MECHANICAL ASPECTS OF BREATHING

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GENERAL CONCEPTS AND TERMINOLOGY

In the chain of events that contribute to the translation of the output of the respiratory rhythm generator into ventilation, the mechanical properties of the respiratory system obviously represent a critical step. Following activation of the respiratory muscles, the magnitude of force generated depends on the physical properties of the inspiratory muscles (*i.e.*, the force-length and force-velocity characteristics). The physical translation of force into inspiratory muscle pressure depends on the configuration of the muscle and the mechanical characteristics of the structure to which the force is applied. Finally, of the total pressure generated by the muscles, part is required to overcome the elastic properties of the respiratory system in order to change lung volume (V), and part is dissipated to overcome the resistive characteristics of the respiratory system in order to move air, i.e., in order to generate flow (***V***) [Fig.1]. Hence, the total pressure generated is equal to the sum of *elastic* (Pel) and *resistive* (or *non-elastic*) (Pres) components, the former proportional to V and 1/C, the latter proportional to ***V*** and R,

$$Ptotal = Pel + Pres = (V \cdot 1/C) + (\boldsymbol{V} \cdot R) \qquad \text{(eq.1)}$$

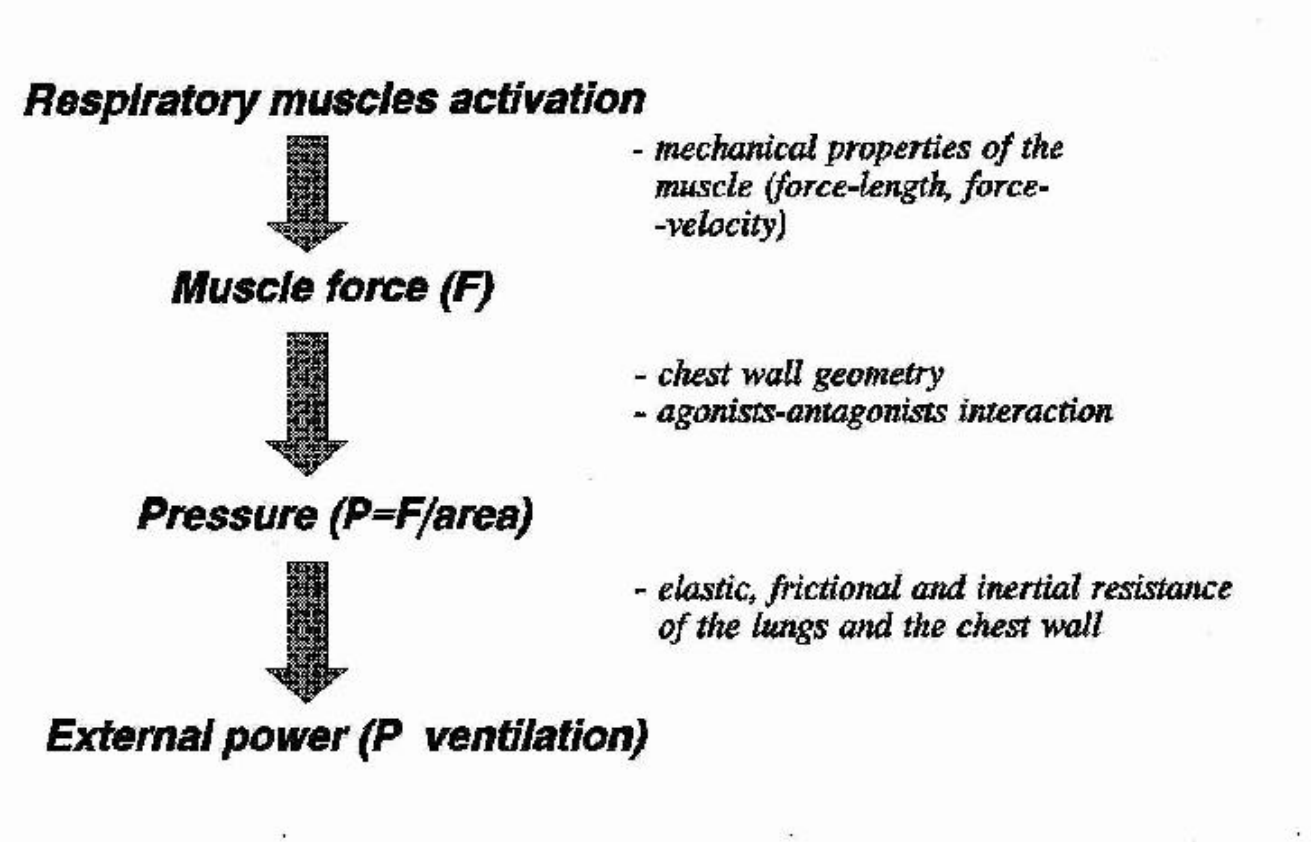

Fig.1. The sequence of events translating muscle activation into ventilation, and the factors involved in each step.

where C (Compliance) and R (Resistance) are proportionality factors determined by, respectively, the elastic and resistive characteristics of the system.

An additional pressure component is required to accelerate the gas, and its magnitude depends on the inertia of the gas and respiratory structures. Because it is usually a small portion of Ptotal, it is often neglected. However, during rapid changes in ***V***, as during high frequency ventilation, the pressure losses due to inertia can become an important fraction of Ptotal.

During *spontaneous breathing,* Ptotal for inflation is generated by the respiratory muscles. Hence Ptotal = Pmus, and inflow can occur whenever (Pmus-Pel) is greater than 0. Normally, during resting breathing, because tidal volume is entirely above the resting volume of the respiratory system (Vr), Pmus is generated by the inspiratory muscles, and expiration is passive. However, in some conditions, like some cases of hyperventilation, the expiratory muscles may become phasically active, and the breathing act occurs not just above, but across Vr. In such a case, inspiration from a lung volume below Vr is the combined result of the recoil of the respiratory system after expiratory muscle relaxation and the active contraction of the inspiratory muscles.

During *artificial ventilation*, Pmus = 0, and the driving pressure (Ptotal) is generated by the ventilator, which opposes Pel and Pres. Whenever Pmus = 0, we say that the system is in a *passive* mode. The passive mode is usually during part of the expiratory phase of the resting

spontaneous breathing cycle. At this time, the elastic pressure stored during inspiration (Pel) becomes the driving pressure generating expiratory flow, i.e., Pel = Pres = $\dot{V}$· Rrs.

Whenever Pmus differs from 0, we say that the system is in an *active* mode; this is of course the case during inspiration in the spontaneously breathing subject, but it can also occur when $\dot{V}$ = 0, such as during breath holding (in which case Pmus = Pel).

Whenever flow is nil ($\dot{V}$ = 0), Equation 1 simplifies to

$$Ptotal = Pel = V \cdot 1/C \qquad \text{(eq.2)}$$

Such a condition is defined as *static*, irrespective of the presence or absence of Pmus. On the contrary, whenever $\dot{V}$ differs from 0, the system is in a *dynamic* condition, again, irrespective of whether the respiratory muscles are active (*e.g.* during spontaneous inspiration) or not (*e.g.* inflation by a ventilator).

A dynamic condition with no changes in volume (V=0), during which

$$Ptotal = Pres = \dot{V} \cdot R \qquad \text{(eq.3)}$$

in the respiratory system can be approached when $\dot{V}$ is very high and V is very small, such as during panting or during high frequency ventilation. During an inspiratory effort against closed airways, because the change in lung volume can be considered nil (and therefore $\dot{V}$ = 0), no external work is performed, and the total pressure (Ptotal = Pmus) is entirely dissipated as heat. In summary, the operational mode of the respiratory system can be

(a) *active* (Pmus > 0) or *passive* (Pmus = 0),

and

(b) *static* ($\dot{V}$ = 0) or *dynamic* ($\dot{V} \neq 0$),

in various combinations. In adult humans, during spontaneous resting breathing, expiration is a *passive-dynamic* event, since the respiratory muscles are usually inactive. A forced expiration is an *active-dynamic* process. Breath holding is usually *active-static*. Relaxation against closed glottis (a common event in the early postnatal hours) is *passive-static*.

A few other conventions need to be emphasized at this point. The pressure across an organ, or trans-mural pressure (across the lung, trans-pulmonary pressure, or across the chest wall, trans-chest wall pressure, or across the respiratory system, trans-respiratory system pressure) is the difference between inside and outside, not vice versa. Atmospheric pressure is considered = 0, such that positive (>0) or negative (<0) pressure values imply values respectively greater or lower than atmospheric.

STATIC MECHANICAL PROPERTIES

As stated above, the respiratory system is in a *passive* mode when Pmus = 0. Obviously, this is the case during artificial ventilation in a paralysed subject, but it can also occur without paralysis after a period of hyperventilation, *i.e.* when arterial PCO_2 is lowered below the threshold for muscle activation.

In an awake adult subject spontaneously breathing, the passive mode is difficult to obtain, and only a few well-trained subjects are able to completely relax their respiratory muscles. In infants, during sleep, passive conditions can be achieved by the experimenter with an occlusion of the airways at any lung volume above the resting volume of the respiratory system. This manoeuver can be easily performed by having the infant breathing through a face-mask, of which the outlet is briefly (less than 1 sec) occluded at end-inspiration. During the brief occlusion, which usually does not disturb the infant's sleep, the increased lung volume triggers the Hering-Breüer reflex, which inhibits the activity of the respiratory muscles [Fig.2].

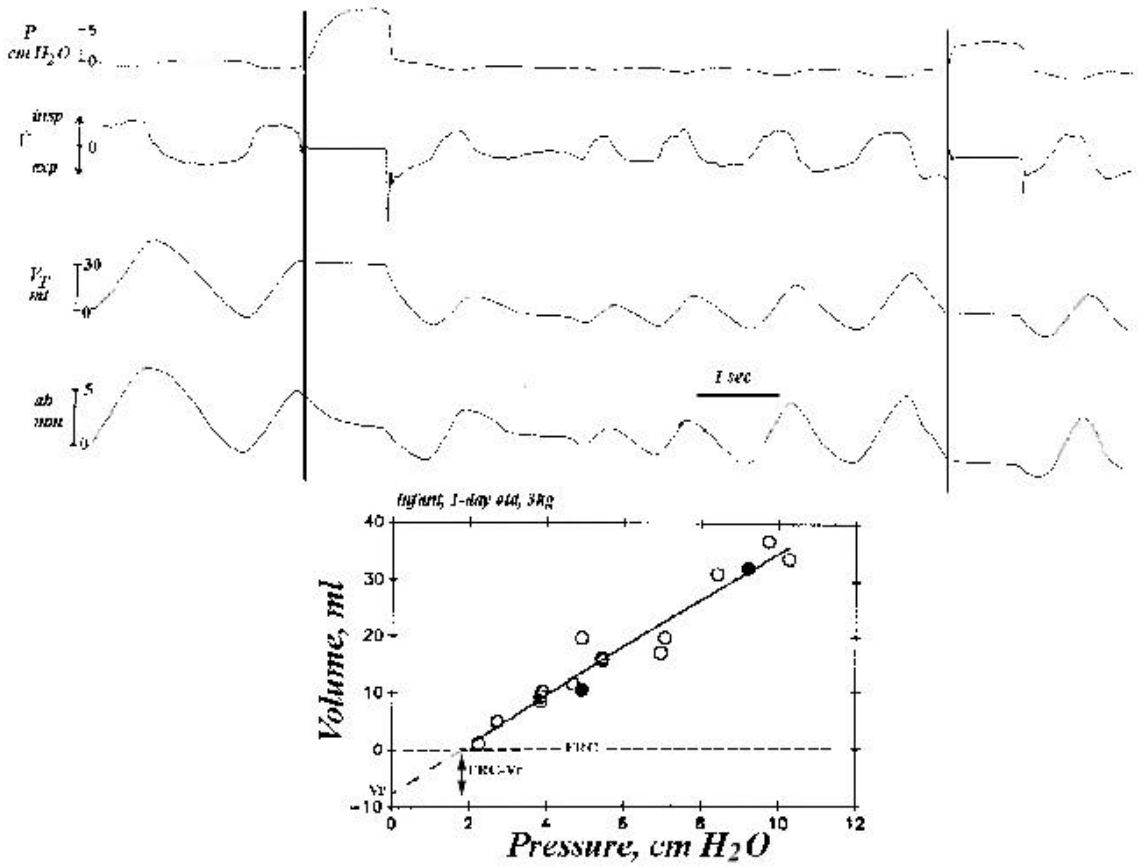

Fig.2 ***Top*****. Experimental records in an infant spontaneously breathing through a face-mask connected to a pneumotachograph. The vertical lines indicate the onset of a brief occlusion of the airways performed by the investigator. As the infant is relaxing against the occlusion, volume (V) remains constant (*i.e.* airflow *V*=0), and airways pressure (P) measured from a side-port of the mask rises to the recoil pressure of the respiratory system for that lung volume. *ab*, anterior-posterior motion of the abdomen. *Bottom.* From the P and V data of a number of occlusions (*i.e.* static-passive conditions), it is possible to construct the P-V curve of the respiratory system, the slope of which represents its compliance**

1. Compliance. When, in passive conditions, ***V***=0, the system is static, and eq.(1) simplifies to Ptotal = Pel = V · 1/C. Volume is usually plotted on the y-axis. The slope of the relationship is called *compliance*, which the reciprocal of *elastance*.*

[*It is important to realize that compliance is the slope of the V-P relationship (Δ V / Δ P), not simply the ratio between the absolute values of the two variables.]

In the example presented in Fig. 2 the pressure across the respiratory system (Prs) is easily measured during the occlusion. Because ***V*** =0 and the subject is relaxed the requirements for static-passive conditions are satisfied.

Crs is not constant throughout the vital capacity range. It decreases as lung volume increases, because Prs increases disproportionately more than lung volume does. Equally, Crs decreases as lung volume decreases below the resting volume. Generally, Crs is measured over the tidal volume range, and over this range Crs is approximately constant.

Crs is contributed by the chest wall and the lungs, and it is often useful to separate the two for the purpose of clinical assessment of the pulmonary function. The only way to partition Crs into its lung (CL) and chest wall (Ccw) components is by measuring the pressure across each of these two structures.

Trans-pulmonary pressure (PL) is the difference between the inside of the lungs (airways pressure, which in static conditions equals mouth pressure) and pleural pressure. Trans-chest wall pressure (Pcw) is the difference between pleural pressure, and body surface, or atmospheric pressure, which is considered 0. Pleural pressure (Ppl) can be measured directly, by connecting a needle-manometer system to the pleural space. However, this invasive and somewhat risky approach would yield regional, rather than average, values of Ppl. Much simpler is the use of a catheter connected to a soft latex balloon; the balloon is positioned in the lower third of the esophagus, a place which in many conditions, at least in the adult man, accurately reflects Ppl. Hence, esophageal, rather than pleural, is the pressure commonly measured, and the two can be considered equivalent.

Dynamic compliance. A schematic tracing from a spontaneously breathing subject is presented in Fig. 3. CL is computed at end inspiration, as $\Delta V / \Delta PL$. Compliance measured in this way is often labelled *dynamic compliance* (Cdyn), a term that may be confusing because it seems to contradict the compulsory requirement of static (not dynamic!) condition for measurements of compliance. In effect, the word *dynamic* is used to stress the fact that the measurement is obtained by taking advantage of a very brief static condition at end-inflation, without interrupting or in any way interfering with the spontaneous breathing. Indeed, Cdyn is a very convenient approach to the assessment of the lung compliance, because does not require any cooperation from the subject.

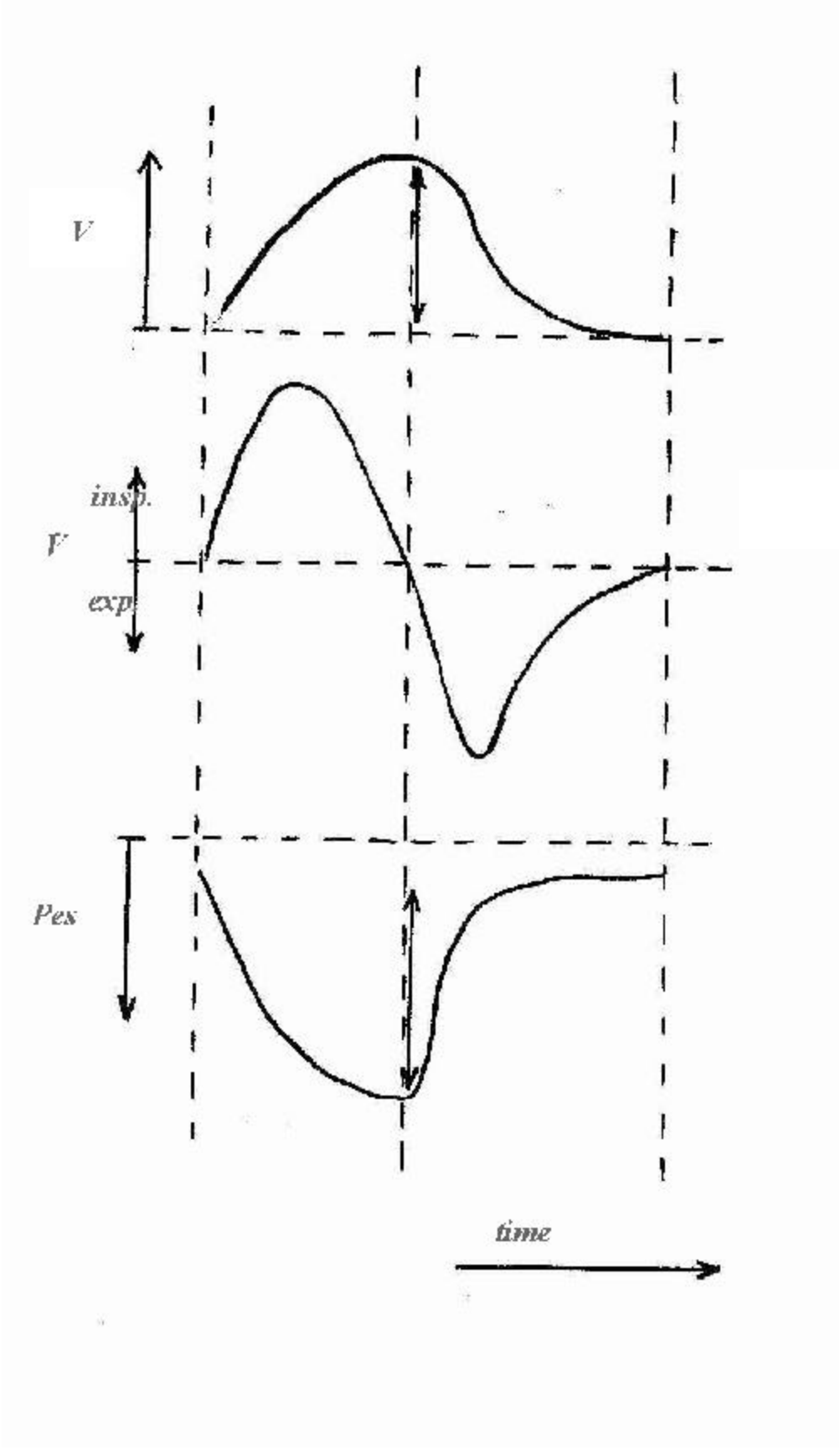
V
insp.
V
exp.
Pes
time

Fig.3. Schematic representation of the changes in lung volume (V), airflow (*V*) and esophageal pressure (Pes) in a subject spontaneously breathing. Lung compliance can be measured at end-inspiration, as $\Delta V / \Delta$ Pes, since at end-inspiration the system is in static mode. Lung compliance measured in this way during spontaneous breathing is often called *dynamic* lung compliance.

It needs to be said, however, that, even in normal subjects, Cdyn can be less than the value measured in static conditions, for example by having the subject definitely breath-holding for a few seconds, and therefore maintaining lung volume constant. Cdyn is decreased mainly because of lung stress relaxation, a phenomenon characteristic of tissue with viscoelastic, rather than purely elastic, properties. Asynchronous mechanical behaviour of peripheral lung units also contributes to the lowering of Cdyn.

Specific compliance. The compliance of a lung depends not only on its intrinsic elastic properties but also on its size or volume. A change in volume per unit pressure change will be larger for a human lung than, for example, a mouse lung. The compliance of a large person would be higher than that of a child or a small person. One approach to consider the influence of size on compliance is that of expressing compliance relative to lung volume. The lung volume usually used for normalization is functional residual capacity (FRC), since it is a volume easily reproducible. The resulting value is called *specific compliance* (Compliance/FRC). For example, an individual with a compliance of 0.18 L/cm H_2O and an FRC of 2.4 L would have a specific compliance of 0.18/2.4 = 0.08 cm H_2O^{-1}. A large man with a compliance of 0.33 L/cm H_2O and an FRC of 4.4 L will have the same specific compliance (0.33/4.4 = 0.08 cm H_2O^{-1}).

Several common pulmonary disorders change CL, including:

- Pulmonary edema: Compliance is reduced when the inflation of some alveoli is prevented. The reduction in compliance is also due in part to an alteration of the surfactant lining and in part to a decrease in alveolar radii.
- Restrictive diseases of the lungs: Compliance is reduced in subjects with pleural, interstitial, or alveolar fibrosis. The presence of excessive scar and collagen tissue contributes to "stiffer lungs". Compliance is also reduced in atelectasis and pneumonia.
- Emphysema: Compliance, if measured is static sustained conditions, is usually increased due to the loss of elastic tissue and the tendency of the alveoli to overinflate. When measured dynamically, however, Cdyn in patients with emphysema can be decreased due to increased airway resistance and uneven filling and emptying of the peripheral airways.

Ccw and Crs can be decreased in obesity, or certain diseases or deformity of the skeleton (*e.g.* scoliosis).

2. Pressure-Volume (P-V) curve of the lung. The P-V curve of the lung can be constructed by having the subject perform a full vital capacity in the step-wise fashion, holding his breath with glottis open at various lung volumes. When V is plotted against PL a curve as shown in Fig. 4 is obtained. Note that the curve obtained on inflation from RV to TLC is different from that obtained on deflation from TLC to RV. This difference reflects the hysteresis of the lungs. This curve would not be too different from that which can be obtained *"in vitro"* on dissected isolated lungs, as long as it was constructed at the same absolute lung volumes.

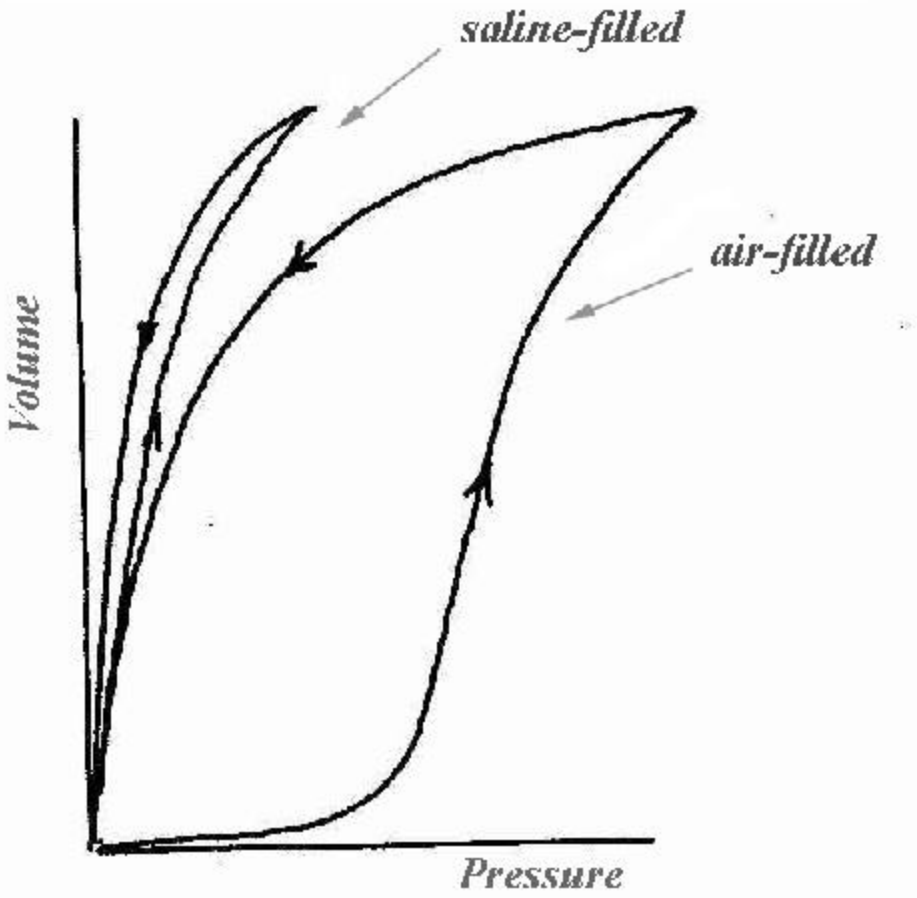

Fig.4. Pressure -Volume relationship of an isolated lung inflated and deflated with air, or with saline, starting from the collapsed state (zero volume)

By comparing this pressure-volume curve, obtained in air-filled lungs, with one obtained by filling the lungs with saline, which abolishes the air-liquid interface [Fig.4] it can be appreciated that the liquid-filled P-V loop is displaced to the left (low lung recoil pressure and high compliance), and has substantially less hysteresis. Hence, during the normal inflation with air, a large portion of lung recoil and hysteresis must be attributed to surface tension forces. Furthermore, on deflation there is a much smaller difference between the air and liquid-filled curves than on inflation. Thus, during normal breathing, surface tension forces are greater on inflation than they are on deflation.

Surface tension can be described as a molecular cohesive force existing in the surface film of all liquids which tends to contract the surface to the smallest possible area. It is commonly expressed in units of dynes per centimetre. A soap bubble on the end of a tube is an example of

an air-liquid system in which the surface tension tends to shrink the surface area. The bubble trans-mural pressure, when it is greater than 0, tends to expand the bubble. The surface tension at the inside and outside surfaces tends to prevent further expansion. Assuming that the thickness of the bubble is negligible, the relationship between trans-mural pressure (P), surface tension (T), and the radius (r) for a soap bubble at equilibrium is given by the following relationship,

$$P = K \cdot T / r \qquad \text{(eq.4)}$$

known as the Young-LaPlace relationship. This expression states that with a constant surface tension the trans-mural pressure increases as the radius decreases. A good example of this principle can be demonstrated with two bubbles of different radii in communication with each other [Fig.5]. P of the small bubble is higher than P of the large bubble; hence, airflow is generated from the smaller into the larger bubble. The hundreds of millions of alveoli within human lungs vary from 75 to 300μ in diameter. They are in communication with each other through conducting airways, intra-alveolar pores, and broncho-alveolar communications. Assume these open alveoli have all a constant and the same surface tension; the system would then be unstable, with small alveoli collapsing and further expanding the larger alveoli. This unstable condition would indeed exist if it were not for a surface-active material (pulmonary surfactant) lining the alveoli. This substance, thought to contain dipalmitoyl lecithin as an essential component, floats on the alveolar surface and helps to stabilize alveolar surface forces. Pulmonary surfactant has a short half-life of 14 hours and therefore must be continually synthesized in the lungs.

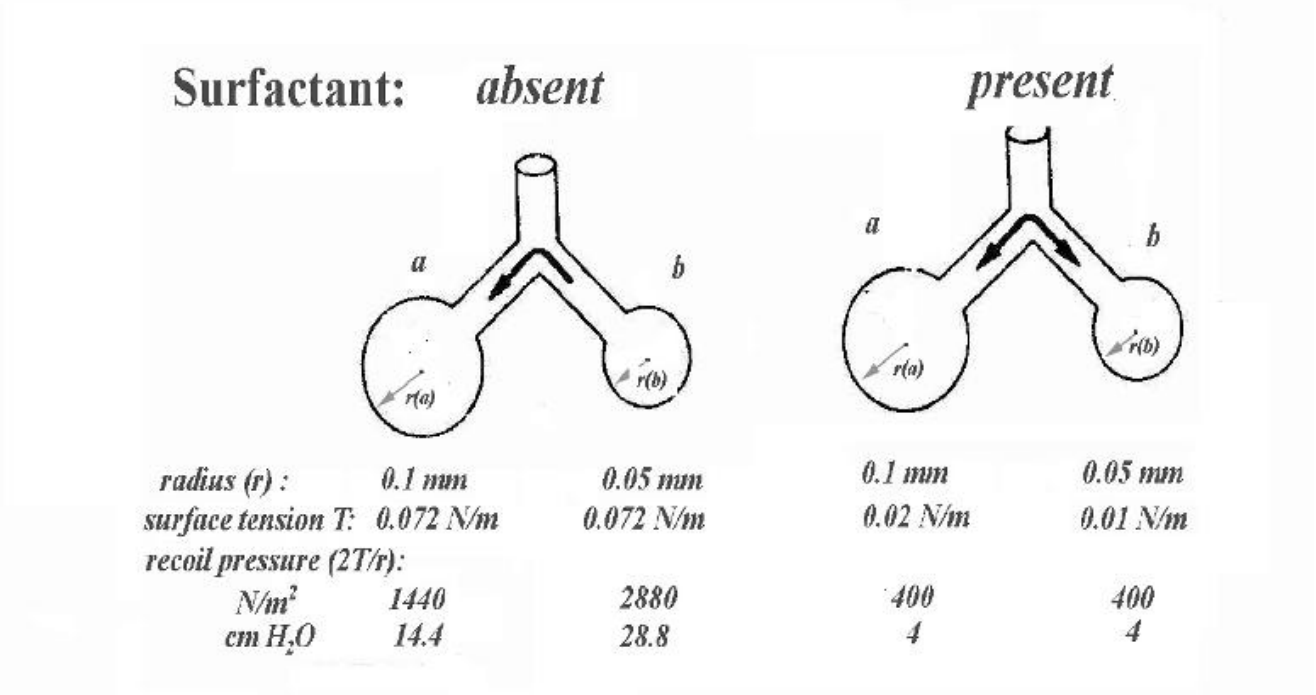

Fig.5. Numerical example to illustrate the importance of changing surface tension (T) in proportion with the radius of curvature (r) of the surface exerting tension. At *left*, in absence of surfactant, two alveoli with different radius generate different pressures. At *right*, surfactant lowers T of the less inflated alveolus, such that its recoil pressure is not higher than that of the bigger one.

The dynamic properties of surfactant permit the alveolar surface tension to change with inflation and deflation, thus keeping the small alveoli from total collapse (or atelectasis) and the larger ones from hyperinflation. It has been suggested that as the radii of the alveoli change, the concentration or thickness of the surfactant layer varies inversely with the area of the surface. Using surface-active material extracted from the lung, it can be shown that as the surface area increases and the surfactant layer is stretched thin, the surface tension approaches that of a plasma film without a surface-active agent. When compressed, this material has the unique ability to decrease the surface tension to less than 5 dynes/cm. Therefore, the collapse of the small alveoli is prevented during deflation because their surface tension is less, minimizing further collapse until the larger alveoli with larger surface tensions have deflated.
In summary, pulmonary surfactant is important in that it
1) promotes alveolar stability: alveoli of varying radii can coexist without a pressure gradient between each other,
2) reduces lung recoil pressure: the low surface tension reduces the muscular effort necessary to inflate the lungs and to keep them aerated.

The synthesis of pulmonary surfactant is one function of the *Type II alveolar cells*. Lamellar inclusion bodies within these alveolar cells go through phases of transformation in which the granular material is lost, presumably through the cell membrane, and floated on to the alveolar surface. The absence of pulmonary surfactant is associated with lung collapse (atelectasis). A reduction in pulmonary surfactant can occur with prolonged inhalation of 100% oxygen. Also, a reduction or complete lack of pulmonary surfactant is often found in the lungs of immature infants. This condition (respiratory distress syndrome) is frequent in premature infants, especially those born to diabetic mothers, and is responsible for the deaths of more neonates than any other perinatal disease.

3. Lung-chest wall coupling. Because Prs is contributed by lungs and chest wall, at any lung volume Pcw= Prs-PL, from which Ccw=?V / ?Pcw. From this, it is also apparent that

$$1/Crs = 1/CL + 1/Ccw \qquad \text{(eq.5)}$$

In an adult man, Crs is about 0.1 L/cm H_2O, equally contributed by CL (0.2 L/cm H_2O) and Ccw (0.2 L/cm H_2O).

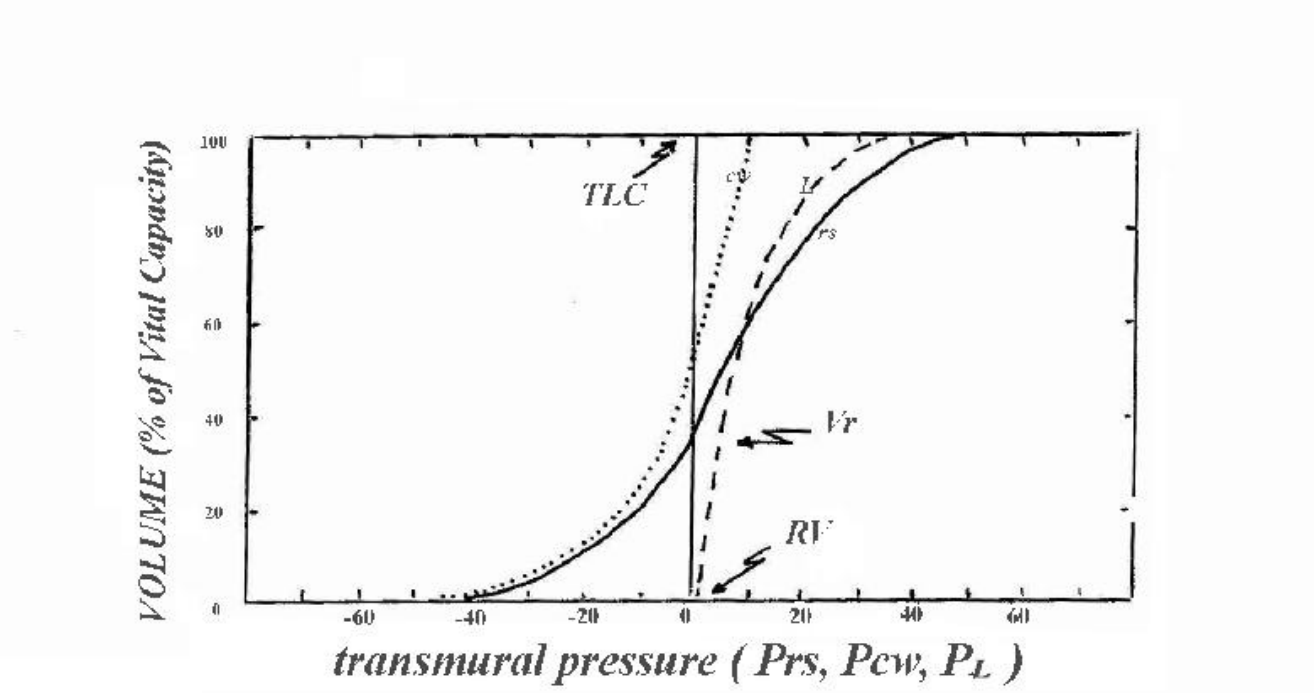

Fig.6. Pressure-Volume relations of the lungs, chest wall and the respiratory system in an adult human subject. Lung volume is expressed in percent of the vital capacity; hence, 0% indicates residual volume (RV) and 100% indicates total lung capacity (TLC). Y-axis indicates the pressure across each individual structure, Prs, Pcw or PL. At the resting volume of the respiratory system (Vr) transpulmonary pressure (PL) has the same absolute value, with opposite sign, of the trans-chest wall pressure (Pcw).

The contribution of PL and Pcw to Prs varies throughout the vital capacity range [Fig.6]. In fact, at very high volume both PL and Pcw are positive, indicating that both structures tend to recoil to lower volumes. Below about 60% of the vital capacity, on the other hand, Pcw is negative, indicating the tendency of the chest wall, quite differently from the lungs, to expand. At the resting volume of the respiratory system (Vr), the negative Pcw value, in absolute terms, equals PL; *i.e.* Pcw + PL=0, and no pressure is applied to the respiratory system (Prs=0). In other words, at Vr, lungs and chest oppose each other, the former tending to collapse, the latter to expand, maintaining a negative value of pleural (or esophageal) pressure; in the adult man, pleural pressure at Vr is approximately -5 cm H_2O. It follows that loss of elastic recoil in the lungs, as in emphysema, will result in an increase in FRC, until a lung volume is reached at which a new equilibrium is established. Conversely, an increase in chest wall compliance, as in infancy, favours the tendency of the lungs to collapse, therefore reducing Vr [Fig.7].

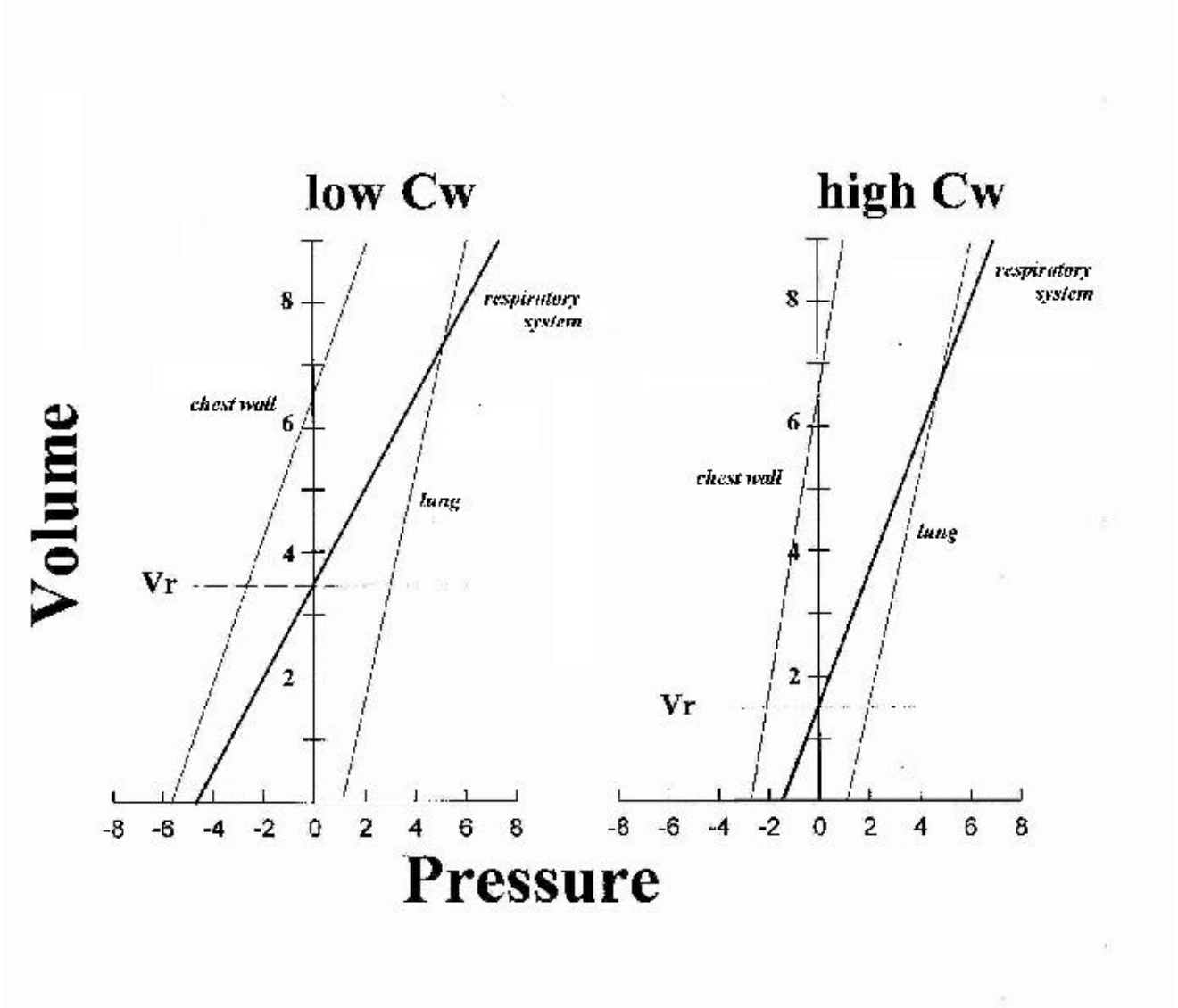

Fig.7. Schematic representation of a change in chest wall compliance (Cw) on the resting volume of the respiratory system (Vr). For simplicity, P-V curves are represented by linear relations.

Total lung capacity (TLC) is reached when the pressure developed by the inspiratory muscles is entirely offset by the elastic recoil of the respiratory system (principally the lungs, which become very stiff at high volumes, cf. Fig.6). Loss of lung recoil permits the inspiratory muscles to shorten further, with the result that TLC is increased. However, because the force that the inspiratory muscles can develop falls off rapidly as lung volume becomes greater, the increase in TLC is usually not very large. Thus, emphysema results in hyperinflation, as indicated by an increase in FRC and to a lesser degree in TLC, and in air-trapping, as indicated by the increase in RV. Because RV is usually increased more than TLC, the vital capacity is generally reduced.

Passive expiration can occur whenever Prs>0, which is the case above Vr. Conversely, passive inspiration could occur whenever Prs<0. A situation of passive inspiration is very uncommon in humans, but it is common in animals (dogs, horses) which normally breathe *across* Vr. In these cases, contraction of the expiratory muscles during expiration brings the system below Vr; therefore, as soon as these muscles relax, part of the next inspiration can occur by passive recoil.

Alveolar pressure can be greatly changed from what simply generated by the passive recoil of the respiratory system by contraction of the respiratory muscles, in other words by adding Pmus to Prs. In these cases, alveolar pressure can reach very high values, as it can be appreciated by making strenuous inspiratory and expiratory efforts against a manometer, without letting air get in or out of the lung. If the manoeuver is repeated at different lung volumes, from TLC to RV, we obtain the curves represented in Fig. 8. The maximal inspiratory pressure decreases with the increase in lung volume, because, by increasing the lung volume, the inspiratory muscles shorten and therefore develop less force. The opposite applies to the expiratory muscles. The area included between the two curves represents the maximal "potential" work that might be developed in one breathing act by the respiratory system. It is called "potential" work because it represents only the maximum theoretic work that can be done by the respiratory muscles when they contract isometrically, and the velocity of contraction is therefore nil. However, during a breathing act, the respiratory muscles contract with a finite velocity. Since the force-velocity relationship of a muscle during shortening states that one is inversely related to the other one (cfr.chapter 4, Fig.6), we can expect that the pressure developed by the respiratory muscle, even at very low speed of shortening (low flows), will always be less than the pressure generated during isometric contraction.

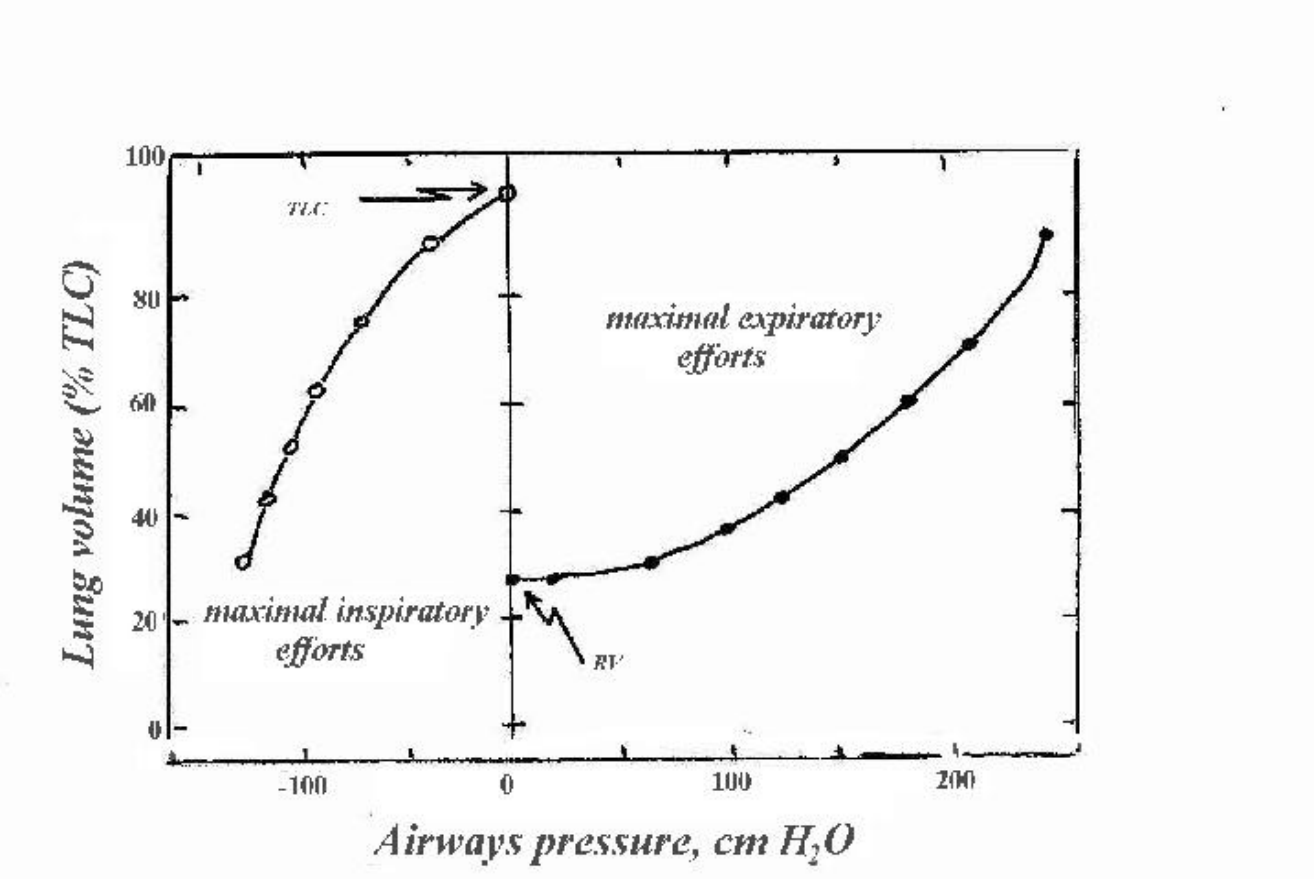

Fig.8. Maximal static inspiratory and expiratory airways pressures generated at lung volumes from total lung capacity (TLC) to residual volume (RV). Volumes are represented in % of TLC. Although the manoeuver is done without generating any flow (i.e. in static conditions), very large positive (expiratory) or negative (inspiratory) pressures slightly decrease or, respectively, increase lung volume because of Boyle's law.

DYNAMIC MECHANICAL PROPERTIES

The generation of airflow through the airways requires a driving pressure. When alveolar pressure (Palv) is negative (*i.e.* sub-atmospheric), and the airways are open, air flows into the lungs; when Palv is positive air flows out. In either case the system is in a *dynamic mode,* because $\dot{V} \neq 0$. When Palv-Pb = 0, also $\dot{V} = 0$, and the system is in a *static mode.* During breathing, the static mode is only at the beginning and the end of inspiration. In between, the system is in dynamic mode, which implies that pressure is needed not only to overcome the elastic resistance to lung volume, but also the frictional (or non-elastic) resistance to air flow, as previously expressed by equation 1.

Consider, as an example, the tracings obtained in a patient artificially ventilated, in whom the total inflatory pressure (Ptotal of eq.2) provided by the ventilator is monitored at the airways opening [Fig.9]. The total resistance of the respiratory system (Rrs) can be calculated at any point in time during inflation as [Ptotal-Pel(rs)] / $\dot{V}$, where Pel(rs) is the elastic pressure component (V/Crs) of Ptotal (eq. 2). The measurement is more accurate at maximal flow, which is usually in the middle third of inflation. A time average inflation resistance can be computed from the chart record by planimetry.

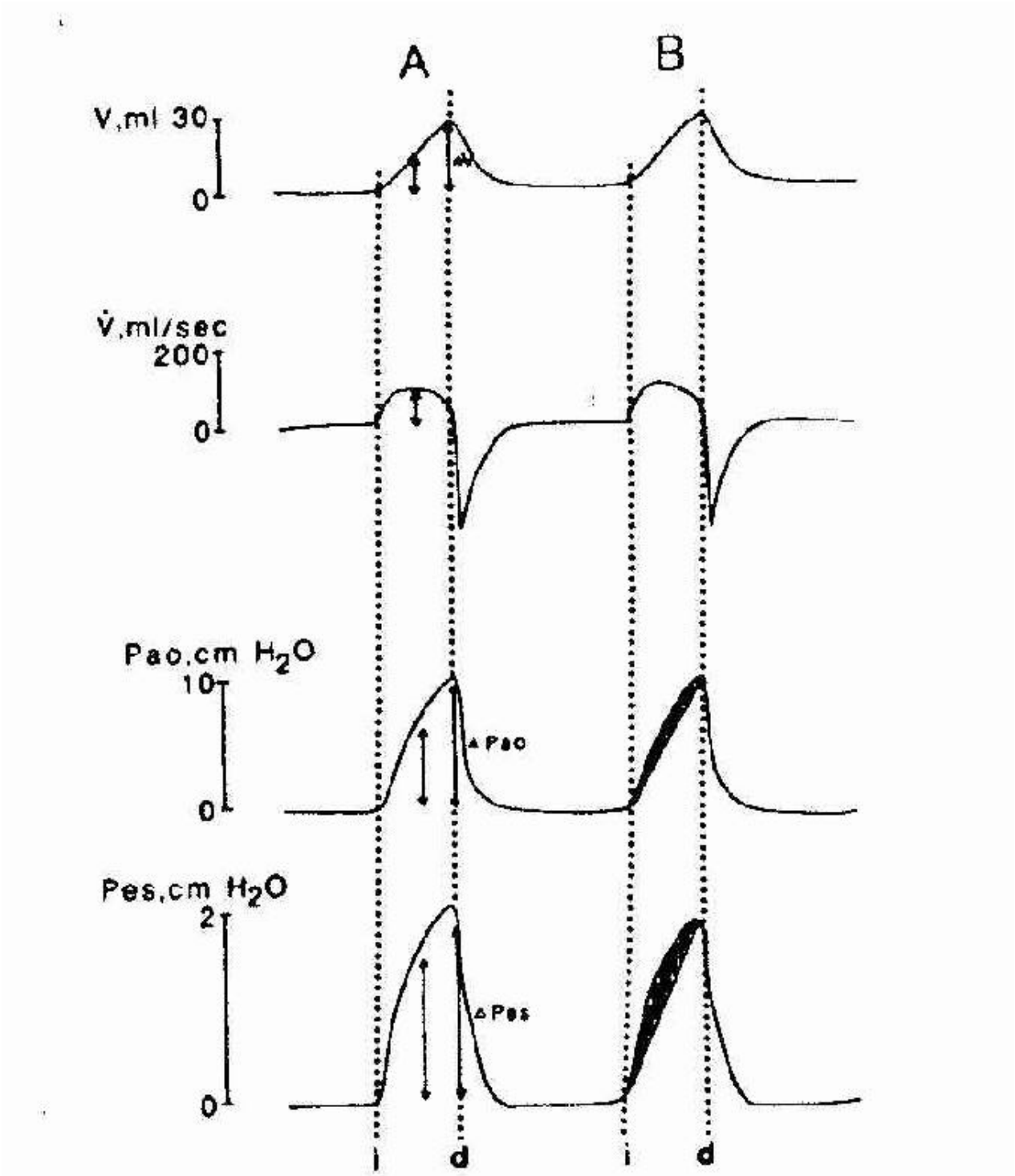
A
B
V,ml 30
0
V̇,ml/sec
200
0
Pao,cm H2O
10
0
ΔPao
Pes,cm H2O
2
0
ΔPes
i
d
i
d

Fig. 9. Changes in lung volume (V), airflow (*V*), pressure at the airway opening (Pao), and esophageal pressure (Pes) in an intubated, artificially ventilated infant. (i, d = beginning of inflation, deflation, respectively). Peak Pao is arbitrarily set at 10 cm H_2O, and ventilator frequency at 40 cycles per minute. For simplicity, Pao at end-expiration has been set at 0, although, normally, infants are ventilated with some positive end-expiratory pressure. *A* and *B* are two consecutive ventilation cycles representing two analytical approaches to the measurement of respiratory system resistance (Rrs), at mid lung volume (*A*), and by planimetry (*B*). Equally, from the Pao-Pes difference it is possible to compute total pulmonary resistance (RL).

Similar approaches can be adopted for the computation of total pulmonary resistance (RL) and chest wall resistance (Rcw), as long as the appropriate pressures, respectively PL (Pao-Ppl) and Pcw (Ppl-atmospheric), are measured.

During spontaneous breathing, RL can be measured following a similar reasoning. For example [Fig.10], at mid inflation, the resistive pressure is the total PL (Pao-Pes) minus its elastic component, and RL = [PL-Pel(L)] / ***V***. Pel(L) at any lung volume during inspiration (V') can be calculated once Cdyn is measured (cf. Fig.3), as Pel(L) = V'/ Cdyn

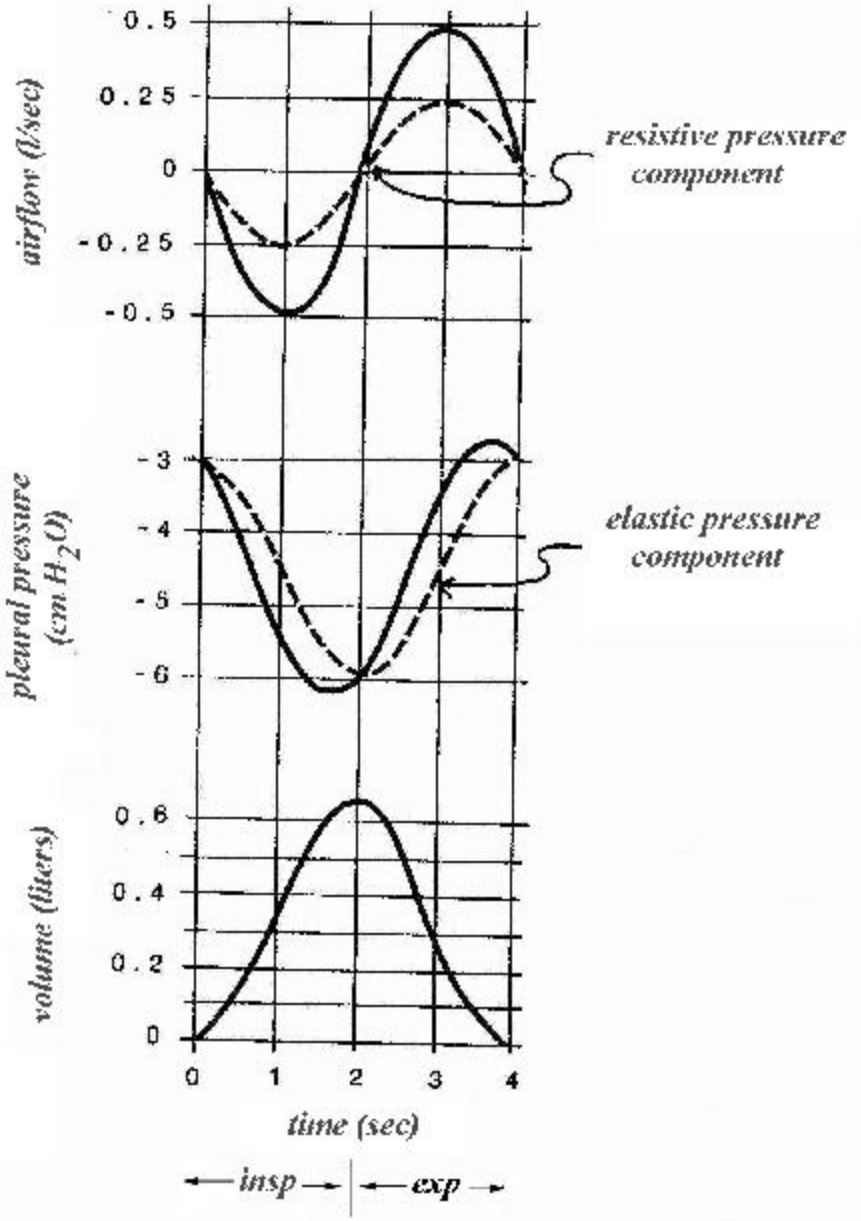

Fig.10. The continuous lines indicate the change in airflow (*V*), lung volume (V) and esophageal (or pleural) pressure during one breathing cycle. The dashed lines indicate the calculated elastic and flow-resistive components of PL. The former is calculated at each lung volume from the value of dynamic lung compliance (Cdyn= ΔV/ΔPL at end inspiration).

1. Pressure-Flow relationship. The airflow pattern can be laminar, turbulent or mixed (cf. Appendix 2). In long, straight, smooth-walled, cylindrical tubes airflow (***V***) increases in proportion to the driving pressure P (*laminar* flow regime). When flow increases beyond the limit set by the Reynolds' number, the flow is turbulent, and the P- ***V*** relationship becomes alinear.

Since in the tracheobronchial tree the total cross sectional area of each airway generation increases greatly toward the periphery of the lung, and the total airflow (***V***) through each airway generation is constant, the linear velocity of the gas decreases toward the lung periphery. Therefore, in the most peripheral airways the flow is more likely to be laminar, whereas turbulency is more likely to occur in the trachea and larger airways. In the upper airways the flow pattern is turbulent or mixed because of the high linear velocity and the complex geometry of the air pathways. The length (*l*) and radius (*r*) of the airways increase with lung volume. Because airways resistance is much more sensitive to changes in *r* than in *l*, resistance falls as lung volume increases. Therefore, the P- ***V*** relationship during inspiration or lung inflation also reflects the influence of lung volume on airways resistance. If one wants to avoid this latter factor, it is possible to construct the *iso-volume* pressure-flow relationships. To this end, P- ***V*** data points are patiently collected during a number of inspiratory and expiratory forced manoeuvres, and the values measured at the same lung volume are joined together in a plot [Fig.11].

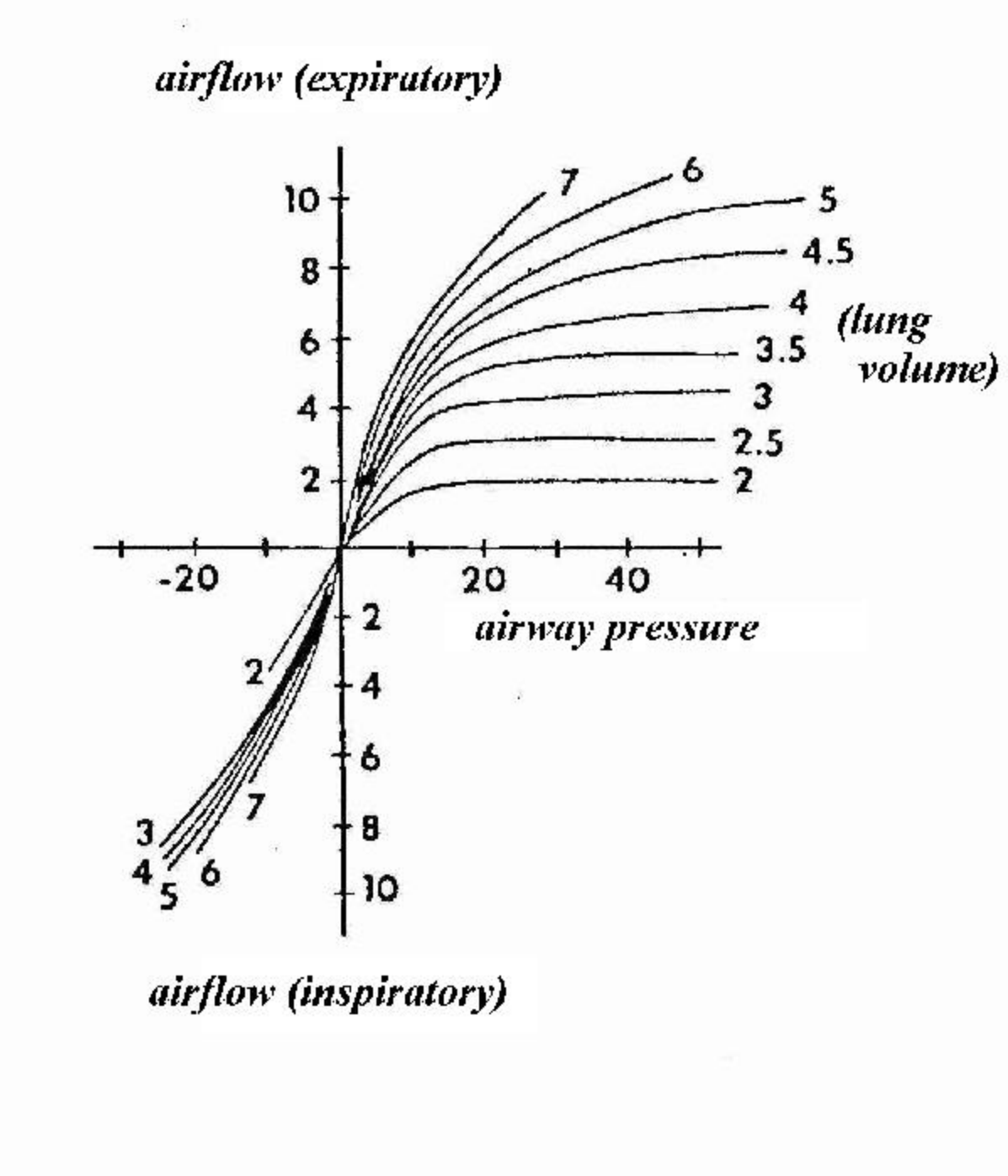

Fig.11. Iso-volume pressure-flow relations. Numbers refer to lung volume (liters). As lung volume increases, the curves become steeper, indicating a decrease in both inspiratory and expiratory resistance. Note that the plateau during the forced expiratory manoeuvres (airflow limitation) is reached at lower pressures when lung volume is low.

At low lung volumes the support applied to the airways by the attached alveolar walls approaches zero and the airways close trapping gas behind them. If this did not occur the alveoli would collapse and large pressures would be required to reinflate them. Thus airway

closure at low lung volumes can be regarded as a protective mechanism. However, as a result of disease processes airway closure can occur at lung volumes higher than normal. This is frequently an early manifestation of disease and the measurement of lung volume at which airways close (*closing volume*) is often used to detect pulmonary abnormalities.

Because flow is not uniformly laminar, the P-***V*** relationship in the airways is not linear, and the Poiseuille's law (P = R · ***V***, cf. Appendix 2) describes it only in first approximation. Rather, the value of resistance depends on the flow rate, and the flow rate at which R is measured needs to be specified. In turbulent flow regime (normally, in the larger airways) gas density affects the value of R. Gas density is increased in hyperbaria, and divers breathing from pressurised tanks have higher airways resistance. The opposite can occur at high altitude, because the hypobaria decreases gas density.

2. Expiratory Flow Limitation. During forced expiration pleural pressure becomes considerably greater than atmospheric, depending upon the intensity of the expiratory effort. Because the lungs have elastic recoil throughout the whole vital capacity range, alveolar pressure is always greater than pleural pressure. Hence, the alveoli have a positive transmural pressure.

However, this positive pressure within the airways decreases from the alveoli toward the mouth (where it is atmospheric); in the trachea the inside pressure is close to atmospheric pressure. Thus at the alveolar end the pressure inside the airways is greater than pleural pressure by a magnitude equal to the lung recoil pressure, whereas at the tracheal end the pressure inside the airway is less than pleural pressure. It follows that at some point along the airways the pressure inside must be exactly equal to pleural pressure (*equal pressure point*, EPP) [Fig.12].

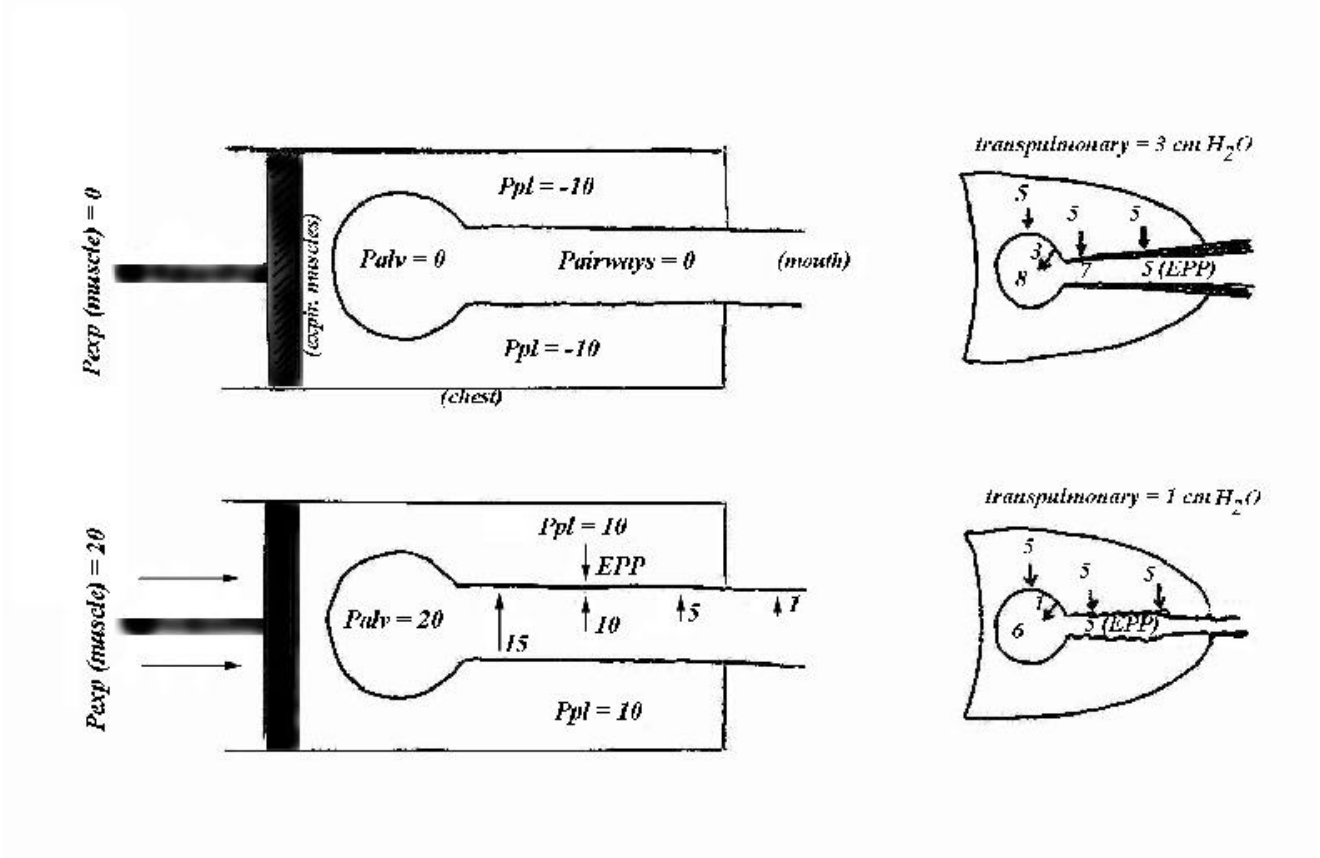

Fig.12. ***Left.*** **The equal-pressure-point (EPP) model. At top, pleural (Ppl), alveolar (Palv) and intra-airways pressures at end-inspiration. At bottom, corresponding values**

during a forced expiration, in which the expiratory muscles generated an expiratory pressure of 20 cm H_2O.
***Right*. Numerical examples of an active, yet not maximal, expiration from the same lung volume, in a subject with normal lung recoil of 3 cm H_2O (*top*), and in a patient with emphysema, with lung recoil of only 1 cm H_2O (*bottom*). In this latter case, EPP is very close to the most peripheral airways**.

From the EPP downstream (*i.e.* in the direction towards the mouth) pleural pressure can exceed the intra-airways pressure, and the airways become dynamically compressed. Of course, this increases the resistance during the forced expiration. Furthermore, the greater the degree of expiratory effort (i.e., the more positive the pleural pressure becomes), the greater the degree of dynamic compression. Thus, with the increase in effort, the driving pressure (*i.e.* alveolar pressure) increases, but also the resistance to flow increases. The result is that eventually the expiratory flow cannot increase any further, and becomes independent of the effort. This is shown by the plateau in the P-***V*** relationship [Fig.11].

Because the location of the EPP depends on the Palv-Ppl difference, *i.e.* on the lung recoil pressure, the lower the recoil, the more peripheral the EPP. Hence, expiratory flow limitation is more easily present during forced expiration at low than at large lung volumes (cf. Fig.11). In patients with decreased lung recoil (*e.g.* emphysema), muscle exercise can be limited by the inability of the respiratory system to breathe out fast enough during the hyperpnea. In fact, in some cases, even during resting breathing the expiratory airflow can be dynamically limited. In these severe cases, the only way to improve the expiratory flow is by breathing at high lung volume (hyperinflation), which increases lung recoil.

3. Partitioning of Resistance. Approximately half of the resistance to flow in the airways is contributed by the upper airways (larynx to mouth), and most of the rest is in large central airways. Switching from nose to mouth breathing reduces upper airways resistance, and is therefore adopted when high flows are needed, as during exercise-hyperpnea. This nose-to-mouth breathing switch, albeit triggered by pressure receptors in the upper passages, seems to be a behavioural response which needs to be learned; infants are thought to be less capable of mouth-breathing than adults, and many mammalian species do not seem able (or perhaps never learn?) to breathe through the mouth.

The resistance to flow of the airways smaller than 2-3 mm diameter is only about 10% of the total. This has profound implications with regard to disease, since even large changes in the resistance of the peripheral airways may have minimal impact on R. As an example, consider the lung model with one central airway of R=9 arbitrary units, leading to two parallel peripheral airways with R=1; hence, together, these two peripheral units contribute 10% of the total R. If one half of all the peripheral airways became occluded, peripheral resistance would double to 2. Total resistance would only increase to 1.1, an increase of only 10%, which could be undetected since is probably within the measurement error. Thus, in the particular circumstances of obstruction in small airways, measurements of RL are an insensitive means of detection, and other methods must be devised.

Tests which detect the lung volume at which airways close (*closing volume*) is one such method. The influence on RL during breathing helium, instead of air, is another test. Helium has a density lower than air but its viscosity is almost the same. Thus, if breathing helium causes a reduction in RL, most of the resistance during air-breathing must be in larger airways where the pressure-flow regime is density dependent (cf. also Appendix 2). If breathing helium causes little reduction in the high value of RL , most of the high resistance must originate in smaller airways where the flow is laminar.

WORK AND COST

The mechanical work which is carried out solely on the lungs during a breathing cycle can be estimated by measuring the changes in the pleural pressure and volume. When these variables are X-Y plotted, a loop is obtained [Fig.13]. The mechanical work necessary to inflate the lungs from functional residual capacity (FRC) to VT is the whole are at the left of the *inflation* P-V curve. Of this, part is required to overcome the elastic resistance of the lung during inspiration, represented by the area at the left of the *lung* static P-V curve (dotted area). Part represents the extra work required to overcome the frictional resistance (white area). Of course, for the same VT, this latter work depends not only on resistance but also on the inspiratory time, *i.e.* on the inspiratory flow rate.

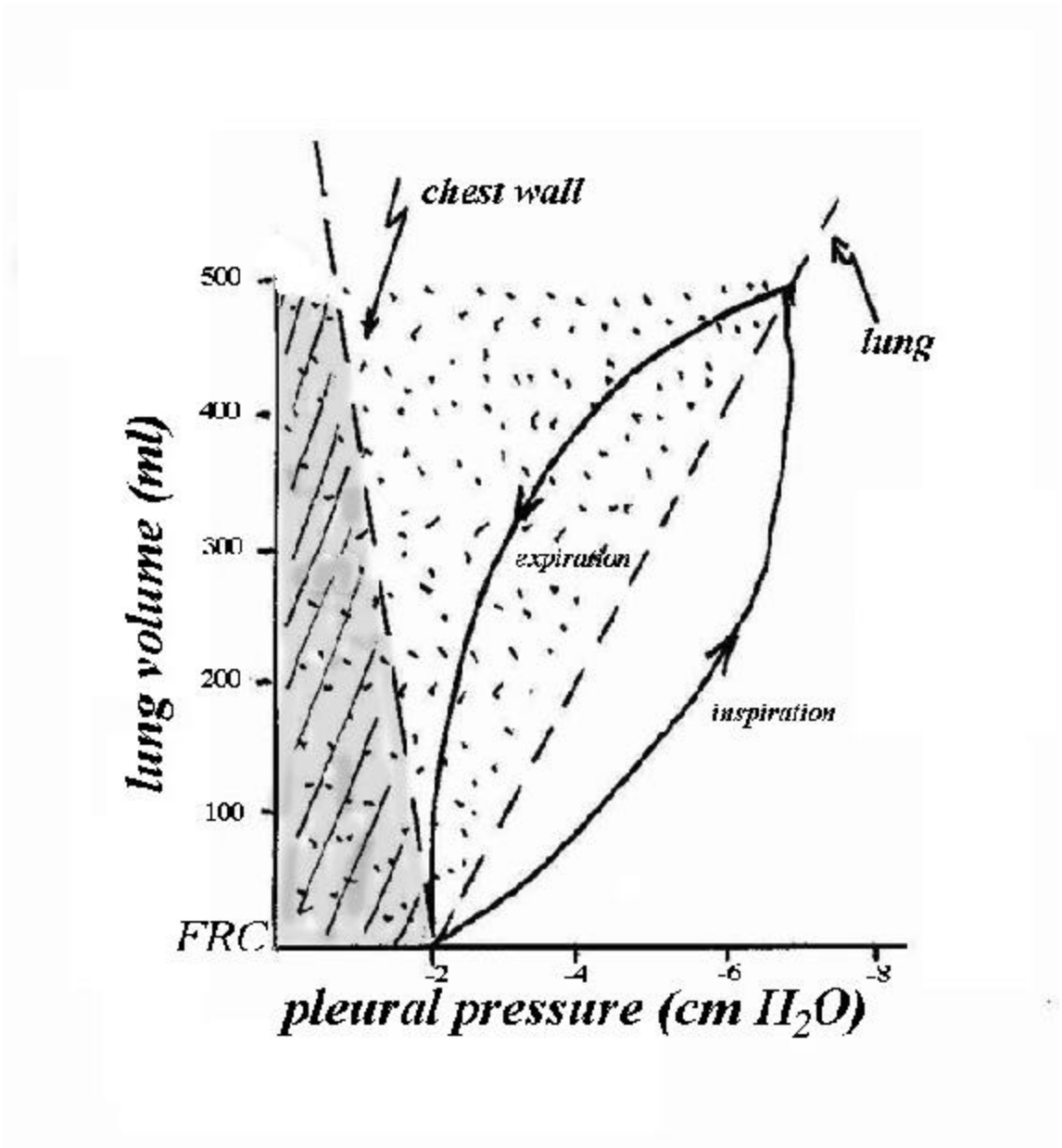

Fig.13. Changes in pleural pressure during inspiration from functional residual capacity (FRC) to VT, and the following expiration (*continuous line, 'inspiration' and 'expiration')*. The *dashed lines* indicate the static P-V curves of lungs and chest wall.

The total inspiratory work is represented by the whole area at the left of the *inspiration* P-V curve. A portion of it (*grey-dotted area with hatching*) is contributed by the expanding action of the chest wall.

During expiration, the work to overcome expiratory resistance is the represented by the area between the *expiration* P-V curve and the elastic static P-V curve of the lung. When this area is less than the elastic energy stored at end inspiration, expiration can be an entirely passive process, not requiring expiratory muscle work. In this case, any remaining energy stored in inspiration and not needed to generate expiratory flow would be dissipated as heat. On the other hand, if the expiratory non-elastic work loop exceeds the elastic energy stored at end-inspiration, expiration cannot be entirely passive, and expiratory muscular work is required.

For the same ventilation, a rapid and shallow breathing pattern reduces the elastic work of breathing, but disproportionately increases the non-elastic component. Conversely, a deep and slow pattern reduces the frictional work, but increases disproportionately the elastic work. During resting breathing in an adult man, the minimum work occurs at a breathing frequency of about 12-15 breaths/min, which indeed corresponds to the most common breathing rates observed at rest.

In order to perform the mechanical work necessary for breathing, the respiratory muscles require oxygen. During quiet breathing, the total oxygen consumption ($\dot{V}O_2$) of the body is between 200 and 300 ml/min. During voluntary hyperventilation, the difference between total $\dot{V}O_2$ and resting $\dot{V}O_2$ should represent the oxygen consumption of breathing. This seemingly straight-forward approach to compute the cost of breathing is, in reality, complicated by a number of assumptions. At any rate, the oxygen cost of breathing has been calculated to range between 0.3 and 1.8 ml/L of ventilation, for values of ventilation up to about 50 L/min, or less than 5 percent of total $\dot{V}O_2$. At levels of ventilation above 50 L/min, the respiratory muscles utilize a greater proportion of the total $\dot{V}O_2$, and, eventually, the respiratory cost can become a very large fraction of total $\dot{V}O_2$.

THE RESPIRATORY SYSTEM IN '*ACTIVE*' MODE

An important question is whether during spontaneous breathing the mechanical properties of the respiratory system are the same as during passive conditions. The answer is that neither during inspiration nor during expiration does the system behave exactly as expected on the basis of passive measurements. During inspiration, the main reason for the difference has to do with the uneven distribution of pressure on the chest wall during muscle contraction, leading to distortion. This has several functional implications, including its effect on the energetics of breathing (see next section). The frequency dependence of Cdyn, mentioned earlier, and the decrease in lung Cdyn as the result of chest wall distortion are additional factors contributing to the difference between active and passive mechanics.

During expiration, neural mechanisms aimed to control the expiratory flow and mean lung volume, including post-inspiratory muscle activity and laryngeal braking, effectively increase the expiratory resistance prolonging the expiratory time constant above its passive value.

1. Chest Wall Distortion. During passive inflation of the respiratory system (*e.g.* by a positive-pressure ventilator) both trans-abdominal pressure and pleural pressure (Ppl) increase. In fact, if we assume no passive tension of the diaphragm (*i.e.* trans-diaphragmatic pressure Pdi = 0), the changes in Ppl and Pab will be the same, and any region of the chest wall (and more specifically its two main compartments, rib cage [or thorax] and abdomen) will be driven by the same uniformly applied pressure, Pab = Ppl.

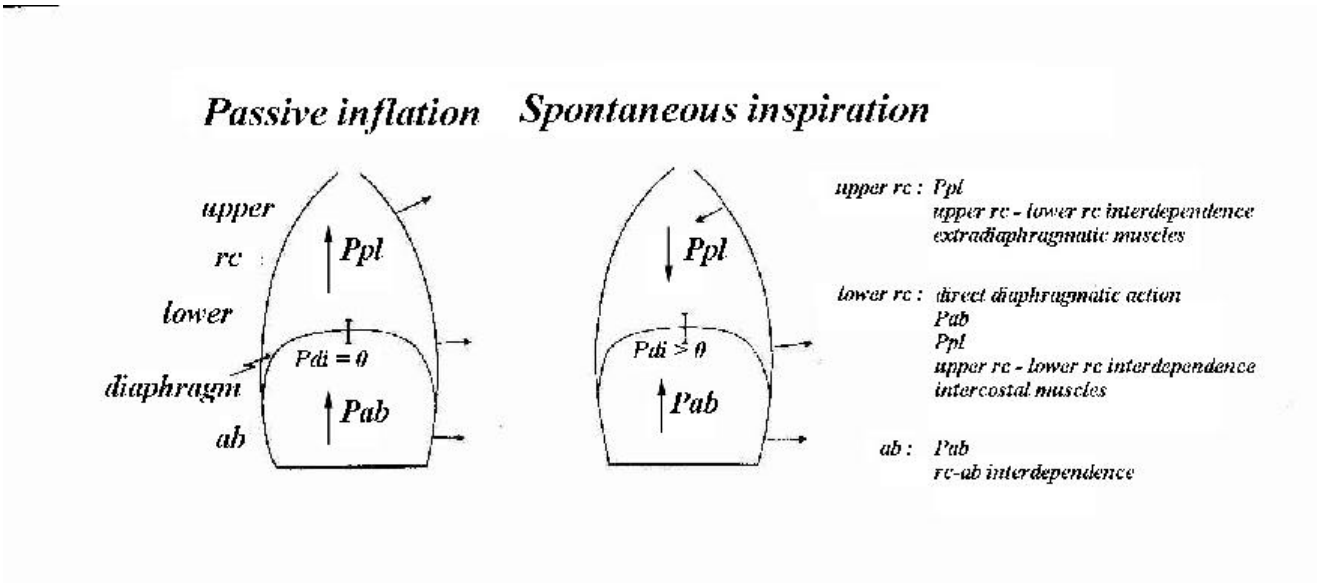

Fig.14. Schema of the pressures applied to the chest wall and its components rib cage (rc) and abdomen (ab) during passive inflation (*left*) and spontaneous breathing (*right*). Arrows from the chest indicate the expected direction of motion in absence of extra-diaphragmatic muscle activity. At extreme right, summary of pressures and forces determining motion of the upper portion of the rc, lower rc, and ab during spontaneous inspiration.
Pdi = trans-diaphragmatic pressure (Pab-Ppl)

In active conditions (Pmus > 0), when the diaphragm is contracting, Pab increases, similarly to the passive inflation, expanding ab. The motion of rc is more complex than in passive conditions, because it depends on the interplay of several factors [Fig.14]. First, Ppl during spontaneous inspiration becomes progressively more subatmospheric, which tends to collapse the rib cage, both in its upper and lower regions. Pab acts on the lowermost part of the rib cage (the apposition area, which faces the cranial part of the abdomen) with an inflatory action. In addition, the lower rib cage can be expanded by the direct outward-pulling action of the diaphragmatic fibers. Hence, differently from the inflation of the respiratory system in *passive* mode, the magnitude of rib cage expansion during diaphragmatic contraction can be quite variable. For the lower portions of the rib cage, the degree of its expansion will depend on the net effect of multiple forces. As far as the upper rib cage, the expected tendency to collapse during diaphragmatic contractions because of the negative Ppl can be partly diminished by the mechanical interdependence with the lower rib cage, and even offset or reversed into outward motion by the compensatory contraction of the intercostal muscles.

It is important to realize that the mechanical arrangement of the mammalian respiratory system is such that diaphragmatic contraction alone results in a tendency for the upper rib cage to collapse inward. This is particularly the case in infancy, when the mechanical coupling between upper and lower rib cage is not very effective because of high chest wall compliance, and the neural proprioceptive control of the intercostal muscles does not operate as in adults. A clear example of the action of the diaphragm on the chest wall is provided by adult humans with no intercostal muscle activity (tetraplegic patients), in whom the upper rib cage paradoxically moves inward during inspiration [see chapter 1, Fig.13]. In normal subjects, therefore, absence of inward motion of the rib cage during inspiration implies that the compensatory action of the extra-diaphragmatic muscles (namely, intercostal muscles) is taking place. In other words, motion of the whole chest wall during *active* breathing as in *passive* conditions should not be

interpreted as absence of distortion, but, rather, as full compensation of distortion. The two concepts are quite different when examined in light of the energetics of breathing.

To the extent that chest wall distortion is defined as the difference in configuration between the active and passive modes, it could be quantitatively evaluated as the difference in linear dimensions of any chest wall region between its active and passive conditions. Of course, the functional interpretation of these differences depends on which region of the chest wall has been sampled; for example, the factors contributing to the rib cage motion at the level of the apposition area may be very difficult to sort out.

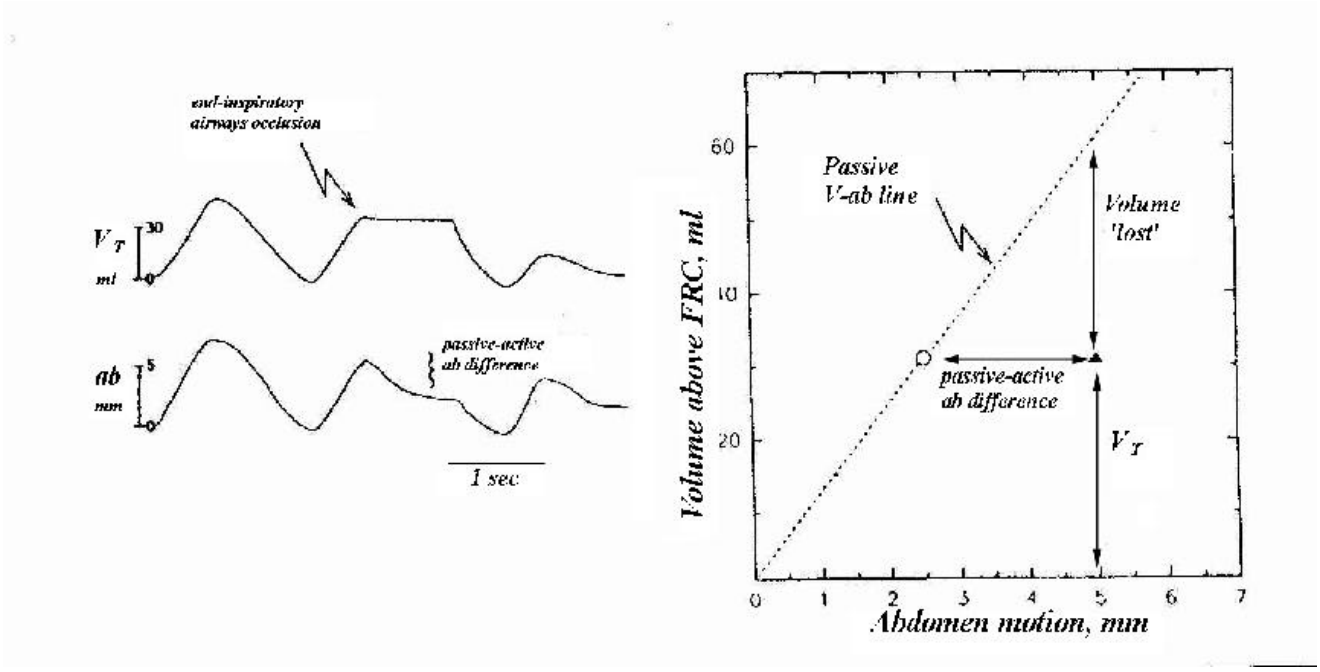

Fig.15. ***Left*****. Records of changes in lung volume (VT) and abdominal anterior-posterior dimension (ab) in a supine infant, spontaneously breathing through a face-mask and a pneumotachograph. At end-inspiration, the airways are briefly occluded by the investigator; as lung volume remains constant, ab decreases from the active end-inspiratory value to the passive value.**
Right**. Abdominal motion-lung volume relation, from the records presented in the left panel. Extrapolation of the passive line above VT assumes linearity**.

An analysis of the net effect of chest distortion on lung volume can be done by comparing the lung volume (or transpulmonary pressure)-Pab relationship between active and passive conditions [Fig.15]. For the same ΔV, Pab (or abdominal expansion, since changes in Pab and motion of the abdominal wall are closely related during resting breathing) is larger during active than in passive inflation. This is true even at end-inspiration (*i.e.* in static conditions), VT being less than the passive ΔV, for the same change in Pab. In infants during resting breathing VT can be only 50% of the passive V, at the same Pab. The volume difference is probably larger in REM sleep (because of the decreased activity of the intercostal muscles) and in the supine posture (because of the higher abdominal compliance compared to the prone position.), whereas it could be less during hyperventilation, as in hypoxia (because of recruitment of accessory respiratory muscles).

2. Expiration. During expiration, in resting conditions, one may expect the profile of the spirogram and airflow to be exactly as in passive conditions, since expiration is driven by the

elastic recoil of the respiratory system. This is often not the case [Fig.16], mainly for two reasons. First, the inspiratory activity does not cease instantaneously at end-inspiration but proceeds during part of the expiratory phase, maintaining some inspiratory pressure (PmusI); hence, the effective recoil pressure of the respiratory system in expiration is less than the passive value by a magnitude which corresponds to PmusI. Second, during expiration the narrowing of the vocal folds by contraction of the laryngeal adductors increases airway resistance, therefore lowering the expiratory flow.

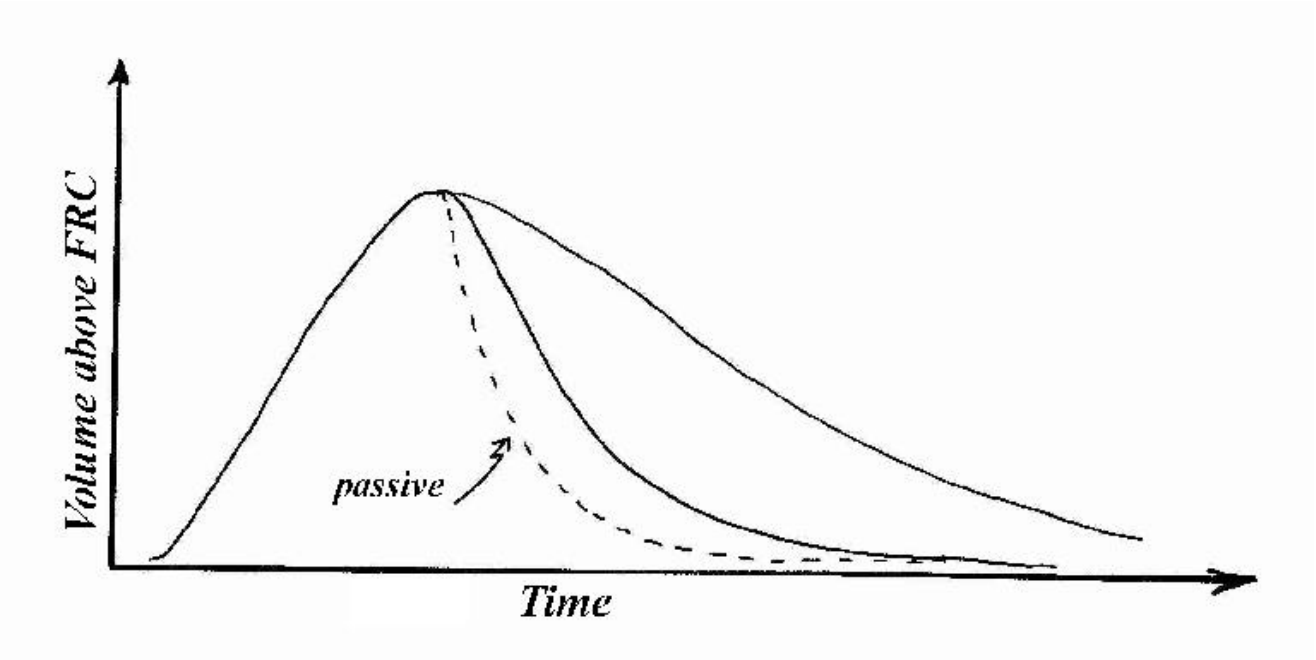

Fig.16. Schematic representation of the spirogram. The dashed line represents the passive expiratory trajectory, as it could be measured in paralysed conditions. The other two trajectories are examples of what is actually observed, with mean expiratory volume higher than the passive value. This is the effect of the combined action of post-inspiratory activity of the inspiratory muscles, and the laryngeal control of expiratory flow.

By reducing the expiratory flow, mean lung volume is higher than it would be if expiration was strictly passive. In fact, during infancy, when these phenomena are much more pronounced than in adulthood, inspiration begins before completion of the previous expiration. The result is that the functional residual capacity (FRC, or end-expiratory level) is dynamically maintained at a lung volume higher than the passive relaxation volume of the respiratory system (Vr). This is particularly important in the infant, who, because of the high chest wall-lung compliance ratio, would naturally tend to have a low Vr [cfr Fig.7]. When the vocal folds are bypassed, as with tracheal intubation in conditions of artificial ventilation, it is common practice to add an end-expiratory pressure of a few cm H_2O, which effectively substitutes the larynx and, by protecting FRC, prevents deflation of the respiratory system to its low passive volume.

3. Implications on the energetics of breathing. The computation of the tidal work of breathing by planimetry from the Ppl-V diagram, presented earlier, allows an estimate of the work performed in moving air in and out of the lungs during each breathing cycle, *i.e.* the *external* work of breathing. During resting conditions, this value would be similar to that computed analytically from the equation of motion of the respiratory system (eq.1), for any V and $\dot{V}$, from the passive values of Crs and Rrs, and assuming a sinusoidal flow pattern.

The *active* work of breathing is likely to exceed these estimates. The main reason for the difference is in the fact that the respiratory muscles, being themselves part of the chest wall, cannot generate a force as uniformly applied to the system as in passive conditions. Indeed, the inflatory action of the main inspiratory muscle, the diaphragm, can be pictured more like that of a piston expanding the abdomen and simultaneously collapsing the upper rib cage than that of a uniform chest wall expander. The result of this uneven distribution of muscle force is that some force is lost in the distortion of the chest wall, instead of being translated into airflow. In addition, the energy produced by muscles working antagonistically, or contracting isometrically, is dissipated without generating any pressure.

Estimates of these pressure losses during *active* conditions have been attempted with numerous approaches and various assumptions. Notwithstanding the difficulties for a quantitative assessment, the general conclusion can be reached that during active breathing the respiratory system behaves as if its impedance was higher than in passive conditions, because of a lower compliance, higher resistance, or both. Estimates of the active work are useful because they offer a more realistic evaluation of the work imposed on the respiratory muscles, and of the cost required, than passive measurements would provide. In addition, *active* values of Crs and Rrs permit more accurate predictions of the ability to protect tidal volume in face of external elastic or resistive loads.