Spontaneous breathing and respiratory support of preterm infants at birth

Pas, A.B. de

CHAPTER 11

Effect of sustained inflation length on establishing functional residual capacity at birth in ventilated premature rabbits

Arjan B te Pas*[1,2], Melissa Siew[3], Megan J Wallace[3], Marcus, J Kitchen[4], Andreas Fouras[6], Robert A Lewis[5], Naoto Yagi[7], Kentaro Uesugi[7], Susan Donath[8], Peter G Davis[1], Colin J Morley[1], Stuart B Hooper[3]

[1] Neonatal Services, Royal Women's Hospital, Victoria 3053, Australia

[2] Division of Neonatology, Department of Pediatrics, Leiden University Medical Center, 2300 RC Leiden, the Netherlands

[3] Department of Physiology, [4]School of Physics, [5]Monash Centre for Synchrotron Science and, [6]Division of Biological Engineering, Monash University, Melbourne, Victoria 3800, Australia

[7] SPring-8/JASRI, Sayo, Hyogo 679-5198, Japan

[8] Murdoch Children's Research Institute, Melbourne Victoria 3052, Australia.

submitted

Abstract

The effect of inflation length on the first inspiratory volume and functional residual capacity (FRC) immediately after birth was investigated. Preterm rabbits (28 days) were randomized into 4 groups to receive a 1, 5, 10 or 20 sec inflation (SI) followed by ventilation with 5 cmH_2O PEEP. Gas volumes were measured by plethysmography and uniformity of lung aeration by phase contrast X-ray imaging for 7 minutes. The first inspiratory volume significantly ($p < 0.001$) increased with inflation duration; from a median (IQR) of 0.2 (0.1-3.1) ml/kg for 1 sec inflation to 23.4 (19.3-30.4) ml/kg for 20 sec SI. The lung was uniformly aerated and FRC and tidal volume fully recruited following 20 sec SI. A 10 sec SI caused a higher FRC ($p < 0.05$) at 7 minutes and a 20 sec SI caused a higher FRC ($p < 0.05$) at 20 sec and 7 minutes than a 1 or 5 sec SI. The mean (SD) time for 90% of the lung to aerate was 14.0 (4.1) sec using 35 cmH_2O PIP . In these rabbits, 10 and 20 sec SI increased the inspiratory volume, produced a greater FRC and a 20 sec SI uniformly aerated the lung before ventilation started.

Introduction

Many preterm infants need positive pressure ventilation during the transition to air breathing at birth to assist lung aeration and the initiation of pulmonary gas exchange. It is possible that an initial sustained inflation (SI) might overcome the long time constant of a liquid-filled lung and facilitate early gas exchange to reduce the need for intubation (1, 2). However, this procedure is not commonly used because of the risk of over-inflating and damaging the lung during the initial inflation (3). Despite this, the international guidelines on neonatal resuscitation state that an initial SI may be beneficial during stabilisation at birth (4). However, a recommended duration for the SI was not provided (4) due to a lack of evidence, as few studies have investigated the use of SIs during ventilation at birth. Although a few physiological and clinical studies have examined the effect of different durations of inflation (1, 2, 5-9), there is currently no consistent view whether it is beneficial or what duration is most appropriate

We have recently used phase contrast X-ray imaging to determine the rate and spatial pattern of lung aeration at birth in spontaneously breathing (10) and mechanically ventilated preterm rabbit pups (11). Using this technique, the entry of air into the lung and its spatial distribution can be imaged and measured breath-by-breath (12).

In this study, we have investigated the effect of SIs of different durations on the recruitment of FRC and tidal volumes from birth. We hypothesized that increasing the duration of the first inflation would increase the recruitment of FRC and tidal volume from the first breath after birth due to the longer time constant for the air/liquid interface to move into the distal airways.

Methods

Animal experiments

All animal procedures were approved by the SPring-8 Animal Care and Monash University's School of Biomedical Science's Animal Ethics Committees. Studies were conducted in experimental hutch 3 of beam line 20B2, in the Biomedical Imaging Centre at the SPring-8 synchrotron in Japan.

Experiments were performed on 6 litters of New Zealand white rabbits using 35 pups delivered at 28 days gestation (term 32 days; 28 days correlates approximately with human infants of 26-28 weeks of gestation). The does were anesthetized (Propofol; 12 mg/kg bolus, 100 mg/kg/h i.v. infusion, then isofluorane 1-2%), intubated and ventilated. The pups were sequentially delivered by hysterotomy, leaving the fetal membranes over the nose and mouth to prevent air entering the lungs. The pups were sedated (Nembutal 0.1 mg intraperitoneal), a topical anesthetic (5% xylocaine) was applied and an endotracheal tube (18 gauge plastic catheter) inserted via tracheostomy; the endotracheal tube was blocked to prevent air from entering the lung before imaging commenced. The fetal membranes were then removed, the umbilical cord ligated and cut and the pup was placed in a water-filled plethysmograph (see below). The pups were then ventilated for 7 minutes while they were simultaneously imaged. After the experiment, pups were killed by anesthetic over-dose.

Plethysmography

Lung gas volume changes were measured using water-based plethysmography (11). The pup was placed in the plethysmograph (head out), which consisted of a sealed water-filled (warmed to 37°C) perspex chamber open to the atmosphere via a water column. The pup's head was located outside the chamber and a rubber diaphragm formed a water-tight seal around the pup's neck. The increase in lung volume caused by lung aeration displaced water from the chamber into the water column and the resulting increase in pressure was recorded electronically using a computerised data acquisition system (Powerlab, ADInstruments Sydney, Australia). The plethysmograph was calibrated before each experiment by measuring the pressure change caused by injecting a known volume of water (1 mL) into the sealed chamber. We recorded FRC, initial volume, tidal volume, minute volume, inspiratory and expiratory times, airway pressure, ventilator rate and gas flow.

Mechanical ventilation

A purpose-built small animal ventilator was used to ventilate pups with air in a time cycled, pressure limited mode (positive pressure ventilation, PPV). Ventilation commenced with a PIP of 35 cmH_2O and an inspiration time of 1, 5, 10 or 20 seconds, depending on the group (see below). After the first inflation, pups were ventilated with a fixed inspiration and expiration time (rate 24/min, 1:1.5 inspiration: expiration ratio), starting with a peak inspiratory pressure of 35 cm H_2O which was then adjusted (increased or decreased by 2 cmH_2O per minute) to generate a tidal volume of about 10 ml/kg, PEEP was set at either 0 or 5 cm H_2O.

Protocol

The pups were randomly allocated to one of the four ventilation groups:
Group 1: PPV from the start (*No SI*).
Group 2: Inflation for 5 s followed by PPV (*5 SI*).
Group 3: Inflation for 10 s followed by PPV (*10 SI*).
Group 4: Inflation for 20 s followed by PPV (*20 SI*).

Phase contrast X-ray imaging

Phase contrast X-ray imaging was used to demonstrate the effect of SI duration on the rate and spatial pattern of lung aeration. Details describing the imaging and analytical procedures have been reported previously (10, 13, 14). The X-ray energy used was 24 keV, the detector

(Hamamatsu, C4742-95HR) was located 2.0 m down stream of the pups and a short exposure time (50 msec) and a relatively long inspiration time (1 sec) were used to minimise motion blur. Image acquisition was triggered by the ventilator at the onset of inspiration, which triggered a sequence of images at 300 msec intervals. A shutter, located upstream from the rabbit pup, prevented radiation exposure between image acquisitions and the timing of each image acquisition was recorded digitally in unison with the plethysmograph recording.

During the 20 sec SI, the rate of increase in air volume within different regions of the lung was measured by dividing the images into quadrants and measuring the air volume in each quadrant (at end-expiration or during the SI) using a phase retrieval analysis (11). This analysis has recently been validated (11) and uses extra-thoracic landmarks to track pup movement between consecutive images to ensure that the relative amount of lung in each quadrant does not change over time. As the amount of lung (thus potential air volume) varies between quadrants, the air volume of each quadrant at each time point was expressed as a percentage of the maximum volume achieved in that quadrant following complete lung aeration.

Analysis

The first inflation volume was calculated by measuring the gas volume at the end of the first inflation. FRC was defined as the volume of air remaining in the lung at end expiration and Vt recruitment refers to the gradual increase in Vt for a given pressure gradient.

FRC was calculated at 20 sec, 1, 3 and 7 min by determining the average FRC following four consecutive inflations at these times. FRC was assumed to be zero at the start of ventilation. To compare the first inflation volume and FRC between groups, a one-way ANOVA followed by a Tukey HSD post-hoc test was used. Significance was defined as $p<0.05$ and data were analysed using SPSS software (SPSS for windows, version 15.0, 2006, Chicago, IL).

Results

Twenty-six of 31 pups were delivered alive and studied. Two pups were excluded because of equipment malfunction. None of the pups developed a pneumothorax, which was verified using imaging. The average pup weight (SD) in each group was: group 1 (no SI) 34.4 (2.4) g, group 2 (5 SI) 40.1 (5.4) g, group 3 (10 SI) 36.2 (2.1) g, Group 4 (20 SI) 37.9 (2.3) g. Each group contained 6 pups.

First inflation volume

Compared to the volume achieved with a normal 1 second inflation (no SI) (median (IQR)), a sustained inflation of 10 and 20 seconds, but not 5 seconds, significantly increased the average volume of the first inflation (table 1, figures 1 and 2). Furthermore, the volume achieved by a 20 second SI was significantly greater than that achieved by a 10 sec SI ($P < 0.05$) and did not result in either total lung or regional over-inflation (figures 1, 2 and 4e-h). Indeed, the gas volume achieved by a 20 second SI (23.4 (19.3 - 30.4) ml/kg) was similar to the end-inflation gas volume measured during the subsequent ventilation period (figure 1), when the pups had recruited a FRC of ~13ml/kg and were ventilated to reach a

Table 1. Median (IQR) FRC at each time for each group.
FRC= Functional residual capacity; SI = Sustained inflation.

Group	First inspiratory volume (ml/kg)	FRC 20 s (ml/kg)	FRC 1 min (ml/kg)	FRC 3 min (ml/kg)	FRC 7 min (ml/kg)
No SI	0.2 (0.1 – 3.1)	7.7 (2.8 – 11.7)	9.7 (9.0 – 13.6)	9.6 (7.3 – 12.0)	8.9 (6.8 – 13.0)
5 SI	4.5 (3.6 – 13.8)	6.0 (2.2 – 10.8)	10.2 (3.4 – 11.3)	12.1 (3.4 – 12.4)	12.3 (2.4 – 12.7)
10 SI	10.4 (9.0 – 13.4) *	8.4 (5.9 – 10.5)	11.2 (10.5 – 13.3)	12.8 (11.7 – 14.3)	13.8 (12.0 – 14.8)*
20 SI	23.4 (19.3 – 30.4)*	12.7 (11.5 – 14.2)*	12.5 (9.2 – 13.1)	12.7 (7.3 – 14.0)	12.4 (7.6 – 15.3)*

* indicates significant difference ($P < 0.05$) compared to no sustained inflation (No SI).

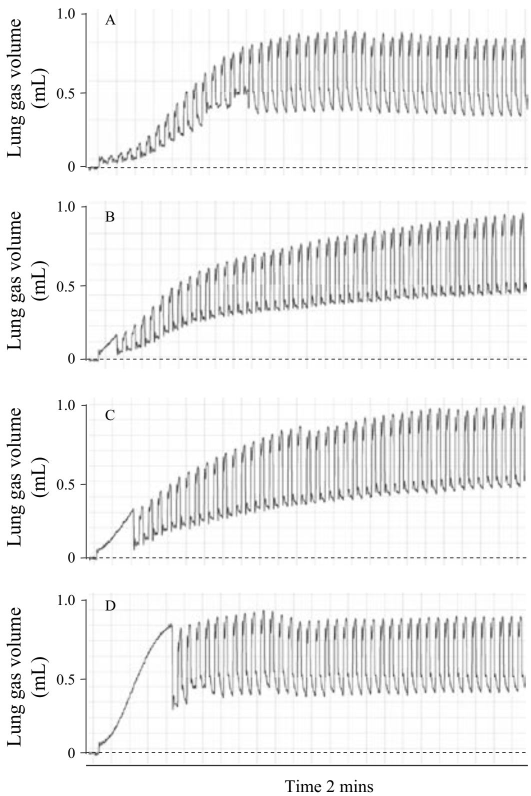

Figure 1. Plethysmograph recordings of lung gas volumes from newborn rabbit pups delivered preterm and ventilated from birth. The first inflation was either not sustained (no SI; ie. 1 sec in duration) (**A**), or sustained for 5 (**B**), 10 (**C**) or 20 (**D**) seconds. Pups were then ventilated initially with a positive end-expiratory pressure (PEEP) of 5cmH_2O and peak inflating pressure (PIP) of 35cmH_2O, changing to achieve a tidal volume of ~10ml/kg.

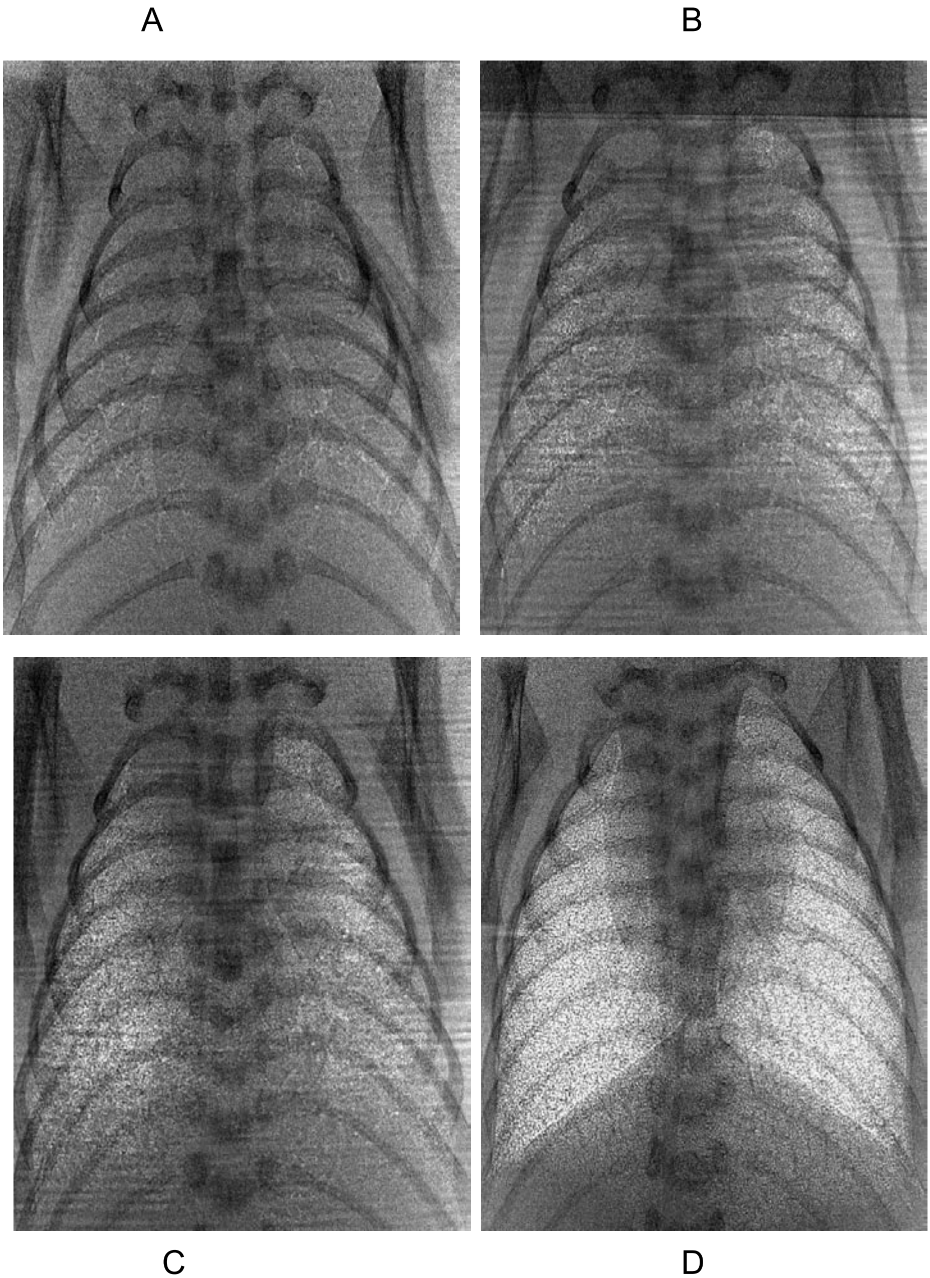

Figure 2. Phase contrast X-ray images acquired at the end of the first inflation after birth in prematurely delivery newborn rabbit pups. The first inflation was either not sustained (No SI; ie. 1 sec in duration) (**A**) or sustained for 5 (**B**), 10 (**C**) or 20 (**D**) seconds.

Vt of ~10ml/kg (figure 1). Furthermore, during the 20 sec SI, although the upper (rostral) regions of the lungs aerated faster than the lower (caudal) regions, resulting in significantly greater volumes between 6-13 secs of the SI (figure 3), relative air volumes were similar in all regions by 20 sec. This indicates that, during a SI, the increase in air volumes in the aerated regions is eventually slow, allowing the other regions to "catch-up" (figure 3).

The phase contrast X-ray images and movie sequences (figures 4 and 5) clearly demonstrate that the spatial pattern of lung aeration is not uniform and that a finite period (~15 secs; figure 3) is required before the lung is uniformly aerated. As determined from the image sequences, a 20 sec SI completely aerated the lungs in 5 of 6 pups, before the onset of positive pressure ventilation (figures 1 and 4e-h). However, a 10 sec SI completely aerated

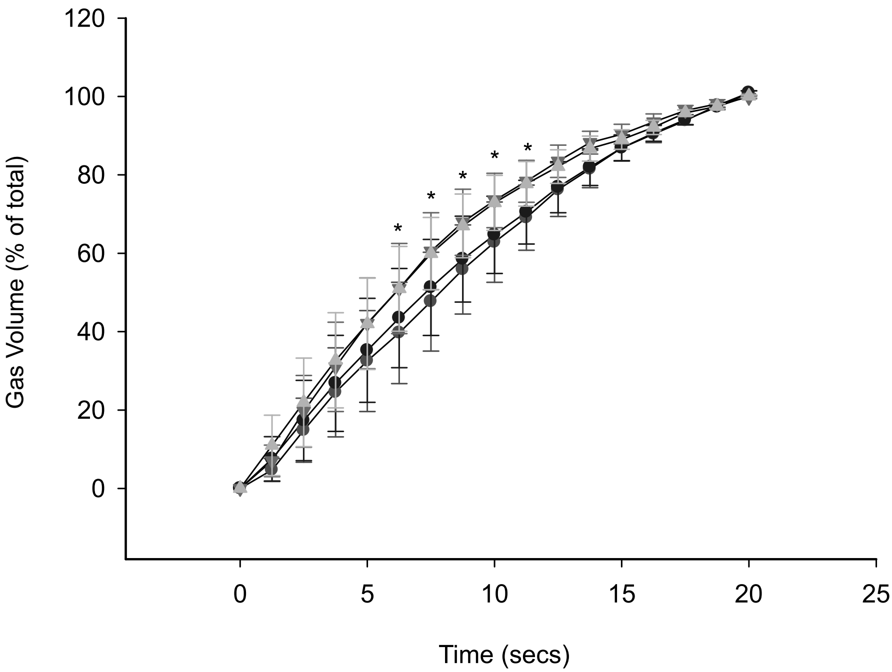

Figure 3. The increase in air volume within different regions of the lung was measured during the 20 sec SI, by dividing the phase contrast X-ray images into quadrants; (●) lower left (left caudal region); (●) lower right (right caudal region); (▼) upper left (left rostral region) and (▲) upper right (right rostral region). Air volumes in each quadrant were measured using a previously described and validated phase retrieval analysis. As the amount of lung (thus potential air volume) varies between quadrants, the air volume of each quadrant was expressed as a percentage of the maximum volume achieved in that quadrant to compare between regions. The relative air volume was significantly greater in both upper (rostral) (▼, ▲), compared with both lower (caudal) (●, ●), regions as indicated by the asterisks. Values are mean ± SEM.

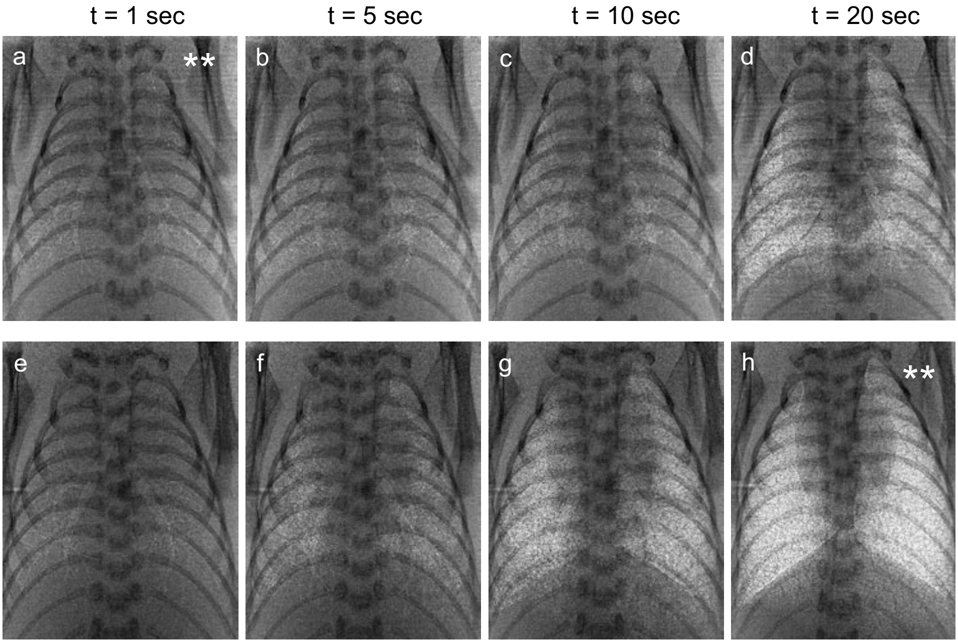

Figure 4. Phase contrast X-ray images acquired at 1 (a & e), 5 (b & f), 10 (c & g) and 20 (d & h) seconds after birth in prematurely delivery newborn rabbit pups ventilated from birth. The first inflation was either not sustained (1 sec in duration; top panel; images a, b, c & d) or sustained for 20 seconds (bottom panel; images e, f, g & h). The double asterisks (**) indicate images acquired at the end of the first inflation. Images acquired after the first inflation were acquired at end-inspiration.

the lungs in only 1 of 6 pups, whereas no pups had completely aerated their lungs following a 5 sec SI (figures 1 and 5a-d).

Assuming the pressure gradient (35 cmH_2O) remained constant throughout the SI, the mean maximum lung inflation rate and minimum resistance for moving the air/liquid interface into the distal airways, was calculated. During the 20 sec SI, the mean lung inflation rate was 3.5 (3.5) mL/kg/sec (range 1.6 to 9.6 mL/kg/sec) whereas after aeration was complete, lung inflation rates during PPV were more than 20 fold higher (81.7 (32.1) mL/kg/sec), despite a lower mean pressure gradient (26 (4.2) cmH_2O). The resistance to lung inflation was 25.3 (29.6) cmH_2O/(mL/kg/sec) during the 20 sec SI whereas during PPV in the same pups, the resistance was nearly a 100 fold lower (0.38 (0.08) cmH_2O/(mL/kg/sec)). The mean time taken to reach 90% (21.5 (5.5) mL/kg) of the 20 sec SI volume was 14.0 (4.1) secs and also varied considerably between pups (8.6 secs to >20 secs).

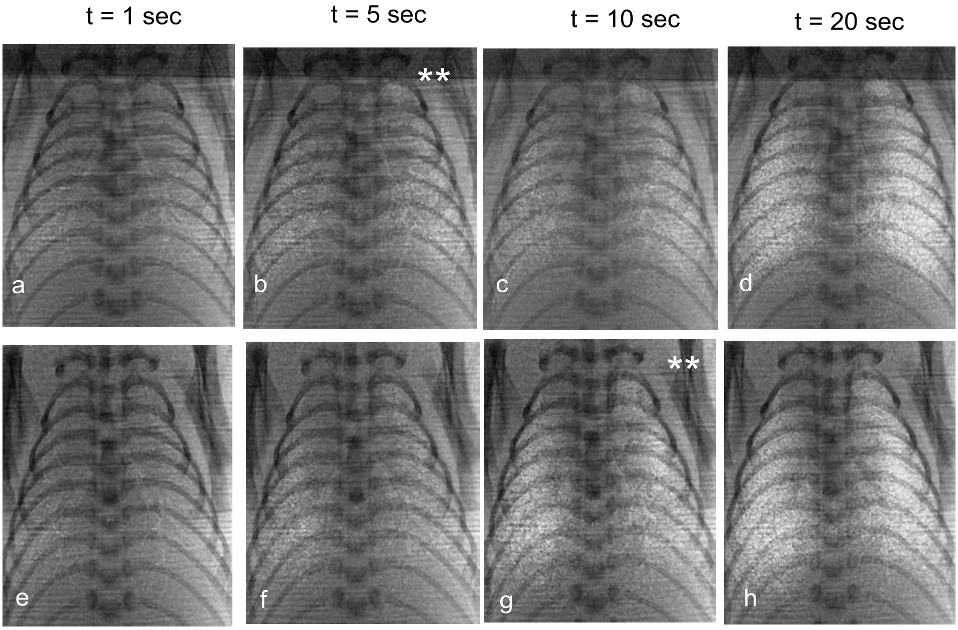

Figure 5. Phase contrast X-ray images acquired at 1 (a & e), 5 (b & f), 10 (c & g) and 20 (d & h) seconds after birth in prematurely delivery newborn rabbit pups ventilated from birth. The first inflation was sustained for either 5 seconds (top panel; images a, b, c & d) or 10 seconds (bottom panel; images e, f, g & h). The double asterisks (**) indicate images acquired at the end of the first inflation. Images acquired after the first inflation were acquired at end-inspiration.

FRC

The median (IQR) FRC of each group at each time point is shown in table 1 and figure 6. Compared to a 1 sec inflation (No SI), a 5 sec SI did not result in a significantly higher FRC at any of the time points measured. However, a 10 sec SI resulted in a significantly higher FRC at 7 minutes after birth and a 20 sec SI resulted in a significantly higher FRC at 20 sec and 7 minutes after birth.

Tidal volume

Following a 20 seconds SI, the tidal volume (Vt) did not increase after the first inflation (figures 1 and 7). As a result, over the first 7 inflations, the mean (SD) expired tidal volumes in the 20 seconds SI group (14.1 (5.1) mL/kg) group were significantly greater than the first 7 inflations in all other groups (No SI, 2.0 (1.8) ml/kg, $P < 0.05$; 5 SI, 4.9 (3.8) ml/kg, $P < 0.001$; 10 SI, 6.6 (2.3) ml/kg, $P < 0.05$). Pups receiving a 10 sec SI gradually recruited Vt over the first 10 breaths. They had significantly ($p<0.05$) larger Vt than pups receiving a 5 sec SI or no SI (figures 1 and 7). Pups not receiving a SI had the slowest tidal volume recruitment.

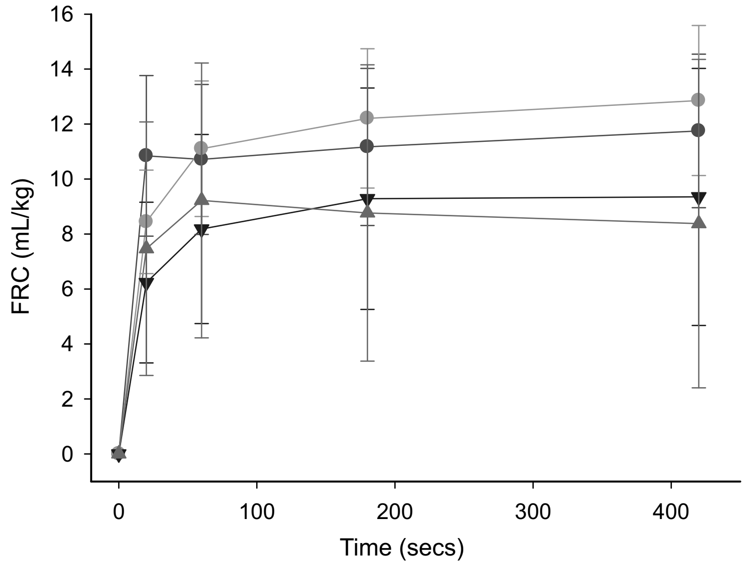

Figure 6. Mean FRC increase with time. Values were derived from prematurely delivery preterm rabbit pups ventilated from birth. The first inflation was either not sustained (1 sec in duration; ▲) or sustained for 5 (▼), 10 (●) or 20 (●) seconds. ▲, ▼, ●, ● = points of measurement at T= 20 seconds, 1, 3, 7 minutes. Values are mean ± SEM.

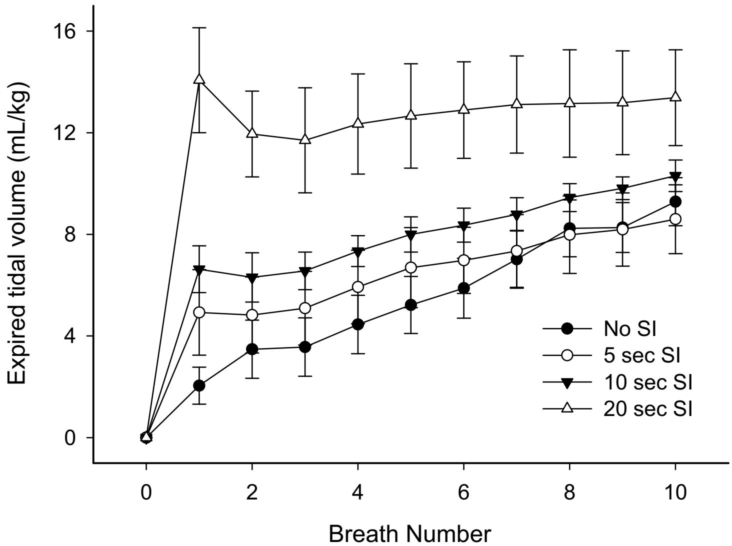

Figure 7. Tidal volume recruitment in prematurely delivered newborn rabbit pups ventilated from birth. The first inflation was either not sustained (1 sec in duration; No SI)) or sustained for 5 (5 SI), 10 (10 SI) or 20 (20 SI) seconds. Values are mean ± SEM.

Discussion

This study has shown that an initial sustained inflation of 20 sec significantly increased the volume of air entering the lung during the first inflation in preterm rabbit pups ventilated from birth using PPV. The phase contrast X-ray images demonstrated that, although the spatial pattern of lung aeration is not uniform during the first sustained inflation, by the end of 20 sec, the lung had completely and uniformly aerated before the onset of PPV. Our data also demonstrated that lung aeration requires a finite time, occurring at a maximum rate of 3.5 (3.5) mL/kg/sec and results in 90% lung aeration within 14.0 (4.1) seconds using an inflating pressure of 35cmH_2O. Furthermore, increasing the duration of the SI from 5 to 10 to 20 sec, significantly increased the FRC at 20 sec and both a 10 and 20 sec SI resulted in a small, but significant increase in FRC at 7 minutes compared to no SI. The phase contrast images show that a 20 sec SI progressively aerated the entire lung without causing over-expansion of regions that rapidly aerated (upper lobes), while slower regions continued to aerate (lower lobes). Over-expanded, regions of the lung bulge out between the ribs and can be clearly seen in the phase contrast images (unpublished observations). However, in figure 4h (acquired at the end of a 20 second SI), gaps between the ribs and the edge of the lung are clearly visible.

In contrast to a 10 and 20 sec SI, almost no gas entered the lung during a 1 sec inflation in pups not receiving a SI (figures 1, 2 & 4). Furthermore, although the application of PEEP facilitated the rapid accumulation of an FRC, during a 1 sec inflation, tidal expansion of the lung was restricted to aerated regions (figure 4). In contrast, tidal expansion of the lung after a 20 sec SI occurred evenly throughout the lung and was comparable to the volume observed after the first breath of spontaneously breathing term rabbit pups.(15).

The inspiratory volume measured during the first breath in healthy term infants were in a similar range to that observed following a 10 sec SI (2, 16-18). Vyas et al, found a strong positive correlation between the first inspiratory volume and the FRC reached after the first breath (16), which is consistent with the findings of this study (figures 1,2,4 &5). The same inspiratory volume was achieved in asphyxiated infants when an initial inflation of 5 seconds was given (2), but not with standard ventilation (19). In our study, because the lung was fully recruited after the 20 sec SI, the pressures used for subsequent inflations were initially too large, resulting in a Vt of ~12mL/kg. Despite reducing the PIP to 26 (4.2) cmH_2O, the Vt remained high, indicating that lung compliance was continuing to increase throughout this period (figure 7).

The FRC measured following the 10 or 20 second initial SI were in the same range as the FRC measured in spontaneously breathing term rabbit pups (10-20 ml/kg) over the same time period (15). This could explain why, in clinical studies, a 10 to 20 SI was more successful in improving gas exchange than a 5 second SI (5, 7-9).

Very preterm infants commonly have problems clearing their airways of liquid at birth. When respiratory support is needed, our results indicate that an initial SI would allow more air to enter the lung before the start of PPV (2, 9). The first breath of spontaneously breathing infants is characterised by a long and deep inspiration followed by a prolonged expiratory phase, which can incorporate expiratory braking manoeuvres (20, 21). During the 20 sec SI, an initial pressure gradient of 35cmH_2O produced a maximal gas flow rate into the lung (lung inflation rate) of only 3.5 (3.5) mL/kg/sec (mean (SD)), compared with 81.7 (32.1) mL/kg/sec during PPV. This indicates that the resistance for moving the air/liquid interface from the proximal into the distal airways during the first inflation is very high (~100 fold higher than during PPV) and that several seconds are required to overcome this resistance and achieve an adequate lung volume for a given inflating pressure. Given the large viscosity difference between air and liquid, it is not surprising that resistance to the first inflation is so much greater than similar inflations following lung aeration.

The high resistance and low flow rates during the first inflation, clearly indicate that inflation times of a second or less are likely to be insufficient to achieve an adequate lung gas volume in an apnoeic animal. This is evident in the phase contrast X-ray images which demonstrated that following a 1 sec inflation, no air entered the distal gas exchange regions of the lung (figures 2 & 4). Some regions were aerated by a 5 sec SI and the numbers of regions were increased further by a 10 sec SI, whereas the lung was fully aerated following a 20 sec SI. These observations are supported by the finding that the mean time taken to aerate 90% of the lung during a SI with an inflating pressure of 35cmH_2O was 14.0 (4.1) secs. However, this time varied considerably between individuals and will be determined by the initial pressure gradient. As the pressure gradient increases, the time constant for complete lung aeration will obviously decrease, but the possibility of over-expansion in lung regions aerating first is likely to be high. Thus, lower pressures and a longer first inflation time would appear preferable.

Although a SI of 20 seconds increased the FRC created at the onset of tidal ventilation, the beneficial effect of a SI on FRC rapidly decreased with increasing ventilation time. As lung gas volume can be lost very quickly in these immature pups in the absence of PEEP, it is not surprising that using PEEP during PPV is more important for maintaining FRC than an initial SI. As all groups were ventilated with PEEP this explains why the difference in FRC observed between groups when measured after 7 minutes of ventilation was small. In the absence of PEEP, we have demonstrated only a very small FRC was achieved with a 20 sec SI, indicating that an initial SI should always be combined with the application of PEEP (9).

The FRC varied markedly between individuals which limited our ability to detect differences between groups. This large variability most likely results from differences in lung maturity between pups. However, it is interesting that the variation in FRC was markedly less at one minute (table 1, figure 6) in pups receiving a 20 sec SI than in all other groups. It is possible that a 20 sec SI at 35 cm H_2O was enough to overcome all the different factors that contribute to the time constant for lung aeration, leading to less variation in FRC. This suggestion is consistent with the finding that the time taken to achieve 90% lung aeration varies considerably (8.6 to >20 sec), but with most (5 of 6) pups fully aerating their lungs within 20 sec.

We used ventilated preterm rabbit pups to demonstrate the principles of how initial inflations of different durations affect FRC, tidal volumes and the uniformity of lung aeration. Although very preterm infants resuscitated under different circumstances (e.g. in a horizontal position), may have partially aerated lungs before ventilation starts due to spontaneous breathing, we believe that the principles displayed in this study are likely to apply to preterm infants. Indeed, the high viscosity of liquid, compared to air, will always increase the resistance to lung inflation in liquid-filled versus air-filled airways, no matter what the species. Thus, a SI inflation of sufficient duration will over-come the different time constants, caused for example by different sized airways, allowing more uniform aeration before PPV begins. On the other hand, if the lung is only partially aerated, during PPV air will preferentially enter and inflate aerated regions because air-filled airways have a much (100 fold) lower resistance than liquid-filled airways. In liquid-filled regions, the air/liquid interface will move distally only after the pressure in the aerated regions exceeds the pressure gradient required to overcome the resistance to liquid movement. If the inflation time is short (<1sec), the airway pressure will only exceed the required pressure briefly during inspiration, thereby greatly increasing the time and number of inflations required to fully aerate and recruit the lung. This contention is supported by the finding that for a given inflating pressure, tidal volumes recruit more slowly in the absence of a SI and that increasing the duration of the SI increases the rate of lung recruitment (figure 7).

In conclusion, during positive pressure ventilation with PEEP after birth, increasing the duration of the initial inflation to 10 or 20 seconds, increased the gas volume entering the lung, allowing ventilation of the distal gas exchange regions from the first inflation. The results demonstrate that uniform lung aeration requires a finite period of time due to the long time constant caused by the high resistance for the air/liquid interface to move through the airways. As a result, in ventilated preterm rabbit pups, a mean initial sustained inflation of 14.0 (4.1) secs is required to mostly (90%) aerate the lungs. Although we measured a larger FRC at 7 minutes with a SI of 10-20 seconds, the effect of a SI on FRC rapidly decreases with increasing ventilation time, indicating that the application of PEEP is also important.

Reference List

1. Hird MF, Greenough A, Gamsu HR 1991 Inflating pressures for effective resuscitation of preterm infants. Early Hum Dev 26:69-72
2. Vyas H, Milner AD, Hopkin IE, Boon AW 1981 Physiologic responses to prolonged and slow-rise inflation in the resuscitation of the asphyxiated newborn infant. J Pediatr 99:635-639
3. Bjorklund LJ, Ingimarsson J, Curstedt T, John J, Robertson B, Werner O, Vilstrup CT 1997 Manual ventilation with a few large breaths at birth compromises the therapeutic effect of subsequent surfactant replacement in immature lambs. Pediatr Res 42:348-355
4. 2006 The International Liaison Committee on Resuscitation (ILCOR) consensus on science with treatment recommendations for pediatric and neonatal patients: neonatal resuscitation. Pediatrics 117:e978-e988
5. Harling AE, Beresford MW, Vince GS, Bates M, Yoxall CW 2005 Does sustained lung inflation at resuscitation reduce lung injury in the preterm infant? Arch Dis Child Fetal Neonatal Ed 90:F406-F410
6. Klopping-Ketelaars WA, Maertzdorf WJ, Blanco CE 1994 Effect of sustained inflations applied directly after cord clamping on lung function in premature newborn lambs. Acta Paediatr 83:1017-1021
7. Lindner W, Hogel J, Pohlandt F 2005 Sustained pressure-controlled inflation or intermittent mandatory ventilation in preterm infants in the delivery room? A randomized, controlled trial on initial respiratory support via nasopharyngeal tube. Acta Paediatr 94:303-309
8. Lindner W, Vossbeck S, Hummler H, Pohlandt F 1999 Delivery room management of extremely low birth weight infants: spontaneous breathing or intubation? Pediatrics 103:961-967
9. te Pas AB, Walther FJ 2007 A randomized, controlled trial of delivery-room respiratory management in very preterm infants. Pediatrics 120:322-329
10. Hooper SB, Kitchen MJ, Wallace MJ, Yagi N, Uesugi K, Morgan MJ, Hall C, Siu KK, Williams IM, Siew M, Irvine SC, Pavlov K, Lewis RA 2007 Imaging lung aeration and lung liquid clearance at birth. FASEB J 21:3329-37
11. Kitchen MJ, Lewis RA, Morgan MJ, Wallace MJ, Siew ML, Siu KK, Habib A, Fouras A, Yagi N, Uesugi K, Hooper SB 2008 Dynamic measures of regional lung air volume using phase contrast x-ray imaging. Phys Med Biol 53:6065-6077
12. Kitchen MJ, Pavlov KM, Hooper SB, Vine DJ, Siu KK, Wallace MJ, Siew ML, Yagi N, Uesugi K, Lewis RA 2008 Simultaneous acquisition of dual analyser-based phase contrast X-ray images for small animal imaging. Eur J Radiol [Epub ahead of print]
13. Lewis RA, Yagi N, Kitchen MJ, Morgan MJ, Paganin D, Siu KK, Pavlov K, Williams I, Uesugi K, Wallace MJ, Hall CJ, Whitley J, Hooper SB 2005 Dynamic imaging of the lungs using x-ray phase contrast. Phys Med Biol 50:5031-5040
14. Kitchen MJ, Paganin D, Lewis RA, Yagi N, Uesugi K, Mudie ST 2004 On the origin of speckle in x-ray phase contrast images of lung tissue. Phys Med Biol 49:4335-4348
15. Lachmann B, Grossmann G, Nilsson R, Robertson B 1979 Lung mechanics during spontaneous ventilation in premature and fullterm rabbit neonates. Respir Physiol 38:283-302
16. Vyas H, Field D, Milner AD, Hopkin IE 1986 Determinants of the first inspiratory volume and functional residual capacity at birth. Pediatr Pulmonol 2:189-193
17. Vyas H, Milner AD, Hopkins IE 1981 Intrathoracic pressure and volume changes during the spontaneous onset of respiration in babies born by cesarean section and by vaginal delivery. J Pediatr 99:787-791
18. Saunders RA, Milner AD 1978 Pulmonary pressure/volume relationships during the last phase of delivery and the first postnatal breaths in human subjects. J Pediatr 93:667-673
19. Boon AW, Milner AD, Hopkin IE 1979 Lung expansion, tidal exchange, and formation of the functional residual capacity during resuscitation of asphyxiated neonates. J Pediatr 95:1031-1036
20. Karlberg P, Cherry RB, Escardo FE, Koch G 1962 pulmonary ventilation and mechanics of breathing in the first minutes of life, including the onset of respiration. Acta Paediatr Scand 51:121-136
21. Mortola JP, Fisher JT, Smith JB, Fox GS, Weeks S, Willis D 1982 Onset of respiration in infants delivered by cesarean section. J Appl Physiol 52:716-724