The Effect of Increased Full Coverage Anti-G Trouser Inflation Pressure on the Cardiovascular Responses to Positive Pressure Breathing

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Abstract

Positive pressure breathing (PPB) provides short term emergency protection against hypoxia in the event of cabin depressurisation in military aircraft operating at altitudes exceeding 40,000 feet. PPB, however, causes significant disturbance to the normal function of the respiratory and circulatory systems, thus limiting the level and duration of pressure breathing that can be tolerated.

The adverse effects of PPB can be lessened by the use of counter-pressure garments, which apply an external pressure to the surfaces of the trunk and the lower limbs. We investigated the potential benefits of increased lower limb counter-pressure as a measure to optimise cardiovascular function during PPB.

A trans-cranial Doppler sonograph was used to measure the cerebral blood velocity (CBV) during PPB whilst wearing full coverage anti-G trousers (FCAGT) inflated to various pressures. Six subjects were exposed to 45mmHg PPB for 10 minutes at ground level, and 70mmHg PPB for 4 minutes at ground level. At each PPB level, subjects were exposed to 4 levels of FCAGT inflation – 1 x PPB pressure, 1.5 x PPB pressure, 2 x PPB pressure, and 2.5 x PPB pressure. Subjects also completed a control during normal breathing at rest. CBV during PPB was lower than CBV during the control condition ($p<0.05$), irrespective of FCAGT inflation level. Heart rate during PPB at a FCAGT inflation pressure of 1 x PPB pressure was greater than heart rate during the control condition ($p<0.05$). In addition, alveolar CO_2 pressure ($PACO_2$) during PPB was lower than $PACO_2$ during the control condition ($p<0.05$), irrespective of FCAGT pressure. We cannot wholly attribute the observed reduction in CBV during PPB to cardiovascular dysfunction, as the reduction in $PACO_2$ during PPB is suggestive of a decreased arterial PCO_2, a factor known to induce cerebral vasoconstriction.

In a second study, a rebreathing based lung function test was used to assess effective pulmonary blood flow (QP_{eff}) and diffusing capacity of the lungs (Dl) during PPB whilst wearing full coverage anti-G trousers inflated to various pressures. Six subjects were exposed to 45mmHg PPB for 2.5 minutes at ground level, and 60mmHg PPB for 2.5 minutes at ground level. At each level of PPB, subjects were exposed to 4 levels of FCAGT inflation pressure – 1 x PPB pressure, 1.5 x PPB pressure, 2 x PPB pressure, and 2.5 x PPB pressure. The subjects also completed a control during normal breathing at rest. QP_{eff} and Dl during PPB was not significantly different to QP_{eff} and Dl during the control condition, irrespective of FCAGT inflation pressure. Heart rate during PPB at a FCAGT inflation pressure of 1 x PPB pressure was greater than heart rate during the control condition ($p<0.05$), and greater than heart-rate during PPB at the other levels of FCAGT inflation pressure ($p<0.05$).

We conclude that cardiovascular function is impaired during PPB whilst wearing FCAGTs inflated to a pressure equal to PPB pressure. In addition, our results demonstrate that near normal cardiovascular function can be maintained during PPB if FCAGTs are inflated to 1.5 x PPB pressure, 2 x PPB pressure, or 2.5 x PPB pressure.

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Introduction

In the event of cockpit pressurisation failure or forced ejection at altitudes exceeding 40,000 feet, aircrew are exposed to the risk of significant hypoxia. At these altitudes, breathing 100% oxygen does not maintain physiologically adequate blood oxygen saturation, due to an insufficient oxygen pressure gradient between the inspired gas and the blood flowing through capillaries in ventilated regions of the lungs. Theoretically, under these conditions a physiologically acceptable inspired oxygen tension could be achieved simply by increasing the absolute pressure of the 100% oxygen breathing gas delivered to the pilot's oxygen mask. Unfortunately, breathing a gas delivered to the airway at a pressure exceeding ambient pressure ('positive pressure breathing') imposes significant physiological penalties, thus limiting the effectiveness of this procedure as a measure to prevent hypoxia following rapid decompression at altitudes exceeding 40,000 feet.

Positive pressure breathing (PPB) adversely affects the normal mechanical function of the respiratory apparatus, resulting in hyperinflation of the lungs and an increased work of breathing. The most significant consequence of PPB is, however, the effect on the circulation. PPB raises intrathoracic pressure, resulting in a displacement of blood from the thoracic cavity and a temporary abolition of the normal peripheral to central venous pressure gradient, and hence a reduction in venous return. Progressive accumulation of the blood displaced from the thorax in the peripheral veins results in an increase in peripheral venous pressure, which continues until a peripheral to central venous pressure gradient is re-established. Thus, during PPB the circulation of blood is maintained at the cost of a reduction in the volume of circulating blood, compromising the supply of oxygenated blood to the brain.

The development of counter pressure garment assemblies has reduced the severity of the adverse effects of PPB. Application of an equal counter pressure to the external surface of the trunk and abdomen almost wholly alleviates the respiratory dysfunction associated with PPB. The addition of lower limb counter pressure, via the use of anti-G trousers, provides some protection against PPB-induced circulatory dysfunction. Research data demonstrate that the degree of cardiovascular protection provided by anti-G trousers during PPB is dependent on the garment design, the extent of lower body surface area coverage, and the inflation pressure of the garment relative to the pressure of the breathing gas.

Earlier standard coverage anti-G trouser designs, which provide bladder coverage of approximately 30% of the lower body surface area below the umbilicus, have been shown to provide only limited protection against PPB induced cardiovascular dysfunction. Although studies have shown that inflating standard coverage anti-G trousers to a pressure up to four times PPB pressure improves cardiovascular function during PPB (Ackles et al, 1978; Gradwell, 1993), available data demonstrate that standard coverage anti-G trousers are incapable of facilitating maintenance of normal circulatory function during PPB (Goodman, Fraser, Eastman, and Ackles, 1992; Goodman, Fraser, Ackles, Mohn, and Pecaric, 1993; Goodman, Freeman, Yang, Hsia, and Chan, 1994).

The recent development of full coverage anti-G trousers (FCAGTs), which provide circumferential bladder coverage of up to 90% of the lower body surface area below the umbilicus, has improved the degree of circulatory protection available to aircrew during PPB (Goodman et al, 1992; Goodman et al, 1993; Goodman et al, 1994).

Theoretically, extended bladder coverage provided by FCAGTs affords the possibility of using garment inflation pressures that are substantially lower than those previously recommended for standard coverage anti-G trousers during PPB. Currently, however, there is no consensus amongst researchers as to the optimum FCAGT inflation pressure during PPB. Establishment of the lowest FCAGT inflation pressure sufficient to facilitate maintenance of normal cardiovascular function during PPB will reduce the discomfort and impaired mobility arising from excessive lower body pressurisation.

The present study aimed to determine the lowest FCAGT inflation pressure that facilitated maintenance of optimum physiological function during ground level PPB not exceeding 70mmHg. Two separate experiments assessed various physiological responses to PPB in subjects wearing a counter pressure

assembly incorporating FCAGTs inflated to various multiples of PPB pressure (1 x PPB pressure, 1.5 x PPB pressure, 2 x PPB pressure, or 2.5 x PPB pressure).

Methods

Phase 1

Six male subjects from the DERA staff gave informed consent to participate in this part of the study. All subjects were aged under 45 years, were medically screened and received positive pressure breathing (PPB) training prior to participation in the study.

Prior to each experimental exposure, an adjustable headband device, incorporating the probe of a transcranial Doppler (TCD) sonograph (Pioneer 4040, Nicolet Biomedical/EME, Madison, USA), was fitted to the subject's head. The TCD probe was placed on the portion of the scalp covering the right temporal region of the subject's skull. The TCD probe emits an ultrasound signal at a constant rate and frequency, which is backscattered and reflected by red blood cells moving through the selected blood vessel at the measurement site. The resultant frequency shift of the ultrasound signal is proportional to the velocity of the blood cells within the selected vessel. A point 2-5mm proximal to the bifurcation in the Middle Cerebral Artery (MCA) at the Circle of Willis was selected as the measurement site. The MCA is considered inextensible, and hence changes in blood velocity are directly proportional to changes in blood flow. Thus, the TCD device allowed non-invasive measurement of a direct correlate of cerebral blood flow. In addition to the TCD device, subjects were fitted with 3 electrodes to enable display of their electrocardiogram (ECG) using a standard 3-lead ECG configuration.

Following instrumentation fitting, subjects donned a representative aircrew equipment assembly (AEA) comprising aircrew underwear, Royal Air Force (RAF) Mk14b aircrew flying coverall, a RAF G-type flying helmet (modified to accommodate the TCD probe), RAF Type P/Q oronasal oxygen mask, representative FCAGTs, and a representative chest counter-pressure garment (CCPG). The FCAGTs provided circumferential bladder coverage of approximately 90% of the lower body surface area below the umbilicus. The CCPG provided bladder coverage of the shoulders, and the anterior and posterior external surfaces of the chest and upper abdomen.

Subjects underwent experimental exposures at two levels of PPB (45mmHg for 10 minutes, and 70mmHg for 4 minutes), at four FCAGT inflation pressures (1 x PPB, 1.5 x PPB, 2 x PPB, and 2.5 x PPB). Thus, subjects completed eight individual PPB experimental conditions. In addition, subjects underwent two control conditions to provide a baseline comparison with data obtained during 10-minute 45mmHg PPB exposures and 4-minute 70mmHg PPB exposures. The control conditions involved normal breathing at ambient pressure, and were identical in all aspects to the PPB experimental conditions, save for the absence of PPB and counter pressure garment inflation.

During all experimental exposures, subjects were seated on a chair positioned in a hypobaric chamber. On each visit to the laboratory, subjects underwent a maximum of three PPB experimental exposures per half day. Experimental exposures were presented to subjects according to a Latin square experimental design, which ensured that no two subjects experienced an identically ordered sequence of exposures.

PPB was initiated using the 'through the wall' method, as utilised by others (Goodman et al, 1993; Goodman et al, 1995). The hypobaric chamber was decompressed, such that the pressure within the chamber was lowered by an amount equal to the required PPB pressure (i.e. either 45mmHg or 70mmHg). Subjects could breathe air at either chamber pressure or the relatively higher pressure of ambient air outside the chamber. A bank of ganged two-way taps acted as a switchover mechanism, which could connect the subject's oxygen mask and CCPG, via gas hoses protruding through the chamber wall, to the relatively higher pressure ambient air, thus enabling simultaneous delivery of PPB and CCPG inflation. The two-way tap system was designed to allow rapid termination of PPB, if required. The FCAGTs were inflated from a compressed air

supply, via integrated control boxes (manufactured locally) linked to solenoid operated valves. The control boxes could be configured to enable the maintenance of any desired FCAGT inflation pressure, up to a maximum of 5 times PPB pressure.

Differential pressure transducers (Celesco transducers, model No. LCVR) measured the pressure in the subject's oxygen mask ('mask cavity pressure'), CCPG, FCAGTs, and in a reference pressure tube, which enabled the pressure differential between the chamber and ambient air to be monitored. The subject's arterial blood pressure and heart rate was recorded using a Finapres 2300 blood pressure monitor (Ohmeda Inc), with the finger cuff secured on the ring finger of the subject's left hand, which was held at heart level during the experimental exposures. The subject's respired gas composition was measured throughout all experimental exposures by a respiratory mass spectrometer (QP9000, Morgan Medical Ltd), configured to measure the relative concentrations of nitrogen, oxygen, carbon dioxide, and argon in the sampled gas. The outputs from the TCD sonograph, respiratory mass spectrometer, the pressure transducers, and the arterial blood pressure monitor, were displayed and recorded using an analogue to digital converter incorporating a data recording system (Maclab/S, ADInstruments) linked to a microcomputer (Apple PowerMac, Apple Computers).

During all PPB exposures, a suitably qualified Medical Officer accompanied the subject in the hypobaric chamber. Subjects could voluntarily terminate PPB at any time, via the use of a thumb-down signal. The Medical Officer terminated PPB if there was any evidence of impending syncope, or if the subject was considered unfit to continue PPB for any reason.

Data Acquisition and Statistical Analysis

Mean arterial blood pressure (MAP), heart rate, cerebral blood velocity, and estimated alveolar carbon dioxide tension data were obtained using dedicated analysis functions within the data recording/analysis software package (Chart, ADInstruments).

The data for each variable were averaged over 1-minute periods of each experimental condition. The data obtained from 45mmHg PPB experimental conditions (including the associated control condition) were separated from the data obtained from the 70mmHg PPB experimental conditions to form two distinct data sets. The mean values in each data set were subsequently analysed using a two-factor (FCAGT inflation pressure and time) analysis of variance with repeated measures. A significance level of $p<0.05$ was adopted as the cut-off point for all main effects. Where main effects were identified, post-hoc analysis (Newman Keuls test) was used to determine which experimental conditions differed from each other.

Phase 2

Six male subjects from the DERA staff gave informed consent to participate in this part of the study. All subjects were aged under 40 years, were medically screened and received positive pressure breathing (PPB) training prior to participation in the study.

Subjects were fitted with 3 electrodes to enable display of their electrocardiogram (ECG) using a standard 3-lead ECG configuration prior to donning the aircrew equipment assembly (AEA). Subjects wore a representative AEA comprising aircrew underwear, Royal Air Force (RAF) Mk14b aircrew flying coverall, a RAF Mk10b aircrew helmet, a modified RAF Type P/Q oronasal oxygen mask, representative FCAGTs, and a representative CCPG. The FCAGTs and CCPG were identical to those used in phase 1 of the study.

Subjects underwent experimental exposures at two levels of PPB (45mmHg for 2.5 minutes, and 60mmHg for 2.5 minutes), at four FCAGT inflation pressures (1 x PPB, 1.5 x PPB, 2 x PPB, and 2.5 x PPB). Thus, subjects completed eight individual PPB experimental conditions. In addition, subjects underwent two control conditions to provide a baseline comparison with data obtained during 45mmHg PPB exposures and 60mmHg PPB exposures. The control conditions involved normal breathing at ambient pressure, and were identical in all aspects to the PPB experimental conditions, save for the absence of PPB and counter pressure garment inflation.

Following garment fitting, subjects were seated on a chair positioned in a hypobaric chamber. On each visit to the laboratory, subjects underwent a maximum of three PPB experimental exposures per half day, with experimental exposures presented to subjects according to a Latin square experimental design, as described previously.

Arterial blood pressure and heart rate were recorded using a Finapres 2300 blood pressure monitor (Ohmeda Inc), with the finger cuff secured on the ring finger of the subject's left hand, which was held at heart level during the experimental exposures. Differential pressure transducers (Celesco transducers, model No. LCVR) measured the pressure in the subject's oxygen mask ('mask cavity pressure'), CCPG, FCAGTs, and in a reference pressure tube, which enabled the pressure differential between the chamber and ambient air to be monitored. The subject's respired gas composition was measured throughout all experimental exposures by a respiratory mass spectrometer (QP9000, Morgan Medical Ltd), configured to measure the relative concentrations of nitrogen, oxygen, carbon dioxide, argon, freon^{22}, and carbon monoxide^{18} in the sampled gas. The outputs from the respiratory mass spectrometer, the pressure transducers, and the arterial blood pressure monitor were displayed and recorded using an analogue to digital converter incorporating a data recording system (Maclab/S, ADInstruments) linked to a microcomputer (Apple PowerMac, Apple Computers) running a data recording and analysis software package (Chart, ADInstruments).

The PPB delivery and FCAGT inflation methods were identical to those used during phase 1 of the study. The experimental configuration during this phase of the study differed substantially to that employed during phase 1, with respect to provision of a facility to enable rebreathing manoeuvres to be performed during PPB. The modified RAF Type P/Q oronasal mask incorporated an occluded inspiratory port and a single common inlet/outlet pathway via the open expiratory port. A short section of rubber hose connected the expiratory port of the modified P/Q oxygen mask to a one-way non-rebreathing valve (PK Morgan), which acted as the junction between the inspiratory and expiratory limbs of a breathing circuit. A two-way tap, placed in the hose linking the mask and the one-way valve, functioned as a changeover mechanism between the breathing circuit and the rebreathing apparatus.

The rebreathing apparatus comprised a two-way tap, which enabled rebreathing bag filling/emptying, connected to a 200mm long metal pipe (of internal diameter 10mm), which extended through a hole in an airtight Perspex box and onwards into a 6-litre rubber rebreathing bag (PK Morgan). The mouth of the rebreathing bag was sealed around the metal pipe at the point where it entered the interior of the Perspex box, such that the pipe extended fully from the mouth of the bag to its distal end. The metal pipe was perforated with several holes, to prevent premature bag closure during inspiratory efforts in the rebreathing manoeuvres. The rebreathing gas was delivered to the rebreathing bag by a calibrated 7-litre capacity gas syringe (Hans Rudolph) that could be connected to the rebreathing bag via a filling/emptying two-way tap. A section of rubber hose connected the inside of the Perspex box to the air outside the chamber and, thus, the inside of the Perspex box was always exposed to the atmospheric pressure of air outside the chamber. This enabled the gas in the rebreathing bag to be pressurised to the same level as the gas delivered to the subject's oxygen mask, via the breathing circuit.

Subjects performed a rebreathing manoeuvre during the final 30 seconds of each experimental exposure. After pressure breathing for 2 minutes, subjects breathed out to residual lung volume, and then started rebreathing a quantity of gas (equal to 80% of their seated vital capacity) from the rebreathing bag. The rebreathing bag contained a gas mixture comprising approximately 3.5% freon^{22}, 10% argon, 0.3% carbon monoxide^{18} ($C^{18}O$), and 17.5% oxygen, in a balance of nitrogen. Subjects rebreathed at a frequency of 25 breaths per minute, for a period of 25 to 30 seconds duration. An audible metronome was used to assist subjects in the maintenance of the required breathing frequency during the rebreathing period. Subjects inhaled and exhaled the full volume of gas contained within the rebreathing bag throughout the rebreathing manoeuvre.

During all PPB exposures, a suitably qualified Medical Officer accompanied the subject in the hypobaric chamber. Subjects could voluntarily terminate PPB at any time, via the use of a thumb-down signal. The Medical Officer terminated PPB if there was any evidence of impending syncope, or if the subject was considered unfit to continue PPB for any reason.

Data Acquisition and Statistical Analysis

Mean arterial blood pressure (MAP) and heart rate data were obtained using dedicated analysis functions within the data recording/analysis software package (Chart, ADInstruments).

The records of argon, freon^{22}, C^{18}O, and carbon dioxide concentration during rebreathing manouevres were transferred from the Chart software to a semi-automated spreadsheet (Excel, Microsoft Corporation) function designed by the authors. Following input of the raw data, the argon, freon^{22}, C^{18}O, and carbon dioxide traces were represented as a series of graphs of gas concentration against rebreathing time. The argon trace was used to select two time intervals: the first equating to the peak inspired concentration of argon during the first inspiration from the rebreathing bag, the second equating to the time interval coincident with complete gaseous mixing between residual gas in the lungs and the gas within the rebreathing bag and associated apparatus. The data point equating to the peak inspired argon concentration was taken as the data point coincident with peak inspired concentration for freon^{22},and C^{18}O also. The argon, freon^{22}, and C^{18}O traces were then normalised with respect to their peak inspired concentrations, such that the plots were transformed into a series of graphs relating fraction of peak inspired concentration against time. The next stage of the analysis involved transforming these plots into graphs plotting the natural logarithm (ln) of the normalised freon^{22} and C^{18}O concentrations against time.

The carbon dioxide trace was used to select six end-tidal expiration sample points, starting with the first expiration following the point of complete gaseous mixing within the rebreathing 'system'. The time between the start of rebreathing and complete gaseous mixing never exceeded 10 seconds, and hence the final expired sample point occurred at a time interval no later than 23 seconds after the start of the rebreathing manoeuvre. The six sampling intervals determined from the carbon dioxide trace were used to obtain six data points from the ln freon^{22} and ln C^{18}O traces. The slope of a straight line plotted through the six data points represents the rate constant of decline in concentration (termed k) for the gas in question. Following determination of k, estimated values for the effective pulmonary blood flow and diffusing capacity of the lungs for carbon monoxide were calculated, in accordance with formulas described by Sackner (1987) and Cotes (1975), respectively.

The MAP and heart rate data were averaged over a 30-second period extending from 80 seconds following the start of each experimental condition. The data obtained from 45mmHg PPB experimental conditions (including the associated control condition) were separated from the data obtained from the 60mmHg PPB experimental conditions to form two distinct data sets. The mean values for heart rate, MAP, effective pulmonary blood flow, and diffusing capacity of the lungs for carbon monoxide in each data set were subsequently analysed using a single factor (FCAGT inflation pressure) analysis of variance with repeated measures. A significance level of $p<0.05$ was adopted as the cut-off point for all main effects. Where any main effects were identified, post-hoc tests (Newman Keuls) were used to identify which PPB experimental conditions differed from each other. A Dunnet's multiple pairwise comparison test analysed differences between PPB experimental conditions and the control condition.

Results

Phase 1

All experimental exposures were completed without untoward incident, with no evidence of pre-syncopal symptoms during any of the PPB exposures.

Cerebral Blood Velocity

Cerebral blood velocity during 45mmHg and 70mmHg PPB was significantly lower than cerebral blood velocity during the control condition, at all FCAGT inflation pressures. The level of FCAGT inflation pressure had no significant effect on the observed decrease in cerebral blood velocity during PPB. Figures 1 and 2 illustrate the cerebral blood velocity measured during 45mmHg PPB and 70mmHg PPB and associated control conditions.

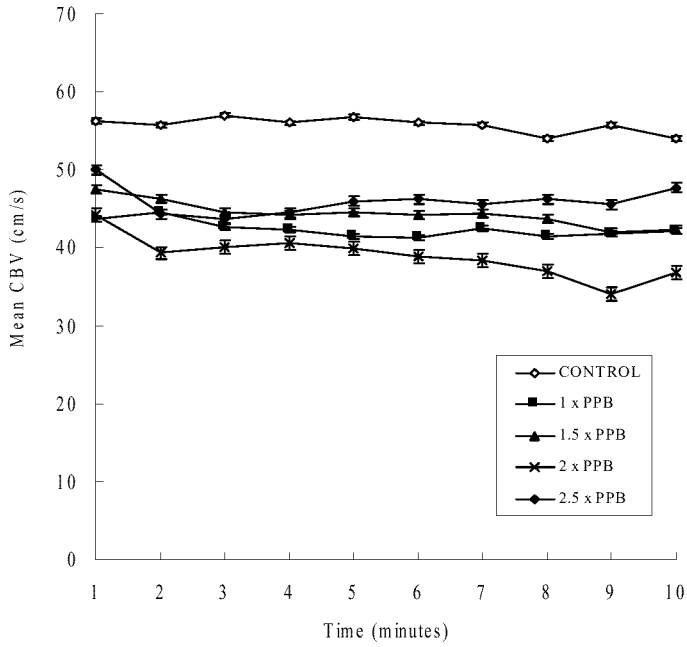

Figure 1: ***Cerebral blood velocity [mean (n=6) 6 SEM] during control condition and during 45mmHg PPB with FCAGTs inflated to various multiples of PPB pressure***

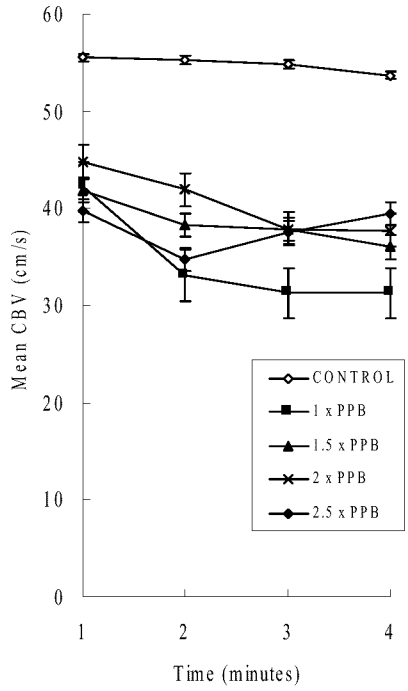

Figure 2: ***Cerebral blood velocity [mean (n=6) 6 SEM] during control condition and during 70mmHg PPB with FCAGTs inflated to various multiples of PPB pressure***

Heart Rate

Heart rate during 45mmHg and 70mmHg PPB with FCAGTs inflated to a pressure equal to PPB pressure was significantly greater than heart rate recorded during the corresponding control conditions. Heart rate during 45mmHg and 70mmHg PPB with FCAGTs inflated to 1.5 x PPB, 2 x PPB, or 2.5 x PPB was not, however, significantly different to heart rate during the control conditions. In addition, heart rate during the first minute of 45mmHg PPB was significantly lower than heart rate recorded at all other intervals during 45mmHg PPB, irrespective of FCAGT inflation pressure. Figures 3 and 4 illustrate the heart rate measured during 45mmHg and 70mmHg PPB and their associated control conditions.

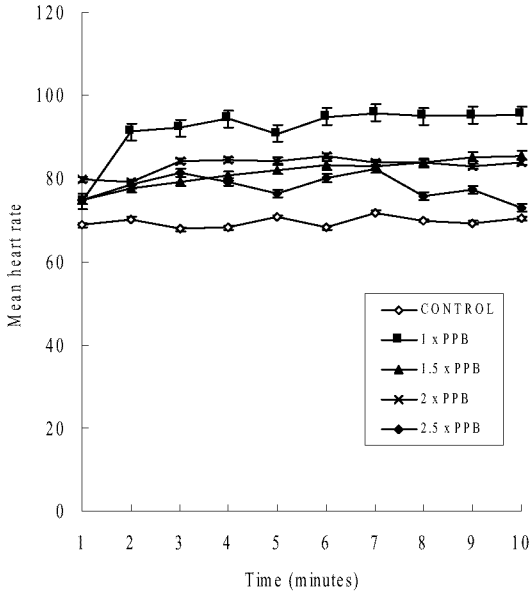

Figure 3: ***Heart rate [mean (n=6) 6 SEM] during control condition and during 45mmHg PPB with FCAGTs inflated to various multiples of PPB pressure***

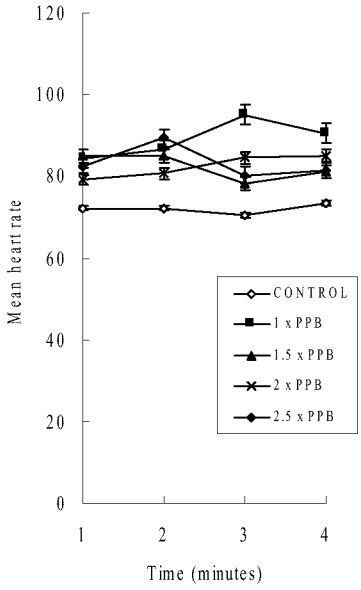

Figure 4: ***Heart rate [mean (n=6) 6 SEM] during control condition and during 70mmHg PPB with FCAGTs inflated to various multiples of PPB pressure***

Alveolar Carbon Dioxide Tension

Alveolar carbon dioxide tension ($PACO_2$) during 45mmHg and 70mmHg PPB was significantly lower than $PACO_2$ during the control condition, at all FCAGT inflation pressures. During 70mmHg PPB with FCAGTs inflated to a pressure equal to PPB pressure, $PACO_2$ was significantly lower than the $PACO_2$ during 70mmHg PPB at all other FCAGT inflation pressures. In addition, $PACO_2$ during the first minute of 45mmHg and 70mmHg PPB was significantly lower than $PACO_2$ recorded at all other intervals during PPB, irrespective of FCAGT inflation pressure. Figures 5 and 6 show the $PACO_2$ measured during 45mmHg and 70mmHg PPB and their associated control conditions.

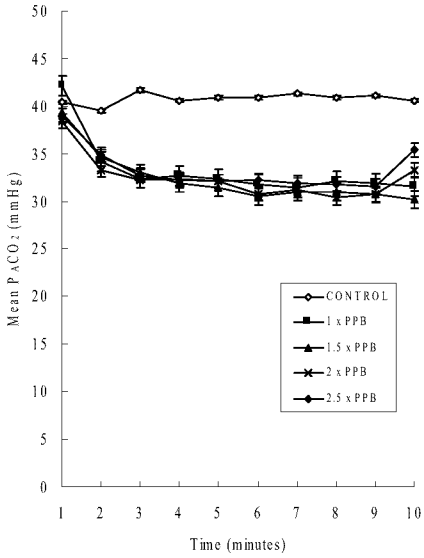

Figure 5: ***Alveolar carbon dioxide tension [mean (n=6) 6 SEM] during control condition and during 45mmHg PPB with FCAGTs inflated to various multiples of PPB pressure***

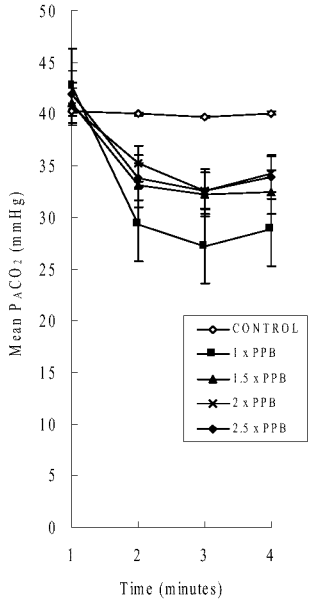

Figure 6: ***Alveolar carbon dioxide tension [mean (n=6) 6 SEM] during control condition and during 70mmHg PPB with FCAGTs inflated to various multiples of PPB pressure***

Mean Arterial Pressure

Mean arterial pressure (MAP) recorded during 45mmHg and 70mmHg PPB was significantly greater than MAP recorded during control conditions, irrespective of FCAGT inflation pressure. The level of FCAGT inflation pressure had no significant effect on the observed increase in MAP during PPB. Figures 7 and 8 illustrate the MAP measured during 45mmHg PPB and 70mmHg PPB and associated control conditions.

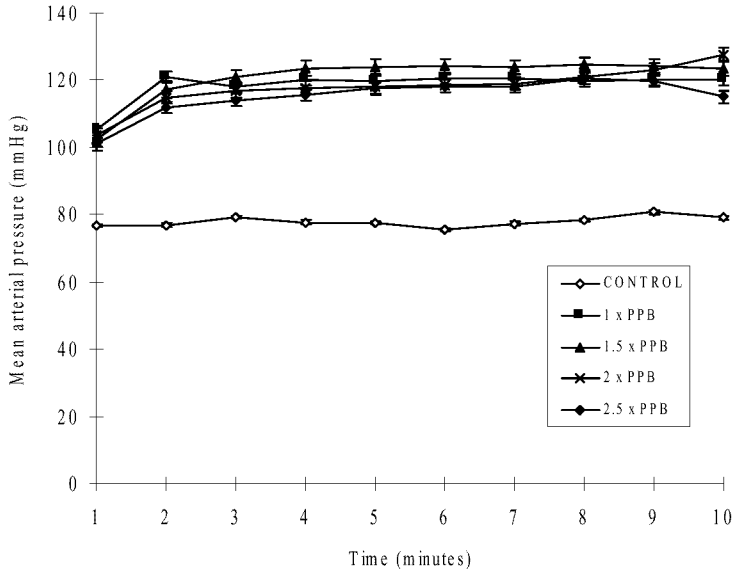

Figure 7: ***Mean arterial pressure [mean (n=6) 6 SEM] during control condition and during 45mmHg PPB with FCAGTs inflated to various multiples of PPB pressure***

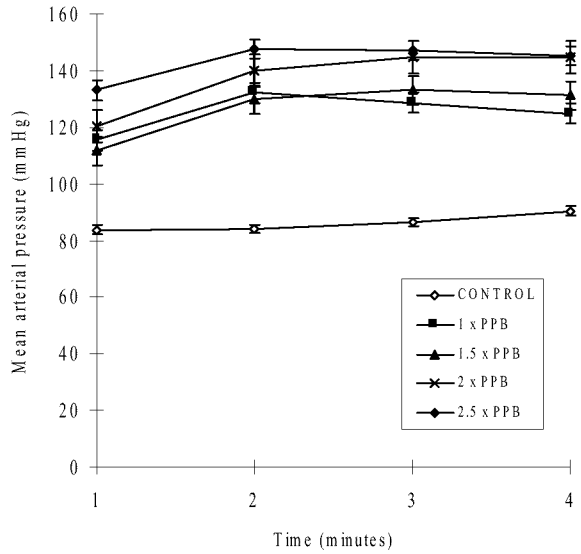

Figure 8: ***Mean arterial pressure [mean (n=6) 6 SEM] during control condition and during 70mmHg PPB with FCAGTs inflated to various multiples of PPB pressure***

Phase 2

All experimental exposures were completed without untoward incident. Six subjects contributed heart rate and blood pressure data at the 45mmHg and 60mmHg positive pressure breathing (PPB) levels. Rebreathing data analysis revealed that two subjects, however, were unable to achieve a reliable mask seal whilst rebreathing during PPB, as evidenced by careful examination of mask cavity pressure records. Therefore, the rebreathing based data included in the statistical analysis were derived from only four subjects.

The diffusing capacity of the lungs for carbon monoxide ($D\mathrm{l}_{CO}$) data were transformed into diffusion coefficients for carbon monoxide (K_{CO}), an expression of $D\mathrm{l}_{CO}$ per litre of alveolar volume. The rebreathing lung volume during PPB was greater than rebreathing lung volume in the control condition, due to an increased residual lung volume (RV) during PPB. The $D\mathrm{l}_{CO}$ has been demonstrated to increase when measured at increased lung volumes (Stam, Hrachovina, Stijnen, and Versprille, 1994) and therefore, transformation of the data into diffusion coefficients prevented erroneous comparisons between $D\mathrm{l}_{CO}$ measured during PPB and $D\mathrm{l}_{CO}$ measured during the control condition.

Effective pulmonary blood flow

The effective pulmonary blood flow measured during PPB was not significantly different to the effective pulmonary blood flow recorded during the control condition, irrespective of FCAGT inflation pressure. Mean effective pulmonary blood flow during 45mmHg PPB is shown in figure 9; the results obtained during 60mmHg PPB are shown in figure 10.

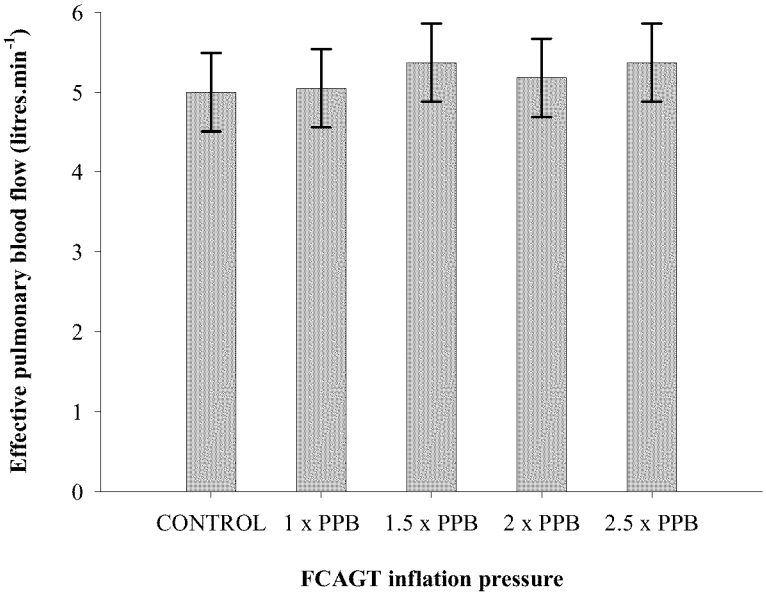

Figure 9: ***Effective pulmonary blood flow [mean (n=4) 6 SEM] during control and during 45mmHg PPB with FCAGTs inflated to various multiples of PPB pressure***

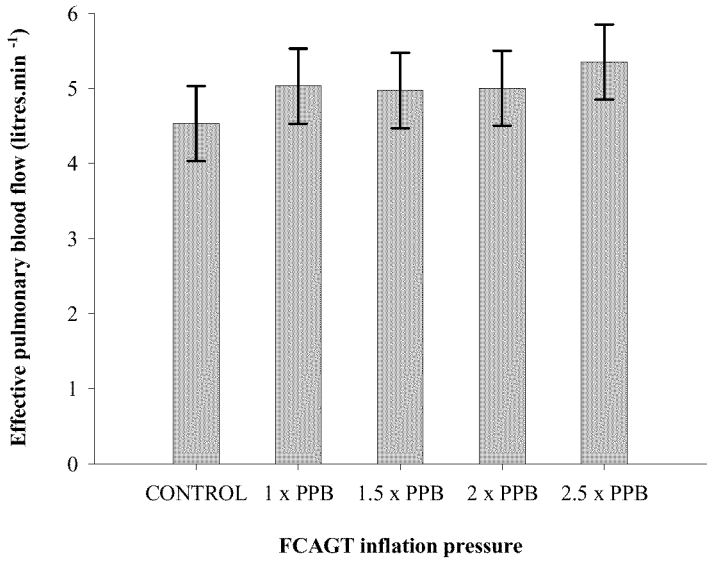

Figure 10: ***Effective pulmonary blood flow [mean (n=4) 6 SEM] during control and during 60mmHg PPB with FCAGTs inflated to various multiples of PPB pressure***

Diffusion Coefficient

The diffusion coefficient measured during PPB was not significantly different to the diffusion coefficient recorded during the control condition, irrespective of FCAGT inflation pressure. Mean diffusion coefficient during 45mmHg PPB is shown in figure 11; the results obtained during 60mmHg PPB are shown in figure 12.

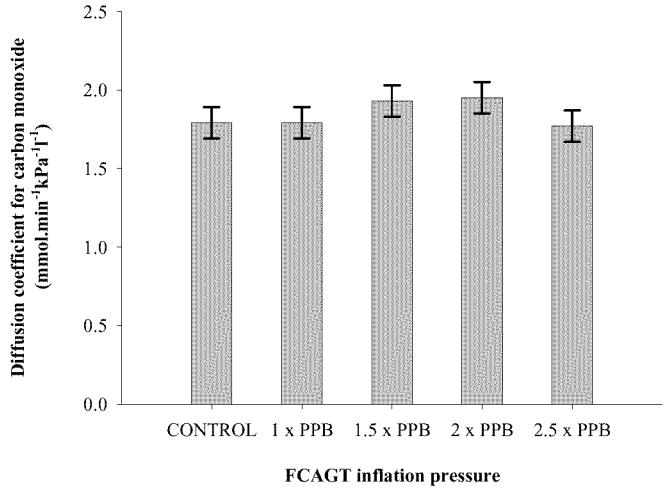

Figure 11: ***Diffusion coefficient for carbon monoxide [mean (n=4) 6 SEM] during control and during 45mmHg PPB with FCAGTs inflated to various multiples of PPB pressure***

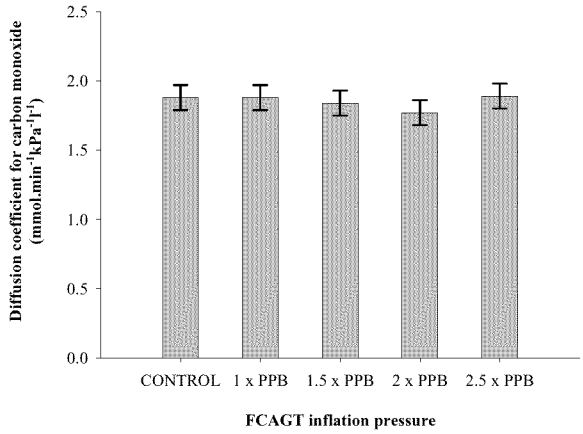

Figure 12: ***Diffusion coefficient for carbon monoxide [mean (n=4) 6 SEM] during control and during 60mmHg PPB with FCAGTs inflated to various multiples of PPB pressure***

Heart rate

Heart rate measured during 45mmHg PPB with FCAGTs inflated to the same pressure as PPB pressure was significantly greater than heart rate recorded during the control condition ($p<0.05$). Heart rate during 45mmHg with FCAGTs inflated to 1.5 x PPB, 2 x PPB, or 2.5 x PPB was not, however, significantly different to heart rate during the control condition.

Heart rate measured during 60mmHg PPB with FCAGTs inflated to a pressure equal to PPB pressure was significantly greater than heart rate during the control condition ($p<0.01$). Heart rate during 45mmHg with FCAGTs inflated to 1.5 x PPB, 2 x PPB, or 2.5 x PPB was not, however, significantly different to heart rate during the control condition. In addition, heart rate during 60mmHg PPB with FCAGTs inflated to a pressure equal to PPB pressure was significantly greater than heart rate during 60mmHg PPB at all other FCAGT inflation pressures ($p<0.05$). Mean heart rate during experimental conditions at 45mmHg PPB and at 60mmHg PPB are shown in figures 13 and 14, respectively.

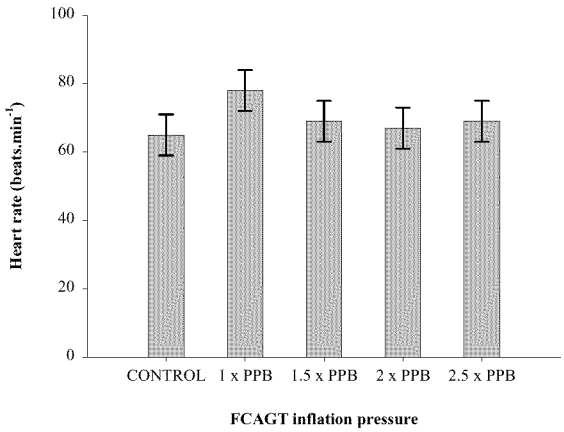

Figure 13: ***Heart rate [mean (n=4) 6 SEM] during control and during 45mmHg PPB with FCAGTs inflated to various multiples of PPB pressure***

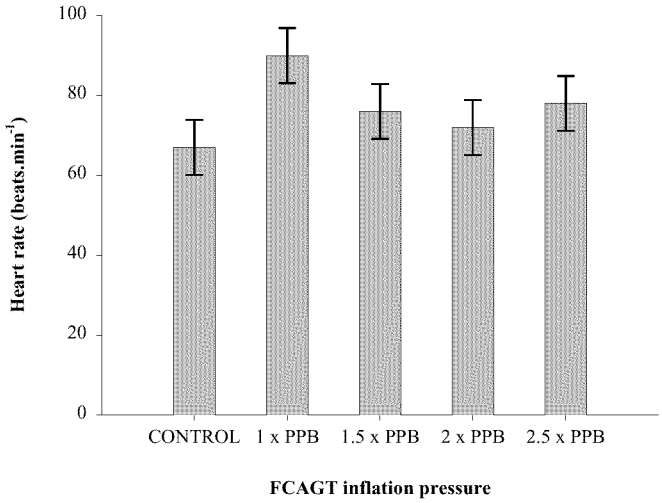

Figure 14: ***Heart rate [mean (n=4) 6 SEM] during control and during 60mmHg PPB with FCAGTs inflated to various multiples of PPB pressure***

Mean Arterial Pressure

At both PPB levels, mean arterial pressure measured during PPB at all FCAGT inflation pressures was significantly greater than mean arterial pressure during the control condition ($p<0.01$).

Mean arterial pressure during the different experimental conditions conducted at 45mmHg PPB is shown in figure 15; the results obtained during experimental conditions at 60mmHg PPB are shown in figure 16.

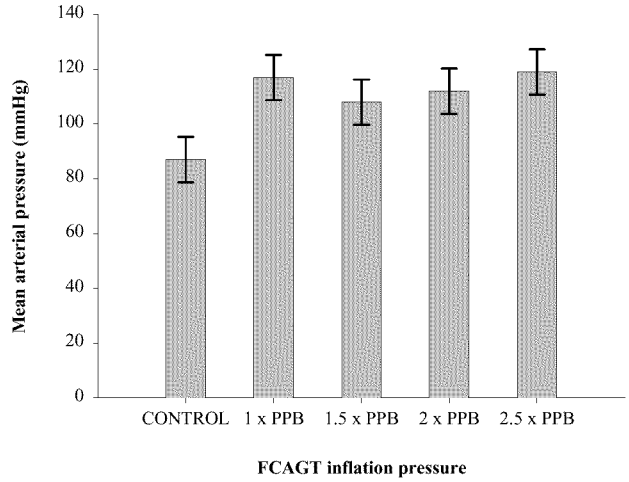

Figure 15: ***Mean arterial pressure [mean (n=6) 6 SEM] during control condition and during 45mmHg PPB with FCAGTs inflated to various multiples of PPB pressure***

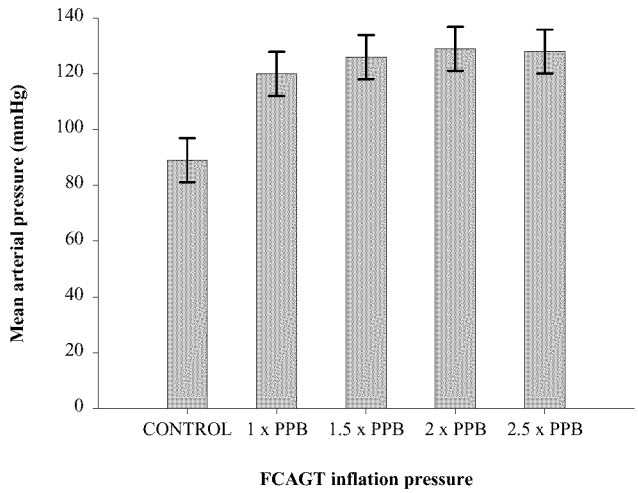

Figure 16: ***Mean arterial pressure [mean (n=6) 6 SEM] during control condition and during 45mmHg PPB with FCAGTs inflated to various multiples of PPB pressure***

Discussion

This study aimed to investigate some of the physiological effects of positive pressure breathing (PPB) in subjects wearing a counter pressure assembly that incorporated full coverage anti-G trousers (FCAGTs) inflated to various multiples of positive breathing pressures. The results of the study show that FCAGTs inflated to 1.5, 2, or 2.5 times PPB pressure facilitated maintenance of near-normal heart rate during 45mmHg, 60mmHg, and 70mmHg PPB, in addition to near-normal effective pulmonary blood flow and diffusing capacity of the lungs for carbon monoxide during 45mmHg and 60mmHg PPB (see Figures 3, 4, 13, 14, 9, 10, 11, and 12). In contrast, during PPB conditions where FCAGTs were inflated to the same pressure as PPB, heart rate increased above control levels (see Figures 3, 4, 13, and 14). In addition, cerebral blood velocity (CBV) and alveolar carbon dioxide tension ($PACO_2$) during 45mmHg and 70mmHg PPB were consistently lower than CBV and $PACO_2$ measured during control conditions (see Figures 1, 2, 5, and 6), irrespective of FCAGT inflation pressure.

The Effect of Positive Pressure Breathing on Heart Rate and Blood Pressure

The increase in heart rate during PPB when FCAGTs were inflated to the same pressure as the PPB gas indicates that normal cardiovascular function was compromised under these conditions. Data from the four subjects who successfully completed rebreathing manoeuvres during PPB suggest that the effective pulmonary blood flow was unchanged during all PPB conditions, compared to that measured during the control conditions (see Figures 9 and 10). The effective pulmonary blood flow is a direct correlate of cardiac output since, during any period of time, the output from the left side of the heart – the cardiac output – must equal the output of the right side of the heart – the effective pulmonary blood flow plus anatomical and physiological shunts via non-ventilated regions within the lungs. Thus, these findings suggest that stroke volume was compromised during PPB when FCAGTs were inflated to a pressure equal to PPB pressure.

Several investigators have illuminated the mechanism underlying an increase in heart rate during PPB. Ernsting (1966) measured intra-esophegal pressure during PPB to demonstrate that a proportion of the increased airway pressure was transmitted to the intrathoracic cavity - the proportion of airway pressure transmitted to the intrathoracic cavity being dependent on the degree of lung distension induced by PPB. Ernsting demonstrated that the increase in intrathoracic pressure induced by PPB was followed by an increase in peripheral venous pressure, accompanied by an increase in peripheral limb volume, until

peripheral venous pressure equalled intrathoracic pressure. This observation confirmed that PPB induced displacement of blood from the thoracic cavity into the peripheral veins. Direct measurement of a subsequent decline in effective right atrial pressure (right atrial pressure minus intrathoracic pressure) led Ernsting to conclude that the observed increase in heart rate during PPB was a reflex mechanism initiated to maintain cardiac output in the face of a declining venous return. In a later study, Balldin and Wranne (1980) directly measured cardiac output (by the thermodilution method) and effective right atrial pressure during PPB at 30mmHg and 70mmHg. They confirmed that an increase in heart rate during PPB followed a decrease in effective right atrial pressure and a subsequent decline in stroke volume.

Recently, Goodman et al (1994) used radionuclide ventricular cardiography to demonstrate that increased heart rate during PPB was associated with a reduced end-diastolic left ventricular volume and decreased stroke volume. In summary, increased heart rate during PPB occurs subsequent to a fall in venous return, and hence cardiac preload, which results in a reduced stroke volume in accordance with the Starling mechanism.

In the present study, therefore, the observation of an increased heart rate during PPB when FCAGTs were inflated to a pressure equal to PPB pressure suggests that in these conditions, venous return to the heart was compromised. In a recent study, Goodman et al (1995) also observed that FCAGTs inflated to the same pressure as the PPB pressure were similarly unable to facilitate maintenance of normal heart rate during PPB. In addition, Goodman et al demonstrated that the increase in heart rate during these conditions was attributable to a reduction in end diastolic left ventricular volume and a subsequent fall in stroke volume. Therefore, it is likely that FCAGTs inflated to the same pressure as PPB pressure do not completely prevent accumulation of blood displaced from the thorax at the onset of PPB in the veins of the lower limbs. Thus, increasing the extent of lower body surface area bladder coverage alone is not sufficient to abolish the adverse cardiovascular effects of PPB observed in previous studies that employed standard coverage garments inflated a pressure equal to PPB pressure (Ernsting, 1966; Ackles et al, 1978).

When FCAGT inflation pressure equalled 1.5 times, 2 times, or 2.5 times PPB pressure, heart rate during 45mmHg, 60mmHg, and 70mmHg PPB was not significantly different to heart rate during the control condition (see Figures 3, 4, 13, and 14). Presumably, increasing FCAGT inflation pressure in excess of PPB pressure reduces the compliance of the veins within the lower limbs, via an increase in local tissue pressure. Therefore, during PPB, a peripheral to central venous pressure gradient can be restored without a significant increase in the volume of blood contained within the lower limb veins, thus preventing a decrease in circulating blood volume. The findings of the present study support the results of a recent investigation that showed that normal cardiovascular function during 70mmHg PPB can be facilitated by a counter pressure assembly incorporating FCAGTs inflated to 2 times PPB pressure (Goodman et al, 1995).

Mean arterial blood pressure was consistently increased from control levels during PPB, irrespective of FCAGT inflation pressure (see Figures 7, 8, 15, and 16). The increase in systemic blood pressure during PPB is a direct effect of increased intrathoracic pressure during PPB, as described earlier.

The control of systemic blood pressure during PPB is complex, and is thought to be influenced by a number of competing factors. In normal conditions, systemic blood pressure is mediated by baroreceptors located in the aortic arch and the carotid artery. These receptors are sensitive to 'stretch', and are thus affected by changes in transmural pressure across the walls of the vessels in which they are situated. If near normal cardiovascular function is maintained during PPB with counter pressure applied to the thorax, the aortic baroreceptors are not subjected to any change in transmural pressure, as the pressure within the heart and the intrathoracic cavity are increased by the same amount. The carotid baroreceptors, however, are located in an area that is not covered by counter pressure garments, and hence, they receive a hypertensive stimulus during PPB. Presumably, the carotid baroreceptors exert a vasodilatory influence during PPB, resulting in an overall increase in MAP that is slightly lower than the increase in intrathoracic pressure induced by PPB. This assumption is supported by the observations of Gradwell (1993), who showed that MAP during PPB with equal counterpressure applied to the thorax *and* neck increases to a level significantly higher than MAP during PPB with counter pressure applied to the thorax alone.

In previous studies (Ernsting, 1966; Gradwell, 1993; Goodman et al, 1995), PPB conditions that elicited an increase in heart rate from control conditions have been associated with a lower than expected increase in MAP. Presumably, relatively lower MAP in these conditions is a reflection of the reduction in venous return to the heart and concomitant reduction in stroke volume. Other investigators, however, have reported no significant differences in the MAP response between PPB experimental conditions, even when a significant difference in the heart rate response to different PPB experimental conditions was identified (Ackles et al, 1978).

The Effect of Positive Pressure Breathing on Effective Pulmonary Blood Flow

The effective pulmonary blood flow was maintained at control levels during 45mmHg and 60mmHg PPB, irrespective of FCAGT inflation pressure. When FCAGT inflation pressure equalled PPB pressure, however, the effective pulmonary blood flow was maintained at the expense of an increase in heart rate (see Figures 9, 10, 13, and 14).

The mechanism that initiates a compensatory increase in heart rate if stroke volume is compromised during PPB is poorly understood. In normal conditions, cardiovascular control is largely mediated by inputs to the cardiovascular control centre from arterial and cardiopulmonary baroreceptors that respond to changes in systemic and intrathoracic vascular pressure changes respectively (Victor and Mark, 1976). Thus, in normal conditions, these inputs are complementary, as a decrease in central venous pressure will reduce end diastolic volume, decrease ventricular contractile force in accordance with Starling's mechanism, and hence reduce systemic arterial pressure. Complementary inputs from arterial and cardiopulmonary baroreceptors will initiate a co-ordinated response in these conditions to increase peripheral resistance, heart rate and ventricular contractility to restore systemic arterial pressure (Victor and Mark, 1976).

As described earlier, the carotid baroreceptors sense an increase in transmural pressure during PPB, and would therefore exert a vasodilatory and bradycardic influence on the circulation, in an attempt to reduce peripheral resistance and cardiac output, and hence reduce carotid artery transmural pressure. Presumably, if venous return is decreased during PPB, cardiovascular control centres in the brain must receive additional inputs that override the carotid baroreceptor input, and initiate responses that attempt to facilitate maintenance of cardiac output, via an increase in heart rate and/or ventricular contractile force. The site of the receptors responsible for these inputs must reside in the intrathoracic cavity, probably within the heart itself or the pulmonary circulation, and these inputs must respond to a decrease in central venous pressure or atrial and/or ventricular distension during diastole.

Goodman et al (1994) recently provided evidence of a coordinated compensatory response to cardiovascular insufficiency during PPB. A Radionuclide ventricular cardiography technique has enabled these investigators to demonstrate that a reduction in end diastolic left ventricular volume during 70mmHg PPB is accompanied by an increase in heart rate *and* a decrease in end systolic left ventricular volume, thus providing evidence of an increase in ventricular contractility during PPB, which must be mediated by a compensatory reflex mechanism.

The Effect of Positive Pressure Breathing on Diffusion Coefficient for Carbon Monoxide

The diffusion coefficient for carbon monoxide (K_{CO}) was maintained at control levels during 45mmHg and 60mmHg PPB, irrespective of FCAGT inflation pressure (see Figures 11 and 12). This observation suggests that the capacity for diffusive gas exchange of carbon monoxide between the alveolar gas and the pulmonary capillary blood was not compromised during PPB, at all FCAGT inflation pressures.

The capacity for diffusive gas exchange of carbon monoxide between the alveolar gas and the pulmonary capillary blood is directly correlated with the capacity for diffusive gas exchange of oxygen between the alveolar gas and the pulmonary capillary blood (Piiper et al, 1979). Therefore, in the present study, PPB did not appear to impair the mechanisms that facilitate uptake of oxygen from the alveolar gas by the pulmonary blood – an observation that has particular relevance to the application of PPB as a procedure to prevent hypoxia in the event of cockpit depressurisation at altitudes exceeding 40,000 feet.

In addition, the maintenance of a normal diffusion coefficient for carbon monoxide suggests that PPB had no significant effect on the pulmonary capillary blood volume, at all levels of FCAGT inflation. The authors have adopted the assumption that PPB had no effect on the diffusing capacity of the alveolar capillary membrane – a proposition supported by Ernsting's (1966) measurement of the effects of PPB on the pulmonary capillary blood volume using Roughton and Forster's (1957) method.

The findings of the present study are, in this respect, unexpected. During PPB with FCAGTs inflated to the same pressure as PPB pressure, heart rate was increased from control levels, suggesting a reduction in venous return, and hence a diminution of thoracic blood volume, as described earlier. Presently, there is no adequate explanation for the observed maintenance of pulmonary capillary blood volume in these conditions.

A maintained pulmonary capillary blood volume during PPB with counter pressure has, however, been observed in chronically instrumented dogs (Williams and Horvath, 1959). These investigators observed that reductions in pulmonary capillary blood volume frequently occurred only when the reduction in *total* circulating blood volume was of sufficient severity to depress cardiac output.

Ernsting (1966) observed a decreased pulmonary capillary blood volume during PPB, but there are a number of significant differences between Ernsting's methodology and the methods employed during the present investigation. The subjects in Ernsting's study wore garments that applied counter pressure to the external surfaces of the thorax and abdomen only. These conditions are known to induce a significantly greater displacement of blood from the thorax than that observed during PPB with counter pressure applied to the external surfaces of the thorax, abdomen *and* lower limbs (Ernsting, 1966). In addition, Ernsting employed the breath hold method to measure $D\mathrm{l}_{\mathrm{CO}}$, a method that may reduce cardiac output during the measurement period (Gotshall and Davrath, 1999). Therefore, cardiac output was probably significantly decreased from control values during Ernsting's measures of pulmonary capillary blood volume during PPB.

The Effect of Positive Pressure Breathing on Cerebral Blood Velocity

Initially, observation of near-normal values for a number of cardiovascular variables during 45mmHg and 60mmHg PPB when FCAGTs were inflated to 1.5 times, 2 times, or 2.5 times PPB pressure appears to contradict the observed reduction in cerebral blood velocity during 45mmHg and 70mmHg PPB at the same FCAGT inflation pressures (see Figures 1 and 2). Even in experimental conditions where FCAGT inflation pressure equalled PPB pressure, the observed increase in heart rate was almost certainly sufficient to restore a near-normal cardiac output. Other investigators who have studied the cardiovascular effects of PPB in subjects wearing modern counter pressure assemblies have reported that a moderate increase in heart rate during PPB at, or below, 70mmHg is able to sufficiently compensate for any observed reduction in stroke volume, hence ensuring maintenance of a near-normal cardiac output (Goodman et al, 1994; Goodman et al, 1995).

Therefore, it is unlikely that the observed reduction in cerebral blood velocity during 45mmHg and 70mmHg PPB seen in the present study was caused by cardiovascular insufficiency induced by PPB itself. The consistently lowered alveolar carbon dioxide tension observed during all PPB experimental conditions in the present study (see Figures 5 and 6) is, therefore, probably responsible for a large proportion of the decrease in cerebral blood velocity during PPB. A reduction in alveolar carbon dioxide tension during PPB occurs as a result of hyperventilation, even in subjects with considerable experience of PPB (Ernsting, 1966).

The significance of hyperventilation during PPB, and the associated hypocapnia, lies in the effect of a reduction in arterial carbon dioxide tension on the cerebral circulation. Hypocapnia is known to reduce cerebral blood flow (Kety and Schmidt, 1948; Markwalder, Grolimund, Seiler, Roth, and Aaslid, 1984), presumably via vasoconstriction in the cerebral circulation. Therefore, the observed decrease in CBV during PPB in the present study may have been entirely attributable to the effects of hyperventilation induced by PPB.

Determination of the Most Effective FCAGT Inflation Pressure for use during Positive Pressure Breathing for Altitude Protection

The findings of the present study suggest that FCAGTs inflated to 1.5 times, 2 times, or 2.5 times PPB pressure are able to facilitate maintenance of near-normal physiological function during 45mmHg, 60mmHg and 70mmHg PPB. In addition, the physiological responses to PPB with FCAGTs inflated to 1.5 times PPB pressure did not significantly differ to the responses observed during PPB with FCAGTs inflated to 2 times or 2.5 times PPB pressure. Therefore, if discomfort and mobility problems are to be minimised, a FCAGT inflation pressure of 1.5 times PPB pressure would appear to be the most effective solution for use during PPB for altitude protection.

Conclusions

The results of the present study suggest that FCAGTs inflated to equal PPB pressure are incapable of facilitating maintenance of near normal cardiovascular function during 45mmHg, 60mmHg, and 70mmHg PPB. Increasing the FCAGT inflation pressure to 1.5 times, 2 times, or 2.5 times PPB pressure is, however, sufficient to abolish some of the adverse effects of 45mmHg, 60mmHg, and 70mmHg PPB observed when FCAGTs are inflated to a pressure equal to PPB pressure.

The observed reduction in cerebral blood velocity during 45mmHg and 70mmHg PPB is probably a direct result of hypocapnia caused by the hyperventilation induced by PPB. The practical significance of decreased CBV during PPB for altitude protection cannot be fully assessed until the effects of PPB when combined with a hypoxic stress on CBV are accurately determined.

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