CHAPTER 2

Whole-body plethysmography

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The word plethysmograph is derived from the Greek plethmos (enlargement), and is related closely to plethus (fullness) and plethora (fullness). Indeed, the fundamental function of a whole-body plethysmograph is the measurement of intrathoracic gas volume (TGV) and volume change. Whole-body plethysmographs have been used to measure changes in lung volume over a range of volumes, from the scale of millilitres to litres. Early reports of whole-body plethysmography to determine thoracic gas volume (TGV) [1] and airway resistance ($R_{aw}$) [2] measured volume changes of the order of millilitres, in terms of associated changes in plethysmograph and alveolar pressures ($P_{a}$), using the constant-volume variable-pressure plethysmograph. Changes in lung volume during compression and decompression of thoracic gas were measured while the subject breathed entirely within the plethysmograph.

An alternative volume-displacement whole-body plethysmograph measured volume changes of the thorax directly, including both changes in volume of gas flowing into and out of the lung and simultaneous changes in compression and decompression of thoracic gas [3]. In contrast to the constant-volume plethysmograph of DuBois et al. [1], subjects breathed in and out across the wall of the volume-displacement plethysmograph developed by Mead [3]. The volume-displacement plethysmograph provided more ready assessment of changes in TGV during extended manoeuvres such as the vital capacity (VC). During such forced manoeuvres, lung volume changes due to compression of thoracic gas were measured, in addition to those associated with gas flow out of the lung.

Subsequent technological developments permitted a combination of the two approaches by using a pressure-compensated volume-displacement or integrated-flow, plethysmograph, described by the groups of Mead and van de Woestijne [4–7], and reviewed by Péslin [8] and Coates et al. [9]. In the combination plethysmograph, the subjects breathe either across the wall of the plethysmograph to the outside to measure total thoracic displacements or within the plethysmograph to measure compression volumes only, excluding air flow into or out of the lung. In this combination plethysmograph, both pressure change in the plethysmograph and the volume displaced through the plethysmograph wall are combined to provide a measure of the volume displacements of the thorax. This approach provides the advantageous frequency response of the pressure plethysmograph with the ability to measure volume displacements over a very wide range of volumes. This approach is now commonly referred to as a "transmural" plethysmograph.

Current technological improvements in whole-body plethysmography provide measurable variables that are less dependent on patient cooperation than in initial implementations [1, 2]. Recent advances in the understanding of chronic obstructive pulmonary disease (COPD) have led to renewed interest in the evaluation of compression
of TGV as an aid to better understanding of dynamic events during the respiratory cycle. Therefore, applications of plethysmographic techniques that include thoracic volume displacements are reviewed as well in this Chapter. However, this Chapter focuses primarily on the use of the variable-pressure constant-volume plethysmograph, as this instrument has been in use most commonly in clinical pulmonary function testing. The clinical measurements of $R_{aw}$ and functional residual capacity (FRC) determined by whole-body plethysmography ($FRC_{pleth}$) are most extensively discussed herein.

**Principles of whole-body plethysmography**

The whole-body plethysmograph consists of a rigid chamber, of comparable size and shape to an enclosed telephone booth, in which the subject sits while breathing through a pneumotachograph. Pressure transducers of different sensitivity are arranged to measure the pressure across the pneumotachograph (flow), the pressure difference across the wall of the plethysmograph and pressure at the airway opening. The fundamental principle of the variable-pressure plethysmograph is that changes in $P_A$ may be inferred from changes in plethysmograph pressure. This is achieved by the process described immediately below.

A shutter mechanism is positioned close to the mouth in the plethysmograph. This shutter may be closed to provide transient airway occlusion. Voluntary respiratory efforts are performed against the closed shutter, during which the change in $P_A$ ($\Delta P_A$), is estimated by recording the change in mouth pressure ($\Delta P_m$). $P_m$ ($P_A$) is plotted against simultaneous plethysmographic pressure changes during respiratory efforts against a closed shutter to measure absolute TGV. The same relationship between alveolar and plethysmographic pressure measured during respiratory efforts against a closed shutter is then extended to dynamic events during free breathing to measure $R_{aw}$, wherein airflow is related to $P_A$.

**Types of plethysmograph**

Three different types of whole-body plethysmograph may be used to measure changes in thoracic volume. These depend on whether the aim is to measure the large volume changes associated with respiratory manoeuvres, such as the VC, or just those which accompany compression and decompression of the gas in the lungs exclusive of changes in volume due to gas flow in and out of the lungs. Suitable changes in transducer sensitivities and mechanical arrangement are incorporated into the different types of plethysmograph.

The constant-volume or variable-pressure plethysmograph is used to measure small volume changes due to compression and decompression of gas within the lungs.

The constant-pressure or volume-displacement plethysmograph is used to measure large changes in lung volume associated with gas flow into and out of the lungs.

The pressure-corrected variable-volume plethysmograph combines the advantages of both the plethysmographs described above. The sensitivity and rapid frequency response of variable-pressure constant-volume plethysmography is provided along with the ability to measure large slow volume changes in the lungs during breathing.

Variable-pressure plethysmograph. The advantage of the variable pressure plethysmograph is simplicity of hardware components and accuracy of the measurement. The small changes in plethysmographic pressure associated with compression/decompression of TGV are recorded using a very sensitive pressure transducer, as shown schematically in figure 1.
The plethysmograph is open to the atmosphere via a small leak with a mechanical time constant of 5–25 s, with most current instruments using a value $<10$ s. This controlled leak minimises slowly occurring pressure changes that are not related to respiratory manoeuvres, such as thermal drift (heating) caused by the presence of a subject breathing within the chamber.

The large volume of the plethysmograph chamber (600–1,000 L) undergoes very small pressure changes during compression and decompression of TGV. Accordingly, the plethysmographic pressure transducer must be very sensitive and stable. It is stabilised against changes in room air pressure during such events as opening or closing of a door by connection of the other side of the plethysmographic pressure transducer to a reference chamber with comparable time-constant to that of the plethysmograph.

In practice, the plethysmographic pressure transducer is calibrated in terms of changes in TGV. This is done by quickly introducing and withdrawing 30–50 mL of air into the plethysmograph chamber at a frequency of approximately 1 Hz. $P_A$: alveolar pressure; $P_m$: mouth pressure; $V_L$: lung volume; $R_{aw}$: airway resistance; TGV: thoracic gas volume; $\Delta V$: change in volume; $\Delta P$: change in pressure. See text for discussion.

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In practice, the plethysmographic pressure transducer is calibrated in terms of changes in TGV. This is done by quickly introducing and withdrawing 30–50 mL of air into the plethysmograph using a motor-driven syringe, to simulate the changes in TGV that occur during decompression and compression of thoracic gas. After such calibration, the measured changes in plethysmographic gas pressure reflect the change in TGV due to compression and decompression of thoracic gas. Changes in calibrated plethysmographic gas pressure are recorded in terms of volume change ($\Delta V$), and known as shift volume. Shift volume is the change in TGV due only to compression or decompression, exclusive of changes due to airflow into and out of the lung, both during occluded respiratory efforts and during breathing within the plethysmograph. Since calibration of the plethysmograph is normally carried out without a subject in the plethysmograph, this calibration must be corrected for the subject’s body volume. Therefore, the body weight of the subject is entered prior to any testing of the subject and is used in the calculation of the final calibration coefficient.

**Volume-displacement plethysmograph.** A volume-displacement plethysmograph measures volume changes of the thorax directly. Subjects breathe in and out across
the wall of the plethysmograph to room air. The increase in lung volume that occurs during inspiration includes the volume of gas inspired plus the additional volume associated with decompression of TGV resulting from the fall in intrathoracic pressure necessary to provide a gradient for inspiratory airflow.

The advantage of the volume-displacement plethysmograph is the ability to measure respiratory manoeuvres such as the slow or forced vital capacity (FVC). Integrated airflow at the mouth can be compared to thoracic volume displacements during forced expiration to provide more physiological information in subjects with hyperinflation or airway obstruction.

Measurement of total thoracic volume displacement is useful, but the original plethysmograph described by Mead [3] required a very sensitive and critically damped direct-reading spirometer, which was technically very demanding to build. Therefore, this construction has been supplanted by the pressure-corrected integrated-flow plethysmograph [6–9].

**Flow plethysmograph.** Comroe et al. [10] pointed out that use of a spirometer connected to a volume-displacement plethysmograph chamber made it difficult to obtain adequate speed of response. Frequency response was improved by adding a signal proportional to plethysmograph pressure to the volume-displacement signal and, subsequently, substituting a pneumotachograph in the wall of the plethysmograph for the spirometer bell [4–6]. Such a pressure-corrected plethysmograph which integrates flow through the plethysmograph wall permits accurate measurement of changes in TGV during forced expiration manoeuvres. Loss of sensitivity with small thoracic volume displacements and possible zero-flow integrator drift are limitations of this approach when measuring TGV; but occlusion of the pneumotachograph in the wall of the plethysmograph converts the flow plethysmograph back into a variable-pressure plethysmograph, allowing more sensitive measurements of TGV. The flow plethysmograph is shown schematically in figure 2.

Some pressure change in plethysmograph air is required to cause movement of air in

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**Fig. 2.** – Schematic representation of a pressure-corrected integrated-flow plethysmograph, illustrating the path of the subject’s breathing through the wall of the plethysmograph to room air. Recording of the volume displacements of the thorax includes those due to airflow into and out from the lung, as well as those due to compression and decompression. Volume displacements of the thorax drive plethysmograph air through a pneumotachygraph in the wall of the plethysmograph, and are recorded by integration of the flow through the plethysmograph wall. $P_{a}$: alveolar pressure; $P_{m}$: mouth pressure; $V_{l}$: lung volume; $R_{w}$: airway resistance; TGV: thoracic gas volume; $ΔV$: change in volume; $ΔP$: change in pressure. See text for further discussion.
and out of the plethysmograph chamber. This pressure change occurs in the large volume of compressible gas within the plethysmograph chamber. Thus, part of the volume displacement is temporarily "lost" in compression or decompression of plethysmographic air and does not reach its equilibrium value until plethysmographic air pressure has returned to atmospheric, as noted by Mead [3]. This volume displacement is "found" within the pressure change of plethysmographic air itself. Thus, as the subject breathes room air through a tube across the wall of the plethysmograph, changes in TGV expand or compress plethysmographic air, and simultaneously displace some air in or out of the plethysmograph across the flow meter in its wall. The volume displaced by compression or decompression of plethysmographic air is recovered by adding an electrical signal proportional to plethysmographic pressure to the measured volume displaced across the plethysmograph wall in the "pressure-corrected" body plethysmograph [4–7]. Because this volume displacement is most commonly recorded by integrating flow through a flow meter in the plethysmograph wall, this type of plethysmograph is often described as a pressure-corrected integrated-flow plethysmograph. It should be emphasised that in this use, the integrated flow is the flow in and out across the wall of the plethysmograph chamber, in contrast to the integrated airflow in and out of the mouth described for the pressure plethysmograph [2].

The measurement of a rapid volume change, such as that encountered during a brief cough or the initial part of a forced expiratory VC utilises the "pressure-correction" shown schematically in figure 3 which is modified from Leith and Mead [7]. Figure 3 shows schematically the initial rapid decrease in TGV during a forced expiration. The trace labelled a) represents an idealised trace of the true volume change for the initial rapid decrease in lung volume, shown as the onset of a square wave. At the onset of this abrupt decrease in TGV, plethysmographic pressure falls rapidly with compression of thoracic lung volume and expansion of plethysmographic air by expiratory muscle effort, then exponentially returns to its initial value, after the volume event is complete (e.g. a brief cough). This pressure change is shown in trace b). The signal from a linear flowmeter in the wall of the plethysmograph is identical in shape to trace b). Integration of this flow signal is shown in trace c). Integrated flow across the plethysmograph wall

![Diagram](image_url)

Fig. 3. – Schematic representation of the basis of "pressure-correction" to account for phase lag between volume displacements of the thorax and those of plethysmograph air through the pneumotachygraph in the plethysmograph wall. $P_{\text{pleth}}$: pressure in the plethysmograph chamber; $V_{\text{pleth}}$: flow across wall of chamber. See text for discussion.
eventually reaches the same level as the true decrease in TGV, but the volume change recorded by integrated flow across the plethysmograph wall is slower because of the temporary "loss" of volume during the initial decrease in plethysmographic air pressure. To recover this contribution, an electrical signal proportional to trace b) is added to the integrated plethysmograph flow in trace c). The sum of these contributions recovers the initial true volume event represented by the solid trace d).

Pressure-corrected integrated-flow plethysmographs provide sensitive recordings of pressure and volume events over a wide range of volume displacements. They permit accurate recording of maximal expiratory flow-volume curves in addition to measurement of TGV, specific airway resistance (s\(R_{aw}\)) and \(R_{aw}\) with the same instrument. Thus, this approach provides the advantageous frequency response and sensitivity of the variable-pressure plethysmograph with additional lung volume displacement recordings over a wide range of volumes, and has been used for measures of true TGV change (including that due to compression of thoracic gas) during either tidal breathing [11] or measurement of the FVC [12]. This combined approach is now commonly referred to as a "transmural" plethysmograph. It permits evaluation of the differences between thoracic gas compression and airway closure, the so-called "trapped gas" [13].

**Measurement notes**

Applications of whole-body plethysmography include physiological evaluation of respiratory mechanical limitations and diagnostic clinical testing. Special applications include paediatric and infant diagnostic testing, which have been extensively discussed by others [9, 14]. The present chapter is restricted to plethysmographic measurements in larger children and adults. While spirometry is the most commonly used pulmonary functional diagnostic test, body plethysmography provides essential additional diagnostic information [15, 16], and usefully includes measurement of both slow and forced vital capacities done in the plethysmograph.

After the subject has entered the plethysmograph, the door is closed with an airtight seal. Approximately 2 min are required for plethysmograph cabin pressure to equilibrate while air in the cabin is warmed and humidified by the subject breathing at rest. During this initial period, the plethysmograph cabin is vented periodically to room air via a solenoid-operated valve. After about 2 min, pressure drift with the valve closed is much decreased and does not interfere with the measurement of s\(R_{aw}\). At this time the subject is asked to close his/her lips tightly around the mouthpiece and breathe normally through the pneumotachygraph. The patient sits erect with head and neck in a neutral posture. A nose-clip is applied to close the nares. The subject is allowed to adapt to the measurement conditions and breathe regularly through the flowmeter for about 30 s before testing is initiated.

A complete whole-body plethysmography, measurement is commonly divided into three standardised measuring sequences whose order may be defined by diagnostic requirements. s\(R_{aw}\) is usually measured first, followed by measurement of TGV and concluding with measurement of the entire range of lung volumes, both slow and forced spirometry. Individual measurement phases can be skipped or repeated, depending on the diagnostic information required and/or the patient’s ability to cooperate. The initial report of whole-body plethysmography first described its application to measure TGV [1] and the description that follows below begins with determination of TGV. The measurement of lung volumes by plethysmography is extensively reviewed by Coates et al. [9] along with detailed discussions of physiological assumptions and technical demands of measuring instruments.
Determination of thoracic gas volume and functional residual capacity

As befits the etymology of body plethysmography, its primary use to measure TGV is considered first. It is noted that while this order corresponds didactically to the historical development of plethysmography and previous literature, in practice, current computer-assisted plethysmographic techniques commonly measure specific resistance first.

Measurement of TGV is done in the variable-pressure constant-volume plethysmograph by making use of Boyle-Mariotte’s law which relates pressure and volume changes to each other under isothermal conditions. Thus, during compression of thoracic gas, its pressure rises and, at constant temperature, the product of pressure and volume remains constant. In the plethysmograph, voluntary respiratory efforts are used to produce changes in alveolar dry gas pressure, \( \Delta P_A \), which are associated with reciprocal changes in TGV, \( \Delta V \). Alveolar dry gas pressure (\( P_A \)) itself is the difference between ambient barometric pressure (\( P_{\text{bar}} \)) and saturated water vapour pressure at body temperature (\( P_{H_2O,\text{sat}} \)), when the glottis is open with no airflow. A shutter mechanism positioned close to the mouth provides for transient controlled airway occlusion, which is utilised in making voluntary respiratory efforts to determine the relationship between plethysmographic pressure and \( P_m \). During these respiratory efforts against the closed shutter, TGV is decompressed and compressed respectively. Because the total amount of gas in the plethysmograph–lung system is constant, \( \Delta V \) causes corresponding changes in plethysmographic gas pressure during compression and decompression of thoracic gas. The change in plethysmographic pressure is then measured in terms of the change in TGV, \( \Delta V \), and denoted shift volume.

With the glottis maintained open, the change in \( P_A \) during respiratory efforts against a closed shutter may be measured by recording the change in \( P_m \). In normal subjects, the change in \( P_m \) closely approximates that in \( P_A \) during panting efforts [1]. However, the assumption that change in \( P_A \) can be measured accurately by \( P_m \) during panting efforts against a closed shutter in patients with airflow obstruction has been questioned. Several groups have reported significant differences between changes in oesophageal pressure and \( P_m \) during panting efforts against a closed shutter in subjects with airflow obstruction [17–22]. This is discussed more extensively in the sections below: Pathophysiological manifestations and Measurement of thoracic gas volume.

When only slow (1 Hz) panting efforts against a closed shutter are utilised [17–22], it is possible to measure changes in \( P_A \) from \( P_m \). \( P_m (P_A) \) pressure is plotted against simultaneous plethysmographic pressure changes (measured as the shift volume) during respiratory efforts against a closed shutter to measure absolute TGV.

The measurement of TGV is summarised by the following equations, for small changes in pressure and volume.

Boyle-Mariotte’s Law : \( P \cdot V = \text{constant under isothermal conditions} \) (1)

During airway occlusion, usually at resting end-expiration, the following equations describe TGV and \( P_A \). The inspiratory or expiratory effort against the closed shutter will decrease or increase \( P_A \) by \( \Delta P_A \), and increase or decrease TGV by a small volume change, \( \Delta V \).

\[
P_A \cdot \text{TGV} = (P_A - \Delta P_A)(\text{TGV} + \Delta V) \quad (2)
\]

Expanding and rearranging equation (2),

\[
\text{TGV} = (\Delta V / \Delta P_A)(P_A - \Delta P_A) \quad (3)
\]

Since \( \Delta P_A \) is very small compared to \( P_A \) (< 2%) it is usually omitted in the differential
term.

TGV \sim (\Delta V / \Delta P_A) \cdot P_A \quad \text{with} \quad P_A = P_{\text{bar}} - P_{\text{H}_2\text{O, sat}} \quad (4)

TGV \sim (\Delta V / \Delta P_A) \cdot (P_{\text{bar}} - P_{\text{H}_2\text{O, sat}}) \quad (5)

As noted above, during the respiratory efforts against the closed shutter, the change in $P_A$ \textit{i.e.} $\Delta P_A$, is recorded as $\Delta P_m$. $\Delta V$, the shift volume, is measured by the calibrated plethysmographic gas pressure transducer.

In whole-body plethysmographs, where $s_{\text{Raw}}$ is measured during shallow panting, TGV is determined at a lung volume that is the most comfortable for the patient. This volume is usually greater than resting FRC, because of comfort factors for normal subjects and because of flow limitation in patients with obstructive lung disease [23, 24]. Accordingly, this volume increment above resting FRC must be subtracted to provide $\text{FRC}_{\text{pleth}}$ [9].

The measured TGV additionally includes any apparatus dead spaces ($V_{d, \text{app}}$) as well as any volume inspired above resting end-expiratory lung volume at the moment of occlusion ($V_{t, \text{occ}}$). Hence $\text{FRC}_{\text{pleth}}$ can be derived from TGV by subtraction of these two volume components.

$\text{FRC}_{\text{pleth}} = \text{TGV} - V_{d, \text{app}} - V_{t, \text{occ}} \quad (6)$

In contrast to gas dilution measurements of FRC ($\text{FRC}_{\text{dil}}$), $\text{FRC}_{\text{pleth}}$ includes all TGV even if some may not be in communication with the airway opening. Thus, the value of $\text{FRC}_{\text{pleth}}$ serves as the methodological anchor for determination of absolute TGV both at residual volume (RV) and total lung capacity (TLC). The measurement procedure for determining $\text{FRC}_{\text{pleth}}$ is more complicated than the recording of $s_{\text{Raw}}$ which is described in the next section, because the subject must respond with normal breathing efforts while ventilation is interrupted by the closed shutter. Therefore, this manoeuvre requires more subject cooperation, and FRC may vary from test to test. In contrast, RV and TLC are more fixed and may be determined immediately after measurement of FRC by slow exhalation to RV followed by inhalation to TLC.

During tidal breathing, the shutter mechanism is activated by the operator using computer control, and closes at the end of the following tidal expiration. Most plethysmographs program shutter reopening at a predetermined maximal occlusion time or after the subject has generated predetermined cumulative inspiratory and expiratory $P_m$ changes against the shutter or a number of zero-pressure crossings. These different criteria were introduced to create reliable test results with optimal comfort for the subject. Subjects should always be informed to remove the mouthpiece from their mouth in the event the shutter does not open or if the subject senses substantial difficulty breathing.

During the occlusion phase the subject is asked to continue normal breathing efforts against the closed shutter. To optimise measurement quality, shutter closure settings are selected to allow recording of at least one positive and one negative $P_m$ change when the shutter is closed. Plethysmographic shift volume and the corresponding $P_m$ changes are displayed on an X–Y graph as shown in figure 4.

As in all pulmonary function evaluations, it is recommended that three replicates of the measurement of TGV are recorded and saved. Quality of the measurement is reflected, in part, by the variability of replicate trials. Quanjer \textit{et al.} [25] suggests a maximal deviation of 5% between the individual trials.

\textbf{Determination of specific resistance}

During assessment of $s_{\text{Raw}}$, it is emphasised that the relationship between airflow and shift volume, initially described by DuBois \textit{et al.} [2] does not define $R_{\text{aw}}$. $R_{\text{aw}}$ is defined
only by combining the measurement of $sR_{aw}$ and the TGV measurement during occluded respiratory efforts [1, 2].

Mouth flow during spontaneous breathing is continuously recorded from the pneumotachygraph and displayed on a graphic X–Y display versus the shift volume produced by thoracic compression and decompression as shown in figure 5. As noted above, the shift volume, $\Delta V$, excludes lung volume change due to gas flow in and out of the lung.

Thermal and humidity effects arise during inspiration of plethysmographic air and subsequent expiration of warm humid alveolar air. Electronic compensation for thermal and humidity effects was introduced to permit tidal breathing [26]; however, current whole-body plethysmographs commonly incorporate algorithms to compensate for thermal/humidity effects so that the graphic X–Y display of the $sR_{aw}$ loop is closed as

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Fig. 4. – Respiratory effort against closed shutter in the same patient as in figures 5–7, showing mouth pressure ($P_m$) plotted on vertical axis and shift volume ($\Delta V$) on the horizontal axis. Expiratory effort results in positive $P_m$ and negative $\Delta V$, and vice-versa for inspiratory effort. The slope of $P_m$ versus $\Delta V$ is proportional to the functional residual capacity determined by plethysmography (FRC$_{pleth}$; 3.8 L). This tracing shows good coordination of the obstructed inspiratory and expiratory efforts, with only small departures from a single line.

Fig. 5. – Tracing of a specific resistance ($sR_{aw}$) loop in a patient with airflow obstruction, showing the slope used for calculation of total $sR_{aw}$ ($sR_{tot}$; 3 kPa·s). Mouth airflow ($V$) is plotted on the vertical axis with inspiratory flows positive and expiratory flows negative. Shift volume ($\Delta V$) is plotted on the horizontal axis with inspiratory shift volumes positive and those during expiration negative. See text for discussion.
completely as possible during inspiration, during tidal breathing, without the need for rapid shallow respirations.

Equation 7 summarises the relationship between mouth flow, $V'$, measured by the flow meter and simultaneously measured plethysmograph pressure, calibrated in terms of shift volume, $\Delta V$, to derive $sR_{aw}$.

$$sR_{aw} = (\Delta V / V') (P_{bar} - P_{H2O,sat})$$ (7)

$sR_{aw}$ is thus determined as the product of dry gas $P_{bar}$ and the ratio of shift volume to mouth flow.

It must be emphasised that the commonly utilised slope of the X–Y display of the $sR_{aw}$ loops in this measuring step does not directly represent $R_{aw}$ (i.e. pressure–flow loops) as often assumed, but is instead, $sR_{aw}$. Thus, the slope does not yield a value for $R_{aw}$, but requires knowledge of TGV prior to calculation $R_{aw}$. The $sR_{aw}$ loop is influenced by $R_{aw}$ and TGV and its inclination rotates clockwise if either $R_{aw}$ or TGV or both are increased.

Acquisition of $sR_{aw}$ data in a whole-body plethysmographic measurement requires little cooperation from the subject, as this is commonly done in current plethysmographs during tidal breathing, rather than using the voluntary rapid shallow panting method originally reported by DuBois et al. [2].

As in all plethysmographic applications, subjects should sit upright and avoid neck flexion or rotation. After adapting to the measuring conditions during tidal breathing through the pneumotachygraph, it is recommended that at least 5–10 $sR_{aw}$ loops should be recorded as one trial. Normally, three replicate trials are recorded and saved. Optimal quality of the recording is achieved when $sR_{aw}$ loops are regular and reproducible with the loop nearly entirely closed, although patients with significant airflow obstruction manifest open loops during expiration.

Numerical parameters calculated from the specific resistance loop. The content of the $sR_{aw}$ loop is often quite complex and is not a simple narrow linear oval loop, especially in the presence of peripheral airway disease, as initially described by DuBois et al. [2]. Since the $sR_{aw}$ loop includes varying flows throughout the tidal breathing respiratory cycle, different investigators have utilised different portions of the loop to approximate a "representative" value for the entire cycle.

The total specific resistance ($sR_{tot}$) [27] and effective specific resistance ($sR_{eff}$) [23] have been well established and both are utilised in clinical laboratories. These approaches, along with use of the linear portion of the $sR_{aw}$ loop between inspiratory and expiratory flow rates of 0.5 L·s$^{-1}$ [28, 29] are designed to provide a linear approximation of $sR_{aw}$. Such linear approximations are generally comparable in patients with normal respiratory mechanics, but all of these approaches manifest interpretative compromises in advanced obstructive lung disease. The specific characteristics of these different approaches are discussed in a subsequent section with physiological interpretation.

Total specific resistance. The $sR_{tot}$, as described by Islam and Ulmer [27], is determined by a straight line between maximal inspiratory and maximal expiratory shift volume points as shown in figure 5.

The outstanding characteristic of $sR_{tot}$ is its sensitivity to partial obstruction of peripheral airways. The potential disadvantage of $sR_{tot}$ would appear to be a greater variability from test to test, as a consequence of using only two points at the extremes of inspiratory and expiratory shift volume.

Effective specific resistance. $sR_{eff}$, as introduced by Matthys and Orth [23], extended the dimensional analysis applied by Jaeger and Otis [30] to integrate effects of variable
flows and nonlinearities of mouth flow-shift volume loops during tidal breathing. They calculated $sR_{\text{eff}}$ during tidal breathing from the quotient of the integrated shift volume–volume loop (flow resistive work of breathing) and the integrated flow–volume loop (fig. 6a). This ratio defines the slope of a line that represents $sR_{\text{eff}}$. Figure 6b shows the placement of this line within the $sR_{\text{aw}}$ loop, defined by performing a least-squared fit of the line of Matthys and Orth [23] to the points that make up the $sR_{\text{aw}}$ loop.

The outstanding characteristic of $sR_{\text{eff}}$ is its reflection of an integrative assessment of airway behaviour throughout the entire tidal breath. Digital integration of the respective loops shown in figure 6a improves the signal-to-noise ratio. $sR_{\text{eff}}$ reflects larger central airways somewhat more prominently than $sR_{\text{tot}}$.

**Specific resistance at 0.5 $L\cdot s^{-1}$**. Dubois et al. [2] initially measured the slope of the $sR_{\text{aw}}$ loop at a defined fixed flow of 1 $L\cdot s^{-1}$, noting small increases of the slope in normal

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**Fig. 6.** – a) Schematic representation of graphic integration of flow ($V'$), volume ($V$), and shift volume ($\Delta V$) parameters, adapted from Matthys and Orth [23], showing flow-resistive work of breathing during inspiration and expiration ($Ai$ and $Af$, respectively) and flow–volume loop during tidal breathing ($Bi$ and $Be$), used in the calculation of effective specific resistance ($sR_{\text{eff}}$). See text for discussion. b) Same tracing of specific resistance ($sR_{\text{aw}}$) loop as in figure 5, but showing the slope resulting from calculation of area ratio shown in figure 6a, equal to $sR_{\text{eff}}$ positioned on the $sR_{\text{aw}}$ loop by regression technique ($sR_{\text{eff}} = 2.7 \text{kPa} \cdot s$). $VT$: tidal volume; $V'E$: expiratory flow; $V'I$: inspiratory flow; FRCpleth: plethysmographic functional residual capacity. See text for discussion.
subjects at 0.75 and 0.5 L·s⁻¹. Subsequently, the flow range has commonly been limited to the relatively linear portion of the $s_{R_{aw}}$ loop between inspiratory and expiratory flow rates of 0.5 L·s⁻¹ [28, 29] for definition of $sR_{0.5}$, as shown in figure 7.

The potential advantage of $sR_{0.5}$ is that it standardises the flow at which resistance is measured. In normal subjects, but particularly in patients with airflow obstruction, resistance is dependent upon flow rate, so this approach offers less inter-individual variability. The parameter $sR_{0.5}$ reflects primarily the behaviour of larger, more proximal airways, with much less sensitivity to peripheral airway abnormalities.

Specific conductance. The reciprocal of $s_{R_{aw}}$ is denoted specific conductance ($s_{G_{aw}}$).

$$s_{G_{aw}} = 1/s_{R_{aw}}$$

(8)

When calculating $s_{G_{aw}}$, it must be defined with respect to which calculation of $s_{R_{aw}}$ is performed, according to the definitions listed in the sections above. The conversion of $s_{R_{aw}}$ to $s_{G_{aw}}$ is not simply a mathematical procedure, but is based on the original observations of BRISCOE and DU BOIS [31] that the major determinant of $R_{aw}$ in normal subjects is lung volume and, accordingly, that the relationship between lung volume and conductance is linear within and between individuals. Thus, $s_{G_{aw}}$ is a "volume-normalised" expression for airway conductance.

Calculation of airway resistance and conductance

Finally, the commonly used clinical parameters of body plethysmography, $R_{aw}$ and $G_{aw}$, are calculated using $s_{R_{aw}}$ and corresponding TGV, as defined below:

$$R_{aw} = s_{R_{aw}}/TGV$$

Or corrected for the average lung volume during tidal breathing, where $V_T$ represents tidal breathing.

$$R_{aw} = s_{R_{aw}}/(FRC_{pleth} + V_T/2) \quad G_{aw} = 1/R_{aw}$$

(9)

In practice, the measurements of TGV are conveniently performed immediately after the $s_{R_{aw}}$ breathing loops; and three replicates are recommended. Quality of the measurement is reflected in part by the variability of replicate trials and, in part, by

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Fig. 7. – Same tracing of specific resistance loop as in figure 5, showing the slope used for calculation of specific resistance 0.5 ($sR_{0.5}$; 2.5 kPa·s). See text for discussion.
how closely the $P_m$ – plethysmograph pressure tracing approximates a straight line. A good quality tracing is shown in figure 4, where departures from the computer regression line are very small over a wide range of $P_m$.

By definition, inaccuracy in the determination of TGV or FRC$_{pleth}$ will cause a proportional error in the estimation of $R_{aw}$ and $G_{aw}$. For this reason, and because it is technically more demanding for patients with airflow obstruction to make respiratory efforts against a closed shutter than for tidal breathing, some clinicians restrict their most careful attention to $sR_{aw}$ and $sG_{aw}$ [23, 27, 30, 32]. Additionally, in many patients with COPD, $R_{aw}$ appears to be nearly within normal limits, due to manifest compensatory lung hyperinflation, especially when measured between 0.5 L$\cdot$s$^{-1}$ inspiratory and expiratory flow. In these cases, $sR_{aw}$ and $sG_{aw}$ still show abnormality, because of the increased TGV maintained during tidal breathing. In a subsequent section, an alternative approach to estimation of TGV during tidal breathing only is described, avoiding voluntary respiratory efforts against a closed shutter [24].

**Spirometric measurement**

It is often convenient to complete a body plethysmographic measurement with spirometric measurements. Commonly this is done immediately after TGV has been determined, using a slow exhalation below resting FRC to minimal lung volume, i.e. performance of an expiratory reserve volume (ERV) effort. This is followed by an inspiratory vital capacity effort (IVC) to TLC, followed by a maximal forced expiration for determination of forced expiratory volume in one second (FEV1) and FVC.

In this way, all the primary pulmonary subdivisions can be recorded as absolute gas volumes. These include TLC, FRC$_{pleth}$ and RV. RV may be calculated by subtracting ERV from FRC$_{pleth}$.

$$RV = FRC_{pleth} - ERV \tag{10}$$

TLC is determined by adding the maximal VC recorded, usually IVC, to RV.

$$TLC = RV + IVC \tag{11}$$

Inspiratory capacity (IC) is the difference between TLC and FRC$_{pleth}$.

$$IC = TLC - FRC_{pleth} \tag{12}$$

The spirometric data described above are conveniently recorded from the flow meter in the whole-body plethysmograph. Issues relevant to spirometry are reviewed and discussed in another chapter of this Monograph. However, it is relevant to note here that, using the "transmural" pressure-compensated integrated-flow plethysmograph it is possible to view the maximal expiratory flow–volume (MEFV) curve with respect to volume displacements of the thorax, including those due to compression, during forced expiration [12]. This is a more reliable method of assessing for the presence of expiratory-flow limitation during resting breathing compared with maximal forced expiration, than spirometry using only integrated mouth flow as the volume axis. Using such a transmural plethysmograph, it is immediately evident that the VC measured from thoracic wall displacements is greater than that measured from integrated flow, because of compression of thoracic gas trapped behind closed small airways at low lung volumes. While this is not important in making clinical decisions, the clinical value of thoracic wall displacements during tidal breathing is a significant issue in patients with chronic airflow obstruction and is discussed below (section Clinical utility of whole-body plethysmography).
Pulmonary function using whole-body plethysmography

Initial interpretation of body plethysmographic parameters usually considers measured values in comparison to established normative data. However, it is often preferable to use the patient as his own control, by assessing the trend of measurements over time or to repeat measurements after therapeutic challenge. Additionally, plethysmography may be repeated after bronchial challenge to assess airway reactivity.

Predicted and limit values for airway resistance

Relatively few studies have established predicted values of $R_{aw}$ in adults. Age differences have relatively unimportant effects, as first noted by BRISCOE and DUBoIS [31]. ULMER and coworkers [33, 34] reported an average $R_{tot}$ for healthy adults of 0.22 kPa·s·L⁻¹ and defined an upper limit of normal $R_{tot}$ as 0.35 kPa·s·L⁻¹. MATTHYS et al. [35] introduced normative equations for $sR_{tot}$ and $sR_{eff}$, and reported an average±SD value for $R_{eff}$ of 0.2±0.0967 kPa·s·L⁻¹.

Recently Vän der Velden et al. [36] compared $R_{tot}$, $R_{eff}$ and $R_{0.5}$ in 78 healthy adults with average±SD values for $R_{tot}$ of 0.19±0.07 kPa·s·L⁻¹, for $R_{eff}$ of 0.15±0.06 kPa·s·L⁻¹ and $R_{0.5}$ of 0.13±0.05 kPa·s·L⁻¹. These comparative values are useful for current guidance. QUANJER [37] tabulated data in 1983, including a large 1970 study of $R_{aw}$ during tidal breathing, in both males and females. He selected an upper limit of normal of 0.3 kPa·s·L⁻¹ for both males and females. However, the age of these data argue for the value of undertaking new studies of normative values for $R_{aw}$, $sG_{aw}$ and, possibly, absolute lung volumes using modern plethysmographs with thermal/humidity effects compensated by numerical algorithms.

In younger children, KLUG and BISGAARD [38] have measured $sR_{aw}$ with the child accompanied by an adult within the plethysmograph. As expected with growth and increase in lung size, $R_{aw}$ decreases with age in children. Predicted values for children have been reported by ZAPLETAL et al. [39].

Predicted value for thoracic gas volumes

Body size and lung size in adults may vary according to ethnic origin and some normative values have been reported by different authors to correspond to populations served in their communities. QUANJER et al. [25] reported standardised values for FRC, RV and TLC with spirometry in adults and ULMER et al. [34] reported standardised values for TGV and FRCpleth in adults. ZAPLETAL et al. [39] reported plethysmographic volumes for children.

Assessment of bronchial reactivity

Measurement of $sR_{aw}$ ($sG_{aw}$) has been used clinically for assessment of bronchial responsiveness. Because $sR_{aw}$ and $sG_{aw}$ are commonly measured during tidal breathing, they are influenced both by $R_{aw}$ as well as changes in resting lung volumes (FRC). Since both resistance and resting end-expiratory lung volume may change during bronchial or therapeutic challenge, $sR_{aw}$ and $sG_{aw}$ provide useful practical assessments of airway responsiveness, even in the absence of a determination of absolute TGV. In adults or children unable to perform the measurement of TGV, $sR_{aw}$ or $sG_{aw}$ provides useful clinical guidance, although American Thoracic Society and European Respiratory Society guidelines suggest separate documentation of $R_{aw}$ and changes in FRC. Such
measures of airway response during tidal breathing are often considered preferable to spirometric assessments [40]. The commonly used limit for bronchoprovocation is a 15 or 20% decrease in FEV\(_1\) relative to control baseline FEV\(_1\). The comparable limit for \(sR_{\text{tot}}\) is 100%, for \(R_{\text{tot}}\) 50% increase and for \(sG_{\text{tot}}\) 40% decrease from baseline, respectively [40].

Therapeutic challenge may be similarly compared to baseline \(sR_{\text{aw}}\) and judged by the degree of reversibility, whether limited in magnitude (partial reversibility) or more complete, such that \(sR_{\text{aw}}\) values reach the normal range. Reversibility, whether partial or complete, can be assessed as the improvement quantified as per cent of the predicted value.

**Interpretations of whole-body plethysmography**

*Pathophysiological manifestations*

While the numerical values of \(sR_{\text{aw}}\) and \(sG_{\text{aw}}, R_{\text{aw}}, G_{\text{aw}},\) and TGV may be compared with normative data where they are available, and for assessment of bronchial and therapeutic challenge, the linear approximations used to derive numerical values provide a limited capacity for the understanding of pathophysiology. Further physiological interpretative information is available from the shape of the \(sR_{\text{aw}}\) loops. The additional value of these graphic displays is analogous to the additional value of the flow–volume curve, relative to simple numerical values of FEV\(_1\) and FVC.

The infrastructure of physiological interpretation of \(sR_{\text{aw}}\) loops is the relationship between airflow measured at the mouth and shift volume \((V' \text{ versus } \Delta V)\). Shift volume represents the volume changes in TGV that occur during compression and decompression of thoracic gas, not including the volume changes due to airflow in and out of the lung, and this shift volume is related to airflow resistance. When airflow resistance is the dominant contribution to shift volume, changes in \(P_A\) and shift volume usually manifest a linear relationship to airflow at the mouth. This is made use of in estimates of \(sR_{\text{aw}}\) between the limits of 0.5 L·s\(^{-1}\) inspiratory and expiratory flows. However, even in normal subjects when airflow rate is substantially larger than 0.5 L·s\(^{-1}\) it is common to observe slight alinearity of \(sR_{\text{aw}}\), as noted in original report of DuBois et al. [2].

Mild obstructive lung disease may manifest as only minimal nonlinearity of \(sR_{\text{aw}}\) loops. However, in advanced obstructive lung disease, it is now well known that dynamic compression of intrathoracic airways is associated with disproportionate increases in intrathoracic pressure relative to airflow. Stanescu et al. [18] and Rodenstein et al. [19] used oesophageal pressure to estimate pleural pressure during respiratory efforts against a closed shutter in patients with airflow obstruction These studies demonstrated that, in the presence of increased airflow resistance, mouth occlusion pressure changes underestimate those of oesophageal (and alveolar) pressure during panting at frequencies >1 Hz. Other investigators confirmed the inaccuracy of TGV measured during panting against a closed shutter at frequencies >1 Hz, and suggested that their results were consistent with nonhomogeneous mechanical properties of airways and lung tissue time constants [17, 22]. Furthermore, in patients with severe airflow obstruction, there may be areas of the lungs that do not communicate with central airways, and, therefore, do not ventilate during tidal breathing, as evidenced by measures of "closing volume" that occur at lung volumes that may exceed FRC [41, 42].

Islam and Ulmer [27] provided a comprehensive evaluation of effects of airway closure using plethysmographic measures of the altered relationship between changes in intrathoracic pressure relative to airflow. They reasoned that the marked narrowing or
closure of small airways that occurred at low lung volumes, defined as closing volume 
[41, 42], should cause an abrupt decrease in plethysmographic gas pressure. They plotted 
apparent $R_{\text{tot}}$ as a function of lung volume, and showed a dramatic increase in apparent $R_{\text{tot}}$ in patients with airflow obstruction at low lung volumes, manifest to a lesser degree in normal subjects [27]. In normal subjects, they determined closing volume at lung volumes below FRC (i.e., within the ERV), which they associated with a significant increase in apparent $R_{\text{tot}}$. In patients with chronic airflow obstruction, they were unable to determine a closing volume because of technical limitations; however, they measured a substantial increase in apparent $R_{\text{tot}}$ within the IC. These authors utilised changes in apparent $R_{\text{tot}}$ as a reflection of compression of gas in nonventilated airspaces. The clinical implication of such changes is discussed below (section Extending the clinical utility of whole-body plethysmography).

Shortly after the report of Islam and Ulmer [27], Matthys and Orth [23] described the contribution of these pathophysiological disturbances to a dissociation between maximal shift volume and maximal flow. They extended the dimensional analysis applied by Jaeger and Otis [30] to integrate these contributions to an "effective resistance" that included the effects of the entire range of variable flows during tidal breathing and nonlinearities in the $sR_{\text{aw}}$ loop. They measured the areas of graphic plots of shift volume versus volume and of flow versus volume during tidal breathing, determined planimetrically during playback of plethysmographic signals recorded on magnetic tape (fig. 6a). They divided the integrated shift volume–volume loop (the flow resistive work of breathing, A in fig 6a) by the flow–volume loop (B in fig 6a) to derive $sR_{\text{eff}}$. They calculated effective resistance from the quotient of $sR_{\text{eff}}$ and mean ventilated lung volume ($FRC_{\text{pleth}} + V_T/2$).

$$R_{\text{eff}} = [(A/B)\frac{(P_{\text{bar}} - P_{H_2O,\text{sat}})}{(FRC_{\text{pleth}} + V_T/2)}]$$  \hspace{1cm} (13)

Matthys and Orth [23] performed these calculations from analysis of signals recorded on magnetic tape; but this is now readily calculated by digital algorithms in modern computer-assisted plethysmographs. Despite the obvious attraction of an integrative approach, such as that of Matthys and Orth, the analysis and interpretation of multiple graphic displays, including flow–volume loops, shift volume versus volume and shift volume versus flow loops, is not feasible in the clinical pulmonary function laboratory. Accordingly, calculation of the numerical value of $sR_{\text{eff}}$ is done by computer algorithm, and the resulting slope is positioned within the conventional $sR_{\text{aw}}$ loop using regression techniques. In this way, $sR_{\text{eff}}$ can be compared conveniently to $sR_{\text{tot}}$ and $sR_{0.5}$ if desired [36].

Since the contributions of dynamic compression of intrathoracic airways and compression of nonventilated lung areas make the $sR_{\text{aw}}$ loops highly nonlinear and contribute to characteristic shapes of the shift volume versus mouth flow X–Y graph displayed in current body plethysmographs, these characteristic shapes are now discussed in detail.

**Characteristic specific resistance loops**

Characterisic $sR_{\text{aw}}$ loops are shown in figure 8. The tracing labelled a) in figure 8 displays a schematic $sR_{\text{aw}}$ loop in a normal subject during tidal breathing, which is shown after numerical software compensations to close the $sR_{\text{aw}}$ loop. Normal subjects manifest a steep linear loop during tidal breathing without hysteresis. In contrast, during voluntary panting efforts, the upper and lower end portions of the loop may become slightly curvilinear. The curvilinearity is in the form of a very slight 'S' shape, analogous to that shown in tracing d), but much less exaggerated. In normal subjects during
voluntary panting, the flattening of the sRaw loop at the upper right extremity (mid-inspiration) and at the lower left extremity (mid-expiration) of the loop are only barely visible, depending on the absolute value of flow rates achieved. While the accepted numerical limits of normality are broad, it is the characteristic shape of the sRaw loop, immediately apparent from direct observation, that guides clinical interpretation.

Tracing b) in figure 8 is typical of subjects with large (central) airway constriction that is relatively uniform (and not a localised stenosis) and without significant small airway obstruction. This might be seen in a patient with mild asthma. Here a linear sRaw loop that is tilted clockwise, manifesting a slope less steep than normal, reflects increased RRaw.

In subjects with normal pulmonary mechanics or uniformly increased large airway constriction, as noted immediately above, the sRaw loop has little or no hysteresis ("openness" of the loop). In patients with nonhomogeneous small airway partial obstruction, the sRaw loop manifests the characteristic shape shown by tracing c) in figure 8. The loop is quite open, especially during expiratory flow. A large shift volume appears at mid expiration, without corresponding increases in expiratory flow. Such alinearities may represent expiratory flow limitation and/or dynamic airway compression. It is well known that expiratory flow limitation and dynamic airway compression may occur during tidal breathing in COPD [41, 42], and this contributes to the characteristic shape of the sRaw loop in tracing c).

Compression of nonventilated airspaces will also contribute to the leftward displacement of the shift volume versus mouth flow tracing. Rodenstein et al. [43] obstructed right lung middle and lower lobes in normal humans to assess the effect of nonventilated airspace on measurement of TGV. They did not report sRaw loops during such obstruction, but the similar TGV reported without and with nonventilated airspaces implies, by definition, that compression of TGV with increases in PA is quantitatively the same without and with nonventilated airspaces. Thus, the relationship between shift volume and airflow will be distorted as in tracing c) by compression of nonventilated airspaces. Changes in plethysmographic volume with compression of gas behind closed airways were demonstrated by Davis et al. [13] and, as noted above, by Islam and Ulmer [27] prior to that.

It may be seen from the shape and direction of tracing c), comparing early expiratory
flow with late expiratory flow at the same value of mouth flow, that shift volume is less early in the expiration compared to late in expiration at the same flow. This hysteresis defines a nonlinear relationship of shift volume to mouth flow that may include contributions of dynamic airway compression and compression of nonventilating airspaces to the overall TGV compression during expiration. The single lines drawn in figures 5–7 represent lines defined as \( s_{R_{tot}} \), \( s_{R_{eff}} \) and \( s_{R_{0.5}} \). It is readily apparent that such a single line drawn for \( s_{R_{tot}} \) reflects a single index that includes important nonlinearities occurring during expiratory airflow. This single line is very different from a "representative" line that might be drawn during inspiratory airflow only or the line corresponding to \( s_{R_{0.5}} \) in tracing c). More important than any attempt to quantify the complex shape of the \( s_{Raw} \) loop by a single index, the X–Y display itself reveals the highly abnormal mechanical behaviour during expiratory airflow in tracing c). These abnormalities include contributions from nonlinear expiratory airflow resistance, dynamic airway compression and compression of nonventilated airspace. The latter two factors contribute to the increased shift volume late in expiration compared to early in expiration, even at an identical mouth flow.

Numerical analysis of tracings in patients similar to those in figure 8c, after dividing by TGV, may be compared with normative values listed above in the section Predicted and limit values for airway resistance. It should be noted that calculation of measured values as per cent predicted may differ in plethysmographs available from different manufacturers. Such calculations should state whether "predicted" is the mean expected value or the upper limit (for resistance) of accepted normal values. Equally importantly, extension of the study of Van der Velden et al. [36] should be undertaken with modern commercially available plethysmographs to confirm their predicted values, including a larger normal population sample and to compare \( R_{tot} \), \( R_{eff} \) and \( R_{0.5} \) in patients with chronic airflow obstruction done at baseline and following therapeutic challenge. The value of such extensions of plethysmography is discussed below in the section Extending the clinical utility of whole-body plethysmography.

Because of mechanical nonhomogenities in the lung and airways in obstructive lung disease, it is not entirely satisfactory to attempt to summarise \( R_{aw} \) by a single number. Future clinical investigations might usefully include discrimination between inspiratory and expiratory \( R_{eff} \), to recognise the predominance of abnormality during expiratory airflow. An alternative distinction can be made by looking at the parameter most commonly used in North America, \( R_{aw} \) between inspiratory and expiratory flow rates of 0.5 L·s⁻¹. It can be seen in tracing c) that the line corresponding to \( s_{R_{0.5}} \) would be substantially steeper (less abnormal) than that for \( s_{R_{tot}} \). This reflects, in part, the smaller flow rates, higher lung volume and lack of dynamic airway compression during late inspiration/early expiration. It is fair to state that inspection of the shape of the \( s_{Raw} \) loop displayed as the X–Y graph is equally useful diagnostically as any single or combination of numerical values.

Tracing d) in figure 8 shows the influence of a fixed or functional stenosis of the upper airways, for example laryngeal abnormality, or paralysis of one vocal cord. This type of "orifice" constriction manifests flow limitation during inspiration, such that, at sufficiently high flows, further increases in driving pressure do not result in any increase in airflow. This reflects localised upper airway obstruction, analogous to that which pertains in the maximal expiratory flow–volume curve. Thus, during forced expiration, when a critical driving pressure for expiratory airflow (intrapleural pressure for forced expiration) is achieved, further increases in driving pressure do not cause any further increases in flow rate. A similar flow limitation may occur in the extrathoracic airway during inspiration, as shown in the upper right portion of tracing d) in figure 8.
Clinical utility of whole-body plethysmography

The utility of whole-body plethysmography is discussed from the perspective of clinical respiratory medicine by Brusasco and Pellegrino [44] and physiological considerations are presented in detail by Pride and Macklem [45].

Measurement of thoracic gas volume

The raison d’être of whole-body plethysmography is the measurement of lung volumes. Accordingly, the first acknowledged clinical benefit of body plethysmography is the definition of restrictive lung disease [46]. Normative data for TGV and pulmonary subdivisions allow definition of restrictive lung disease as distinct from obstructive, in the presence of a reduced VC. Definition of abnormally increased lung volumes in obstructive lung disease is a further appropriate clinical use of whole-body plethysmography. While lung volumes can be measured by gas dilution techniques, it is well known that dilution techniques measure only the volume of ventilated airspaces. Accordingly, when whole-body plethysmography is combined with dilution measures of lung volumes, the volume of trapped gas is estimated by the difference between FRCpleth and dilutional FRCHe. Because FRC varies to some degree from breath to breath, a further comparison of calculated RV determined with dilution and plethysmography provides useful information concerning trapped gas.

The voluntary rapid shallow obstructed respiratory efforts described by DuBois et al. [1] appear to permit equilibration of intrathoracic gas and Pm, and, accordingly, a realistic estimate of changes in PA from Pm measurements in normal subjects. However, in the presence of intrathoracic airway obstruction, rapid obstructed panting efforts overestimate TGV because the change in Pm underestimates the change in PA [18, 19]. Stanescu et al. [18] and Rodenstein et al. [19] investigated normal and asthmatic subjects. They compared changes in mouth pressure with those of oesophageal pressure during obstructed panting efforts and showed that in normal subjects Pm and oesophageal pressures during panting efforts against a closed shutter were comparable. However, in the presence of airflow obstruction, changes in Pm significantly underestimated those in the oesophagus, taken to be equal to PA changes during respiratory efforts against a closed shutter. Airway obstructions were either diffuse, as in asthmatic subjects, or in the lower trachea, induced in normal subjects by inflating a balloon in the lower trachea. This group then bypassed the upper airways with a cuffed endotracheal tube and showed comparable occlusion pressure changes between the endotracheal tube opening and the oesophagus. They concluded that an increased degree of airflow obstruction, increased compliance of the upper extrathoracic airways and increased rate of panting all combine to cause the underestimation of PA change by Pm, and consequent overestimation of TGV. This work and that of others [17, 20–22] resulted in a recommendation of panting at 1 Hz to optimise the measurement of TGV.

Thus, the assumption implicit in the original work of Dubois et al. [1] by use of changes in Pm to represent changes in PA during panting efforts against a closed shutter has been demonstrated to be unwarranted in patients with significant airflow obstruction, unless very slow panting efforts are performed. However, such slow panting efforts require considerable coordination on the part of the patient, and, in practice, tidal breathing is much more reliably assessed in current commercial plethysmographs with the aid of computer-assisted compensation for thermal and humidity effects.

A second assumption is that the changes in body volume during panting efforts against a closed shutter are essentially only those of TGV. This assumption has been reinforced
by Brown et al. [47], who investigated the effects of panting efforts at different volumes within the VC and with different amounts of abdominal air introduced into the stomach via a nasogastric catheter. They reported that when panting efforts were performed near RV and near TLC, discrepancies of 3–5% of true TLC could be related to abdominal gas volume, but when panting efforts were performed at FRC the effect of abdominal gas volume on measurement of TGV was negligible. The simplest form of Boyle-Mariotte’s Law used in manual calculations of TGV [1] has been evaluated by Coates et al. [11] who included calculation of TGV using the complete Boyle-Mariotte’s law equation (Equation 3, section Determination of thoracic gas volume and functional residual capacity) and demonstrated errors in the order of ±3% during panting and ±2–9% during a single inspiratory effort against a closed shutter as recommended for children [48]. Although such discrepancies are not likely to influence clinical decisions, the authors argued that they are easily avoided using modern computational methods in automated whole-body plethysmographs [49].

The foregoing analysis and review of efforts to optimise the measurement of FRCpleth has emphasised the cooperation required of the patient, including panting efforts against a closed shutter at a controlled low frequency in addition to maintenance of an open glottis during obstructed respiratory efforts. These constraints prompted Agrawal and Agrawal [24] to measure TGV during tidal breathing without obstructed respiratory efforts. These authors reasoned that since sRaw is expressed numerically by the product of TGV and Raw, addition of a known resistance in the respiratory path would permit determination of TGV by subtraction. Thus:

\[ s_{Raw1} = Raw \cdot TGV \]  
\[ s_{Raw2} = (Raw + R_{add}) \cdot TGV \]  
Subtracting Equation 14 from Equation 15 yields:

\[ s_{Raw2} - s_{Raw1} = R_{add} \cdot TGV; \text{ and } TGV = (s_{Raw2} - s_{Raw1})/R_{add} \]  

It is implicit in these equations that TGV must be constant between tidal breathing without and with the added resistance, airflow at which sRaw is measured must be the same without and with the added resistance; and that airway mechanics can be modelled as a linear system. These authors measured sRaw manually from an oscilloscope screen at the onset of inspiration up to 0.5 L·s\(^{-1}\) inspiratory flow without and with added resistance. The added resistance was brought into the respiratory path by a shutter valve which permitted replicate measures of sRaw with and without added resistance in a constant-volume plethysmograph. Any change in FRC associated with switching of the shutter valve could be measured by integrated airflow; however, no changes in FRC were observed. Thus, the first two assumptions are warranted. The assumption of linear behaviour without and with an added resistance in front of the mouth may be questioned in patients with airflow obstruction and nonhomogeneities in lung mechanical properties. Accordingly, the authors measured TGV during tidal breathing without and with the added resistance, and compared these results with TGV measured during panting at FRC. Good agreement between the two methods was obtained in normal subjects and a limited number of asthmatic and COPD patients in whom baseline Raw ranged from 0.1–1.5 kPa·s·L\(^{-1}\) [24].

The advantage of estimating lung volume in this manner is that tidal breathing only is required. Agrawal and Agrawal [24] measured sRaw manually, and it remains to be determined whether modern computer-assisted plethysmographs will provide comparable FRCpleth results during respiratory efforts against a closed shutter and during tidal breathing without and with added resistance. It is the authors’ opinion that this approach
is worthy of further investigation as it presents a convenient approach to the measurement of TGV that is likely to be more easily applicable to a wide variety of patients.

**Measurement of airway resistance**

Measures of $R_{aw}$ made in a whole-body plethysmograph demand the constraints and linear approximations described in previous sections. Accordingly, a single number defining "resistance" is not entirely satisfactory in patients with substantial airflow obstruction. Nonhomogeneous lung mechanical properties, expiratory flow limitation and airway closure all contribute to the highly nonlinear shapes of the $sR_{aw}$ loops described in previous sections. Limitations of interpretation imposed by the linear approximations described in sections Numerical parameters calculated from the specific resistance loop, Pathophysiological manifestations, and Characteristic specific resistance loops point to the clinical utility of direct visual inspection of the $sR_{aw}$ loops themselves. In addition to calculating resistance by any of the alternative linear approximations, the shape of the $sR_{aw}$ loop provides improved understanding of the patients' pathophysiology.

Plethysmographic $sR_{aw}$ can be measured both during rapid shallow breathing (panting) and during tidal breathing. The initial description of $sR_{aw}$ [2] utilised rapid shallow breathing to minimise thermal effects. This had the added advantage of resulting in full opening of the vocal cords [50]. However, one disadvantage of panting respirations is that they are almost invariably performed at lung volumes significantly larger than resting FRC [23, 24], necessitating further corrections to optimise accuracy [9, 11]. Furthermore, controlling panting frequency at a rate of 1 Hz [17–22], as well as requiring substantial coordination of the patient’s respiratory efforts, also increases the likelihood of variable glottic opening [50]. Krell et al. [32] demonstrated that quiet breathing $sR_{aw}$ was equivalent to that obtained during panting. Subsequently, with improved computer-assisted compensation algorithms [49], it was possible to program commercial whole-body plethysmographs to measure $sR_{aw}$ during tidal breathing, at normal resting FRC.

Pulmonary resistance, including $R_{aw}$ and tissue viscance, is also available during tidal breathing from the measurement of oesophageal pressure, although this invasive procedure is both more time consuming and more uncomfortable for the patient. Respiratory resistance is available during tidal breathing using the method of forced oscillation, and is described in another chapter in this monograph. Neither pulmonary resistance nor forced oscillatory resistance has yet achieved the clinical acceptance of whole-body plethysmography. Interestingly, the forced oscillation technique was first introduced by DuBois et al. [51] in the same year that this group first published the plethysmographic measurement of $R_{aw}$.

The clinical utility of plethysmographic measurements of $R_{aw}$ and $sR_{aw}$ is attested to by the fact that they have been considered the "gold standard" for decades for assessing airway function. In patients with significant airflow obstruction, $sG_{aw}$ is commonly assessed. This permits lung hyperinflation to be taken into account. Normative values are available for $R_{aw}$, $sR_{aw}$, and their reciprocals, $G_{aw}$ and $sG_{aw}$ [33–36].

The choice of which measure of resistance is clinically most useful varies among different investigators and in different countries. Some investigators emphasise the advantage of $R_{tot}$ because it includes the effects of multiple mechanical abnormalities associated with advanced peripheral airway obstruction. Against this is the disadvantage of test-to-test variability, due to its derivation from only two points (maximal inspiratory and expiratory shift volumes) of the $sR_{aw}$ loop. Other investigators prefer $R_{eff}$, because it integrates the entire ranges of flow, shift volume and lung volume of the complete tidal breath, and may thus be expected to offer less within-individual variability. Others argue against the perceived advantages of both these approaches to approximate "resistance"
because of their sensitivity to nonflow-resistive mechanical effects due to compression of nonventilating air spaces and also sensitivity to dynamic expiratory intrathoracic airway compression and expiratory flow limitation during tidal breathing. These mechanical abnormalities, albeit related to pressure dissipation during airflow in patients with chronic airflow obstruction, are largely excluded from the calculation of $R_{0.5}$. For these reasons, most North American clinicians utilise $R_{0.5}$, which is derived from a standardised flow range between late inspiration, $+0.5 \text{ Ls}^{-1}$, and early expiration, $-0.5 \text{ Ls}^{-1}$, on the sRAW loop (fig. 7). This calculation results in a lower resistance than either $R_{\text{eff}}$ or $R_{\text{tot}}$ because it is minimally affected by dynamic airway compression or compression of nonventilating airspace. As such, it reflects primarily the resistance in larger central airways, is relatively insensitive to changes in peripheral airways and manifests less test-to-test variability within an individual.

The effects of dynamic airway compression and compression of nonventilating airspaces lead to a dependence of $R_{\text{tot}}$ and $R_{\text{eff}}$ on breathing pattern itself, namely the degree to which patients with chronic airflow obstruction "force" their expiratory effort. During resting tidal breathing in normal individuals, expiratory airflow is largely, if not entirely, produced by stored elastic energy in the chest wall. However, even in normal subjects, LORING and MEAD [52] have shown that resting breathing is associated with a variable degree of active abdominal muscle recruitment. This active expiratory muscle recruitment is much more marked in patients with chronic airflow obstruction. Such patients commonly utilise active expiratory muscle effort to aid expiratory airflow and manifest expiratory flow limitation even during resting tidal breathing [53]. Depending upon the patient's unique individual sensation of their breathing, they may contract their expiratory muscles to a variable degree during resting tidal expiration, and this active expiration may change variably with therapeutic challenge. The degree of expiratory muscle effort will directly influence calculated $R_{\text{eff}}$ and $R_{\text{tot}}$ because greater efforts cause greater shift volumes without corresponding increases in expiratory airflow in the presence of expiratory flow limitation.

It is clear that there are marked differences between "instantaneous" airflow resistance during inspiration and expiration in patients with chronic airflow obstruction. These differences may be appreciated graphically by direct visual inspection of the sRAW loop. They may be appreciated numerically by deriving separate inspiratory and expiratory values of $R_{\text{eff}}$, again using the integrated areas of shift volume–volume and flow–volume loops, as denoted $A_I/A_E$ and $B_I/B_E$ for inspiration and expiration separately in figure 6a. Comparable numerical representation of the mechanical abnormalities that occur during expiration using $R_{0.5}$ or $R_{\text{tot}}$ is not possible due to the definition of these quantities based on the sRAW loops. Instead, graphic display of the sRAW loop is required to appreciate the prominence of such abnormalities during the expiratory phase [2, 54–56].

However, current computer-assisted plethysmography makes it possible to calculate "instantaneous" values of airflow resistance, provided TGV is known. During breathing within the constant-volume plethysmograph, airflow resistance in the lung requires small amounts of compression of thoracic gas during expiration and expansion of thoracic gas during inspiration, resulting in the "shift volumes" measured by the pressure change in the plethysmograph. Calculation of $R_{\text{aw}}$ requires measures of $P_A$ and airflow. During free breathing, shift volume can be used to record an index of changes in $P_A$, because shift volume is the product of TGV, and the change in alveolar pressure, $\Delta P_A$, divided by initial $P_A$. In other words, the fractional change in $P_A$, $[\Delta P_A]/(P_{\text{bar}}-P_{H_2O,\text{sat}})$, integrated over TGV causes a change in TGV equal to shift volume, which, in turn, results in plethysmographic pressure change. In this way, shift volume provides an index of $\Delta P_A$ provided TGV is known. It must be emphasised, however, that plethysmographic pressure change during breathing is not equal to $\Delta P_A$. It is much smaller in magnitude than $\Delta P_A$, and reflects the fractional $\Delta P_A$ amplified by TGV.
The instantaneous relationship between $\Delta V$, TGV and $P_A$ may be written as:

$$\frac{\Delta P_A}{(P_{\text{bar}} - P_{H_2O,\text{sat}})} = \frac{\Delta V}{\text{TGV}} \quad (17)$$

This is a restatement of Boyle-Mariotte’s law that, under isothermal conditions, the fractional change in $P_A$ is equal to the fractional change in TGV. Equation 17 may be rearranged as follows:

$$\Delta P_A = (P_{\text{bar}} - P_{H_2O,\text{sat}})(\Delta V/\text{TGV}) \quad (18)$$

Thus, instantaneous $P_A$ during free breathing can be defined using the product of dry gas $P_{\text{bar}}$ and the ratio of shift volume to TGV, if TGV is known. This is done by the computer, continuously in time, from measured signals of shift volume, volume and airflow after respiratory efforts against a closed shutter have been utilised to calculate TGV. Instantaneous $R_{aw}$ ($iR_{aw}$) is then defined by the ratio of instantaneous $P_A$ to instantaneous airflow. This computer calculation has only recently been implemented, and provides a convenient display of $R_{aw}$ throughout the tidal breath, except at end-expiration and end-inspiration, where $iR_{aw}$ is undefined because airflow is zero, as shown in figure 9.

It should be noted that $R_{aw}$ calculated in this manner includes nonlinearities in flow resistance and effects of expiratory flow limitation, and also what may be considered by some to be "inappropriate" attribution of compression of trapped gas to flow resistance. Expiratory flow limitation contributes variably to apparent $R_{aw}$ as a function of respiratory effort: the greater the expiratory muscle effort, the larger the calculated expiratory $R_{aw}$ at a fixed flow rate. Nevertheless, these contributions may be

![Fig. 9](image-url)
appropriately considered "resistive". Compression of trapped gas during expiration and decompression during inspiration are not related to airflow per se, but, nevertheless, contribute to the total dynamic $P_A$ burden during breathing. More importantly, the degree of trapped gas in patients with airflow obstruction is likely to be related much more prominently to small airway obstruction than to larger more central airways. Thus, this $R_{aw}$ will be more sensitive to small airway obstruction than $R_{0.5}$ and $R_{eff}$.

It may be seen in figure 9 that there is a progressive increase in calculated $R_{aw}$ throughout expiration, consistent with the known effects of mechanical abnormalities during expiratory air flow in patients with airflow obstruction. The envelope of values of $R_{aw}$ in figure 9 includes wide variability of $iR_{aw}$ throughout the course of the tidal breath in patients with severe airflow obstruction. For comparison, it may be noted that $R_{0.5}$ will be approximately equal to the $iR_{aw}$ values just before end-inspiration, while $R_{tot}$ and $R_{eff}$ values will fall near the middle of the expiratory $iR_{aw}$ envelope. This representation may serve as a useful extension of plethysmographic technique, as noted in the section below.

**Extending the clinical utility of whole-body plethysmography**

This review draws to its conclusion by extending the exploration of clinical implications of the complexity of the relationship between shift volume and airflow. As noted above, this complexity has resulted in three different numerical approximations to measure resistance derived from different linear approximations of the shift volume–airflow relationship. The limitations of rapid shallow panting efforts have been described and the resultant improvements offered by tidal breathing in the determination of resistance in patients with airflow obstruction.

The potential for tidal breathing estimation of TGV by addition of a known resistance in front of the mouth has been introduced [24], and will await further investigation using modern computer-assisted plethysmographs that provide numerical compensation for thermal and humidity effects during tidal breathing. Investigations in patients with airflow obstruction should include baseline measures and the response to acute bronchodilation to fully utilise the scope of experimental conditions in which this approach might be applicable.

Further investigations that extend the work of Van der Velden et al. [36] in patients with chronic airflow obstruction will provide useful comparisons of the different numerical approximations to measurement of resistance. Such investigations will usefully include response to acute bronchodilation with $\beta$-agonists on the one hand and short-acting anticholinergics on the other, in the same patients. In this way, the relative sensitivity to primarily proximal or distal airway bronchodilation of $R_{tot}$, $R_{eff}$ and $R_{0.5}$ can be assessed in patients with airflow obstruction, with bronchodilator effects in primarily proximal or distal airways.

The relationship between calculated $iR_{aw}$ and lung volume during the tidal breath has recently been demonstrated (section above, Measurement of airway resistance). Extension of these studies may prove to be a useful representation for clinicians, permitting a graphic impression of change in apparent $iR_{aw}$ within the tidal breath. Further investigations are necessary to define the relative sensitivity of $iR_{aw}$ and expiratory $R_{eff}$ to interventions that affect primarily larger proximal or smaller peripheral airways.

The relationship between shift volume and lung volume itself is now considered. As noted in section Spirometric measurement, the VC measured plethysmographically from thoracic wall displacements is larger than that measured from integrated airflow in patients with chronic airflow obstruction [12]. Similarly, Islam and Ulmer [27] have shown that the plethysmographic change in apparent $R_{tot}$ that occurs with airway closure in patients with chronic airflow obstruction may become manifest in some cases at
volumes greater than \( \text{FRC}_{\text{pleth}} \). Thus the tidal volume measured from thoracic wall displacements must also be larger than that derived from integration of airflow in some patients with chronic airflow obstruction.

This relates importantly to the work of O’DONNELL and co-workers [57–59] who have shown that a significant limitation to exercise in patients with chronic airflow obstruction relates to the severe dyspnoea that occurs when end-tidal inspiration encroaches on TLC. This implies that thoracic muscle volume displacements are an important limiting factor. The work performed by thoracic respiratory muscles includes not only flow resistive work, but also that required to move the elastic structures of the thoracic wall itself. The thoracic muscles move the thorax, and their volume displacements are those of the thoracic wall, including compression and decompression of trapped gas. The volume displacement of the thorax is systematically underestimated by integration of airflow in patients with chronic airflow obstruction. It can be appreciated by a plethysmographic measure of thoracic volume displacements, such as is readily available from the pressure-compensated integrated-flow whole-body plethysmograph.

Thus, it would appear that respiratory limitation in patients with chronic airflow obstruction may be explored in the future by stimulated ventilation in an appropriate whole-body plethysmograph. Efficacy of treatment interventions, whether pharmaceutical or rehabilitative, may be assessed by their effects on the ability of patients with chronic airflow obstruction to improve thoracic volume displacements. Alternatively, treatment efficacy may be assessed by changes in plethysmographic closing volume relative to TLC in such patients.

**Summary**

The aim of this chapter has been to describe the unique and clinically relevant information provided by whole-body plethysmography. Primary among this information is the measurement of absolute TGV. Plethysmographic TGV (\( \text{FRC}_{\text{pleth}} \)) is considered the gold standard of absolute volume measurements and includes the nonventilated airspace. Because the whole-body plethysmograph provides a measure of true change in TGV, an increased use of the combination pressure-corrected integrated-flow (transmural) plethysmograph is to be expected in the evaluation of patients with chronic airflow obstruction. The use of thoracic volume measurements rather than integrated mouth flow has provided more precise characterisation of pulmonary mechanical parameters as a function of lung volume.

The clinical measurement of plethysmographic airflow resistance is also considered to be the gold standard, and is more widely applied than either pulmonary resistance measured invasively via oesophageal balloon or forced oscillatory resistance measured noninvasively. It is emphasised that the plethysmographic measurement of resistance requires two separate measurements: first, that of \( sR_{aw} \), and secondly, the measurement of TGV itself. Both plethysmographic and forced oscillatory resistance are influenced by the subject’s spontaneous breathing pattern and both require further complementary measurements to define more precisely the extent of pathophysiological disturbances in patients with chronic airflow obstruction. Measurement of resistance as a function of lung volume provides a useful extension of currently utilised methodology and more clearly delineates effects of small airway obstruction. Technological developments have now permitted incorporation of the transmural function in commercially manufactured plethysmographs, thereby expanding the utility of whole-body plethysmography, and increasing its utility in distinguishing
between flow resistive and compression effects, both dynamic airway compression and
airway closure (nonventilated airspaces). While this capability has hitherto been
utilised primarily in FVC efforts, increased interest in new treatments for COPD may
stimulate use of this capability during tidal breathing. Whole-body plethysmography
may be further developed to include measurement of TGV during tidal breathing
without panting efforts against a closed airway shutter, and measurement of
instantaneous $R_{aw}$ during tidal breathing.

The sensitivity of plethysmography imposes demands for vigilance on the operator,
who must ensure stable body posture, attention to physical support of the oral cavity
and cooperation of the subject during testing procedures. Cooperation may be
improved by careful instructions to the patient, careful attention to the patient during
testing and informing the patient that they can remove the mouthpiece if breathing
becomes obstructed or too difficult. Posture must be supported to maintain subject
comfort and the instrument mouthpiece must be brought to an appropriate level for
the subject to avoid unusual neck posture. The usual clinical testing procedure of at
least three replicate measures may be usefully augmented by increased testing
replicates in circumstances where acute response to intervention is desired.

**Keywords:** Airway resistance, shift-volume, thoracic gas volume.

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