

## **SERIES "STANDARDS FOR INFANT RESPIRATORY FUNCTION TESTING: ERS/ATS TASK FORCE"**

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# **Tidal breath analysis for infant pulmonary function testing**

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*Tidal breath analysis for infant pulmonary function testing. J.H.T. Bates, G. Schmalisch, D. Filbrun, J. Stocks, on behalf of the ERS/ATS Task Force on Standards for Infant Respiratory Function Testing. ©ERS Journals Ltd 2000.*

**ABSTRACT:** The aim of this position paper is to provide recommendations pertaining to software and equipment requirements when analysing tidal breathing measurements in infants. These guidelines cover numerous aspects including terminology and definitions, equipment, data acquisition and analysis, and reporting of results, and highlight areas in which further research is needed before consensus can be reached.

When collecting tidal breathing data in infants and children, equipment dead space and resistance must be minimized, all sources of leak eliminated, and a flowmeter with appropriate frequency response and linearity employed. Inspired gases should be corrected to body temperature, barometric pressure and saturated with water vapour conditions and efforts made to eliminate the various sources of drift in volume that can occur. In addition, the analogue-to-digital converter used to sample data must be capable of adequately resolving the highest and lowest flows required by the study. An adequate sampling rate must be used; 50–100 Hz may be sufficient for the determination of timing and volume parameters, especially in older infants, but rates of 200 Hz are recommended for analysis of the tidal breathing flow/volume loop and other sensitive parameters such as time to peak tidal expiratory flow/expiratory time.

The potentially most troublesome aspect of tidal breath analysis from the computational point of view is the identification of the beginning and end of inspiration and expiration.

Once methods and equipment for the measurement and analysis of tidal breathing in infants have been standardized, there is an urgent need to establish appropriate reference ranges for various key parameters so that they may be used more effectively in the clinical setting. Implementation of these recommendations should help to ensure that such measurements are as accurate as possible and that more meaningful comparisons can be made between data collected in different centres or with different equipment.

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The present document represents one of a series [1–6] that is being produced by the European Respiratory Society/American Thoracic Society Task Force on standards for infant respiratory function testing. The aim of this task force is to summarize what is currently seen to be good laboratory practice, and to provide recommendations for both users and manufacturers of infant lung function equipment and software. These recommendations have been developed after widespread communication on an international level and are directed towards

future developments in this field, including the use of more automated and standardized equipment than has been used in the past. It is recognized that this document will need to be updated regularly in response to advances in both technology and knowledge regarding the application and interpretation of these tests under different circumstances. In the meantime, every attempt has been made to avoid being too prescriptive in order to allow for future developments, while at the same time offering guidance as to minimum standards for those developing

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equipment and performing tests. It is anticipated that acceptance and application of these recommendations will be of particular value when attempting to compare data between centres, develop or use reference data, or participate in multicentre trials which use tidal breathing parameters as outcome measures.

An infant's breathing pattern measured during tidal breathing contains significant physiological information pertaining to a number of processes related to respiratory control and pulmonary mechanical function. Such information is encapsulated within a number of conceptually

straightforward parameters. The most fundamental parameters contained in the flow and volume signal, tidal volume ( $V_T$ ), respiratory frequency ( $f_R$ ), and inspiratory ( $t_I$ ) and expiratory time ( $t_E$ ), are shown in figure 1a and b.  $f_R$ , which is calculated as  $60/(t_I+t_E)$ , is also referred to as respiratory rate (RR). These basic parameters can be used to calculate quantities pertaining to the more detailed aspects of the pattern and magnitude of tidal breathing, such as the time to peak tidal expiratory flow ( $t_{PTEF}$ ) as a proportion of  $t_E$  ( $t_{PTEF}/t_E$ ), minute ventilation ( $\dot{V}_E$ ), mean inspiratory flow ( $\dot{V}_T/t_I$ ) and the duty cycle ( $t_I/\text{total breath time}$  ( $t_{tot}$ )). In addition, tidal breathing flow/volume loops may be plotted for visual inspection and evaluation of parameters such as the volume expired up to the time of peak expiratory flow ( $V_{PTEF}$ ) or defined flow in relation to exhaled volume (fig. 1c). It may also be useful to derive certain composite parameters, such as  $V_{PTEF}$  related to  $V_T$  ( $V_{PTEF}/V_T$ ). However, the purpose of this document is not to provide a theoretical background to the factors determining tidal breathing patterns during early life, nor to comment on the potential clinical significance (or irrelevance, in some instances!) of the innumerable parameters that can be calculated from recordings of tidal breathing. For this, the reader is directed to the existing literature, much of which has been summarized recently [7]. The intent is rather to stress the various factors during data acquisition, analysis and reporting of tidal breathing parameters that can lead to systematic errors between different recording systems.

Obtaining tidal breathing parameters requires nothing more than the measurement of flow or volume at the mouth and nose during a period of regular breathing. However, there are a number of considerations pertaining to the analysis of tidal breathing data that make it somewhat less than trivial. The most problematic issue, from a practical point of view, is the precise detection of the onset of inspiration and expiration. The problem of automatically segmenting breaths into their inspiratory and expiratory phases is thus considered in the present document. Other practical issues such as the collection of airflow data and the derivation of a drift-free volume signal from such data are also considered. Some of these practical issues are influenced by the task in hand. For example, investigations into the control of breathing require the determination of not only the magnitude of but also the variability in  $V_T$ ,  $t_I$ , and  $t_E$ . On the one hand, this requires measurement of a large number of breathing cycles, which cannot be performed with the conventional combination of face mask and pneumotachometer (PNT) due to their relatively high apparatus dead space; thus alternative approaches are usually required [8]. On the other hand, a relatively low sample rate (10–50 Hz) will often suffice for such studies. By contrast, when attempting to analyse the mechanical components of the tidal breathing signal, a relatively low number of consecutive, reproducible and artefact-free breaths need to be recorded, but at a higher sampling rate.

Because of the complexities of using noninvasive body surface measurements to obtain quantitatively accurate assessments of tidal breathing parameters, and the lack of any standardized approach to such measurements, the current document is limited to direct measurements of airflow and volume at the airway opening. Nevertheless, some of the recommendations within may be pertinent if alternative approaches are used.

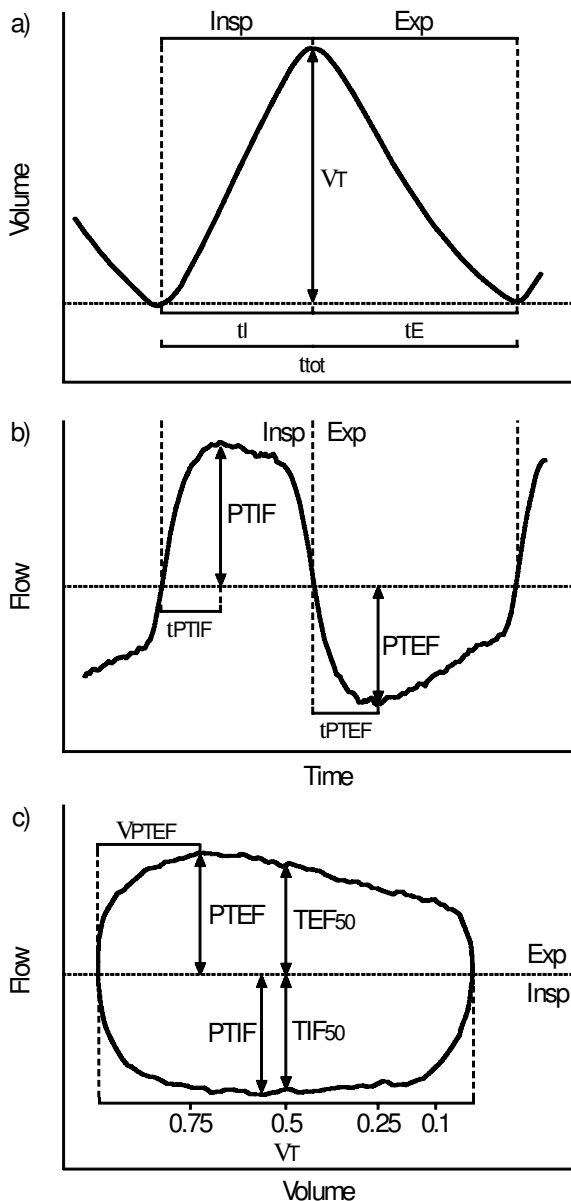


Fig. 1. – Tidal breathing parameters of: a) the flow; and b) volume signals; and c) the flow/volume loop. The tidal expiratory ( $TEF_{50}$ ) and inspiratory flow when 50% of tidal volume ( $V_T$ ) remains in the lung ( $TIF_{50}$ ) are shown; other values of  $TEF_x$  and  $TIF_x$  correspond to the different  $V_T$  on the scale bar. Insp: inspiration; exp: expiration;  $t_I$ : inspiratory time;  $t_E$ : expiratory time;  $t_{tot}$ : total breath time;  $PTIF$ : peak tidal inspiratory flow;  $PTEF$ : peak tidal expiratory flow;  $t_{PTEF}$ : time to peak expiratory flow;  $t_{PTIF}$ : time to peak inspiratory flow;  $V_{PTEF}$ : volume expired before  $PTEF$  attained.

## General procedures

In the present paper, tidal breathing is taken to be the natural physiological state of undisturbed regular breathing. Measurements are commonly performed during quiet sleep, which, in older infants, is usually associated with active inspiration and passive expiration. In order to record periods of "undisturbed breathing", there should be negligible influence of the measuring equipment [9]; thus tidal breathing should be assessed prior to more complex investigations. For example, although it is certainly possible to measure tidal breathing parameters immediately after insertion of an oesophageal catheter, the values obtained will be significantly different from those measured prior to catheter insertion. Meaningful comparison of tidal breathing parameters within and between infants, or interpretation with respect to "reference values", are only possible if the measurement conditions are the same. Careful documentation of measurement conditions and equipment characteristics during tidal breathing measurements is therefore essential.

Contrary to common belief, collection of undisturbed quiet tidal breathing data is not a trivial undertaking, as even the application of a face mask can stimulate breathing [10, 11]. Consequently, measurements should only be made after a sufficient adaptation period has been allowed to elapse after attachment of the measurement equipment. This is not a problem if there is negligible additional dead space involved, such as with the flow-through technique [8]. However, when using a conventional mask and PNT, the apparatus dead space limits the duration of measurements [12]. Furthermore, the smaller the infant, the greater the impact of the apparatus dead space. Careful preparation is therefore necessary to minimize the adaptation period, especially when studying newborns.

Careful use of equipment in order to ensure patient safety remains the responsibility of the operator [1]. Routine safety measures in the pulmonary function testing laboratory include: 1) availability of full resuscitation equipment, including suction, at the site of infant lung function testing, plus a suitable alarm system; 2) the presence of two individuals (other than parents) during testing, one of whom has prime responsibility for the infant's wellbeing; the infant must never be left unattended; 3) continuous physiological monitoring (and ideally recording), including at least pulse oximetry; 4) use of transparent face masks; and 5) adherence to the hospital-specific protocol for sedation or anaesthesia.

Further details regarding measurement conditions which may influence infant safety or the accuracy and reproducibility of results have been published previously [5, 13]. The measurement procedure can be summarized as follows. 1) The infant should be lying supine with the neck and/or shoulders supported in the midline in slight extension. This position should be stabilized by use of a neck roll or head ring. If an alternative posture is used, this should be stated clearly in any publication. 2) The infant should be fed, dry, clean and comfortably clothed. 3) The face mask should cover mouth and nose and be placed with minimal pressure while also being airtight. To prevent any air leaks, a thin sealing ring of silicon putty is often helpful.

## Equipment

Airflow and volume, determined by numerical integration of airflow, are the basic signals of tidal breathing analysis (fig. 1). Airflow is usually measured at the airway opening using a PNT connected to a face mask. Although both respiratory inductance and "face-out" body plethysmography have been used to record tidal breathing signals, the former only provides quantitatively accurate measurements if there has been previous calibration using a PNT and the measurement conditions remain very stable [14], whereas the latter is too expensive and cumbersome for routine bedside application. A detailed description of devices available for the measurement of flow, and hence volume, has been published recently [15]. The reader is also referred to the document in the present series on specifications for equipment and software used for infant pulmonary function testing for further details and justification of the recommendations presented below [1, 3].

### *Face mask*

Different types of mask are used, based largely on local preference and availability. The dead space of the face mask and flowmeter may have a marked influence on the pattern of breathing, with respect to both magnitude and timing, thereby altering the very parameters that the investigator is trying to assess. In preterm and sick neonates, even when a small face mask and a very-low-dead space flowmeter are used, the total apparatus dead space may exceed the infant's own dead space and present a considerable load, thereby precluding anything but brief intermittent recordings. In such infants, the use of the dead-space-free-flow-through technique is recommended [8].

In order to aid international standardization the following recommendations are made: 1) report brand and size of mask and whether the mask has an air-filled cuff, since the mask dead space depends significantly on the cuff pressure; 2) document other aids to improving airtight placement (*e.g.* silicon putty or Vaseline); 3) minimize dead space and report whether measures to reduce mask volume are used (*e.g.* shortening of the mask port or putting silicon putty in the mask); and 4) measure the dead space of the mask by water displacement and subtract 50% of this volume to estimate the effective dead space [1, 16].

### *Flowmeter*

The conventional transducer employed for measurement of respiratory flow is the combination of PNT and differential pressure transducer. Attention is restricted to this device in the present document, although several new devices, such as ultrasonic flowmeters and hot wire anemometers [17], are currently being developed and validated for use in infant respiratory function measurements. A number of general considerations concerning instrumentation and measurement technique pertain to the measurement of flow and its recording using a computer. These are as follows. 1) The flowmeter should be a low-resistance low-dead-space device. Flowmeters

for measurements in preterm infants should have a dead space of <1.5 mL. Unfortunately, the apparatus dead space of most modern devices arises largely due to the necessary connecting ports, and so possibilities for dead space reduction are limited. In any case, the connection between PNT and mask must be minimized without disturbing the linearity of the flowmeter [15]. 2) Minimizing the resistance of the infant lung function equipment is important since the overall resistance of the equipment may not only dramatically change the respiratory pattern in spontaneously breathing babies but also interfere with triggering devices in those who are ventilated. Any significant increase in resistance increases the expiratory time constant and potentially influences the end-expiratory level. This, in turn, affects any measurements that are volume-dependent, including various tidal breathing parameters. The need to design future apparatus with as low a resistance as possible within the constraints of simultaneously attaining a low dead space and high resolution cannot be overemphasized. 3) The combined resistance of the apparatus (including any valves, capnographs, *etc.*) should be <20% of the infant's intrinsic resistance at the mean flows likely to be encountered [1]. Thus, as a rough guide, the combined apparatus resistance should not exceed 1.2 kPa·L<sup>-1</sup>·s at 50 mL·s<sup>-1</sup> in spontaneously breathing preterm infants, 0.7 kPa·L<sup>-1</sup>·s at 100 mL·s<sup>-1</sup> in term neonates and 0.5 kPa·L<sup>-1</sup>·s at 300 mL·s<sup>-1</sup> in infants and young children. 4) The response of the flowmeter should be linear over the range of flows encountered. The extent to which a PNT remains linear over an extended range is critically dependent on design features such as whether it is a capillary-, screen- or variable orifice-type device and the geometry of any integral connections. It is therefore essential that the manufacturer provides accurate details and that the user checks the range of flows over which the flowmeter provides accurate recordings. The approximate linearity ranges required for various sizes of infant are 0–100 mL·s<sup>-1</sup> in preterm infants and neonates of 2–4 kg, 0–300 mL·s<sup>-1</sup> in infants of 4–10 kg and 0–500 mL·s<sup>-1</sup> in preschool children of 11–15 kg. In practice, flowmeters with a linear range of 0–10 L·min<sup>-1</sup> are commonly used in preterm infants and neonates, whereas those with a range of 0–35 L·min<sup>-1</sup> are used for obtaining tidal breathing measurements in older infants and young children. 5) If a PNT has a nonlinear response over the desired flow range, it may be possible to effectively linearize it by characterizing the response and inverting it digitally. This can reduce dead space by allowing the use of a smaller-calibre PNT. However, it must be ensured that the response characteristics of the device remains constant over a prolonged period, after repeated disinfection and on exposure to different respired gases. 6) The flowmeter should have a flat frequency response over a frequency range sufficient to encompass the majority of the power in the measured signals [1]. For tidal breathing signals, it is probably sufficient to have a flat frequency response up to 10 Hz. If the transducer itself does not have a flat frequency response over this range, it may be possible to render it flat by digital compensation of the sampled data [18]; however, this is only possible if the response of the device is linear. 7) If a PNT with metal screens or capillaries is used, it should be heated to body temperature to avoid condensation on the resistive element.

Major changes in screen resistance, and hence measured flows, can occur within <1 min of placing an unheated PNT into a ventilator circuit; thus this practice is strongly discouraged. 8) Despite such heating, PNTs with screens or capillaries in the ventilator circuit are highly susceptible to obstruction by secretions, leading to falsely high measured flows and possible danger to the patient. Therefore, these PNTs should only be used by qualified personnel while the patient is under direct observation [19]. 9) The geometry of the connectors on either side of the PNT screen affects the overall pressure/flow characteristics of the device. It is therefore important that the connectors be as symmetrical as possible on either side of the PNT, and that the PNT is calibrated *in situ* in exactly the same configuration as that to be used with the subject [15]. 10) If the inspired gas differs significantly from room air (*e.g.* by increased inspiratory oxygen fraction ( $F_{I,O_2}$ )), it may be of different viscosity to room air, and therefore have different PNT calibration factors. In such a case, either the PNT should be calibrated with the inspired gas or the room air calibration factors should be scaled by the relative differences in gas viscosity [15]. For measurements during artificial ventilation, continuous  $F_{I,O_2}$  correction at the bedside is advantageous [19]. The influence of changes in gas viscosity and density on the behaviour of the PNT vary according to precise design and should be both stated by the manufacturer and checked by the user.

## Data collection

### Calibration of equipment

Equipment calibration has significant influence on the calculated results and should be performed with the utmost care and according to the recommendations of the manufacturer. Reliable measurements are unachievable with an unsuitable or defective calibration device. It is therefore vital that: 1) calibration is performed under identical circumstances to and with the same equipment configuration as during measurements; 2) the calibration tools are checked periodically; this requires that any calibrated syringes or rotameters are returned to the manufacturers of such devices on a regular basis according to the recommendations for any specific device (*e.g.* 12 monthly for precision syringes) or whenever any deviation is suspected; 3) qualified personnel, who understand both the procedure and the signals and parameters displayed, perform the calibration; 4) manual calibration is performed to check the automatic calibration procedures; and 5) any deviations in inspired gas viscosity are taken into account in the PNT calibration.

### Data acquisition

Data acquisition requirements for infant respiratory function testing are dealt with elsewhere in this series [3]. Only those aspects of particular pertinence to tidal breathing analysis are referred to below. As discussed previously [3, 15], it is crucial that the analogue flow signal is passed through anti-aliasing filters with appropriate frequency cut-offs prior to sampling, in order

to satisfy the Shannon sampling theorem and avoid the potentially insidious problems of aliasing. The flow data are sampled by an analogue-to-digital (A/D) converter, which maps a specified voltage range in to a number of equally spaced binary numbers. It is crucial that the incoming voltage signal from the flow transducer occupies as much of the allowable voltage range of the AD converter as possible if maximum resolution is to be attained. For example, if the flow ranges  $\pm 30 \text{ L}\cdot\text{min}^{-1}$  and is digitized using a 12-bit A/D converter, the maximum resolution of the recorded flow signal is  $60 \text{ L}\cdot\text{min}^{-1}/2^{12}$  (*i.e.*  $14.6 \text{ mL}\cdot\text{min}^{-1}$ ). For this reason, together with the need to minimize apparatus dead space and resistance, a range of PNTs are probably needed to accommodate infants of different ages undergoing different types of respiratory function test in any one centre. The manufacturer should document both the flow range and number of bits of the A/D converter.

### Sampling rate

The necessary sampling rate is determined by Shannon's theorem and the clinical purpose of the tidal breathing analysis. The sampling interval ( $\Delta t$ ) between flow data points determines the resolution of all identified time points such as the beginning and end of inspiration and expiration. Consequently, identified time intervals such as  $t_I$  and  $t_E$  have uncertainties of  $2\Delta t$ . For example, with an  $f_R$  of  $60 \text{ breaths}\cdot\text{min}^{-1}$  and a sampling rate of 100 Hz ( $\Delta t=10 \text{ ms}$ ), the measurement error in  $t_I$  and  $t_E$  can be up to 4%. A sampling rate of 100 Hz has been shown to be normally adequate when calculating only  $V_T$  and  $f_R$  (see *Appendix*), whereas greater time resolution may be required in rapidly breathing infants or for the measurement of certain parameters such as  $t_{PTEF}/t_E$ . Sampling rates of  $\geq 200 \text{ Hz}$  are, therefore, recommended for acquisition of tidal breathing data if such analyses are to be performed, particularly in small rapidly breathing infants [8].

During data collection and/or replay, time-based displays of flow and volume are required together with simultaneous displays of flow/volume loops and relevant trend data [20]. These assist in the recognition of air leaks and behavioural state. Of particular importance is the determination of when the infant has adapted to the presence of the face mask. Exactly how to make this determination remains debatable. The decision to commence recordings must be based on the operator's own experience plus observation of the displayed signals in order to ascertain that: 1) the breathing pattern is regular, stable and representative for that infant; 2) there is no trend in instantaneous  $f_R$  (*i.e.* a stable mean  $f_R$  has been achieved); and 3) the signals are technically acceptable (*e.g.* no leaks, artefacts or excessive volume drift).

Once the infant has adapted to the mask and is sleeping quietly and breathing regularly, tidal breathing should be recorded in epochs of 30–60 s. These should be repeated over the next 5 min and at a later interval if a measure of reproducibility is desired. The number of recorded breathing cycles to use for evaluation depends on the variability of the signals, but should allow the investigator to select several epochs for evaluation. It is recommended that each epoch should contain at least 20 cycles.

The essential general information which should be recorded when measuring any lung function parameters in infants have been described previously [1]. For a tidal breathing study, the additional data include time since last feeding, start and end time of measurement, and adaptation time.

## Signal processing

### Numerical integration

Typically, the primary measured signal is flow. This must be integrated with respect to time to produce volume; this is most conveniently performed using a computer. There are a variety of numerical integration methods available, all of which connect adjacent data points with some kind of curve and then sum the calculated areas beneath each curve segment. The more sophisticated methods make more accurate interpolations between the data points than simpler algorithms, but at the expense of greater complexity. One of the simplest numerical integration methods is the so-called trapezoidal rule (fig. 2). This assumes that the sampled data points of the flow signal are connected by straight lines, and that the volume increment between the  $i$ th and  $(i-1)$ th data points ( $\Delta V_i$ ) is given by:

$$\Delta V_i = \Delta t (V_i + V_{i-1})/2, \quad (1)$$

where  $V_i$  and  $V_{i-1}$  are the flow at the  $i$ th and  $(i-1)$ th data points. The  $\Delta V_i$  are then summed to yield the total area under the curve:

$$V = V_0 + \sum_{i=1}^n \Delta V_i, \quad (2)$$

where  $V_0$  is the volume at which integration of flow begins (which would normally be zero if integration begins at the start of inspiration).

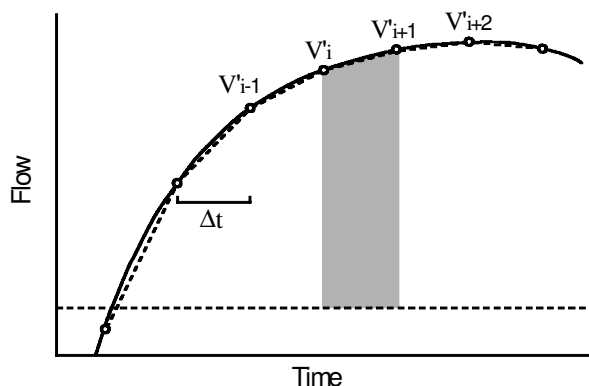


Fig. 2. – Illustration of the trapezoidal rule. The flow signal (—) is integrated by joining its data points using straight lines (---) and calculating the area under each line segment using Equation 1.  $\square$ : volume increment between the  $i$ th and  $(i+1)$ th data points.  $\Delta t$ : sampling interval;  $V_{i-1}$ ,  $V_i$ ,  $V_{i+1}$  and  $V_{i+2}$ : flow at  $(i-1)$ th,  $i$ th  $(i+1)$ th and  $(i+2)$ th data points.

Numerical integration is always in error when the original continuous curve is represented by some kind of approximation function between the sampled points. However, these errors decrease as the data sampling rate increases and the sampled points become more closely spaced. For most respiratory applications, the integration error incurred with the trapezoidal rule is probably negligible with a data sampling rate of 200 Hz.

#### *Volume drift*

When flow is integrated to yield volume, an upward or downward drift in the volume baseline is invariably seen. Some degree of drift is expected for purely physiological reasons. For example, the respiratory exchange ratio (*i.e.* carbon dioxide production/oxygen consumption) is usually  $\sim 0.8$ , *i.e.* the volume of  $O_2$  absorbed by the lungs is 20% greater than the volume of  $CO_2$  excreted. This is reflected in a slightly greater volume of gas being inspired than expired with each breath. Also, if the inspired air is not warmed to body temperature and prehumidified, the volume of gas expired with each breath can be increased by up to 5% (see discussion of body temperature, barometric pressure and saturated with water vapour (BTPS) conditions below), relative to that inspired, by a gain in water vapour content. These physiological effects contribute to a gradually increasing or decreasing volume measured at the mouth, but not to a real change in baseline lung volume.

In addition to the physiological factors discussed above, the following methodological factors also contribute to volume drift.

*Temperature changes between inspired and expired gas.* If inspired air is not warmed to body temperature before passing through the PNT, it has a different viscosity and density to expired air, which causes the PNT to register the transit of an equal number of molecules differently between inspiration and expiration. Variations in temperature may also affect the physical dimensions of the PNT due to the coefficients of thermal expansion of its components.

*Changes in gas composition between inspiration and expiration.* Inspired and expired gases differ in their partial pressures of  $O_2$  and  $CO_2$ . This leads to slight differences in the viscosities of the gas mixtures, with concomitant effects on the flows registered during inspiration and expiration by the PNT.

*Leaks.* Any leaks between the airway opening and PNT, whether through the mask seal or around a tracheal tube, cause a discrepancy between the volume registered by the PNT and that entering or leaving the lungs, and hence a drift in volume. This problem is most likely to occur immediately after mask displacement, if the infant moves or in a pressurized system (*e.g.* during artificial ventilation).

*Zero offset in flow calibration.* If the true zero flow is registered as some finite value, then integration of this offset over time results in a linear drift in volume with a slope equal to the offset. Accurate delineation of the zero flow point is more difficult as the sensitivity of the PNT

decreases, which generally occurs as the linear range increases. The resolution of the A/D converter used to sample the flow also sets a limit on how accurately the zero flow point can be identified. Therefore, perfect offset compensation is never possible. To prevent this volume drift, a dead band around the zero flow, in which all values are set to zero, is used in some devices. However, a dead band can hamper breath detection, especially when flow is very low; thus its use and the flow thresholds of the dead band should be described by the manufacturer of the equipment [21].

*Imperfections in the pneumotachometer response.* If the transducer for measuring flow does not function as a perfect measuring instrument (which is always the case to some degree and may be significantly so under dynamic conditions), it is unlikely that the inspiratory and expiratory flows are measured equally. This produces asymmetries in the recorded flow. Such asymmetry can often be seen in measurements from infants intubated with small endotracheal tubes due to the geometric differences on either side of the PNT.

#### *Correcting volume drift*

The analysis of tidal breathing data requires the examination of data records containing a substantial number of breaths (typically  $\geq 20$ ) obtained during regular breathing. In principle, it might be possible to avoid drift in volume in such a data record by preconditioning the inspired gas to BTPS conditions, continuously monitoring gas partial pressures in both the alveoli and the pulmonary arterial and venous blood to correct for respiratory exchange ratios not equal to unity and eliminating all the methodological factors discussed above. However, this is extremely difficult, if not impossible, in practice. Consequently, it is never known how much of the baseline drift in volume is due to drift and how much represents a true change in absolute lung volume. Also, because the subject is assumed to be in the physiological steady state when data are recorded, the assumption is generally made that functional residual capacity (FRC) remains more or less constant throughout the study period. Such a situation is thus forced on the measured volume signal by some kind of drift correction algorithm which first assesses the drift and then removes it. This does not, of course, mean that FRC must be identical from one breath to the next, but merely that there is no net upward or downward trend in FRC over a period containing many breaths.

Off-line drift correction algorithms commonly define the drift in volume as the slope of the straight line fitted to the end-expiratory points in an epoch of tidal breaths (fig. 3). In order to avoid any outliers skewing the regression, it may be useful to exclude those end-expiratory points with the greatest deviations and then refit the line. This line is then subtracted from the volume to remove the drift, and the mean level of the new end-expiratory points adjusted to zero. There are also other ways in which volume can be drift-corrected, such as subtraction of a curvilinear baseline instead of a straight line, or rezeroing of volume at the end of every breath (which requires breath detection; see below). Different dedrifting algorithms usually lead to slight differences in the

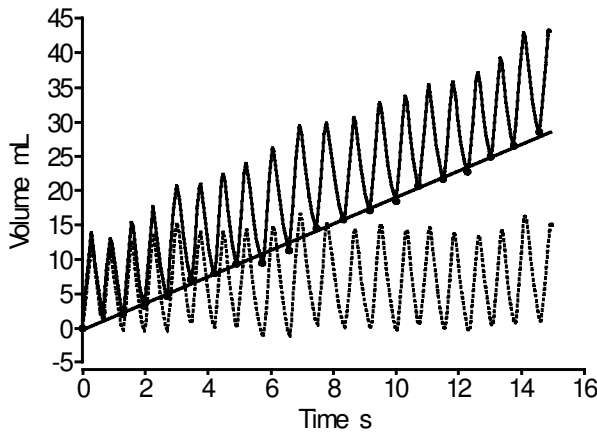


Fig. 3. – Example of volume drift correction. The oscillating volume signal drifting upwards (—) has a straight line that characterizes its drift. Subtracting this line from the volume yields a drift-corrected signal that oscillates about a stable baseline (- - -).

subsequently estimated values of breathing pattern parameters. However, given that drift correction is merely an empirical operation, it is probably appropriate to select a correction algorithm on the basis of robustness and ease of implementation as much as anything else. For the user of breath analysis software, it is important to know which method of drift correction has been implemented. It is also useful to be able to switch off the correction procedure, so that real changes in FRC can be tracked over short periods when the recorded flow signal is sufficiently accurate.

A particular problem with automated drift correction algorithms is that they can mask the presence of significant differences between inspiratory and expiratory  $V_T$ , such as might arise from air leaks in the breathing circuit or severe PNT asymmetries. Consequently, the magnitude of the correction made for volume drift should always be monitored. The drift magnitude (Drift) is usefully defined as the mean drift per breath divided by the mean  $V_T$  over the epoch of volume being analysed, given as a percentage by:

$$\text{Drift} = 100 \frac{\Delta V}{\sum_{i=1}^N V_{T,i}} \quad (3)$$

where  $\Delta V$  is the drift of the volume baseline over  $N$  complete breaths and  $V_{T,i}$  is the  $i$ th  $V_T$ . An unusually large drift magnitude is indicative of a methodological problem, such as the presence of a large air leak.

The end-expiratory lung volume has a significant influence on many tidal breathing parameters [2, 4, 5]. Once the volume has been dedrifted, zero volume is generally defined as the mean end-expiratory level (EEL). This should be displayed on the time-based trace to ensure that it is representative of the data, with the user being given the option to adjust it if necessary.

The variability of the end-expiratory values that are scattered around the "zero" EEL can then be used to assess the stability of the EEL. A preliminary suggestion is that, after correcting the volume signal for drift, the mean EEL is established from 20–30 breaths, with the variation in

individual end-expiratory points from this mean EEL being used to calculate the  $sd$  of the EEL. This could then be expressed relative to the absolute magnitude of the  $V_T$  for within- and between-subject comparisons.

During on-line measurements, rezeroing of the volume at the beginning of inspiration may be helpful in stabilizing the display. However, during off-line evaluation, the true EEL after drift correction should be used so that breath-to-breath variations can be detected. The practice of presenting inspired and expired volumes separately (*i.e.* above and below the zero axis respectively) should be discouraged, since much information about the breathing pattern is lost, including any instability of the EEL or volume drift. Whichever procedure is used to stabilize the volume signal for display, there should always be the means to disable this, and the user must ensure that the procedure does not mask the presence of leaks.

#### *Body temperature, barometric pressure and saturated with water vapour conditions*

Errors of up to 11% may occur if inspiratory flow and volume are not converted to BTPS conditions. If  $V_T$  is expressed as the mean of the inspired ( $V_{Ti}$ ) and expired volumes ( $V_{TE}$ ), which is the recommended practice except in intubated babies, in whom inspiratory leak may be a problem, neglecting to convert this to BTPS conditions leads to an underestimation of ~5%. Unfortunately, correcting to BTPS conditions is not always straightforward. For example, if tidal breathing measurements are made when background gas flow is superimposed on the exhaled gas, the precise BTPS correction factor to apply may be unknown [22]. Also, although it is generally assumed that expired gas is at BTPS conditions, there may be some deconditioning of expired gas before it reaches the PNT in practice (personal communication, J. Reinstaedtler, International Applications, Erich Jäger GmbH, Höchberg, Germany). For the purposes of standardization, and to avoid any systematic bias between different systems for assessing tidal breathing and other parameters of respiratory function in infants, it is currently recommended that inspiratory flow be corrected to BTPS conditions using the following equation:

$$V'^{BTPS} = V'^{ATP} T_b (P_{amb} - P'_{H_2O,amb}) / T_{amb} (P_{amb} - P_{H_2O,T_b}) \quad (4)$$

where  $V'^{BTPS}$  and  $V'^{ATP}$  are flow under BTPS and ambient temperature and barometric pressure conditions,  $T_b$  and  $T_{amb}$  are the thermodynamic body (310.2 K) and ambient temperature and  $P_{amb}$ ,  $P_{H_2O,T_b}$  and  $P_{H_2O,amb}$  are the ambient pressure and water the vapour pressure at 100% humidity at  $T_b$  (6.3 kPa) and of the ambient gas; the latter can be approximated by:

$$P_{H_2O,amb} = (RH_{amb} P_{H_2O,x}) / 100, \quad (5)$$

where  $RH_{amb}$  is the relative humidity of the ambient gas (as a percentage) and  $P_{H_2O,x}$  the water vapour pressure at 100% humidity at a temperature of  $x$ .

BTPS corrections are obviously not necessary when the infant inspires air which has been preconditioned to BTPS conditions, such as during plethysmographic measurements of airway resistance using a heated rebreathing bag [5]. However, data collected under the latter conditions are unsuitable for tidal breathing analysis due to the inevitable stimulation of breathing under these conditions [23].

### Automatic breath identification

One of the main challenges in tidal breathing analysis, from the point of view of the computer programmer, is the automatic identification of the beginning of inspiration and expiration for each breath in a series. This involves pattern recognition, which is notoriously difficult for computers, even though human observers might find the task easy. Indeed, it is no trivial matter to come up with an algorithm that works all the time, and never misses breaths or identifies ones that do not exist. Once the individual inspirations and expirations have been identified, determining  $V_T$ ,  $f_I$ ,  $f_E$  and  $f_R$  for each breath is essentially straightforward.

In recent years, there have been several attempts to identify the most robust type of breath identification algorithm [24]. The most frequently used algorithm for breath detection is based on flow thresholds, as shown in figure 4. The choice of flow threshold is critical because it must be higher than the noise level in order to prevent false triggering but low enough to detect small breaths. Ideally, the flow threshold should depend on age, but most algorithms use a fixed value for all subjects. This can lead to poor identification of breaths, especially in small babies with rapid or irregular breathing patterns. In commercial devices, the flow threshold used should be clearly given by the manufacturer, together with any plausibility tests [24]. Once the flow threshold has been crossed, a threshold algorithm must search back to the last zero crossing of flow to find the precise time of the inspiratory/expiratory transition [7, 8].

The *Appendix* analyses two breath detection algorithms that have been used in a number of previous investigations. One algorithm identifies the zero crossings of a smoothed flow signal, and the other identifies zero crossings in flows

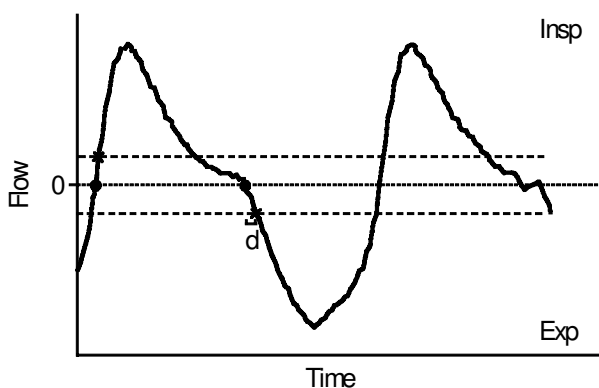


Fig. 4. – Illustration of a flow threshold (---) algorithm for the detection of the beginning of inspiration (insp) and expiration (exp). ● : recognized start of insp/exp; x: verification of insp/exp d: time delay between recognition and verification.

that bracket peak flow magnitudes above a set threshold. Although these algorithms do not represent everything that is possible in automatic breath detection, they serve to illustrate some of the key problems involved, and demonstrate that different algorithms can perform differently under certain circumstances.

### Data evaluation and reporting

Tidal breathing measurements should be accompanied by high-resolution graphic display showing the measured flow and volume signals plotted against time and against each other. These plots should be of sufficient clarity to allow manual validation of the calculated breathing pattern parameters because, despite apparently clear definitions, correct measurement of these parameters is often not straightforward. In particular, automatic determination of the start and end of each breath can be unreliable if the shape of the volume signal differs significantly from the typical normal form shown in figure 1b (see *Appendix*). Automatic breath detection should thus be accompanied by visual confirmation which requires adequate display of the measured signals, something which has rarely been available from commercial devices in the past.

Evaluation of the measured flow and volume signals is commonly performed off-line, beginning with replay of the stored signals and selection by the operator of suitable epochs for analysis. Data that are not accepted for analysis should not be deleted, as they may be valuable in retrospect. In the final report of a tidal breathing analysis, the total number of breaths recorded and the number of these selected for analysis should be given. The mean and SD, or coefficient of variation, should be reported for all parameters. The report should also include essential patient characteristics [1], representative time-based signals and flow/volume loops, together with a parameter table of individual trials and a statistical summary.

### Reference data

In order to use tidal breathing analysis effectively in the clinical setting, it is important to know: 1) the influence of growth and maturation (including gestational and post-natal age) on the various tidal breathing parameters; 2) the influence of demographic factors, such as sex and ethnic group, on tidal breathing parameters; 3) the normal intra- and interindividual variability of the parameters at every age; and 4) the diagnostic value (if any) of the various parameters. Unfortunately, despite repeated efforts over the last 50 years to establish reference values for ventilatory parameters in healthy infants, knowledge regarding the biological development and clinical/diagnostic value of most tidal breathing parameters remains sparse. Although some so-called "reference data" have been published, these values are highly specific to the equipment used and the behavioural state of the specific population studied and cannot be recommended for general use. This problem needs to be addressed urgently in the near future once equipment and measurement conditions have been standardized.



## Conclusions

The study of tidal breathing in infants and children begins with the measurement of flow at the mouth during quiet breathing. When collecting flow data it is important that: 1) a snugly fitting face mask is used to minimize air leaks, with the dead space of the mask being estimated at 50% of its physical volume; 2) a flowmeter with appropriate frequency response and linearity is employed; 3) efforts are made to eliminate the various sources of drift in volume that occur when flow is integrated with respect to time; 4) the A/D converter used to sample the flow signal can adequately resolve the largest and smallest flows required by the study; 5) the flow is filtered for anti-aliasing and sampled so as to satisfy the sampling theorem (a sampling rate of 100 Hz appears to be sufficient for the determination of time and volume parameters, but rates of 200 Hz are necessary for analysis of the tidal breathing flow/volume loop and other sensitive parameters such as  $t_{PTEF}/t_E$ ); and 6) inspired gases are corrected to BTPS conditions.

Once the data have been collected, certain key signal processing considerations must be attended to, as follows: 1) flow must be integrated to obtain volume using an appropriate numerical integration algorithm (trapezoidal integration is sufficiently accurate for most applications involving data sampled at  $\geq 100$  Hz); 2) a drift correction algorithm must be employed to eliminate the inevitable upward or downward drift of the volume baseline obtained from integrating flow; and 3) the magnitude of the drift in volume should be monitored for indications of a possible air leak.

The potentially most troublesome aspect of tidal breath analysis from the computational point of view is the identification of the beginning and end of inspiration and expiration. It would clearly be advantageous if the computer were to perform this labour-intensive task. However, it may not be possible to devise a completely automatic algorithm that works satisfactorily in every case; thus some means of quality control by visual inspection is desirable to ensure appropriate segmentation of individual breaths. Once the individual breaths in a flow record have been successfully identified, it is relatively straightforward to calculate the various indices of the breathing pattern that may be of interest.

Once the methods and equipment for measuring and analysing tidal breathing in infants are standardized, there is an urgent need to establish appropriate reference ranges for various key parameters so that they may be used more effectively in the clinical setting.

## Appendix: automatic breath identification

In this appendix, two algorithms for automatic breath identification are examined in order to illustrate some of the issues and difficulties involved. These algorithms are: 1) an algorithm that identifies the zero crossings of a smoothed flow signal, the "smoothed" algorithm; and 2) an algorithm that identifies zero crossings in flow that bracket peak flow magnitudes above a set threshold, the "threshold" algorithm.

## The smoothed algorithm

This algorithm identifies the beginning of inspiration and expiration in each breath from the points at which flow crosses zero. This requires two conditions to be satisfied: 1) there is no significant zero offset in flow; and 2) flow only changes sign at the inspiratory/expiratory transitions. The first condition is ensured with reasonable accuracy in a first pass over a data record containing a number of breaths by subtracting the mean of the flow signal from itself. The second condition is more problematic because cardiogenic oscillations in flow together with other extraneous noise sources can cause flow to cross zero at multiple points within a breath. This is particularly prevalent at the end of expiration, at which point the magnitude of flow is low. For this reason, the smoothed algorithm first identifies the beginning of expiration in each breath, corresponding to the peaks in volume, as these are generally less obscured by extraneous oscillations.

*Breath identification.* To eliminate the problem of spurious zero crossings, the flow signal is first smoothed by calculating its running mean using a window length of  $N$  data points. The smoothed signal ( $V'_s$ ) is then:

$$V'_s(i) = (1/N) \sum_{j=i-N/2}^{i+N/2} V_j \quad (6)$$

For  $N=2,4,6, \dots$ , the smoothed flow signal tends to show fewer high-frequency noise-generated oscillations than the flow signal. If  $N$  is chosen properly, only the low-frequency oscillations in flow corresponding to complete breaths are left in the smoothed flow. Figure 5 shows an example of the result of this smoothing operation on the flow signal from a single breath. Figure 5 also shows that the smoothing operation shifts the positions of the zero crossings. Therefore, the crossings in the smoothed flow signal cannot be taken as the final positions of the inspiratory/expiratory transitions in flow. The final positions of the beginning of expiration are found as follows. First, the smoothed flow signal is examined for

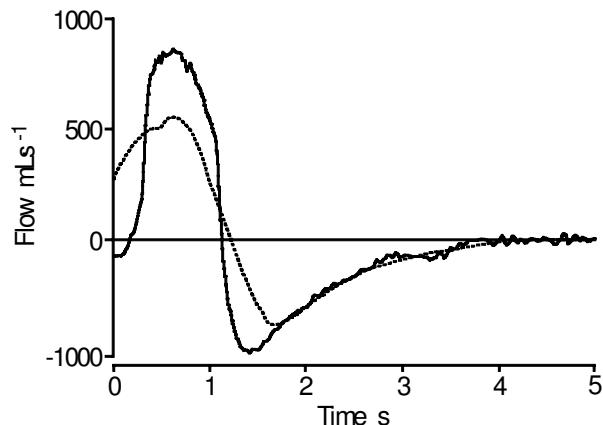


Fig. 5. – Smoothing a signal using a running mean. Note the multiple zero crossings towards the end of expiration in the original flow signal (—). The smoothed flow signal (---) was obtained by smoothing flow using a 1-s running mean, eliminating the multiple zero crossings.

those points at which it crosses zero from positive to negative. These points are close to, but generally not coincident with, the beginning of each expiration. Therefore, the flow signal is next integrated to obtain volume, and the positions of the volume minima are located between those time points at which the beginnings of expiration were previously located in the smoothed flow signal. The regions between these volume minima are then researched for their maxima, which are the true beginnings of expiration.

Note that, if  $N$  is too small, not all the spurious zero crossings will be eliminated in the smoothed flow signal by the above procedure. Similarly, if  $N$  is too large, some of the real breaths may be eliminated.

Generally speaking,  $N$  should correspond to a window length of approximately one breath period, but this obviously varies with the particular data record being analysed. It is therefore not possible to specify a single value of  $N$  that works in every case. For this reason, the smoothed algorithm interacts with the operator for the determination of  $N$ . The operator is prompted for a suitable value, and is then shown the resulting breath identification as a volume signal. If the operator decides that some breaths have been missed or incorrectly identified, a different value of  $N$  may be tried. This process is repeated until breath identification is satisfactory. This interactive process may not be suitable for general clinical applications, as the operator may not have the expertise and/or the time necessary to go through the visual quality check procedure described above. For general use, it may, therefore, be best to use a default length for the smoothing window that works well in most situations. Nevertheless, it is clearly advisable to have some means of resorting to visual quality control, so that an expert can deal with questionable cases that have not been dealt with unambiguously by the algorithm.

*Volume drift correction.* At this stage, however, the volume signal will probably still contain some residual drift that has failed to be eliminated by subtraction of the mean flow. This residual drift is removed by identifying the volume minima between each inspiratory/expiratory transition, and then adding a constant to the flow so that, when it is reintegrated, these volume minima lie along a regression line with a slope of zero. In other words, the FRC is forced to vary about a horizontal baseline (fig. 3). Finally, the maxima and minima for each breath are identified in the drift-corrected volume signal.

At this point, the volume signal has been corrected for drift and the beginning of each expiration identified together with the volume minima for each breath. The  $V_T$  for each breath is then simply the mean of  $V_{T,I}$  (the difference in volume between the beginning of the corresponding expiration and the preceding lowest point) and  $V_{T,E}$  (the difference in volume between the beginning of expiration and the subsequent lowest point). Identifying  $t_I$  and  $t_E$  might seem equally trivial, merely requiring identification of the time differences between each inspiratory/expiratory transition and its preceding or succeeding lowest point. However, even with smoothing, cardiogenic oscillations in the tail of a long slow expiration can produce significant variation in the timing of the lowest point because the volume signal is so flat in this region. For this reason,  $t_I$  is determined by starting at each

transition from inspiration to expiration and working backwards until the volume comes within 5% of the lowest point in the preceding breath. The time interval between this point and the start of the preceding expiration is taken as  $t_E$ .

### The threshold algorithm

*Breath identification.* The threshold and smoothed algorithms both identify transitions between inspiration and expiration from zero crossings in flow. However, spurious crossings, such as those due to cardiogenic oscillations toward the end of expiration, are eliminated in a different manner in the threshold algorithm. In this algorithm, all zero crossings in flow are first identified. Next, the peak magnitudes of flow, either positive or negative, between each zero crossing are found. Finally, pairs of zero crossings are discarded if they are separated by a peak flow whose magnitude is less than a certain threshold. Figure 6 shows the zero crossings in flow from a single breath. The crossings separated by low-magnitude peaks are discarded. The flow threshold for discarding zero crossings varies according to age. In preterm infants and newborns it may be as low as  $10 \text{ mL}\cdot\text{s}^{-1}$ , whereas, in infants beyond the neonatal period ( $>4 \text{ kg}$ ), a threshold of  $\sim 30 \text{ mL}\cdot\text{s}^{-1}$  usually works well. As with the smoothed algorithm, a fixed threshold may not work in every case; thus the user is given the option of changing the threshold until satisfactory results are obtained. Unfortunately, it is not possible to specify a single threshold that will suit every situation. If the threshold is too low, false breaths may be detected, but, if the threshold is too high, real breaths may be missed. The most robust algorithms are those in which a flow threshold is combined with some additional plausibility criteria [24].

*Volume drift correction.* Volume drift correction is achieved by the threshold algorithm in the same way as by the smoothed algorithm; that is the end-expiratory volumes are made to lie along a horizontal regression line.  $V_T$  is obtained identically by both algorithms. Using the threshold algorithm,  $t_I$  and  $t_E$  are determined from the time intervals between successive zero crossings, which

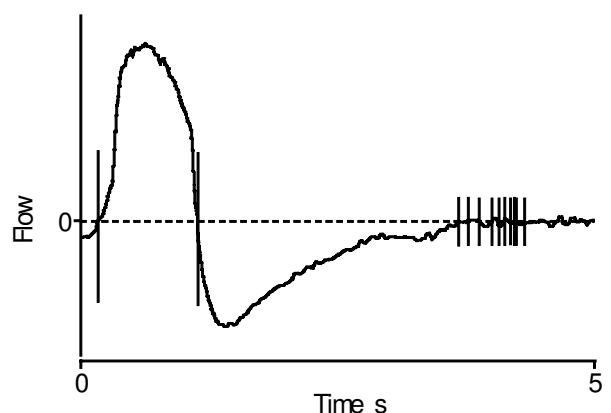


Fig. 6. – Zero crossings in flow (vertical lines). Those crossings separated by low-magnitude peaks in flow (in this case, those toward the end of expiration) are discarded, leaving only those crossings that define the transitions between inspiration and expiration.

differs somewhat from the smoothed algorithm. Note that the time resolution of both algorithms as used in the present study are determined by the data sampling rate, because zero crossings in flow are determined to the nearest data point. With a data sampling rate of 100 Hz, for example, going to the nearest data point gives timing estimates accurate to within 10 ms, which is probably sufficient when simply measuring  $V_T$  and  $f_R$ , but could introduce significant errors when determining short  $t_{PTEF}$ . Since greater accuracy in zero crossing determination is easily obtained by interpolating between the two data points that span zero, this should probably be carried out as a general rule.

#### Comparison of smoothed and threshold breath identification algorithms

Figure 7 shows two 40-s records of flow used to test the algorithms. These records were obtained from infants of 34–38 weeks gestational age, and represent two types of signal: 1) regular ventilation in which the individual breaths are clear and well defined; and 2) ventilation in which there are large rapid oscillations in flow within one of the breaths towards the end of the record (this was deliberately chosen as an extreme example for testing the algorithms and would not be considered a suitable epoch for the analysis of tidal breathing parameters when used to reflect lung mechanical properties).

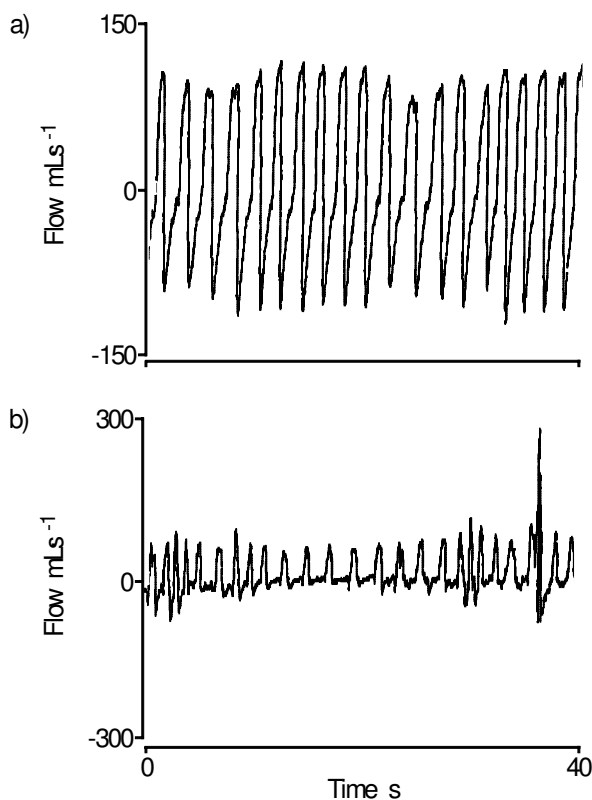


Fig. 7. – The two flow records used to test the breath identification algorithms: a) clear well-defined breaths; and b) somewhat less regular breaths with, in particular, some high-amplitude rapid oscillations in the third-from-last breath.

Table 1. – Tidal breathing parameters identified from 18 consecutive breaths determined by the smoothed and threshold algorithms\*

	Smoothed	Threshold
$V_T$ mL	66.6±3.7	66.6±3.6
$t_I$ s	0.75±0.07	0.76±0.07
$t_E$ s	1.31±0.19	1.29±0.19

Data are presented as mean±SD. \*: from flow record shown in figure 7a. The smoothed algorithm was implemented using a 2-window to calculate the running mean; the threshold algorithm was implemented with a flow threshold of 10 mL·s<sup>-1</sup>.  $V_T$ : tidal volume;  $t_I$ : inspiratory time;  $t_E$ : expiratory time.

Neither the smoothed nor the threshold algorithm presented any difficulty in correctly identifying the breaths shown in figure 7a. The  $V_T$ ,  $t_I$  and  $t_E$  obtained using the two algorithms are given in table 1. The slight differences between the values of some of the parameters returned by the two algorithms are no doubt due to the differences in the way that the beginning of inspiration is defined. In the smoothed algorithm it is the point at which the volume comes within 5% of its lowest point when working backwards from the peak, whereas, in the threshold algorithm, it is simply the lowest point in volume. Thus the threshold algorithm gives a more accurate estimate when the troughs in volume are well defined, as in the data set considered. The smoothed algorithm, in contrast, is more robust to the presence of cardiogenic oscillations at the end of a long expiration, when flow is low and volume is sensitive to having its minimum displaced a large distance by noise.

The two algorithms did not fare equally when considering the flow record shown in figure 7b, however. The smoothed algorithm easily identified the breaths correctly, but the large rapid oscillations in flow towards the end of the record caused problems for the threshold algorithm. These oscillations do not correspond to true breaths, as figure 8 clearly shows. However, the threshold algorithm was unable to eliminate them as candidates because their peak magnitudes were comparable to those of real breaths, and so they were not detected by the flow threshold. This example illustrates the key difference between the way in which the smoothed and threshold algorithms operate. The smoothed algorithm involves a filtering operation that manipulates the frequency content of flow in order to separate spurious high-frequency events from lower-frequency true breaths. The threshold algorithm, in contrast, considers the amplitude characteristics of flow which, in this example, are similar for both spurious oscillations and true breaths.

It thus appears that the threshold algorithm is unable to function successfully in all cases in which the smoothed algorithm does succeed, indicating that using a frequency filtering operation to identify breaths is better than using an approach based simply on amplitude discrimination in cases in which periods of irregular breathing are to be examined. This is particularly relevant in cases in which long-term recordings to investigate regulation of breathing patterns are being undertaken. During routine respiratory function testing, this should be less of a problem as the operator should select epochs of regular breathing.

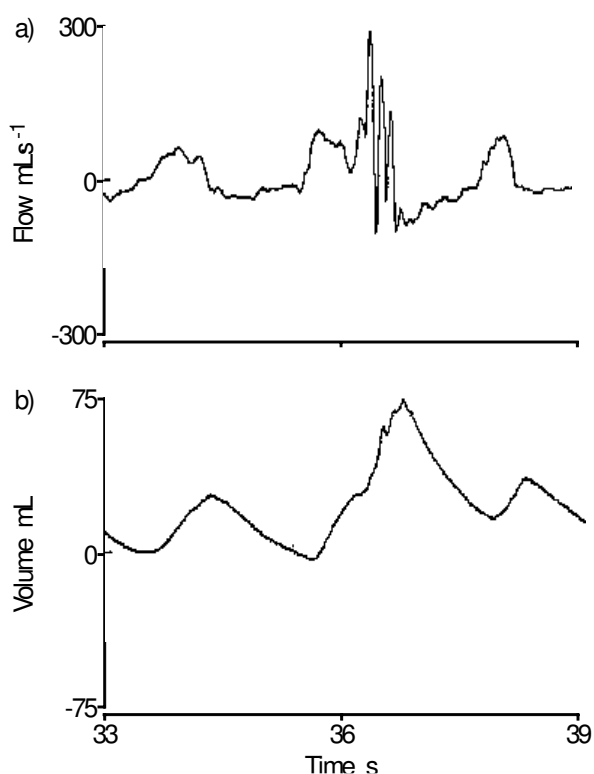


Fig. 8. – A a) 6-s segment near the end of the flow record shown in figure 7b; and b) the corresponding volume signal. The middle breath contains several large oscillations in flow with peak magnitudes that are as large as (or larger than) those of true breaths in the record. Consequently, the threshold algorithm cannot distinguish them from true breaths. The smoothed algorithm, in contrast, is successful at discarding these oscillations because it smooths them out in a low-pass filtered version of flow prior to looking for zero crossings to determine inspiratory/expiratory transitions.

SCHMIDT *et al.* [24] investigated a number of algorithms applied to newborns and found similar results; in most cases all algorithms agreed, but there were always a few difficult situations in which some algorithms outperformed others. Thus it seems somewhat doubtful an algorithm can ever be devised that works all the time without operator intervention. Nevertheless, it would clearly be advantageous to have an algorithm for clinical use that functions, at least most of the time, without user interaction. One possibility for dealing with difficult cases would be to use the combination of a threshold algorithm with various feasibility criteria [24] and to discard all identified breaths that fall outside some agreed range (e.g.  $\pm 10\%$ ) of the mean VT or  $t_{tot}$ .

#### Effects of data sampling rate

The rate at which a flow or volume signal is sampled influences the values of breathing pattern parameters. A low sampling rate obviously gives reduced temporal resolution of timing parameters such as  $t_I$  and  $t_E$  as shown above. In order to test the influence of data sampling rate on estimation of VT,  $t_I$ ,  $t_E$  and  $t_{tot}$ , the smoothed algorithm was used to analyse the flow records shown in figure 7 when resampled at 75, 50 and 25 Hz (the original

sampling rate being 100 Hz). In both cases, the flow signals were analysed using a smoothing window of 2 s.

VT was particularly insensitive to changes in data sampling rate, as might be expected because it is a measure of signal amplitude rather than timing. The mean VT obtained from each of the test signals did not change by more than 0.1% as the sampling rate was dropped from 100 to 25 Hz. The timing parameters  $t_I$  and  $t_E$  were somewhat more affected, changing by up to 0.7% as the sampling rate dropped from 100 to 75 Hz, by up to 2% as the rate dropped to 50 Hz and by up to 3.5% as the rate dropped to 25 Hz. Interestingly, the remaining timing parameter  $t_{tot}$  changed by only up to 0.1% over this range of sampling rates, indicating that errors in estimating  $t_I$  were compensated for by virtually equal and opposite errors in  $t_E$ . These results suggest that a data sampling rate of 100 Hz is adequate for accurate estimation of VT,  $t_I$  and  $t_E$  (and hence  $f_R$ ). Indeed, for most applications, a rate of 50 Hz is probably adequate if it is only these parameters that are to be analysed. Nevertheless, when timing parameters such as  $t_{PTEF}/t_E$  are to be calculated, especially in very small babies with a rapid  $f_R$ , a sampling rate of 200 Hz is recommended.

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