrodes were accomplished by interposing a sterile buffer between the patient and the electrode at the wound site and also at a mucosal surface. The two site and two pH electrode calibration allowed for in vivo recalibration once daily and at the conclusion of the monitoring period to correct for any drift of the Ag/AgCl skin electrode used to complete the circuit.[18] This method is typical for calibrating oesophageal pH electrodes currently in use today (operating instructions for model MI506/508 Esophageal pH Meter, Miecroelectrodes Inc., Londonderry, New Hampshire, USA). In our series and in other reports, no complications of this procedure have ever been noted—for example, bleeding, infection, additional trauma—using this technique as, in effect, it is no different than inserting a 21 gauge needle subcutaneously.

Limb blood flow was measured in the in the lower limb contralateral to the previously placed tpH electrode. The method of occlusion plethysmography was used in most patients, as adapted by Krauss *et al*[26] or the simpler method of impedance plethysmography, as described by Costeloe *et al.*[27] These two methods provide nearly identical measurements of limb blood flow per 100 ml of limb tissue in newborn babies in our hands and as reported by Costeloe.[27] Results obtained with both methods also agreed favourably with those of other investigators.[27][28]

Before and after transfusions, an index of arterial oxygen (CaO_2) and venous oxygen (CvO_2) contents was calculated in individual patients as follows: (haematocrit/3) x (% saturation) x (1.35 ml O_2/g haemoglobin). Dissolved O_2 was considered to be negligible and was not accounted for. Banked adult blood has 2,3 diphospoglycerate (2,3-DPG) concentrations roughly equal to those circulating red cells from normal preterm neonates; concentrations subsequently increase several hours after infusion.[23][24] Consequently, we made no attempt to account for any presumptive improvement in oxygen transfer that may result from the increase in the in vivo percentage of adult haemoglobin, as our measurements were made in the first hour of monitoring immediately after the transfusion.

Oxygen delivery was calculated as the product of CaO_2 multiplied by measured limb blood flow. Regional consumption was assessed by determining the difference between aortic and vena caval O_2 contents multiplied by limb blood flow. Peripheral vascular resistance was calculated by dividing limb blood flow by the measured mean aortic blood pressure. Alveolar-arterial oxygen tension difference ($A-aDO_2$) was calculated from the alveolar gas equation using aortic oxygen and carbon diox-

Table 1   Effect of packed red blood cell transfusions (PRBC) on tissue pH and cardiopulmonary status (mean (SD) values)

Clinical variable	Booster transfusions PRBC (n=21)		Anaemia/shock PRBC (n=4)	
	Before	After	Before	After
Heart rate (bpm)	155 (15)	151 (15)	142 (12)	138 (14)
Systolic blood pressure (mm Hg)	49 (10)	53 (12)†	34 (2)	40 (4)
Haematocrit (%)	34 (5)	43 (7)‡	24 (8)	39 (7)‡
Respiratory rate (breaths/minute)	43 (14)	41 (15)	38 (7)	41 (4)
A-aDO$_2$ (mm Hg)	203 (143)	183 (148)*	171 (71)	168 (57)
pH$_a$	7.36 (0.09)	7.35 (0.06)	7.21 (0.11)	7.8 (0.04)
tpH	7.27 (0.33)	7.38 (0.33)†	7.17 (0.32)	7.26 (0.59)*
Base deficit (mEq/l)	5.2 (3.8)	5.7 (2.8)	9.1 (8.8)	8.3 (3.6)
Gestational age (weeks)	29 (2)		29 (1)	
Weight (g)	1120 (342)		1037 (97)	
Volume infused (ml/kg)	13 (2)		16 (6)	
Time infused (hours)	3.3 (0.8)		2.8 (1.2)	
No of patients	15		2	

* P < 0.05, † P < 0.01, ‡ P < 0.005.

ide tensions and assuming a water vapour pressure of 47 mm Hg.

Average values are reported in the results: the standard deviation is indicated to represent the variability of the tabulated group parameters. Grouped data before and after a transfusion were compared using the paired t test.

Results

Twenty one transfusions of PRBCs were electively given to 15 ventilated, VLBW infants with an average haematocrit of 34 (5). This resulted in a significant increase in haematocrit, systolic blood pressure, and tpH, and a fall in the A-aDO$_2$ (table 1). Arterial pHa, heart rate, and respiratory rates were unchanged. To assess better the impact of an increase in red cell mass in patients who also required volume expansion, four additional transfusions in two patients with haemorrhagic shock were analysed separately and found to respond similarly to those electively transfused for anaemia alone (table 1). In both groups of patients tissue surface pH was lower than arterial blood pH yet this difference did not achieve significance due to a wider range of values for tpH. The mean (SD) FIO$_2$ in the anaemic group was 0.38(0.16) and 0.46(0.20) in the patients in shock.

To assess better the potentially independent effects of blood volume expansion and changes in red blood cell mass, we examined the effects of colloid infusions on monitored variables in five of the same patients studied above plus an additional nine not previously monitored for

PRBC transfusion. Due to some differences in indications, patients receiving fresh frozen plasma (FFP) (5 for abnormal clotting, 3 for chest tube drainage) or 5% albumin (3 for low protein, 3 for chest tube drainage) were less clinically homogenous than those in the anaemia and haemorrhagic shock groups, yet all of them had similar normal range heart rates, respiratory rates, and blood pressures before intervention (table 2). None of the colloid treated patients was anaemic (haematocrit > 35) at the time of study, all had base deficits similar to those of the previous PRBC patients as well as similar A-aDO$_2$ (table 2). The only significant change in status after colloid infusion was a non-physiologically significant fall in the haematocrit from 43 (9) to 38 (9). The mean (SD) FIO$_2$ in the colloid group was 0.59(0.25).

To determine whether blood flow, oxygen delivery, or both parameters, changed in response to PRBC transfusions, we measured limb blood flow during seven blood transfusions in five additional patients. Once again PRBC infusions were associated with a significant increase in blood pressure, haematocrit, and tpH and a fall in A-aDO$_2$ (table 3). As expected, oxygen delivery increased (table 3); however, unexpectedly, so did the base deficit, from 4.1 (3.5) to 6.1 (1.9) mEq/l. Other monitored variables were unchanged, although lactate (table 3) and catecholamine values fell (mean (SD) norepinephrine 578(433) to 508(249) and epinephrine 118 (74) to 105 (58) pg/ml; n= 4 patients; results courtesy of Dr Bernard Mirkin, NorthWestern University) consistent with impaired oxygen delivery and decreased cardiac work.[29] Of additional interest is our observation that the PRBC infusates had a substantial lactate content and a non-physiologically low pH plus a large base deficit (table 4).

Measured oxygen consumption across the aorta and vena cava tended to increase after transfusion in the five patients in whom it was successfully determined both before and after the transfusion. This suggested the intriguing possibility that supply dependent oxygen consumption existed in neonates. To assess better this possibility, measured regional oxygen consumption was plotted against limb oxygen delivery for the five patients studied in table 3. Data were accumulated at various times during

Table 2   Effect of colloid infusions on tissue pH and cardiopulmonary status (mean (SD) values)

Clinical variable	Colloid infusion FFP (n=8), albumin (n=6)	
	Before	After
Heart rate (bpm)	145 (18)	144 (15)
Systolic blood pressure (mm Hg)	52 (12)	51 (12)
Haematocrit (%)	43 (9)	38 (9)*
Respiratory rate (breaths/minute)	43 (12)	43 (13)
A-aDO$_2$ (mm Hg)	256 (161)	236 (171)
pH$_a$	7.31 (0.05)	7.32 (0.04)
tpH	7.18 (0.26)	7.18 (0.32)
Base deficit (mEq/l)	5.7 (2.6)	5.4 (3.6)
Gestational age (weeks)	31 (2)	
Weight (g)	1255 (216)	
Volume infused (ml/kg)	11 (5)	
Time infused (hours)	1.3 (0.9)	
No of patients	11	

* P < 0.01; pHa: arterial blood pH.

Table 3 Effect of "booster" PRBC transfusions on limb blood flow (mean (SD) values)

Clinical variable	Before	After
Heart rate (bpm)	143 (11)	141 (8)
Systolic BP (mm Hg)	50 (6)	55 (5)*
Limb flow (ml/min/100 ml tissue)	11.4 (4.4)	11.3 (5.7)
Resistance	3.6 (1.8)	4.3 (1.7)
Haematocrit (%)	33 (4)	43 (6)†
O_2 Delivery (ml/O_2/min/100 ml tissue)	1.5 (0.7)	2.0 (0.9)*
O_2 Consumption (ml/O_2/min/100 ml tissue; n=4 patients)	0.37 (0.31)	0.47 (0.35)
Respiratory rate (breaths/minute)	43 (14)	38 (10)
A-aDO$_2$ (mm Hg)	259 (144))	234 (134)*
pH$_a$	7.35 (0.06)	7.31 (0.01)
tpH	7.29 (0.04)	7.34 (0.05)†
Base deficit (mEq/l)	4.1 (3.5)	6.1 (1.9)*
Lactate (min/l)	3.1 (2.6)	1.9 (0.5)
Gestational age (weeks)	29 (2)	
Weight (g)	1342 (452)	
Volume infused (ml/kg)	15 (1)	
Time (hours)	3	
No of patients	5	
No of transfusions	7	

* P < 0.05, † P < 0.01, ‡ P < 0.001.

Table 4 Mean (SD) characteristics of PRBC transfused in table 3

Factor	PRBC (n=7)
pH	6.89 (0.04)
Base deficit (mEq/l)	25 (2)
Lactate (mM/l)	5.2 (1.0)
Haematocrit	64 (5)
Capilliary total protein (g/dl)	6.1 (0.8)

their hospital course and in most cases, in relation to the timing of the transfusion (figure 1). A significant but not powerful (r = 0.53, P < 0.05) linear correlation was observed without any sign of a change in slope consistent with the change to a critical O_2 plateau.[9][10]

Discussion

"Booster" packed red blood cell transfusions (increasing RCM) improved oxygen delivery and tissue surface pH with minimal effects on systemic haemodynamics, and *without* changing lower limb (peripheral) blood flow in ventilated preterm neonates with hyaline membrane
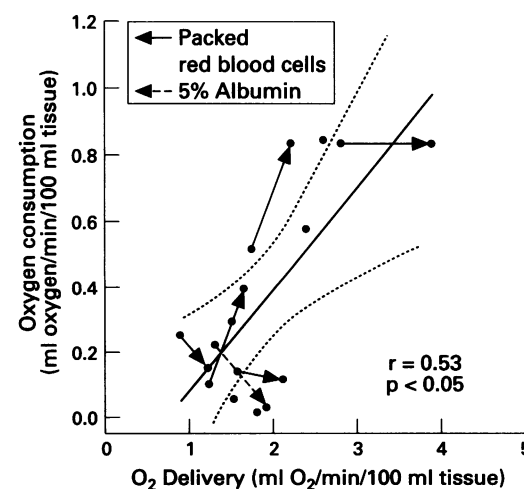

Figure 1 Results obtained from five patients who received six transfusions: five PRBC (solid arrows depict data obtained before to after infusion); one albumin (dotted arrow). In some patients an additional data point was added to illustrate the wide range of variability in this group of ventilated, sick VLBW infants. no consistent clinical or cardiovascular correlation between oxygen delivery and consumption following transfusion was identified.

disease (neonatal RDS) (tables 1 and 3). The observed muscle level tissue acidosis existed in the presence of a normal systemic arterial pH, a moderate base deficit, and raised blood lactate values, suggesting that there was a sub-clinical deficit in organ level oxygen delivery or its utilisation, as originally hypothesised. Although other metabolic causes for tissue acidosis are possible in the acute phases of neonatal RDS,[30-34] altered aerobic metabolism seems to be the most likely.[11]

Each of our patients received transfusions while being managed under radiant warmers. For this reason we believe it is unlikely that basal levels of oxygen consumption or cellular metabolism could have changed substantially during the study period. They could not, therefore, have accounted for the improved tpH observed under the conditions of our brief protocol (maximum of 6 hours from start to finish of data collection). On the other hand, in view of the normal oxygenation and haemodynamic status in the "booster" transfusion group (even before transfusion), we suspect that the low tpH may, in fact, be indicative of a cumulative manifestation of iatrogenic losses of RCM accumulating over the first few days after birth.

Estimates of iatrogenic blood losses average 23 millilitres per patient in acutely ill VLBW neonates (10 to 15 ml/kg),[1] making some form of empiric red cell replacement strategy commonplace[22-25] in order to maintain the RCM. Typical recommendations include infusion of banked blood when 5% or 10% of the estimated total blood volume is removed or when the haematocrit drops below 40 in ventilated patients, as in our study.[22-25] These booster transfusions result in clear haemodynamic benefits such as decreased cardiac output, decreased oxygen consumption, and an increase in blood pressure.[5][35-37] While these recommendations are based on sound physiological principles,[8][9][22-25] they address the *average* systemic requirements for oxygen delivery and not any particular organ specific needs. None of these approaches provides information on the *critical oxygen delivery* necessary to avoid anaerobic metabolism for any particular regional vascular bed.[9][10] Therefore, the identification of a low tpH in this study suggests that regional acidosis is a more common problem than ordinarily appreciated during the acute phases of neonatal RDS, and that it is not reflected in systemic indices of oxygenation. Furthermore, we suggest that iatrogenic anaemia may contribute to the maldistribution of regional peripheral blood flow and oxygen delivery that may already exist during neonatal RDS.[1] Interestingly, although empiric guidelines for transfusion may not be the earliest markers for identifying the need for red cell replacement therapy, they were still quite appropriate when viewed using our method of analysis.

Additional support for a subclinical deficit in regional oxygen delivery comes from other observations, showing that a greater magnitude of improved tpH occurred following PRBC transfusions for haemorrhagic shock than for

transfusions for anaemia alone (table 1). By comparison, colloid infusions increased *neither* the tpH nor changed blood pressure, heart rate, the extent of metabolic acidosis or gas exchange (table 2). Previous reports show a 1-2 mm Hg increase in blood pressure, but no change in heart rate, and variable effects on gas exchange.[36] [38-42] In contrast, both tpH and blood pressure increased after PRBC (tables 1 and 3). Taken together, and as the RCM could *not* possibly have increased after colloid infusion, we interpret the stable tpH in association with a significant fall in haematocrit (table 2)[38] [39] as one of several possibilities. Either an increase in regional blood flow occurred to maintain oxygen delivery, an increase in O_2 extraction, or a change in the cellular metabolic rate. Thus from our data and other reports, it seems that the only clinically relevant haemodynamic effect of infused colloid (in patients without perfusion deficits) is to cause a transient rise in colloid osmotic pressure that may help to mobilise interstitial fluids (not measured in this protocol).[36] [38-42]

Whether viewed as a systemic blood volume problem or a regional O_2 delivery issue, red cell transfusions are needed to maintain the RCM in acutely ill ventilated VLBW neonates. However, there are infectious, thrombotic, allergic and graft versus host disease risks associated with infused blood products.[8] [22-25] Infusion of stored blood is also associated with transiently low concentrations of 2,3-diphosphoglycerate (2,3-DPG), less red cell deformability, and evidence of splanchnic ischaemia in septic adult patients as assessed by gut tonometry.[43] If these problems arose in our neonates, we would have expected an adverse effect on tpH; yet tpH increased along with the circulating base deficit (tables 1 and 3). Both observations were consistent with improved cellular oxygen transport and the transient accumulation of a new acid load. Indeed, when measured, there was a substantial administration of lactate anion and titratable acid (table 4).[24] [44] Unlike septic adults,[43] no clinically important signs of transfusion reaction, abdominal distention, or ileus were noted after PRBC transfusion.

The A-aDO_2 also improved after PRBC transfusions, suggesting that better intrapulmonary oxygen transfer occurred, presumably due to better matching ventilation with perfusion. Although a capillary leak syndrome might have existed in these RDS patients,[45] the A-aDO_2 did not worsen after either colloids or PRBC (tables 1 to 3). These observations further indicated that no particular cardiopulmonary benefit could be gained by infusion of protein solutions in normotensive patients with hyyaline membrane disease, as previously noted.[38-42] Alternatively, the failure to improve a low tpH in patients who received colloid infusions may stem from their cells somehow being "sicker"—for example, eight of 14 in this group had clotting abnormalities and one had bacterial growth on blood culture)(table 2)—than those ventilator-dependent VLBW neonates who were electively transfused only to maintain their haematocrit at > 40. Although we were not able to resolve this issue in our

series, it may be appropriate to extrapolate certain findings from the published findings on adults and animals.

In sepsis or in adult RDS, acidosis and maladaptive oxygen delivery are believed to result from a pathological release of various endogenous cytokines that interfere with O_2 utilisation and cellular metabolism even in the presence of normal levels of oxygen delivery.[11] [33] [34] In our anaemic neonates, we favour an interpretation implicating deficits in neonatal oxygen carrying capacity over a cytokine mediated effect on cellular metabolism, as limb blood flow was unchanged but tpH increased after PRBC transfusion. On the other hand, oxygen delivery alone is unlikely to be the exclusive cause of low tpH in the colloid group (table 2). Consequently, suspicion of a cytokine based neonatal multiorgan failure/ systemic inflammatory response syndrome cannot be entirely dismissed in ventilated VLBW neonates at this time.[46] [47]

Lastly, an unexpected finding in this series was an *apparent* supply dependency of oxygen consumption in the lower limb, as indicated by the absence of the expected oxygen delivery plateau in the range depicted (fig 1). Although we did not initially set out to determine these correlations, the phenomenon of supply dependent oxygen consumption is well characterised in animal models and in published findings on adult RDS.[9] [13] [33] [34]

For purposes of our comparisons, we assumed that 1 millilitre volume of neonatal lower limb tissue (calf) roughly equalled ≤ 1 gram of body weight (water weight). Working with this ratio (which would tend to overestimate actual blood flow per kilogram of body weight), most of our results for oxygen consumption and delivery per 100 ml of tissue volume (table 3 and fig 1) were at or below the minimum critical O_2 delivery rate of 2.1 ml O_2 per 100 g body weight (adult or paediatric tissue[10] [11] [35-37]) the *anaerobic threshold* for adult patients with RDS. [10] [11] Whether the putative causes of this phenomenon in the adult (cytokines, bacterial toxins, and altered metabolism[30-34]) apply to neonates remains to be determined. In any case, in neonatal patients, organ level deficits in oxygen delivery have not been identified before. It is also apparent from our data that there is no consistent association within subjects between oxygen delivery and consumption—an increase in delivery is equally likely to accompany an increase or a decrease in consumption. Moreover, whether treatments should be administered to acutely ill neonates to increase O_2 delivery to supranormal levels is unknown.[48] [49] What is known is that in subacute states, evidence indicates better weight gain and less apnoea and bradycardia when the haematocrit is maintained above 30% in growing preterm neonates recovering from hyaline membrane disease.[22-25] [35] [50]

In summary, we found that packed red blood cell transfusions corrected a subclinical tissue acidosis (low tpH) without affecting arterial pH or lower limb blood flow (table 5). This observation correlated with an increase in regional oxygen delivery, as measured directly.

Table 5   Comparison of magnitude of change in absolute value of monitored variables (mean (SEM) values)

Clinical variable	Booster PRBC transfusion (n=21)	Anaemia/shock PRBC transfusion (n=4)	Colloid infusion (FFP/albumin) (n=14)	Booster PRBC transfusion + blood flow (n=7)
Heart rate (bpm)	−3 (3)	−4 (5)	−1 (2)	−2 (3)
Systolic blood pressure (mm Hg)	+4 (2)‡	+6 (3)	−1 (1)	+5 (2)*
Limb flow (ml/min/100 ml tissue)				−0.1 (1.0)
Resistance				+0.7 (0.4)
Haemocrit (%)	+9 (1)	+15 (7)	−5 (1)†	+10 (1)‡
O_2 delivery (nl/O_2/100 ml tissue)				+0.5 (0.2)*
O_2 consumption (ml/O_2/min/100 ml tissue; n=4 patients)				+0.10 (0.09)
Respiratory rate (breaths/min)	−2 (3)	+3 (3)	0 (3)	−5 (6)
A-aDO_2	−20 (11)*	−3 (11)	−20 (13)	−25 (11)*
pH_a	−0.01 (0.02)	+0.07 (0.04)	+0.01 (0.01)	−0.04 (0.03)
tpH	+0.11 (0.04)†	+0.09 (0.23)*	0.0 (0.04)	+0.05 (0.01)†
Base deficit (mEq/l)	+0.5 (0.7)	−0.8 (3.7)	−0.3 (0.8)	+2.0 (0.9)*
Lactate (mM/l)				−1.2 (0.9)

* $P < 0.05$, † $P < 0.01$, ‡ $P < 0.001$.

The data also suggest a pattern of pathological supply dependent oxygen delivery and are comparable with similar observations in adults with RDS. Colloid infusion provided no measurable cardiovascular or metabolic benefit to these patients and we believe it should be avoided as treatment where oxygen delivery is at issue and leaky pulmonary capillaries exist.

Historical footnote to this report

The data in this report were originally obtained and analysed between 1978 and 1980. When the information was originally obtained, the scope of the project was focused on determining whether a tissue surface pH electrode could serve as a suitable adjunct to the newly developed and recently marketed transcutaneous oxygen and carbon dioxide electrodes. Other investigators had applied the technique in adults to evaluate blood pH and had noted that tpH indeed reflected blood pH except during perfusion deficits when tissue pH was substantially lower. Thus the need to obtain a blood sample to measure blood pH was *not* abrogated. We expanded our original project specifically to address the issues of blood flow in babies by measuring limb blood flow using the technique of occlusion plethysmography. Results were obtained and published as an abstract and then were left to lie dormant as little interest remained for a new clinical device that could not distinguish between blood flow or blood pH without an independent measurement.

Recently, it became quite apparent to one of us (EFL) that a new understanding of the relation between oxygen delivery, oxygen consumption, and patient status had arrived in clinical medicine specifically with regard to the use of gut tonometry in patients at risk for multiorgan failure. It became obvious that we had relevant data that might be useful to our clinical colleagues and which might bear directly on the issues of "booster" transfusion as well as on controversies surrounding the use of crystalloid versus colloid infusions in premature newborns.

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