Continuous Airway Pressure with Oxygen Minimizes the Metabolic Lesion of 'Pump Lung'

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Water distribution and energy status of the lung were measured in ten rabbits at two hours of hypothermic cardiopulmonary bypass (CPB) with left heart venting and incision of the parietal pleurae. During CPB, half the animals had their airways open to room air at ambient atmospheric pressure (ZEEP), and the remainder had their lungs inflated (CPAP) at a pressure of 5 cms H₂O with the oxygen-enriched (70–75 per cent) gas mixture exiting from the disc oxygenator. In both the ZEEP and CPAP groups, there was more than doubling of the pulmonary extravascular sodium-free water (intracellular) space and reciprocal reduction of the pulmonary extravascular sodium (extracellular) space, compared with 12 control animals not undergoing CPB. In the ZEEP group, there was an 18-fold increase in the pulmonary lactate/pyruvate (L/P) ratio compared with controls, and the pulmonary energy charge (E.C.) was significantly less than in controls (0.74 ± 0.02 vs. 0.89 ± 0.01). In the CPAP group the pulmonary L/P ratio was 2½ times control values and the pulmonary E.C. was virtually identical with that of the control group.

These data suggest that CPB results in a shift of fluid from the pulmonary interstitium into the pulmonary intracellular compartment with no net increase in total pulmonary extravascular water. The data also suggest that pulmonary deflation during CPB results in a significant pulmonary energy deficit which can be

prevented by keeping the lung inflated with an oxygen-enriched gas mixture during CPB.

Key Words

SURGERY: cardiovascular; cardiopulmonary bypass; VENTILATION: airway pressure; continuous positive pressure.

Several animal studies^{1–3} and one clinical study⁴ have suggested that positive pressure ventilation during CPB results in decreased static^{1,3} and dynamic compliance,^{2,4} decreased pulmonary surfactant² and increased pulmonary shunting,³ relative to either static inflation or passive deflation.^{1–3} Whether to statically inflate or passively deflate the lungs during total cardiopulmonary bypass (CPB) appears to be a matter of personal choice of the anaesthetist.

Static pulmonary inflation with oxygen results in sustained delivery of oxygen to the alveolar-capillary membrane during one-lung anaesthesia,⁵ and active ventilation of the unperfused lung *in vitro*, with air, results in improved pulmonary energy status relative to passive deflation *in vitro*.⁶ Therefore it is not beyond possibility that, during total CPB, when the lung receives neither ventilation nor perfusion via the pulmonary artery, static pulmonary inflation (CPAP) with an oxygen-containing gas mixture would confer a degree of metabolic protection which would be absent with pulmonary deflation (ZEEP).

Cell volume regulation appears to be largely dependent upon at least one and perhaps two or more membrane pumps which extrude sodium and are fueled by ATP.⁷ Cell swelling also results from hypothermia, even in the absence of energy depletion.

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tion.⁸ Therefore CPB might result in pulmonary cell swelling related to the associated hypothermia of CPB, even if pulmonary energy status is normal.

Thus it was decided to study pulmonary parenchymal water distribution, energy status, and lactate levels at two hours of CPB at 32°C in the rabbit, with static inflation (CPAP) and with passive deflation of the lungs (ZEEP).

Methodology

1 Animal Model

A / EXPERIMENTAL GROUPS

Twenty-two male albino rabbits, weighing 3.37 ± 0.11 kg, were divided into three groups, namely control (12 animals), two-hour CPB with 5 cms H₂O static pulmonary inflation (CPAP) (five animals), and two-hour CPB with pulmonary deflation (ZEEP) (five animals).

B / INDUCTION OF ANAESTHESIA

All animals were anaesthetised with intravenous thiopentone 50–75 mgm/kg body weight, to enable tracheostomy and ventilation with a tidal volume of 25 ml at a respiratory rate of 40 breaths/minute. The ventilatory gas was 50 per cent oxygen in nitrous oxide, with 0.5 to 2.0 per cent halothane. All animals received 2 mgm of pancuronium bromide intravenously after performing the tracheostomy.

C / POST-INDUCTION MANAGEMENT

(i) Control Group

Following induction of anaesthesia, a midline

sternotomy was performed and the hilum of the right lung was double clamped. The lung was resected and immediately frozen in tongs immersed in liquid N₂. A sample of blood was obtained from the left atrium using a heparinized syringe.

(ii) CPB Groups

In both CPB groups (CPAP and ZEEP), femoral arterial and central venous lines were inserted following induction of anaesthesia. Via a midline sternotomy, aortic root and right atrial cannulae were inserted to enable institution of CPB. The left atrium was cannulated to enable left atrial decompression during CPB, measurement of left atrial pressure, and sampling of pulmonary blood at the end of CPB.

The CPB circuit consisted of a 24-disc plexiglass oxygenator with a heat exchanger enabling reduction of perfusate temperature to 32°C, using a Haake model E12 heating/circulating pump. Perfusion flow rate during CPB was 300 ml/minute, using a Harvard peristaltic pump number 1215 with Tygon tubing. The priming volume of the circuit was 100 ml of solution containing 6 mEq KCl, 1000 units of heparin, and 9 mEq of sodium bicarbonate, in a base of Ringer's Lactate solution. The animal was anticoagulated with 3000 units of heparin intravenously prior to commencing CPB, and at one hour of CPB a further 1000 units of heparin was administered.

Following institution of full flow CPB, the heart was continuously fibrillated with an electric current of 15 volts at 7 hz of 3 msec duration from a Scientific and Research Instruments stimulator, via two electrodes sutured to the right and left ventricle respectively. During CPB, blood volume in the oxygenator was maintained by automatic infusion of 7.5 per cent sodium bicarbonate solution using a Radiometer Copenhagen PHM 82 pH meter attached to a Radiometer Copenhagen TTT80 titrator, and by infusion as required, of Ringer's Lactate solution. At the time of institution of ventricular fibrillation with the electric stimulator, the gas flow of 2 L/minute of 5 per cent CO₂ in oxygen to the oxygenator was augmented with 2 L/minute of 50 per cent O₂ in N₂O from the anaesthetic machine, enabling addition of halothane to the oxygenator, to control elevated perfusion pressures during CPB. Methoxamine was added, as needed, to the perfusion circuit using a Sage Instruments syringe pump model 355 to control low perfusion pressures during

Abbreviations

CPB	cardiopulmonary bypass
CPAP	CPB with static pulmonary inflation (5 cms H ₂ O)
ZEEP	CPB with passive pulmonary deflation (0 cms H ₂ O)
VV/TS	ratio of pulmonary vascular volume to pulmonary tissue solids
TEVLW/TS	ratio of total extravascular lung water to pulmonary tissue solids
EVSS/TS	ratio of pulmonary extravascular sodium space to pulmonary tissue solids
EVSW/TS	ratio of pulmonary extravascular sodium-free water to pulmonary tissue solid

CPB. A perfusion pressure of 80 torr was thus maintained. With the onset of total CPB (onset of ventricular fibrillation) the left atrial cannula, which drained into the venous line of the CPB circuit, was unclamped, effecting left atrial decompression. At the same time, both pleurae were incised in all animals. In five animals undergoing CPB, the gas exiting from the oxygenator (having an estimated oxygen concentration of about 72 per cent) was used to generate 5 cms static inflation pressure of the lungs via the tracheostomy tube – these five animals constituted the static inflation (CPAP) group. In the other five animals undergoing CPB, the tracheostomy tube was left open to room air, resulting in deflation of the lungs, thereby constituting the deflation (ZEEP) group.

During total CPB the arterial perfusion pressure, central venous pressure, left atrial pressure, and temperature of the arterialized infusion fluid were recorded every 15 minutes. Arterial blood gases and hematocrit were measured at one and two hours of CPB. At two hours of CPB the right pulmonary hilum was double clamped, and the lung was rapidly resected and frozen in tongs immersed in liquid N₂.

II Tissue Analyses

A / GENERAL PRINCIPLES

(i) Tissue Compartments

The apparent volume of distribution of haemoglobin in homogenized lung, using the cyanmethemoglobin method,⁹ was used to determine tissue vascular volume (VV). Calculation of tissue and blood wet/dry ratios enabled derivation of total extravascular lung water (TEVLW) and extravascular tissue solid (TS). Measurement of the apparent volume of distribution of sodium in the lung was used to determine the total tissue sodium space, from which, by knowing tissue vascular volume and left atrial blood haematocrit, was derived the extravascular sodium space (EVSS). The EVSS was taken as a measure of the tissue interstitial fluid compartment.^{10–12} The total extravascular lung water space minus the extravascular sodium space (TEVLW–EVSS) therefore represents the extravascular sodium-free water space (EVSFW) which was taken as a measure of the extravascular intracellular space in the lung.

In order to relate these compartments to a

common reference point, all pulmonary fluid compartments were equated to the pulmonary extravascular tissue solid (TS). Therefore the data are presented as VV/TS, TEVLW/TS, EVSS/TS and EVSFW/TS ratios. The equations used to calculate these ratios are found in the appendix.

Clearly, using sodium as an extracellular marker leads to overestimation of the extracellular space and underestimation of the intracellular space inasmuch as sodium is also present inside the normal cell, albeit in a much lower concentration (15–28 mmoles/litre).¹³ If, as appears likely,⁷ cell swelling is related to decreased extrusion of sodium from the cell, then the use of sodium as the discriminator between the extracellular and the intracellular compartments would underestimate the degree of cellular swelling and overestimate the size of the extracellular compartment. Therefore the decrease in sodium space and increase in sodium-free water space reported below likely underestimate the degree of cellular swelling which must be inferred from the results obtained in the two CPB groups (CPAP and ZEEP).

(ii) Tissue Metabolic Status

Tissue oxygen deficit results in conversion of pyruvic acid to lactic acid due to blockage of the Krebs cycle,^{14,15} resulting in an increase in tissue lactate/pyruvate ratio (L/P ratio). Therefore the pulmonary L/P ratio was used as an index of local pulmonary hypoxia resulting from CPB with CPAP and CPB with ZEEP.

In 1967, Atkinson¹⁶ proposed that the relative concentrations of adenosine tri-, di- and monophosphate (ATP, ADP, AMP) within each cell carefully regulate rates of energy production and utilization so that under normal circumstances the value of $(ATP + \frac{1}{2} ADP)/(ATP + ADP + AMP)$, defined as the 'energy charge', is rigorously maintained between 0.85 and 0.90.¹⁵

The energy charge has become a widely accepted index of cellular energy metabolism¹⁵ which correlates with cell viability.^{17–19} Therefore in the present paper energy status is assessed by determining the energy charge of the lung.

B / ANALYTIC METHODOLOGY

The frozen lung was homogenized (powdered) using a mortar and pestle, chilled in liquid N₂. The tissue was kept continuously immersed in liquid N₂. For each of the following determinations, a sample

of tissue powder in liquid N₂ was placed on a pre-chilled balance. As the liquid N₂ in the sample evaporated, the sample reached a stable final weight which was recorded, and the still frozen tissue sample was added to the appropriate liquid for each of the three analyses described below.

(i) Tissue and Blood Haemoglobin

Approximately 100 ml of frozen tissue powder was weighed and added to 5000 microlitres of Drabkin's Reagent and homogenized immediately with a Brinkman Instruments Polytron homogenizer for 15 seconds. The sample was spun at 5000 rpm at 5°C for ten minutes. The supernatant was removed and its optical transmittance at 540 nm was measured using a Turner spectrophotometer, to ascertain haemoglobin content. To measure blood haemoglobin, 20 microlitres of blood was added to 5000 microlitres of Drabkin's Reagent and the optical transmittance was measured in the same manner.

(ii) Tissue and Plasma Sodium

A 250–300 mgm sample of frozen powdered lung was added to approximately six times its weight of distilled water and homogenized in the Polytron homogenizer. The tissue and water weights were recorded. To 300 microlitres the resultant homogenate, 33 microlitres of 100 per cent trichloroacetic acid (TCA) was added. Following mixing and centrifugation, 200 microlitres of supernatant was added to 800 microlitres 10 per cent TCA. Following mixing, the resultant liquid was directly assayed for sodium content in a Technicon Auto-Analyzer Flame Photometer IV. Left atrial plasma was similarly analyzed for sodium by diluting 20 microlitres of plasma in 1000 microlitres of 10 per cent TCA.

(iii) Tissue and Blood Wet/Dry Weights

Approximately 1 ml of the tissue homogenate used to determine the tissue sodium content was weighed, dried at 50°C for four days, and reweighed. Left atrial blood was similarly weighed, dried, and reweighed.

(iv) Tissue Metabolism

Approximately 200 mgm of frozen powdered lung was weighed and added to 2 ml of chilled 6 per cent perchloric acid, homogenized with the Polytron homogenizer, and stored on ice. The sample was spun at 8000 rpm for ten minutes at 0°C and the supernatant was neutralized to pH 7.5 using KOH. The added volume of KOH was recorded. Using

standard fluorescent photometric techniques, tissue content of ATP, ADP, AMP, pyruvate and lactate was assessed^{20–22} and expressed as the lactate/pyruvate ratio and the energy charge, as defined above.

III Calculations

The formulae used to calculate the tissue fluid compartments are presented in the Appendix.

IV Statistical Analysis

Data are presented as the mean $\pm$ the standard error of the mean (S.E.M.). Statistical comparison between groups was performed using the two-tailed Student's t-test for unpaired data. Differences with a probability of less than five per cent ($p < 0.05$) were taken to be statistically significant. The following code is used to portray levels of significance of between-group comparisons (Tables I, II):

* differs from control group, $p < 0.05$

** differs from control group, $p < 0.01$

*** differs from control group, $p < 0.001$

§ differs from CPAP group, $p < 0.05$

§§ differs from CPAP group, $p < 0.01$

§§§ differs from CPAP group, $p < 0.001$

Results

There were no significant intergroup differences relative to CPB except as noted in Table 1. The results of tissue analysis are presented in Table II. Total extravascular lung water was modestly reduced in the CPAP group. There was reduction by one third to one half in the pulmonary extravascular sodium space of both experimental groups (CPAP and ZEEP) with no significant difference between the two. There was a 2- to 2½-fold increase in the extravascular sodium free water space in both experimental groups (CPAP and ZEEP) with no significant difference between the two. The lactate/pyruvate ratio was elevated almost 2½-fold in the CPAP group and 18-fold in the ZEEP group. The energy charge was significantly reduced to a mean of just below 0.75 in the ZEEP group.

Discussion

The nature and significance of the pulmonary dysfunction following CPB is not as yet clearly defined. While systemic hypoxia is a major manifestation,^{23–29} it appears that gas exchange abnor-

TABLE I Animal and perfusion data for control, CPB with static inflation (CPAP) and CPB with Passive Deflation (ZEEP) of Lungs (mean $\pm$ S.E.M.)

Time	Analysis	Control	Animal Group	
			CPAP	ZEEP
Prior to CPB	Body wt. (kg)	3.53 $\pm$ 0.11	2.65 $\pm$ 0.15**	3.69 $\pm$ 0.07§§
	Haematocrit	0.413 $\pm$ 0.006	0.355 $\pm$ 0.012**	0.348 $\pm$ 0.020
At 1 hr CPB	(arterial)			
	PO ₂ (torr)	—	267.8 $\pm$ 10.5	219.2 $\pm$ 29.8
	Pco ₂ (torr)	—	27.6 $\pm$ 1.1	32.2 $\pm$ 1.4§
	[H ⁺] (nmol/l)	—	42.0 $\pm$ 2.0	51.0 $\pm$ 5.0
	Haematocrit	—	0.128 $\pm$ 0.017	0.138 $\pm$ 0.007
At 2 hrs CPB	(arterial)			
	PO ₂ (torr)	—	293.8 $\pm$ 9.1	243.0 $\pm$ 19.0
	Pco ₂ (torr)	—	27.6 $\pm$ 1.1	29.4 $\pm$ 2.0
	[H ⁺] (nmol/l)	—	41.0 $\pm$ 2.0	49.0 $\pm$ 5.0
	Haematocrit	—	0.122 $\pm$ 0.012	0.134 $\pm$ 0.008
Parameter average during CPB	PP (torr)	—	83.3 $\pm$ 2.0	85.2 $\pm$ 1.8
	CVP (torr)	—	6.5 $\pm$ 1.2	3.9 $\pm$ 1.1
	LAP (torr)	—	3.1 $\pm$ 1.9	1.8 $\pm$ 1.0
	Temp (°C)	—	31.9 $\pm$ 0.0	31.9 $\pm$ 0.1
Quantity administered during CPB	R/L (ml/kg)	—	176.9 $\pm$ 37.2	137.7 $\pm$ 11.1
	HCO ₃ (ml/kg)	—	87.7 $\pm$ 8.8	73.7 $\pm$ 14.8
	Total (ml/kg)	—	264.6 $\pm$ 42.0	211.4 $\pm$ 21.8
	Methoxamine (mg/kg)	—	0.20 $\pm$ 0.09	0.05 $\pm$ 0.05

PP = mean perfusion pressure during CPB (mean of readings taken every 15 minutes during CPB), in torr.

CVP = mean central venous pressure during CPB, in torr, derived as was PP above.

LAP = mean left atrial pressure during CPB, in torr, derived as was PP above.

Temp = mean perfusate temperature during CPB, in °C derived as was PP above.

R/L = Ringer's Lactate.

HCO₃ = 7.5 per cent sodium bicarbonate solution.

Total (ml/kg) = Ringer's Lactate plus 7.5 per cent sodium bicarbonate solution.

TABLE II Pulmonary Tissue Analyses for Control, CPB with Static Inflation (CPAP) and CPB with Passive Deflation (ZEEP) of the Lungs (mean $\pm$ S.E.M.)

Tissue Analysis	Control n = 12	Animal Group	
		CPAP n = 5	ZEEP n = 5
VV/TS	2.6 $\pm$ 0.2	2.0 $\pm$ 0.3	2.5 $\pm$ 0.2
TEVLW/TS	3.9 $\pm$ 0.1	3.3 $\pm$ 0.3*	3.6 $\pm$ 0.2
EVSS/TS	3.2 $\pm$ 0.0	1.4 $\pm$ 0.4***	2.0 $\pm$ 0.1***
EVSW/TS	0.7 $\pm$ 0.1	1.8 $\pm$ 0.1***	1.6 $\pm$ 0.3**
Lactate/Pyruvate	10.0 $\pm$ 1.1	23.7 $\pm$ 3.0***	183.2 $\pm$ 33.6**
Energy Charge	0.89 $\pm$ 0.01	0.89 $\pm$ 0.01	0.74 $\pm$ 0.02***§§

n = number of animals.

For abbreviations, see table at beginning of article.

malities are less consistent in more recent clinical studies.^{30,31} Until the present study there do not appear to have been any quantitative assessments of intra-vs-extracellular distribution of pulmonary

fluid or of pulmonary metabolism, related to management of the airway during CPB.

The present study examined the rabbit lung at two hours of hypothermic CPB with a disc oxygenator,

left heart venting and incision of the parietal pleural. The data reveal that with ZEEP and with CPAP, the pulmonary extravascular sodium-free water space is more than double control values while the total pulmonary extravascular water compartment is not elevated. This indicates a substantial shift of water from the pulmonary interstitium to the intracellular compartment of the lung.

Studies of pulmonary microscopy after completion of CPB for human open-heart surgery have revealed cellular swelling, interstitial oedema and aggregation of polymorphonuclear leucocytes in the pulmonary capillaries.³³⁻³⁴ These abnormalities occurred both with disc³⁴ and with bubble oxygenators,³³ and with CPAP^{32,33} and with ZEEP³⁴ applied to the airway during CPB. Filtration of pump prime and cardiectomy suction with dacron-wool appeared to prevent these microscopic abnormalities.³³ A study in dogs indicated that application of CPAP with 100 per cent oxygen during CPB without left heart venting, prevented cellular swelling although mild interstitial oedema was present at two hours of CPB.³⁵ In all of these studies there was the likelihood of elevated pulmonary hydrostatic pressure either when coming off CPB³²⁻³⁴ or during the CPB without concurrent left heart decompression.³⁵

Total pulmonary extravascular water has not been found to be elevated following aortic³⁶ or mitral³⁷ surgery or coronary artery surgery with left heart venting during CPB,³¹ regardless of airway management during CPB, unless left atrial pressures were elevated after surgery³⁷ or unless pulmonary artery pressures were high during CPB due to inadequate left heart venting.³⁸ Subsequent increases in total pulmonary extravascular water correlated with subsequent increases in left atrial pressures.³¹ However, since these studies used double indicator methods, areas of non-perfusion in the lungs might have led to calculation of falsely low values.³⁹ The present study used direct methods to ascertain the total pulmonary extravascular water, and also found no evidence of increased total pulmonary extravascular water at two hours of CPB with left heart venting. This study does suggest, however, a very significant redistribution of extravascular water into the cellular compartment from the interstitium of the lung. This is consistent with the microscopic evidence of cellular damage pre-

viously reported.³³⁻³⁵ The lack of concurrent interstitial oedema in the present study may perhaps be explained by the maintenance of a low left atrial pressure up to the point of lung biopsy at two hours of CPB, whereas the clinical microscopic studies which revealed interstitial as well as cellular oedema³²⁻³⁴ were performed after weaning from CPB, during which time left atrial pressures were likely elevated, since fibrillatory arrest rather than cold cardioplegia was in use at the time of those studies. Likewise, the animal model which showed interstitial as well as cellular oedema at two hours of CPB did not include left heart venting.³⁵

Taken together, these various studies suggest that in the absence of elevated hydrostatic pressure in the pulmonary capillary bed during and/or after CPB, there is development of cellular oedema due to a shift of fluid from the interstitium of lung into the parenchymal cellular compartment. In the human³²⁻³⁴ and in the rabbit (present study), unlike in the dog,³⁵ this cellular swelling is not prevented by application of CPAP with an oxygen-enriched gas mixture to the airway during CPB.

The mechanism underlying the pulmonary cellular oedema associated with CPB is not completely clear. However, its association with microaggregates³²⁻³⁵ and its reported prevention by careful filtration of all fluids entering the CPB circuit³³ suggest that cellular damage may be caused by such microaggregates gaining access to the lung via the pulmonary vascular circuit during partial CPB and via the bronchial vascular circuit throughout CPB. Avoidance of a blood/gas interface by using a membrane oxygenator perhaps might also reduce the problem. The present study suggests that the cellular oedema which appears to have occurred is not due to significant energy depletion since the ZEEP group, which had an 18-fold increase in L/P ratio and a significant decrease in energy charge (E.C.), had no greater increase in extravascular sodium-free water than did the CPAP group, which only had a 2½-fold increase in L/P ratio and a normal E.C. It is also possible that pulmonary hypothermia results in a sufficient inhibition of cell membrane metabolism to result in cell swelling. This occurs in other tissues when hypothermic.⁸

The present study appears to be the first investigation of pulmonary energy status during CPB. The data indicate a substantial pulmonary energy deficit during CPB apparently on a hypoxic basis,

when the lung is allowed to collapse with open parietal pleurae. The addition of 5 cms H₂O of CPAP to the airway, with an oxygen enriched gas, prevents this metabolic insult to the lung.

The mechanism underlying the metabolic protection provided by CPAP during CPB is conjectural. One possibility is that CPAP results in delivery, by diffusion, of oxygen to the alveolar capillary membrane via the airway to enable it to adequately maintain aerobic glycolysis. One of the authors (JRH) has previously demonstrated that ventilation of the totally unperfused rabbit lung *in vitro* for three hours results in a significantly better energy state and less lactate production than does passive deflation.⁶ A recent study of one-lung anaesthesia in the dog revealed that addition of 5 cms H₂O of CPAP with 100 per cent oxygen to the airway of the unventilated lung resulted in on-going delivery of oxygen to the blood perfusing the unventilated lung.⁵ Whether such continuous diffusion of oxygen down to the alveoli occurs when CPAP is added to the airway of a lung which does not have pulmonary vascular perfusion to cause active oxygen uptake by passing blood is not known. Alternatively, the metabolic protection conferred upon the lung by CPAP during CPB might simply be the result of improved bronchial vascular perfusion of the lung due to mechanical expansion of the lung.

The functional implications of cellular swelling and energy depletion in the lung during CPB may be reasonably straightforward. Endothelial and alveolar cell swelling would result in increased pulmonary vascular resistance, increased ventilatory dead space, decreased static and dynamic compliance, and an increased AaDO₂. These have been reported to follow CPB.^{14,31,35-38} A pulmonary energy deficit would impair surfactant production, which has been reported following CPB.²

In summary, this study indicates that at two hours of hypothermic CPB with left heart venting, in the rabbit, there is doubling of the pulmonary extravascular sodium-free water space at the expense of the pulmonary extravascular sodium space, with no increase in total pulmonary extravascular water. This implies a substantial shift of fluid from the interstitium into the cells of the lung, by two hours of vented CPB. The data also reveal that if the lungs undergo major collapse for two hours of CPB they suffer significant hypoxic energy deficit which is preventable by maintaining static pulmonary ex-

pansion with an oxygen-enriched gas mixture during CPB.

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Résumé

La distribution de l'eau et la fonction de l'énergie du poumon ont été mesurées chez dix lapins après deux heures de pontage d'hypothermie cardiopulmonaire (CPB) avec le côté gauche du cœur aéré et l'incision de la plèvre pariétale. Durant l'hypothermie cardiopulmonaire (CPB), cinq animaux sont restés avec le tubage trachéal ouvert à l'air avec pression atmosphérique ambiante (ZEEP). Les cinq autres animaux ont eu les poumons gonflés à la pression de 5 cms H₂O (CPAP) par le mélange de gaz (oxygène 70–75 pour cent) provenant du disque oxygénateur. Chez ces deux groupes (ZEEP et CPAP) on a observé un doublement d'espace d'eau sans sodium dans l'espace extravasculaire du poumon (intracellulaire), et une réduction réciproque d'espace de sodium extravasculaire du poumon, comparé avec les douze animaux de contrôle non-traités avec pontage d'hypothermie cardiopulmonaire (CPB). Chez le groupe ZEEP (pression à zéro), le quotient de lactate/pyruvate du poumon était 18 fois supérieur à celui du groupe de contrôle, et la charge de l'énergie pulmonaire était moins significative que celle des animaux de contrôle (0.74 ± 0.02 vs 0.89 ± 0.01). Chez le groupe CPAP, le quotient de lactate/pyruvate du poumon était deux fois demi et celui des valeurs de contrôle et la charge de l'énergie était virtuellement identique à celle du groupe contrôle.

Ces données suggèrent que par suite de CPB, il y a un déplacement de liquide de l'interstitium pulmonaire à l'espace intracellulaire du poumon sans aucune nette élévation du contenu total de l'eau dans l'espace extravasculaire du poumon. Ces données suggèrent aussi que la déflation pulmonaire pendant le CPB provoque un déficit d'énergie pulmonaire qui peut être évité si l'on garde le poumon gonflé avec un mélange de gaz riche en oxygène pendant l'hypothermie cardiopulmonaire.

Appendix

A Calculation of Tissue Fluid Compartments

The following formulae were used to calculate pulmonary fluid compartments:

1. Pulmonary Vascular Volume (VV)

$$(1) \quad VV = \frac{[Hgb]_{tiss}}{[Hgb]_{blood}} \times \frac{20}{5020} \times \frac{(5000 + \text{tissue weight})}{\text{tissue weight}}$$

where

$[Hgb]_{tiss}$ = concentration of haemoglobin in the tissue homogenate

$[Hgb]_{blood}$ = concentration of haemoglobin in the left atrial blood

tissue weight = weight, in milligrams, of frozen tissue powder added to the Drabkin's Reagent

2. Total Tissue Sodium Space (TSS)

$$(2) \quad TSS = \frac{[Na]_{tissue}}{[Na]_{plasma}} \times 0.1088 \times \frac{(\text{tissue weight} + \text{vol H}_2\text{O})}{\text{tissue weight}}$$

where

$[Na]_{tissue}$ = concentration of sodium in tissue supernatant

$[Na]_{plasma}$ = concentration of sodium in left atrial plasma

tissue weight = weight, in milligrams, of frozen tissue powder added to distilled water

vol H₂O = volume of distilled water, in microlitres, to which tissue powder was added

0.1088 = correction factor for the different dilutions of tissue and blood

3. Total Tissue Water (TTW)

$$(3) \quad \frac{\left(\frac{\text{tissue weight}}{\text{tissue weight} + \text{Vol H}_2\text{O}} \times \text{wet weight homog} \right) - \text{dry weight homog}}{\frac{\text{tissue weight}}{\text{tissue weight} + \text{Vol H}_2\text{O}} \times \text{wet weight homog}}$$

where

tissue weight = tissue weight as in Equation (2).

Vol H₂O = volume of distilled water as in Equation (2)

wet weight homog = weight of homogenate sample prior to drying, in milligrams

dry weight homog = weight of homogenate sample after drying, in milligrams

4. Total Extravascular Lung Water (TEVLW)

$$(4) \quad \frac{\text{wet weight blood} - \text{dry weight blood}}{\text{wet weight blood}} \times VV$$

where

TTW = total tissue water as calculated in Equation (3)

wet weight blood = weight of left atrial blood sample prior to drying expressed in mgms

dry weight blood = weight of left atrial blood sample after drying expressed in mgms

VV = vascular volume as calculated in Equation (1)

5. Tissue Extravascular Sodium Space (EVSS)

$$(5) \text{ EVSS} = \text{TSS} - \text{VV}(1 - \text{Hct})$$

where

TSS = Total sodium space as calculated in Equation (2)

VV = tissue vascular volume as calculated in Equation (1)

Hct = haematocrit of left atrial blood, expressed as a decimal portion of unity

6. Extravascular Sodium-Free Water Space (EVSFW)

$$(6) \text{ EVSFW} = \text{TEVLW} - \text{EVSS}$$

where

TEVLW = total extravascular lung water as calculated in Equation (4)

EVSS = extravascular sodium space as calculated in Equation (5)

7. Extravascular Tissue Solids (TS)

$$(7) \text{ TS} = \frac{\text{dry weight homog}}{\frac{\text{tissue weight}}{\text{tissue weight} + \text{Vol H}_2\text{O}} \times \text{wet weight homog}} - \left(\frac{\text{dry weight blood}}{\text{wet weight blood}} \times \text{VV} \right)$$

where

dry weight homog = weight of homogenate sample after drying, as in Equation (3)

wet weight homog = weight of homogenate sample before drying, as in Equation (3)

tissue weight = tissue weight as in Equation (2)

vol H₂O = volume of distilled water added to tissue powder, as in Equation (2)

dry weight blood = weight of left atrial blood sample after drying, as in Equation (4)

wet weight blood = weight of left atrial blood sample before drying, as in Equation (4)

VV = tissue vascular volume as in Equation (1)

In order to relate pulmonary fluid compartments to a common reference point, all compartments are expressed as a proportion relative to the pulmonary extravascular tissue solids (TS).

Therefore, the data are presented as

VV/TS = pulmonary vascular volume per extravascular tissue solid [Equations (1) and (7)]

TEVLW/TS = total extravascular lung water per extravascular tissue solid [Equations (4) and (7)]

EVSS/TS = tissue extravascular sodium space per extravascular tissue solid [Equations (5) and (7)]

EVSFW/TS = tissue extravascular sodium-free water space per extravascular tissue solid [Equations (6) and (7)]

B Calculation of Energy Charge (E.C.)

$$\text{Energy Charge} = \frac{\text{ATP} + \frac{1}{2} \text{ADP}}{\text{ATP} + \text{ADP} + \text{AMP}}$$

where

ATP = concentration of adenosine triphosphate in micromoles per gram wet weight of tissue

ADP = concentration of adenosine diphosphate in micromoles per gram wet weight of tissue

AMP = concentration of adenosine monophosphate in micromoles per gram wet weight of tissue

C Calculation of Lactate/Pyruvate Ratio

Lactate/Pyruvate = concentration of lactate in micromoles per gram wet weight of tissue divided by the concentration of pyruvate in micromoles per gram wet weight of tissue.