Mechanical Events In Physiopathology Of Idiopathic Pulmonary Emphysema: A Theoretical Analysis

S Nazari

Citation

Abstract
Lung volume reduction (LVR) surgery, now quite frequently used as a therapeutic option in lung emphysema, is aimed at advantageously interfering with the structural alterations of bronchoalveolar architecture and the thoracic cage and diaphragm changes characterizing the emphysema. All the changes of the emphysematous parenchyma are triggered by interalveolar septa rupture. The purpose of this article is to analyze this main pathogenic event and its purely mechanical consequences, which are the only ones that can be expected to be modified by LVR, independently of the nature and extent of the etiopathogenic process that brought the septa to the condition in which their rupture was possible.

INTRODUCTION
The etiopathogenesis of lung emphysema is quite complex and its details not yet completely clarified; in fact apart from forms in which it is possible to prove an alteration in the elastic properties of the lung caused by a genetically defined a-1 antitrypsin deficiency (1), in the majority of cases the origin is certainly related to prolonged action on the lung parenchyma of a variety of physical and chemical agents (cigarette smoke, toxic substances, etc.) which can produce the anatomopathological picture of emphysema (2,3).

It has recently been proved, however, that simple lung volume reduction (LVR) has beneficial effects in selected patients, by causing a rearrangement of the residual lung and thoracic cage-diaphragm disposition.

The purpose of this article is, therefore, to analyze the physiopathology of emphysema, confining this analysis to the mechanical events in the fine pulmonary architecture and thoracic cage-diaphragm disposition, that are the only factors that can be expected to be modifiable by LVR.

SURGICAL PHYSIOPATHOLOGY
Despite the fact that the nature, extent and severity of the alveolar membrane alterations probably differ according to the underlying pathogenic agent, a common element characterizes the final picture of emphysema due to any pathogenic agent, i.e. rupture of the interalveolar septa. This elementary injury triggers a series of consequences, essentially mechanico-structural, in the delicate and interconnected bronco-alveolar architecture whose final rearrangement conditions, at least in part, the clinical symptoms. The direct effects of this main event can be summarized in the following points.

- Intrapulmonary air collection- surrounding parenchymal collapse
  The alveolar sacs that form the acina, i.e. the lung functional unit, have an organized architectural structure that, chiefly because of the uniform and particular characteristics of elasticity of the alveolar walls, but also because of the complex interalveolar communication system (poles of Kohn) and surfactant, guarantees harmonious, uniform expansion and ventilation of the alveoli during the respiratory cycle.

- The simple rupture of a relatively small number of interalveolar septa through the immediately consequent redistribution of the elastic forces, causes an important alteration in lung architecture characterized essentially by the creation of
intraparenchymal air spaces and by the collapse of adjacent healthy parenchyma.

A useful and clarifying simulation of the mechanism of the lung structure disarrangement resulting from septa rupture is offered, in a two-dimensional model, by interrupting a series of threads in an elastic net, distended at moderate tension over a finite surface (Fig. 1). In this model, statically similar to lung structure, the interruption of an individual thread, simulating the rupture of an alveolar septum, generates a new structural arrangement in which at least four components can be recognized:

1. the rupture of an alveolar septum puts two contiguous alveoli in wide communication, creating a bigger individual air space, with an air/alveolar wall ratio less favorable for gas exchange (Fig. 1);

2. the contemporaneous redistribution of the net elastic forces in consequence of the lack of the balancing action of the interrupted septum, acts in a radial sense on the newly formed space, further magnifying its dimensions (Fig. 1, hatch) and

3. reducing in proportion that available to the bordering alveoli;

4. moreover in this new structural arrangement the elastic forces of the net are not shared in a harmonious, uniform way on all the walls of the newly-formed space. Due to pure geometric distortion, the stress concentrates on some of the threads bordering these newly-formed spaces; this then creates more favorable conditions for their subsequent rupture leading to further enlargement of the emphysematous space (Fig. 2).

Figure 1
Figure 1: An elastic net with a relatively wide mesh, distended under moderate tension over a finite surface, offers a two-dimensional mechanical model useful for understanding the modifications of pulmonary structure following the simple rupture of a septum. The rupture of a septum not only puts two adjacent alveolar spaces in communication, creating a bigger air space with an air-alveolar membrane ratio less favorable to gaseous exchanges, but because of the lack of the stabilizing effect of the interrupted septum, the elastic recoil of the net acts in a radial sense further widening the newly-formed air space (orange area), necessarily at the expense of the spaces bordered by the surrounding meshes.
Figure 2

Figure 2: This mechanism becomes more evident as the number of interrupted septa increases. It is easy to understand from this model that the creation of wide air spaces in emphysema is a direct consequence of the rearrangement of the elastic forces of the lung to a level of lower tension, in a direct mechanical response to the septal rupture. It is also evident that creation of large intrapulmonary air spaces as a consequence of the centrifugal collapse of the lung parenchyma following septal rupture, does not presuppose an increase of pulmonary volumes but their simple redistribution; in particular this process is completely independent of the expansion of the thoracic cage, ventilation and changes of pressures in the respiratory tree, all of which are, however, able to further enhance this pathogenic mechanism. With this model it is also evident that, due to geometric distortion, the intrinsic elastic recoil of the net does not act on the septa bordering the newly-formed spaces in a uniform way, loading some of these with greater stress (arrows), and thus putting them at more risk of rupturing, necessarily perpetuating the pathogenic mechanism of the emphysema. Although the lung is obviously a three-dimensional structure the mechanico-structural alterations are qualitatively the same as those illustrated in the above two-dimensional model. (In red are the shapes of the 14 meshes whose treads were interrupted. The net was distended prevalently along its vertical axis to enhance evidence of the uneven stress repartition on bordering septa.)

It is interesting to note that this architectural distortion takes place automatically as a direct consequence of the rearrangement of the lung elastic forces to a level of lower tension after the rupture of the alveolar septum; in particular this process is completely independent of the expansion of the thoracic cage, ventilation and changes of pressures in the respiratory tree (bronchial obstruction), all of which, however, are able to further enhance this pathogenic mechanism.

At initial stages some degree of thoracic cage expansion results from the re-equilibrium of its own intrinsic elastic force to the new condition of the emphysematous lung, whose increased compliance now causes a smaller inwards traction on the thoracic cage. This spontaneous, thoracic cage recoil activated expansion cannot, however, exceed 70% of the TLC, which is approximately the static equilibrium point of the thoracic cage.

The greater part of thoracic cage enlargement ("barrel chest") and flattening of the diaphragm, so characteristic of emphysema, cannot thus be a direct physical consequence of bullous formation, except in those infrequent cases in which a valve mechanism causes forced entrapment of air in the bullae. These modifications of the thoracic cage and diaphragm are rather expressions of an active compensatory mechanism (23), taking place presumably only when the lesions are so extensive as to impair gas exchange, which is finalized at improving the ventilation of the residual healthy parenchyma. This compensatory increase in volume of the thoracic cage in fact maintains the emphysematous space distended up to the point at which the healthy alveoli can be ventilated; in the absence of this compensatory mechanism Tidal Volume would be preferentially directed into the more compliant emphysematous spaces, leaving the healthy parenchyma under ventilated.

The relationships between the lesions due to rupture of the alveolar septa and static lung volumes are represented in fig. 3.
**Figure 3**

Figure 3: At septal rupture (1), the elastic pulmonary recoil acts in a radial sense on the newly-formed air space, which is further widened at the expense of a proportional collapse of the confining parenchyma (2); to this is added a modest expansion of the thoracic cage due to rearrangement of its intrinsic elastic forces to the increased pulmonary compliance (3). Static pulmonary volumes are little affected. Only in a second phase, triggered by respiratory inadequacy, is the important expansion of the thoracic cage and lowering of the diaphragm actively established; this results in an increase in the Total Lung Capacity and in particular the RV, in order to achieve ventilation of the healthy parenchyma (4).

On the basis of these considerations it can be easily understood that, given the large functional reserve of the lung, the rupture of interalveolar walls can generate large air chambers without necessarily involving extensive destruction of lung parenchyma, but causing serious underventilation or collapse. The active overexpansion of the thoracic cage and deeper mobilization of the diaphragm have the aim of moving the TV to a greater volume of the TLC (Fig 3,3), where the preferential ventilation of the functional parenchyma is possible after overexpansion of the emphysematous areas.

The relatively limited capacity of expansion of the thoracic cage and of the diaphragm, in comparison to the theoretical ability of the lung to generate large intraparenchymal air spaces by the above mentioned mechanism (Fig. 4), provides probably the strongest rational basis for surgical treatment of emphysema.

**Figure 4**

Figure 4: In pulmonary emphysema the expansion of the thoracic cage and the lowering of the diaphragm gradually move the tidal volume towards the upper limit of the Total Lung Capacity, in order to allow ventilation of the healthy residual parenchyma, after overexpansion of the more compliant emphysematous spaces. It is easy to foresee that this compensatory mechanism soon reaches maximal expansibility of the thoracic cage and diaphragm, which is quite limited in respect to the hypothetical capability of the emphysematous lung to generate large intraparenchymal air spaces.

It is interesting to note that, from a purely mechanical point of view, the forces that determine the structural modifications of lung architecture in emphysema are the same as those involved in spontaneous pneumothorax, the consequences differing only because of the different relationships between the pleural space and the interrupted alveolar wall. In fact, both in pneumothorax and in emphysema, as a result of rupture of the alveolar wall (subpleural in the case of pneumothorax), the elastic recoil of the lung causes a new condition of smaller expansion of the healthy lung parenchyma (Fig. 5). In the case of pneumothorax, in the absence of pleural adhesions, the lung elastic recoil collapses the parenchyma entirely or up to the point at which the pleuropulmonary laceration becomes obliterated or excluded from ventilation; the collapse then occurs in a centripetal direction with respect to the injury and favors its recovery. In emphysema, the injury being intrapulmonary, the rearrangement of the lung elastic recoil to a state of minor distension is realized, necessarily, in a centrifugal sense with respect to the initial injury, toward the thoracic wall and the mediastinum, that are in this case fixed points of support. This allows to clearly understand that, as in pneumothorax it is not the intrapleural air that collapses or compresses the lung (except in tension pneumothorax) so in
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Emphysema are not the bullae that cause the surrounding lung collapse and thoracic cage enlargement; rather it is surrounding lung elastic recoil and then active, compensatory, thoracic cage enlargement that widen the air spaces resulting from interalveolar septal rupture.

**Figure 5**

Figure 5: After the initial injury the elastic pulmonary recoil stabilizes the parenchyma in a condition of lowered tension both in pneumothorax and in emphysema. Pulmonary collapse in pneumothorax occurs in a centripetal direction with respect to the main injury (pleuro-alveolar laceration) favoring its obliteration. In the case of emphysema, on the other hand, the pulmonary collapse occurs in a centrifugal direction with respect to the injury, towards the thoracic wall and the mediastinum, which in this condition represent points of fixed support towards which the pulmonary parenchyma is attracted in its uneven collapse, thus widening the intrapulmonary air space. The hatched polygon in red indicates the rearrangement of the thoracic wall elastic recoil to a condition of greater expansion due to the lesser inward traction on it by the decreased lung elastic recoil.

Of course the increase of airways pressure resulting from bronchial obstruction further enhances the pathogenic mechanism of the emphysema. Since however in essential emphysema bronchial obstruction takes place only in expiration, the resulting increased airway pressure may act rather as a stress factor triggering septal rupture; moreover since this mechanism may take place only when the emphysematous changes are so extensive to allow bronchial obstruction to occur, it cannot have a role in the primary causes of the disease. The final parenchymal arrangement instead depends mainly on the residual lung elastic recoil and active thoracic cage-diaphragm compensatory modifications, active throughout the entire respiratory cycle, that set the emphysematous spaces to their final dimensions.

The analogy with pneumothorax could be useful for understanding that, in essential emphysema as in pneumothorax, the prevailing clinical problem, at least in a certain phase of the evolution of the illness and in some patients, might be that of excessive air collection in the thorax which prevents the residual healthy lung from being efficiently ventilated, rather than diffuse deterioration “per se” of the alveolar membrane.

**DEAD SPACE**

We may hypothesize that these newly-formed air spaces can be anatomically arranged within the lung in such a way that they may interfere with the tidal volume air in two different ways, obviously variably mixed in the clinical occurrences.

At one extreme (Fig. 6, A) we may theoretically hypothesize that the newly-formed air space is positioned in such a way that it is ventilated by a fraction of the tidal volume that is then expired unmodified. The effect of this condition is, therefore, confined to the subtraction, from the tidal volume, of the corresponding quota of air that could not participate in the respiratory exchanges. The extremely unfavorable ratio between the volume of the emphysematous spaces and the ability of gas exchange at their walls does not allow significant modifications of the concentration of the gases in this volume during the respiratory cycle. Using an electrical analogy we could imagine that the newly-formed air spaces in this condition are arranged “in parallel,” with respect to those in which respiratory exchange occurs. They can thus be considered as an expansion of the anatomical dead space (D), interposed between the trachea and the active alveolar surface. In this condition the expired air, that necessarily has low oxygen and elevated carbon dioxide concentrations, becomes, at least in part, re-breathed in the following cycle, thus bringing a gaseous mixture with pressure gradients less favorable for physiological
respiratory gas exchange into contact with the active alveolar membrane.

The amount of Tidal Volume that ineffectively enters both these spaces at each respiratory cycle can be assumed to have the same nature as the so called ‘physiological dead space’ (quantified by the Bohr mixing equation) and, obviously, its value depends on the compensatory mechanisms of the emphysema. In fact rebreathing from expanded dead space and hypoventilation of residual healthy parenchyma are the mechanisms responsible for the ensuing hypercapnia in more serious cases of emphysema.

Figure 6
Figure 6: The newly-formed air spaces generated by septal rupture could have a direct effect on gas exchanges, depending on their relationship with tidal volume air and with the functional alveolar membrane. Two extreme conditions, which are variably mixed in the single case, can be hypothesized. In the condition shown in A the tidal volume air deflected into the air chamber does not participate in respiratory exchanges and is expired nearly unmodified; in fact even in the case that the wall of the bulla is perfused, the ratio between the surface of exchange and the volume of air space is so unfavorable that it can not significantly alter the concentration of the gases during the respiratory cycle (like in “alveolar dead space”). In the condition shown in B, on the other hand, the air of the newly-formed air space mixes with that of the tidal volume before the latter enters into contact with the surface of active exchange and vice versa. This implies re-breathing of part of the expired air with the same consequence as that of an increase of the “anatomical dead space”.

In contrast with pneumothorax, the extra air collected in the thorax in emphysema communicates with the Tidal Volume and this causes extra problems. Ventilation of these intrapulmonary emphysematous spaces is, in fact, largely ineffective and may cause hypercapnia.

We may then anticipate that the gas exchange efficiency of the patient with emphysema largely depends on his ability to direct the major portion of Tidal Volume towards the residual healthy parenchyma; this is achieved by expansion of the thoracic cage and diaphragm that distend emphysematous spaces to the point at which their walls become less distensible than those of the healthy parenchyma so that Tidal Volume is preferentially directed towards the latter. This causes the Tidal Volume to be driven at increasing levels of TLC (Fig. 4); these mechanisms (thoracic cage and diaphragm distension), however, have a limited reserve and soon bring the patient's tidal volume to the upper limits of the TLC, with significant increase of the respiratory work.

As the disease progresses the thoracic cage cannot expand further and an increasing fraction of the TV becomes ineffective for gas exchanges, being diverted towards the emphysematous spaces; this may mark the passage between a compensated clinical situation into unbalanced end stage emphysema.

In an attempt to make a more detailed analysis of this aspect we can speculate that the Volume/Pressure (V/P) curve (compliance) of the emphysematous patient could theoretically be considered as resulting from the combination of the V/P curve of the emphysematous spaces and that of the residual healthy parenchyma. Since the latter can be reasonably assumed to be the same, with regard to its mechanical properties, as in the normal lung, the V/P curve of the emphysematous spaces can be calculated by subtracting the normal lung curve from the whole lung curve (Fig. 7). In other words we know from the physiological V/P curve that at any given pressure the normal lung would occupy a certain volume; we may then reasonably expect that at any given pressure that part of the volume measured in the emphysematous patient exceeding that which the normal lung would have at the same pressure, can be attributed to the emphysematous parenchyma. Using this calculation, step-by-step computation of the emphysematous volumes at unit increases of pressure would generate the V/P curve of the emphysematous spaces.

This allows some interesting consideration. As easily
predicted the final part of the emphysematous spaces curve is nearly horizontal and has a very low \( \frac{DV}{DP} \) ratio (compliance); this means that their volume changes very little with increasing pressure. Since the TV is shared between the healthy and emphysematous lung according to their respective \( \frac{DV}{DP} \), it can be predicted that when the emphysema is still limited, the expansion of the thoracic cage and diaphragm, finalized to take advantage of this difference in the V/P curves, is able to move the TV up to the point at which it can be directed preferentially into the healthy residual parenchyma (Fig. 7, A). Thus if the residual parenchyma has normal exchange capabilities, the emphysema may be quite efficiently compensated.

When the thoracic cage expansion reaches its upper limit, the collapse of parenchyma resulting from further septal ruptures can no longer be compensated for; this generates a condition (Fig. 7, B, blue dashed area), in which the TV cannot be driven at the horizontal part of the emphysematous spaces \( \frac{DV}{DP} \) curve; accordingly the ventilation of the physiological volume of healthy lung implies that the TV should be nearly twice the normal; this means greater displacement of the thoracic cage and thus increased respiratory work. As the disease progresses a proportionally smaller part of the TV may be directed towards functional alveolar surface and respiratory insufficiency ensues in spite of the presence of potentially functional, collapsed parenchyma.
Figure 7

Figure 7: The Volume/Pressure curve (V/P) (compliance) of the emphysematous patient (blue lines) can be theoretically considered as resulting from the combination of the V/P curve of the emphysematous spaces and that of the residual, potentially healthy lung. Since the latter can be assumed to be the same, in regard to its mechanical properties, as that of normal lung (black line), the V/P curve of the emphysematous spaces (red continuous line) can be calculated by subtracting the normal lung curve from the whole lung curve (dashed lines and black arrow) (see text). As can be easily predicted the final part of the emphysematous spaces' curve is nearly horizontal and has a very low V/P ratio (compliance), i.e. in this part of the curve their volume changes very little with increasing pressure. Since the TV is shared between the healthy and emphysematous lung according to their respective DV/DP, it can be predicted that when the emphysema is still limited, the residual healthy lung elastic recoil first and then the active expansion of the thoracic cage and diaphragm, all finalized to take advantage of this V/P curve difference, are able to move the TV up to the point of V/P curve at which it can be directed preferentially into the healthy residual parenchyma (A). If the residual parenchyma has normal exchange capabilities, the emphysema may be then quite efficiently compensated. The limit of this compensatory process is set by the maximal expansibility of the thoracic cage and diaphragm (B, gray dashed arrow); as the disease progresses after this limit is reached an increasingly significant part of the TV is ineffectively directed into the emphysematous spaces. A condition (B, blue dashed area) may then ensue in which the TV cannot be driven at the horizontal part of the emphysematous spaces DV/DP curve; accordingly the ventilation of the physiological volume of healthy lung necessarily implies that the TV should be greater than normal (nearly twice in the example); that means a greater displacement of the thoracic cage and thus increased respiratory work. As the disease progresses still further respiratory insufficiency ensues with a mechanism that is intuitively analogous to that of pneumothorax (i.e. inability to ventilate a potentially functional residual parenchyma). Interestingly enough while LVR reduction in a clinical situation such as that depicted in B improves the TV sharing ratio between potentially healthy and emphysematous parenchyma, LVR in the clinical condition depicted in A would involve sacrifice of the healthy parenchyma included in the surgical specimen without improving the TV sharing which is already maximal. Curves of end-stage emphysema and normal lung were redrawn from references 2 and 5; the curve of compensated emphysema was arbitrarily drawn in an intermediate position between the above.

Figure 8

In the first phases of the disease, the still strong elastic recoil of the residual healthy lung is able, alone, to keep the emphysematous spaces distended up to the more horizontal part of their V/P curve; this can explain why the emphysematous space V/P curve of Fig. 6, left diagram, is more horizontally oriented than that of the normal lung. As the disease progresses the elastic recoil of the residual healthy lung, proportionally collapsed, is no longer sufficient for this purpose and an active over expansion of the thoracic cage is established to achieve the same final result, i.e. to
keep the emphysematous spaces distended up to the part of their V/P curve in which the TV is preferentially directed into the residual healthy lung. With further disease progression these compensatory mechanisms reach their limits and an increasing portion of the TV is ineffectively directed into the emphysematous space.

Obviously the extrapolated curve shown in fig 7 does not give any information about the anatomical distribution of the emphysematous space in respect to that of the residual healthy parenchyma and in particular whether the emphysematous spaces are collected in large bullae or are evenly disseminated throughout the lung. In spite of this and other approximations (see notes 2 and 3) the graphs in fig 7 outline the amount of air collected in the emphysematous space in proportion to the residual healthy parenchyma and to the Tidal Volume, allowing easy imagination of the magnitude of rebreathing if the compensatory mechanism offered by the thoracic cage/diaphragm fails in sparing these air spaces from the majority of Tidal Volume ventilation.

**BRONCHIAL OBSTRUCTION**

The obstructive syndrome, which is a constant part of the clinical picture of emphysema (2, 3), is also a consequence, essentially mechanical, of interalveolar septa rupture. The obstructive syndrome is created by two different mechanisms (3).

On the one hand the radial action that the lung elastic recoil commonly exerts on the wall of the smaller airways decreases unevenly, in proportion to the severity of the emphysematous injuries, with significant distortion of their lumen (Fig. 8). This distortion is responsible for the obstruction during both inspiration and expiration and is largely independent of the lung volumes (3).

On the other hand during expiration, the obstruction of more proximal tracts of the bronchial tree takes place as a consequence of the altered relationships between intrapleural and intraalveolar pressures in the emphysematous patient (Fig. 9), themselves direct consequences of the altered relationship between thoracic wall and lung compliance ($C_{rs}$).

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**Figure 9**

Figure 8: The alveolar septal rupture disarranges the radial action of the elastic pulmonary recoil on the smaller airways with lumen distortion, creating conditions more favorable to their collapse and occlusion. These distortions cause obstacles to ventilation both in inspiration and expiration, and are largely independent of the lung volumes (3).

In fact, in healthy subjects expiration is an entirely passive process, driven by the elastic recoil of the lung which generates a positive pressure inside the airways along a decreasing gradient from the alveoli to the trachea, due to the intrinsic resistance of the airways. The thoracic cage does not participate actively in the mechanism of expiration; as a matter of fact its static equilibrium point is nearly 70% of Total Lung Capacity (TLC) and thus at a volume far superior to that at which the tidal volume is physiologically driven. Thus, the intrinsic elastic recoil of the thoracic cage simply acts as a counterbalance to that of the lung, directed oppositely, throughout the entire respiratory cycle; this allows the intrapleural pressure to be kept negative throughout. This occurs even during expiration after forced inspiration, in spite of the fact that the elastic recoil of the thoracic cage, distended beyond its static equilibrium point (~70% of TLC), acts in the same direction as that of the lung. In fact, even at the peak of forced inspiration it is still inferior to the intrinsic recoil of the lung; accordingly, a negative intrapleural pressure is maintained throughout the entire respiratory cycle in this condition as well.

As a consequence of the compensatory mechanism of the emphysema, the thoracic cage is actively, abnormally dilated and the tidal volume moved to higher values of the TLC, possibly reaching and even passing the static equilibrium point of the thoracic cage; accordingly the counteraction of the thoracic cage intrinsic recoil to that of the lung gradually decreases and is less effective in keeping a negative intrapleural pressure during expiration. On the other hand
the lung elastic recoil decreases significantly as a consequence of the emphysematous lesions. Eventually the increased, inverted, elastic retraction of the thoracic cage expanded over its static equilibrium point, might overcome the decreased intrinsic recoil of the lung with direct effects on the intrapleural pressure, which reaches zero and may even become positive during the expiration. When the intrapleural pressure equals that inside the airways, generated by intrinsic elastic recoil of the lung, conditions enhancing expiratory bronchial obstruction ensue.

Since inner airway pressure, generated by lung elastic recoil, is lowered in proportion to the severity of the emphysema, as the disease progresses the obstruction occurs earlier during the expiration, causing a progressively larger Residual Volume (RV). When the emphysema further worsens with onset of dyspnoea, the intervention of the accessory respiratory muscles during expiration might further increase intrapleural pressure, causing expiratory obstruction at larger lung volumes.

**CONCLUSION**

In conclusion in severe emphysema the expiratory driving force tends to be the active depression of the thoracic cage rather then, physiologically, the lung elastic recoil; this can generate positive intrapleural pressure and then obstruction of the large bronchi. Pursed lip expiration, a common maneuver in patients with emphysema, may increase the large airway inner pressure during expiration, thus counteracting obstruction to some extent.
Figure 10
Figure 9: In the normal subject expiration is a passive process, entirely conditioned by lung elastic recoil which creates a positive pressure in the airways, decreasing from the alveoli to the trachea due to the internal resistance of the airways. In the range of the tidal volume the elastic intrinsic recoil of the thoracic wall (red arrows) acts in an opposite direction to that of the lung, being directed toward its point of static equilibrium, situated at about 70% of the Total Lung Capacity. It thus acts as a counterbalance to the lung elastic recoil (black arrows), in such a way that negative intrapleural pressure is generated. In emphysema the elastic recoil of the thoracic cage, expanded beyond its static equilibrium point, is less effective in counteracting the lung elastic recoil, also reduced, and thus in keeping the intrapleural pressure negative; on the other hand the reduced lung elastic recoil generates a proportionally lower pressure within the airways. In the final phase of expiration, when the lung elastic recoil is very small, the intrapleural pressure could become positive (4). At the point of the bronchial tree at which the endobronchial pressure equals the intrapleural pressure, the conditions for collapse of the airways ensue. In serious emphysema with dyspnea, the expiratory muscles may be involved (green arrows), thus generating, in the early phases of expiration, a positive intrapleural pressure. The bronchial obstruction then tends to occur at an earlier phase of expiration, at greater pulmonary volumes. A compensatory mechanism is provided by pursed-lip expiration by which the patient is able to increase endobronchial pressure, enhancing the patency of the principal airways even in the presence of positive intrapleural pressure.

EFFECTS ON THE PULMONARY VASCULAR NETWORK

Only in very extreme conditions is the parenchymal destruction so extensive as to involve significant reduction of the pulmonary vascular network, causing pulmonary hypertension; as a matter of fact when pulmonary hypertension is present alone or in association with right ventricle hypertrophy and failure (2,3) it is more commonly the result of the changes induced by chronic bronchitis or other frequently associated lung diseases (2,3). In the extreme cases, usually with hypercapnia, the obstructive syndrome may cause a significant impairment of venous return to the heart during expiration (4).

CONCLUSION II

Pneumothorax and pure idiopathic emphysema have interesting physiopathologic analogies; in both cases in fact the lung elastic recoil produces a condition of collapse or under expansion of the healthy parenchyma with generation of intrathoracic, physiologically ineffective air spaces; however, the extra intrathoracic air of emphysema communicates with the tidal volume and this causes further problems.
When the thoracic cage reaches its maximal expansion, in the final stage of the disease, a progressively smaller part of the TV may be directed towards residual, functional alveolar surface and respiratory insufficiency may ensue from a mechanism analogous to that of pneumothorax (i.e. inability to ventilate potentially functional residual parenchyma).

It is then intuitively evident that clearance of intraparenchymal air in emphysema, albeit partial and not selective such as is obtained with lung volume reduction (LVR), could have the same importance as the positioning of a thoracic drain for removal of the same air from the pleural space in a pneumothorax.

**LUNG VOLUME REDUCTION (LVR)**

On the basis of the above considerations, the objective of surgical treatment of emphysema should be to selectively eliminate the newly-formed intraparenchymal air spaces in order to restore normal ventilation of the residual, underventilated/collapsed parenchyma.

This objective is easily achievable, and is in fact current clinical practice, at the more favorable extreme of the hypothesizable situations, i.e. when all the newly-formed air space is localized in confluent bullae in a well identified part of the lung (17-19).

What does not exist, at present, is a tool or technique for obtaining the selective removal of intraparenchymal air collections when they are diffuse and extensive as occurs more commonly in emphysema. The physiopathogenic mechanism above mentioned does, however, allow us to reasonably hypothesize that simple reduction of the lung volume even with sacrifice of a part of “working” parenchyma, might allow more effective ventilation of the residual lung, thus globally improving respiratory exchanges. This therapeutic hypothesis, recently popularized (20-22) by Cooper (23-24) draws on an approach undertaken in the past by Brantingan (17,19), then coldly received by the scientific community (25).

Of course it seems difficult to hypothesize a curative result from the removal of part of a lung, even though only partially functional, in a patient already near the limits of his respiratory function. It might, therefore, be interesting to make detailed theoretical predictions, based on the pathogenic mechanisms described, of the purely mechanical effects of LVR on each of the above considered effects of septal rupture.

For exemplary purposes we can hypothesize, at the least favorable extreme of the clinical events, a case of serious, uniformly diffuse emphysema in which the TLC is increased, for example, by 50% (i.e. TLC=9 liters; normal value = 6 liters in a healthy 50 y.o. man, 1.70 m tall) (Fig. 10). In this case reducing the volume by a third, as recommended by Cooper (15), would mean a 3 liter lung volume resection.

**Figure 11**

Figure 10: The figure schematizes a case of serious, uniformly diffuse emphysema in which the TLC is increased by 50% (i.e. TLC=9 liters; normal value = 6 liters in a healthy 50 y.o. man, 1.70 m tall) before, during and after 3 liters lung volume resection. In the early postoperative phase the intrathoracic space generated by lung volume reduction is obliterated by a corresponding retraction of the thoracic cage and elevation of the diaphragm, as well as overexpansion of the residual lung. This brings the tidal volume towards more physiological levels of TLC, improving the ventilatory mechanics and lowering the respiratory work. See text for the other effects of LVR.

**EFFECTS OF LVR ON THORACIC CAGE AND DIAPHRAGM MOBILITY**

Obviously the lung volume reduction results in the formation of an equal amount of free intrathoracic space. Immediately after surgery this space is obliterated in part by retraction of the thoracic cage and elevation of the diaphragm, and in part by over-expansion of the residual parenchyma, as can be easily documented at chest X-ray and CT scan (22,23). The ratio in which these two components occupy the space resulting from LVR can obviously vary from patient to patient and may be difficult to predict preoperatively.

On a theoretical basis however the more severe the emphysema in the remaining parenchyma, the more
compliant the residual lung and accordingly the more extensive the portion of intrathoracic space that will be made available by LVR occupied by its overexpansion. Fig. 10 demonstrates the hypothesis that, after 3 liters of lung volume have been removed by surgery, the free intrathoracic space is occupied in equal parts by expansion of the residual lung and retraction of the thoracic cage and diaphragm, thus resulting in a 1.5 liter reduction of TLC.

Thus LVR has an immediate, important effect on the thoracic cage and diaphragm which return towards more physiological positions (23, 24, 25), lowering respiratory work and improving ventilatory mechanics.

Moreover that part of the intrathoracic space occupied by thoracic cage/diaphragm retraction after LVR in true diffuse emphysema obviously provides the residual lung with a corresponding extra expansion reserve of the thoracic cage and diaphragm into which to gradually expand along the natural, active compensatory mechanism of emphysema, the causes of which are not affected by LVR.

**EFFECTS OF LVR ON RESIDUAL HEALTHY PARENCHYMA COLLAPSE AND ON TV SHARING BETWEEN HEALTHY AND EMPHYSEMATOUS SPACES**

It may be interesting to try to evaluate the respective proportions of re-expansion of potentially healthy, collapsed areas and emphysematous lesions of the residual lung. This can be a complex problem to solve considering the reciprocal interferences of the V/P curves of these different zones of the residual lung in the expansion process.

We may, however, reasonably expect that if the LVR is carried out in end-stage emphysema, as represented in Fig. 7, B, i.e. when the emphysematous space can no longer be kept expanded up to the more horizontal part of the V/P curve, most of the space will be occupied first and in prevalence by overexpansion of the emphysematous spaces and only in the remaining part by expansion of residual healthy parenchyma. This is substantially identical to the situation occurring during the evolution of the disease, when the extra space made available by thoracic cage enlargement and diaphragm flattening is utilized for overexpansion of the emphysematous space in order to drive the Tidal Volume preferentially into the residual healthy parenchyma.

In this regard LVR can be viewed simply as an extension of the physiological compensatory mechanism of the emphysema, but unfortunately involving resection of that part of still healthy alveolar spaces included in the surgical specimen.

It is interesting to note that improvements of the TV sharing ratio between healthy and emphysematous spaces cannot be expected if the LVR is carried out in a condition like that represented in Fig. 7, A, in which the emphysematous spaces are already kept distended as adequately as possible by the natural compensatory mechanism of the emphysema.

**EFFECTS OF LVR ON DEAD SPACE**

Although LVR does not affect the anatomical relationships between the emphysematous spaces and residual healthy parenchyma, the redirection the Tidal volume into the residual healthy parenchyma by the increased distension of emphysematous spaces and the improved mechanics of ventilation certainly decrease the “physiological dead space” and rebreathing from the emphysematous spaces. CO2 has, in fact, been shown to be decreased after LVR even though at the beginning of the clinical experience hypercapnia was considered a contraindication to surgery.

**EFFECTS OF LVR ON BRONCHIAL OBSTRUCTION**

The retraction of the thoracic cage towards more physiological expansion values also implies that its intrinsic elastic recoil, together with the regained normal diaphragm motility, returns to counteract better that of the lung, likewise increased by over distension after LVR, in keeping the intrapleural pressure negative; moreover the residual lung overdistension causes an increase of the lung recoil generated airways expiratory pressure. Accordingly bronchial obstruction is also immediately improved. It is interesting to note that it was this foreseeable effect on bronchial obstruction that provided the rational basis of the first attempts at surgical treatment of emphysema by Brantigan in the fifties (17, 18, 19).

**EFFECTS OF LVR ON ALVEOLAR MEMBRANE EXCHANGE EFFICIENCY**

Obviously no effect at all can be expected on the causes of the disease and thus on the alterations of the alveolar membrane that brought the septa to the condition in which their rupture was possible as well as on its gas diffusion capacity.

**COMMENT**

Although the qualitative prediction of the purely mechanical effects of LVR is quite straightforward, the quantification of these effects and their impact on gas exchanges in the single
Clinical result (residual lung, which are obviously essential for a good evenly diffuse emphysema. Also the conditions of the minimal in large apical bullae resection but may be not so in parenchyma sacrificed with the surgical specimen, which is extremes is certainly the quota of potentially healthy expressions in between. One difference between the two physiopathologic process which may have a whole range of maybe more limited, are the two extremes of a similar LVR clinical results are to some extent unpredictable and improvement, and uniformly diffuse emphysema, where thoracic cage/diaphragm compensatory mechanisms to continue.

Consistent with the above physiopathologic views, a test able to quantify the TV sharing between healthy and emphysematous spaces would theoretically allow the selection of the point in the natural history of the disease at which LVR would be most strongly indicated, i.e. when the diaphragm and thoracic cage expansion is no longer able to keep the emphysematous spaces distended up to the point at which the TV is preferentially directed into healthy parenchyma; in fact, LVR at an earlier stage would involve sacrifice of functional parenchyma, adding very little to the respiratory function.

Finally, objective data on the long-term evolution of emphysema in the residual lung of patients treated by volume reduction are still not available on a large scale and thus the real duration of the functional advantage obtained in this way is not known; it can be hypothesized, however, that this is related to the progression of the emphysema itself to which LVR simply offers extra thoracic space for thoracic cage/diaphragm compensatory mechanisms to continue.

On the other hand, although the emphysema in this theoretical analysis has been considered uniformly diffuse, in clinical practice it is frequently possible to guide the resection to selected areas of lung parenchyma where the emphysematous lesions are more marked, often the upper lobes. Accordingly a standardized surgical technique for upper lobe tailored resection has been described (s3).

As a matter of fact localized large apical bullae, whose resection invariably results in a significant functional improvement, and uniformly diffuse emphysema, where LVR clinical results are to some extent unpredictable and maybe more limited, are the two extremes of a similar physiopathologic process which may have a whole range of expressions in between. One difference between the two extremes is certainly the quota of potentially healthy parenchyma sacrificed with the surgical specimen, which is minimal in large apical bullae resection but may be not so in evenly diffuse emphysema. Also the conditions of the residual lung, which are obviously essential for a good clinical result (s3), may differ between the two extremes, being perhaps more frequently better in predominantly localized upper lobes emphysema than in true diffuse disease or when emphysema mainly involves the lung bases, as often occurs in cases of a-1 antitrypsin deficiency.

Accordingly literature reports (s28,s29,s30,s31,s32,s33) have shown that the most significant clinical improvements were obtained in patients with emphysematous changes mostly localized to the upper lobes; when the emphysematous lesions were very serious and/or when they mainly involved the lung bases, as often occurs in cases of a-1 antitrypsin deficiency, objective and subjective results of LVR were significantly less marked (s3).

The amount of functional gain obtained with LVR, despite being in most cases subjectively and objectively appreciable, is certainly not equal to that obtained by a single lung transplantation (s3).

**CONCLUSION III**

Septal rupture in lung emphysema generates underexpansion/collapse of the confining parenchyma and large, diffuse air collections; to allow preferential direction of TV into residual healthy parenchyma, the thoracic cage and diaphragm are soon overexpanded up their maximal limits; when this limit is reached serious respiratory insufficiency may ensue even before a significant amount of parenchyma is destroyed by the pathogenic process.

The resection of part of the lung, in particular from areas more involved by the emphysematous changes, may bring the tidal volume back again towards more physiological values of thoracic cage and diaphragm expansibility, decreasing respiratory work and improving ventilatory mechanics. LVR involves also overexpansion of the residual lung that brings the emphysematous spaces up to a part of their V/P curve in which the TV fraction ventilating potentially healthy surrounding parenchyma is increased. The improvement of bronchial obstruction is consequent to the improved interaction between the thoracic cage elastic recoil, increased by its retraction, and that of the residual lung, also increased by its overexpansion, thus allowing the generation of an efficient negative intrapleural pressure; moreover the increased elastic recoil of the distended residual lung generates an higher air ways expiratory pressure, also counteracting bronchial obstruction.

LVR also provides new space into which the residual lung may gradually overexpand should the disease progresses, continuing in the natural compensatory mechanism.
In spite of different opinions (35,36,37,38) at its onset, LVR is now a current therapeutic option for many emphysematous patients; how long the improvements last, however, has still to be demonstrated in large-scale trial.

References

1. Huet-Duvillier G; Balduyck M; Watrigant Y; Sesboue R; Thiebaut C; Lafitte JG; Degand P. Relationship between a mild alpha1 proteinase inhibitor deficiency and respiratory symptoms in a family. Ann Clin Biochem 1995;32:545-9


13. Argenziano M; Moazami N; Thomashow B; Jellen PA; Gorenstein LA; Rose EA; Weinberg AD; Steinglass KM; Ginsburg ME. Extended indications for lung volume reduction surgery in advanced emphysema. Ann Thorac Surg 1996;62:1588-97

14. Brenner M; Yusen R; McKenna R Jr; Sciurba F; Gelb AF; Fischel R; Swain J; Chen JC; Kafie F; Lefrak SS. Lung volume reduction surgery for emphysema. Chest 1996;110:106-19


16. Cooper JD; Patterson GA; Sundaresan RS; Trulock EP; Yusen RD; Pohl MS; Lefrak SS. Results of 150 consecutive bilateral lung volume reduction procedures in patients with severe emphysema. J Thorac Cardiovasc Surg 1996;112:1319-29


23. Holbert JM; Brown ML; Sciurba FC; Keenan RJ; Landreneau RJ; Holzer AD. Changes in lung volume and volume of emphysema after unilateral lung reduction surgery: analysis with CT lung densitometry. Radiology 1996;201:793-7

24. Gelb AF; Zamel N; McKenna RJ Jr; Brenner M. Mechanism of short-term improvement in lung function after emphysema resection. Am J Respir Crit Care Med 1996;154:945-51


26. Gelb AF; McKenna RJ Jr; Brenner M; Fischel R; Baydur A; Zamel N. Contribution of lung and chest wall mechanics following emphysema resection. Chest 1996;110:11-7

27. Sciurba FC; Rogers RM; Keenan RJ; Slivka WA; Gorcsan J 3rd; Ferson PF; Holbert JM; Brown ML; Landreneau RJ. Improvement in pulmonary function and elastic recoil after lung-reduction surgery for diffuse emphysema [see comments]. N Engl J Med. 1996;334:1095-9

28. Cooper JD, Patterson GA Lung volume reduction surgery for severe emphysema Semin Thorac Cardiovasc Surg 1996;8:52-60


30. Gissert HA; Trulock EP; Cooper JD; Sundaresan RS; Patterson GA. Comparison of early functional results after volume reduction or lung transplantation for chronic obstructive pulmonary disease J Thorac Cardiovasc Surg 1996;111:296-306


appropirate in the treatment of emphysema? No [editorial]
Am J Respir Crit Care Med 1996;153:1205-7

38. Little AG. Lung volume reduction. A breath of fresh air?
Author Information

Stefano Nazari, MD
Staff Thoracic Surgeon, Department of Surgery, Foundation Alexis Carrel, University of Pavia