Lung function in awake healthy infants: the first five days of life

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ABSTRACT: Our main aim was to determine an appropriate time for lung function measurements in infants, prior to environmental influences upon their respiratory tract.

Tidal flow-volume loops, respiratory system compliance (Crs) and resistance (Rrs) (single breath passive occlusion technique) were measured in 24 healthy, awake infants, at one hour and on the following four days of life to investigate variability and reproducibility over time. Possible differences in lung function were sought between the 12 vaginally-delivered and 12 Caesarean section-delivered infants.

Tidal volumes increased each day, but significantly so only from Day 0 to Day 1. The expiratory flow-time ratios (time to reach peak expiratory flow to total expiratory time (T_{EPI}/T_{TOT}) and tidal expiratory flow at 75% to peak flow (TTE_{75}/PTEF)) and expiratory flow-volume ratio (volume to reach peak expiratory flow to total expiratory volume (V_{PEF}/V_{TOT})) were significantly smaller on Day 1 than Day 0, but did not change significantly thereafter. Crs and Rrs were lower on Day 0 than later. Intra-individual variation remained stable for tidal flow-volume parameters throughout the study, but was significantly higher during Day 0 and Day 1 for Crs and Rrs. There were no significant differences related to mode of delivery of the infant.

We conclude that, for epidemiological purposes, tidal lung function parameters may be measured from Day 2 to Day 4, and that they are not influenced by mode of delivery of the infant.

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Epidemiological studies concerning the development of childhood asthma may benefit from lung function measurements in newborn infants before environmental factors have exerted an impact upon their respiratory tract. However, the methods available have, until now, usually depended on the infant being sedated or in deep sleep [1]. Recently, it has been shown [2] that measurements of tidal flow-volume (TFV) parameters and passive exhalation can be performed in awake infants, and with less influence by the testing procedure than when performed during sleep.

With the widespread use of lung function testing in neonates, there is concern about standardization of the measurements regarding methodology, intra-individual variation over time [1], and reproducibility of measurements. Further studies of pulmonary physiology in healthy infants in the awake state has also been requested [3]. Furthermore, studies have demonstrated a tendency towards lower tidal volumes at 2 h of life in infants delivered by Caesarean section (CS) compared to normally-delivered infants [4, 5]. This difference should be abolished by approximately 6 h of life, and is probably due to a slower resorption of pulmonary fluid in CS-delivered infants [6, 7].

The main aim of the present study was to determine the appropriate time for measurements of TFV loops and passive respiratory mechanics during the first few days of life in awake infants. Therefore, the study set out to define the variability and reproducibility of the parameters by serial measurements in awake healthy infants. We also wanted to determine whether differences in lung function related to mode of delivery could be detected in awake infants with the methodology used.

Subjects

The first 26 eligible newborn infants of mothers with normal pregnancies were included, after informed consent from the parents. Fourteen infants were delivered vaginally and 12 infants were delivered by elective CS for maternal or mechanical reasons. Inclusion criteria were: vaginal delivery without serious complications, or elective CS due to causes not related to the health of the baby; Caucasian infants of minimum 37 full weeks gestational age; Apgar score of at least eight at 1 and 5 min; no signs of respiratory or other disease at one hour of age. Two infants were excluded (both vaginally-delivered), one because of respiratory problems after two days, and the other due to suspected inherited disease. Thus, 12 healthy infants were tested in each group.

Mean gestational age for all infants was 39.6 (39.1–40.1, 95% confidence interval) weeks, mean length was 50.1 (49.4–50.8) cm, and mean birth weight was 3.49 (3.3–3.7) kg. The infants delivered by CS had significantly lower
gestational age of 39.0 (38.4-39.7) weeks (p<0.01) than the vaginally-delivered infants (40.2 (39.6-40.8) weeks), but they did not differ significantly in birth length or weight.

One test was missed on Day 1 and one on Day 2 (Day 0 being the day of delivery), and one infant was not tested on Day 2 and 3, due to phototherapy in the neonatal ward in a different building.

**Methods**

**Procedure**

All infants were tested as close to one hour of life as possible (55–90 min at the start of measurements), and then at approximately the same time of day for the next 4 days, mainly between 9 a.m. and 2 p.m. Measurements were performed as the infants were quietly awake, (eyes open during parts of the test, responding to stimulation with bodily movement and displaying active limb movement without stimulation). Thus, feed (breast feeding) was given from 5 min to 3 h prior to testing. The parents were present during at least one of the tests. The infants were positioned in the same semi-recumbent manner during all tests.

**Measurements**

Measurements of TFV loops and single breath passive exhalation parameters were performed with the Sensormedics 2600 system. This system consists of an IBM-PS2/50Z (80286) computer, with an outboard microprocessor controlled (8085) analogue-to-digital conversion module. The module is a proprietary design with 15 channels for conversion, multiplexed through three 14-bit D/A's, which perform digital offset, range and conversion, at a speed limited to less than 10 µs per point in track mode.

Flow was measured using a pneumotachograph (8311 series, Hans Rudolph, Missouri, USA), with a flow range of 0–10 l/min. The transducer system measured flow with the use of a screen pneumotachograph (Hans Rudolph) and a Validyne differential pressure transducer (DP-250 transducers) (commercial versions of the MP-45) at ±2 cmH₂O and ±100 cmH₂O, respectively. Volume was derived by the digital integration of the flow signal. As there was no analogue integrator, the only drift in the volume signal may have occurred as a result of a flow offset. Volume derivation from the flow signal occurred at a sampling frequency of 256 samples·s⁻¹, so that no volume loss occurred at any flow within the range of the pneumotachograph and at the volume resolution specification.

The pneumotachograph was fitted to a close-fitting face mask (infant size) with an air inflated cuff to ensure that no leaks occurred (Vital signs inc.). Dead space of the system was 2.4 ml, and that of the face mask was approximately 8.5–11 ml. Calibration of the flow and volume signals was performed with a known volume delivered by a precision syringe (Hans Rudolph). As a known volume was passed through the pneumotachograph, and as volume was integrated from the flow signal, any error in volume had to be directly related to the scaling of the flow signal. The flow signal gain was digitally adjusted by the computer, to attain the correct integral.

**Signal processing**

Additionally, there was a 128 point linearization correction table, divided between 64 point expiratory flow and 64 point inspiratory flow set. Each 64th of the flow range had a correction factor, to linearize the system to be within the ±3% specification for flow and volume. This linearization corrected for both a linearity and asymmetry within the entire pneumotachograph, tubing, transducer and electronic system. The linearization was accomplished by pushing precision volumes through the pneumotachograph at the full range of flows. The computer system then calculated the correction factors for each 64th of the full range of the pneumotachograph, separately for inspiration and expiration.

As there was no analogue integrator, the difference between integration drift and leak was determined by taking the mask off the infant's face. Without flow through the mask, if the volume signal displayed on the monitor continued to rise or fall, then drift was evident.

The ratio of time until peak flow to total expiratory time (TPE/TPE) was calculated by separate measurements of the time to peak expiratory flow and total expiratory time, using the computer. These measurements were performed at a sampling frequency in excess of 250 s⁻¹. The volume until peak flow to total expiratory volume (VPE/VPE) was calculated, using the computer to sort through the flow and volume pairs to find the highest flow. The volume exhaled to the point of peak flow was calculated as a percentage of the total exhaled volume.

Respiratory system mechanics were measured, using the single breath, passive occlusion technique. Following several breaths to establish a stable baseline, automatic occlusion of the airway was initiated at end inspiration with the system's pneumatic slide valve, and alveolar pressure (P₀) was recorded. The baseline was determined by the end-expiratory level of each breath visualized first during real time volume and flow to time trace, and subsequently by a stored picture with volume to time trace. Acceptance, or rejection, of the curve was performed manually if there was a visual drift in the baseline [2], but no mathematical acceptance limit was defined. Occlusion was maintained until relaxation of the respiratory system against the shutter and equilibration of the alveolar and airway pressure was verified by the computer recording a plateau pressure within ±0.125 cmH₂O for 100 ms. The sampling frequency (256 Hz) and resolution of the airway pressure signal (0.025 cmH₂O) enabled assurance that the plateau was stable for 25 consecutive sample data points.

The passive exhalation flow-volume loops obtained upon slide valve opening, were stored and used for calculation. A linear segment, late in the decelerating flow-volume curve, was selected and a least squares best fit line was drawn and extended to cross the volume axis at zero flow and the flow axis at zero volume. Respiratory system compliance (Crs) was calculated from the volume intercept and plateau pressure, using the formula: 

\[ \text{Crs} = \frac{\text{expired volume}}{\text{plateau pressure}} \]
The study was approved by the Regional Medical Ethics Committee, and informed consent from the parents was obtained prior to inclusion in the study.

**Statistical analysis**

Possible differences related to test day and between groups were analysed, using the analysis of variance with repeated measurements. Results are given as means with 95% confidence intervals in parentheses, unless otherwise stated. The intra-individual coefficient of variance for each test is given as a group mean value. Possible differences in lung function related to gender, gestational age, or mode of delivery. Thus, results given in Table 1 are the mean values of the TFV-loops in all infants each day.

**Results**

There were no significant differences in lung function or intra-individual variation of lung function measurements at any time related to gender, gestational age, or mode of delivery. Thus, results given in Table 1 are the mean values of the TFV-loops in all infants each day.

The respiratory rate in all infants was significantly higher at one hour (p<0.01) than on the remaining days. In vaginally- born CS-delivered infants the respiratory rate fell further (although not significantly) on Day 4 (to 57 and 61 breaths-min⁻¹, respectively).

Tidal volumes (given in Table 1 as expiratory volume-kg⁻¹ birth weight) were lower at one hour than at any other time (p<0.01), and increased, although not significantly, throughout the study period. Total mean expiratory volume was 19.5 (17.9-21.0) ml on Day 0, and 22.1-25.6 ml during the next four days. Expiratory flow rates did not differ significantly at any time. Tₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑelectronically corrected. Intra-individual variation of lung function measurements was calculated from analysis.

The respiratory system resistance (Rₛ) was calculated from the flow intercept and plateau pressure according to the formula: Rₛ=time constant/C.rs [8]. The resistance measurements were corrected individually for the size of the pneumotachograph, but the time constant was uncorrected.

Four representative TFV loops were stored for analysis, each chosen from a series of breaths during established tidal breathing. These curves were chosen from eight loops: four stored in the computer and the last four breaths. The curves were selected from tidal breaths, with stable volume and shape of the loops as possible, and the respiratory rate being as low as possible. The results given for each child are the mean of these four curves.

The results of the single breath, passive occlusion measurements are the mean of the 6-15 accepted curves obtained in each test. Curves with irregular pressure plateaus, or where a best fit line could not be placed, were excluded from analysis.

The study was approved by the Regional Medical Ethics Committee, and informed consent from the parents was obtained prior to inclusion in the study.

**Table 1. Tidal flow-volume parameters during the first five days of life (Day 0 (approximately one hour of age) until Day 4)**

| Day   | Respiratory rate breaths-min⁻¹ | Expiratory volume ml·kg⁻¹ birth weight | Tₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑelectronically corrected.

<table>
<thead>
<tr>
<th>Day 0</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=24</td>
<td>n=23</td>
<td>n=22</td>
<td>n=23</td>
<td>n=24</td>
</tr>
<tr>
<td>Respiratory rate breaths-min⁻¹</td>
<td>81 (74-95)*</td>
<td>67 (60-73)</td>
<td>66 (60-72)</td>
<td>65 (59-71)</td>
</tr>
<tr>
<td>Expiratory volume ml·kg⁻¹ birth weight</td>
<td>5.6 (5.3-5.9)**</td>
<td>6.4 (5.9-6.8)</td>
<td>6.8 (6.0-7.6)</td>
<td>6.9 (6.5-7.3)</td>
</tr>
</tbody>
</table>
| Tₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑelectronically corrected.

**Table 2. Passive exhalation measurements during the first five days of life (Day 0 (approximately one hour of age) until Day 4)**

<table>
<thead>
<tr>
<th>Day</th>
<th>Crs kg⁻¹ ml cm H₂O kg⁻¹</th>
<th>Rs cm H₂O ml⁻¹ s⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 0</td>
<td>0.88 (0.77-0.91)*</td>
<td>0.023 (0.014-0.035)**</td>
</tr>
<tr>
<td>Day 1</td>
<td>1.25 (1.08-1.42)</td>
<td>0.040 (0.031-0.050)</td>
</tr>
<tr>
<td>Day 2</td>
<td>1.35 (1.18-1.52)</td>
<td>0.044 (0.033-0.054)</td>
</tr>
<tr>
<td>Day 3</td>
<td>1.27 (1.14-1.40)</td>
<td>0.047 (0.039-0.054)</td>
</tr>
<tr>
<td>Day 4</td>
<td>1.23 (1.12-1.33)</td>
<td>0.047 (0.039-0.056)</td>
</tr>
</tbody>
</table>

Measurements of compliance (Crs) per kg birth weight, and resistance (Rₛ) of the respiratory system were performed at one hour of age (Day 0) until the fifth day of life (Day 4). Results are given as mean with 95% confidence interval in parentheses, for all infants (based on individual mean values from the number of occlusions performed).
The present study in awake neonates demonstrated significant changes in tidal breathing have promising prospects, as the only cooperation required is a quietly breathing baby. Although commonly recommended [9], deep sleep (in neonates) or sedation (in infants) are not required, as has been shown previously [2]. As sedation is cumbersome, not medically advisable in severely ill infants with respiratory disease, and not acceptable for ethical reasons in healthy infants in several countries (including Norway), further studies on respiratory mechanics in infants based upon tidal breathing in various arousal states have been encouraged [10]. Measurements in the present study were, therefore, performed in awake infants, using the criteria for wakefulness described in our previous study [2], and at approximately the same time of day throughout the study, to avoid possible differences in lung function related to diurnal variation.

The tidal volumes related to postnatal age found in the present study agree with the results of HAGNERIUS et al. [4] of 5.2-5.8 ml·kg⁻¹·bodyweight at 30 min of life, as well as those of FISHER et al. of 16.4-22 ml at 60 min of life and 20.5-28.5 ml at 3-5 days of life [11].

The tidal volume and respiratory pattern flow in the present study are supported by the findings of FISHER et al. [11], measuring infants at 10, 60 and 90 min and 3-5 days of life. Peak flow occurred relatively later in the respiratory phase at one hour of age (10 min of age in their study), than at later observations.

The intra-individual variations in TFV volumes remained similar throughout the study. GUPTA et al. [12], in a study of tidal volume during the first 3 days of life (in sleeping infants), found a stable mean CV of 13-14%, whereas FISHER et al. [11] found the CV of tidal volume somewhat lower 3-5 days of life (24-25%) than at one hour of life (29-32%). The mean CV of $T_e/T_i$ in our study (20-26%) is lower than that of a similar ratio, the time of peak expiratory flow ($T_e$) expressed as a percentage of $T_i$, used by FISHER et al. [11] which ranged from 23-37%. The reproducibility of our results during the first five days of life in awake infants is, thus, within the range described by others.

We found an increase in Rs from one hour to one day of life. This has not, to our knowledge, been reported previously. MURUTA [6] maintains that Rs in healthy infants stabilizes before one hour of age, remaining stable the first day of life subsequent to an initial decrease following the first breath.

The intra-individual variability of Crs and Rs in the present study have also been demonstrated by others [12-14]. The same tendency to a higher CV of Crs on Day 1 than later, as found in the present study, has also been described by GUPTA et al. [12]. As our results in awake infants are comparable to those of others, the single breath passive occlusion technique is attractive, as it is

**Table 3.** Coefficient of variation of tidal breathing parameters and passive exhalation measurements during the first five days of life (Day 0 (approximately one hour of age) until Day 4)

<table>
<thead>
<tr>
<th></th>
<th>Day 0</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expiratory volume</td>
<td>6.7</td>
<td>6.9</td>
<td>5.8</td>
<td>6.7</td>
<td>5.5</td>
</tr>
<tr>
<td>$T_e/T_i$</td>
<td>21.7</td>
<td>20.5</td>
<td>19.7</td>
<td>26.1</td>
<td>23.2</td>
</tr>
<tr>
<td>$V_e/V_i$</td>
<td>21.7</td>
<td>19.3</td>
<td>19.0</td>
<td>24.4</td>
<td>21.6</td>
</tr>
<tr>
<td>TEFu/PTEF</td>
<td>8.2</td>
<td>9.3</td>
<td>9.0</td>
<td>9.7</td>
<td>10.9</td>
</tr>
<tr>
<td>Crs/kg⁻¹</td>
<td>21.9*</td>
<td>20.5*</td>
<td>15.5</td>
<td>15.7</td>
<td>15.9</td>
</tr>
<tr>
<td>Rs</td>
<td>29.1</td>
<td>23.0</td>
<td>26.2</td>
<td>21.1</td>
<td>20.1</td>
</tr>
</tbody>
</table>

**Table 4.** Tidal breathing parameters at one hour of life in infants delivered vaginally and by Caesarean section

<table>
<thead>
<tr>
<th></th>
<th>ND</th>
<th>CS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory rate</td>
<td>77</td>
<td>80</td>
</tr>
<tr>
<td>breaths·min⁻¹</td>
<td>(59-94)</td>
<td>(60-99)</td>
</tr>
<tr>
<td>Expiratory volume</td>
<td>19.6</td>
<td>19.3</td>
</tr>
<tr>
<td>ml</td>
<td>(17.9-21.4)</td>
<td>(16.5-22.1)</td>
</tr>
<tr>
<td>$T_e/T_i$</td>
<td>0.42</td>
<td>0.45</td>
</tr>
<tr>
<td>(0.33-0.51)</td>
<td>(0.38-0.53)</td>
<td></td>
</tr>
<tr>
<td>$V_e/V_i$</td>
<td>0.48</td>
<td>0.51</td>
</tr>
<tr>
<td>(0.38-0.57)</td>
<td>(0.43-0.48)</td>
<td></td>
</tr>
<tr>
<td>TEFu/PTEF</td>
<td>0.83</td>
<td>0.86</td>
</tr>
<tr>
<td>(0.75-0.92)</td>
<td>(0.81-0.90)</td>
<td></td>
</tr>
<tr>
<td>Crs</td>
<td>2.84</td>
<td>3.32</td>
</tr>
<tr>
<td>ml·cmH₂O⁻¹</td>
<td>(2.2-3.5)</td>
<td>(2.3-4.1)</td>
</tr>
<tr>
<td>Rs</td>
<td>0.023</td>
<td>0.024</td>
</tr>
<tr>
<td>cmH₂O·ml⁻¹·s</td>
<td>(0.0074-0.028)</td>
<td>(0.011-0.037)</td>
</tr>
</tbody>
</table>

Measurements of tidal flow volume parameters as well as compliance and resistance of the respiratory system are given for infants delivered vaginally (normal delivery (ND)) and by Caesarean section (CS) at one hour of age. Results are given as mean values with 95% confidence intervals in parentheses. There were no significant differences between the groups at one hour of life. For further abbreviations see legend to tables 1 and 3.

the days, as shown in table 3. The CVs for the individual tests of $T_e$ were significantly higher during the first two tests ($p<0.01$ Day 0 to Day 1; $p=0.05$ Day 1 to Day 2) than on the remaining three days. No such differences were found for CV of Rs (table 3).

There were no significant differences in TFV parameters, Crs or Rs between the infants delivered vaginally or by CS. The results for the two groups at one hour of life are shown in table 4.

**Discussion**

The present study in awake neonates demonstrated significant changes in intra-individual variation. As passive occlusion measurements changed significantly from Day 0 to Day 1, with the intra-individual variation remaining higher during the first two compared to the remaining three days, the optimal time for Crs and Rs measurements seems to be Day 2 to Day 4. We could not demonstrate any significant differences in lung function related to mode of delivery, employing the current techniques in awake, healthy neonates.

Measurements of lung function in neonates based upon tidal breathing have promising prospects, as the only cooperation required is a quietly breathing baby. Although commonly recommended [9], deep sleep (in neonates) or sedation (in infants) are not required, as has been shown previously [2]. As sedation is cumbersome, not medically advisable in severely ill infants with respiratory disease, and not acceptable for ethical reasons in healthy infants in several countries (including Norway), further studies on respiratory mechanics in infants based upon tidal breathing in various arousal states have been encouraged [10]. Measurements in the present study were, therefore, performed in awake infants, using the criteria for wakefulness described in our previous study [2], and at approximately the same time of day throughout the study, to avoid possible differences in lung function related to diurnal variation.

The tidal volumes related to postnatal age found in the present study agree with the results of HAGNERIUS et al. [4] of 5.2-5.8 ml·kg⁻¹·bodyweight at 30 min of life, as well as those of FISHER et al. of 16.4-22 ml at 60 min of life and 20.5-28.5 ml at 3-5 days of life [11].

The changes in tidal expiratory flow pattern in the present study are supported by the findings of FISHER et al. [11], measuring infants at 10, 60 and 90 min and 3-5 days of life. Peak flow occurred relatively later in the expiratory phase at one hour of age (10 min of age in their study), than at later observations.

The intra-individual variations in TFV volumes remained similar throughout the study. GUPTA et al. [12], in a study of tidal volume during the first 3 days of life (in sleeping infants), found a stable mean CV of 13-14%, whereas FISHER et al. [11] found the CV of tidal volume somewhat lower 3-5 days of life (24-25%) than at one hour of life (29-32%). The mean CV of $T_e/T_i$ in our study (20-26%) is lower than that of a similar ratio, the time of peak expiratory flow ($T_e$) expressed as a percentage of $T_i$, used by FISHER et al. [11] which ranged from 23-37%. The reproducibility of our results during the first five days of life in awake infants is, thus, within the range described by others.

We found an increase in Rs from one hour to one day of life. This has not, to our knowledge, been reported previously. MURUTA [6] maintains that Rs in healthy infants stabilizes before one hour of age, remaining stable the first day of life subsequent to an initial decrease following the first breath.

The intra-individual variability of Crs and Rs in the present study have also been demonstrated by others [12-14]. The same tendency to a higher CV of Crs on Day 1 than later, as found in the present study, has also been described by GUPTA et al. [12]. As our results in awake infants are comparable to those of others, the single breath passive occlusion technique is attractive, as it is
simple to perform, may be performed in awake patients [2], and is well-recognized [10].

We found no significant differences in lung function related to mode of delivery of the infant as determined by TFV parameters or passive exhalation measurements. This is supported by other studies [4, 6], which demonstrated tendencies, but not significant differences, in tidal volumes and respiratory rates related to mode of delivery of the infant during the first few hours of life. However, due to the low number of subjects in each group, the results must be interpreted with caution.

Methodological concern may arise, as analysis was based upon only four selected tidal breaths during each TFV loop measurement. However, these four loops were selected from a minimum of eight breaths according to the criteria stated, and the results obtained have been in agreement with others [4, 11].

Optimal parameters used to describe shapes of flow-time or flow-volume loops have so far not been defined. The ratios of time or volume until peak expiratory flow, $T_{mT}/T_s$ [10, 15–17] and $V_{mV}/V_s$, respectively, reflects the shape of the expiratory flow pattern. The ratio $T_{EF}/V_{EF}$ describes the rate of decline of the distal part of the expiratory flow-volume loop, as the $T_{mT}/T_s$ ratio quantifies the flow-time relationship and the $V_{mV}/V_s$ ratio quantifies the flow-volume relationship. Although controversies exist [10] concerning the importance of these ratios in tidal breathing, studies of the relationship between tidal flow-time curves and the development of wheezy lower respiratory tract illnesses in childhood [15, 16] have demonstrated the $T_{mT}/T_s$ ratio to be predictive of later wheezing episodes.

The mean CV has commonly been used to describe intra-individual variation in lung function [11, 12, 17]. As there is concern about the value of CV to express stability or reproducibility of any given method, other statistical methods for testing stability are at present being developed [18]. However, in order to compare our results to those of others, the mean CV, although not optimal, is still valid and meaningful, and thus employed.

The high respiratory rates in the present study are unlikely to be explained by the use of a face mask, even though this increased the dead space. It has recently been shown that using the same type and size face mask (Vital Signs Inc.) as in the present study, respiratory rate was lower than with the use of inductance plethysmography (Respitrace®) [17].

Tidal breathing parameters may become important in evaluating lung function in healthy neonates, as measurements are relatively easily performed in awake subjects. Furthermore, if prediction of respiratory illness is possible at an early age, it is important to study lung function before environmental factors have had time to influence the respiratory tract, as soon as stabilization of lung function after birth has occurred. Thus, the present study has demonstrated that an appropriate time for performing TFV and passive exhalation measurements in awake healthy infants seem to be Day 2 to Day 4, indicated by the stability of measurements in this period, regardless of mode of delivery of the infant.

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References