Panlobular Emphysema: Anatomy and Pathodynamics

John P. Wyatt, M.D., Vernon W. Fischer, and Herbert C. Sweet, M.D., F.G.C.P.
St. Louis, Missouri

Contemporary pathologic investigations indicate the existence of several distinctive disease patterns within the syndrome "chronic bronchitis and emphysema." One characteristic form, labelled centrilobular emphysema, has now been recognized and accepted as a distinct entity in which the fundamental lesion is a selective and progressive destruction of the respiratory bronchiole in the mid-portions of the secondary lung lobule. A second type of emphysema, equally as common as the centrilobular form, has been identified as panlobular emphysema on the basis of its uniform air membrane distension and fenestrations throughout the secondary lobule. The functional disturbances in ventilation, gas distribution, and intrapulmonary vascular dynamics and the progressive structural alterations which further categorize this form of chronic pulmonary emphysema are analyzed in this contribution.

Materials and Methods

A battery of morphologic technics, comprising whole lung paper section, intravascular latex injection, including bronchial artery patterns, corrosion vinylite vascular casts, broncho-angiography, stereoscopy and heart weight analysis of right and left ventricle and septum, had been applied to 275 pairs of emphysematous lungs selected at necropsy. The technical details of the above anatomic methods have been described elsewhere. In this contribution, 102 examples of panlobular emphysema type are analyzed, including 20 cases in emphysematous individuals who had been studied several times during life by multiple lung function tests, including a physiologic testing shortly before death.

In an effort to correlate in greater detail antemortem functional tests with postmortem observations, supplemental morphologic technics of a semi-quantitative nature have been devised.

1. The degree of pulmonary resistance was determined on lungs removed shortly after death. The lungs, with pleura intact, separate or paired, were placed in an air-tight plethysmograph after bronchial or tracheal cannulation. A Servo drum spirometer, with an intrinsic resistance of less than 0.1 mm. Hg, was connected to the plethysmographic chamber and the lung airway cannula. Pressure and flow changes of the lung were recorded by an electronically calibrated Sanborn apparatus and Lilly manometer. A water manometer recorded positive and negative pressures within the chamber. Multiple pressure and expiratory flow-rate readings in duplicate were obtained. With known pressure and flow readings, resistance (ml. H₂O/liters/sec.) was calculated from the formula:

\[
\text{flow (liters/sec.)} = \frac{\text{Pressure (cm. H₂O)}}{\text{Resistance}}
\]
2. From these lungs, whole lung paper sections were prepared. The degree of macrosection emphysema was determined for the whole lung by a method described previously,1 (Fig. 1). The good correlative index between postmortem estimation of emphysema with antemortem residual volume studies validates this quantitative morphologic method.

3. As Starr8 and Burton9 have shown that informative functional evaluations of the circulatory pathways can be made in the cadaver, postmortem transfusion of the intact lungs with radioactive Fe35 blood was performed. After circulation was achieved, the blood was retained within the lung by hilar clamping. Regional and whole lung survey of the injected vascular bed was obtained by two methods. Whole lung radiographs were made on sensitive x-ray film; later, utilizing the grid technic, the whole lung paper section was cut up into “cells” measuring 1 cm x 250 µ thick. The amount of retained radioactivity in each cell was determined by a scintillation counter and compared with normal lungs treated in an identical fashion. With this method the total pulmonary vascular bed, capillary as well as arteriolar, is filled, whereas with an Iodine131 labelled propyl-iodone (Dionosil) agar injection10 only the arteriolar bed (down to 60 µ) is filled.

4. The entire vascular bed was filled with radiopaque microtrast. After formalin fixation, whole lung paper sections, cut at 250 µ were subjected to soft tissue x-ray (35 kv, 1.5 ma 10 min.). The whole lung historadiogram revealed the over-all distribution of the arteriolar-capillary bed as related to the whole lung respiratory tissue.

Following postmortem injection of differentially colored microtrast, the capillary bed of the entire lung field was examined under the stereoscope.

RESULTS

The Lung Lobule

A brief recapitulation of our patho-anatomic knowledge of the secondary lobule is a requisite for a clinical-pathologic classification of emphysema. The secondary lobule11 is composed of numerous primary

![Figure 1: Grid method to determine degree of macrosection emphysema. Paper macrosection, reduced one-fourth natural size.]
lobules derived from respiratory bronchioles, usually 10 to 20 in number. These respiratory bronchioles are concentrated in the apical or middle portions of the secondary lobules, divide in a trichotomous fashion and are demarcated at the periphery by a connective tissue envelope, (Fig. 2).

In the superior, lateral and lateral-basal regions of the lung field, the definition of the secondary lobule is distinct, but is not as well delimited in the medial (hilar) areas of the lung. This variation in the connective tissue demarcation is probably responsible for the circumscribed appearance of bullae in the anterior/superior and lateral fields, and the diffuseness of emphysematous alterations in the medial lung regions, as collateral air drift is unimpeded in these latter areas due to the absence of

Figure 3: Complete vascular bed of a secondary lobule filled with latex (white); paralobular vein draining this secondary lobule seen at left. Frozen section, 125 μ, x4.
anatomic barriers of connective tissue. In the medial lung fields, orientation of the secondary lobule is best obtained by blood vessel studies. The centrally situated lobular artery (80-120 μ) gives origin to the terminal helical arteriole (40-60 μ) which forms the coarse stream (20 μ) and fine reticular capillary bed (8-12 μ). These capillaries drain into the paralobular veins which are situated in the connective tissue septa at the periphery of the secondary lobule, (Fig. 3). The pathoanatomic value of the secondary lobule in the categorization of emphysema is reflected in recent investigations utilizing angiographic and bronchographic findings.

**Macroanatomy of Panlobular Emphysema**

1. The whole lung paper section used as a screening technic to determine the type of emphysema, indicated that the paramount anatomic feature is an even, diffuse overdistension and early dissolution of the air sacs (Figs. 4, 5, and 6). This alteration was confirmed under the stereoscope with alveoli measuring between 230 and 240 microns, (Figs. 8 and 9). The uniform degree of alveolar distension allowed one to look through the patent air ducts into the second and third “tier” of air sacs, (Figs. 10 and 11).

With this *en face* view, the air sacs were seen to be ironed out, creating a shallow basin for each alveolus. The presence of numerous elliptical or irregularly shaped lacunae in the abnormally stretched air sac walls was a constant finding. These alveolar wall fenestrations, described earlier by Adriani, Loeschcke and Macklin (Fig. 11) have sharply delimited borders. There was a marked variation in the calibre of the fenestrated openings, giving a labyrinthine appearance, (Figs. 12 and 13). These breaches increased in number and size as the degree of emphysema ad-
Advanced. Advancement of the disease entailed a marked deficiency of alveolar tissue. This uniform disappearance of respiratory tissue reduced the secondary lobule into septated locules measuring up to 700-800 microns in diameter, (Fig. 13). These microbullous fields appeared as regular air pools separated by radii of connective tissue extending from the central portions of the secondary lobule out to the periphery, (Fig. 7). Connective tissue strands which contained intravascular latex bridged bullous formations diffusely situated throughout the lung, (Fig. 14). The by-pass vessels contained within these strands measured up to 160 μ in diameter.

Control measurements of air sacs at all ages were made. At the ages of 55 and 65, the average air sac diameter was 130 microns up to a maximum of 170 microns, (Fig. 15). A number of normal lungs from individuals between 75 years and 92 years of age revealed the average air sac measurement was approximately 200 microns with a disproportionate increase between air duct and alveolar diameters.

2. A conspicuous feature in all generalized forms of panlobular emphysema was an emphysematous state much more advanced in the lower lobes of the lungs. This is in contrast to generalized centrilobular emphysema in which the major concentration of disease is usually in the upper half of the lung.\(^\text{3,4}\)

3. Another distinctive aspect was the diffuse distribution of pigmentary material over the air sac walls throughout the affected lung, (Fig. 6), in contrast to pig-

---

**Fig. 5**: Normal lung, 45-year-old male, for comparison with Figs. 6 and 7. Arteries and veins, black filled with latex. Segment of whole lung paper section, x2. **Fig. 6**: Moderate degree of emphysema showing uniform hyperexpansion and air sac rupture. Carbonaceous pigment diffusely scattered over air sac walls. Segment of whole lung paper section, x2. **Fig. 7**: Uniform microbullous fields throughout several secondary lobules of Miller. Segment of whole lung paper section, x2.
4. In numerous examples of extensive emphysema without evidence of sclerosing bronchial disease or alterations of the thoracic skeleton, a diffuse chronic bronchitis and extensive bronchiectasis was demonstrated by postmortem bronchograms. This bronchiectasis was characterized by numerous cylindrical dilatations of the bronchi extending out to the terminal bronchioles. The cardinal feature of this bronchiectasis was flaccidity. In the control series, the bronchial outlines were smooth, tapering, and evenly filled. The contrast between the markedly ectatic large bronchi and the control bronchograms was striking, (Figs. 16a and b). The bronchial wall deformities were best demonstrated in the advanced degrees of emphysema. Bronchiectasis in chronic bronchitis is distinct from the better known localized fibrosing "surgical bronchiectasis."

A large number of cases were shown to have a mild chronic bronchitis and a normal postmortem bronchogram. In this group, the emphysematous state was moderate in degree and extrapulmonic pathologic conditions such as occluding hilar masses or a deformed thorax were not found.

**Histopathology**

**Bronchi**

In those specimens with diffuse ectasis and multiple sacculations of the large bronchi, the outstanding change was the presence of mucous gland hyperplasia, between muscle components and elastic tissue. In advanced emphysema, there was atrophy of the associated musculature, but little scar formation. There was an increase in width between the supportive cartilaginous plates with some fragmentation of the elas-  

tica.

Even in lung specimens showing lesser degrees of anatomic emphysema and without bronchial dilatation and distortions, some degree of gland hyperplasia in cartilaginous bronchi was present. From this contribution it is apparent that chronic bronchitis is a frequent associative lesion with emphysema, as has been emphasized by British investigators.19,20

---

**FIGURE 8:** Normal adult lung with average air sac measurement approximately 120 microns. (Each micrometer division 120 microns.)

**FIGURE 9:** Early panlobular emphysema with duct ectasis. Air sacs measure 180 microns. (Each micrometer division 180 microns.)
Figure 10: Moderate panlobular emphysema, with marked ductal ectasis and air sac rupture. Air sac fields measure 240 microns. (Each micrometer division 120 microns).

Figure 11: Moderate to advanced panlobular emphysema showing bullous fields and numerous fenestrations in air sac walls. Bullous formations measure from 300-500 microns.

Figure 12: Advanced emphysema with bullous fields measuring up to 2 mm. Breaches in alveolar walls present. (Each micrometer division 180 microns).

Figure 13: Final stage of panlobular emphysema with lobular atrophy. Connective tissue strands bridging bullous fields contain intravascular latex. All lung fields viewed through AO stereoscope, x10. (Each micrometer division 180 microns).
FIGURE 15: Schematic figure illustrating increase of air sac size in age and in emphysema.

FIGURE 16A: Normal bronchogram demonstrating slender, tapering, regular bronchial profiles. Micropaque insufflation. Figure 16B: Diffuse ectasia of bronchi showing beading, sacculation and tortuosity in generalized panlobular emphysema. Micropaque insufflation.
**Air Ducts and Sacs**

Histopathologic examination confirmed the macroanatomic observations on the diffuse destruction of the lung parenchyma within the secondary lobules. Conventional staining procedures yielded no additional information of value pertinent to the pathogenesis of this disease.

**Pulmonary Vasculature and Heart Weight Analysis**

Postmortem angiography revealed a diffuse thinning-out of the arterial pattern. The corrosion cast offered a panoramic view of the vasculature. A basic feature of these vascular casts was a generalized denudation of the arterial and arteriolar channels throughout the lung field, (Fig. 17). A frequently observed finding was the predominance of arterial-arteriolar withering in the basal and anterior half of the lung fields. The paravertebral and apical fields showed much less denudation although the emphysema was generalized. Venous arcades, spider formations, abnormally distended and tortuous pulmonary venous channels were frequently observed, associated with the prominence of large draining segmental veins, (Figs. 18a and b).

The whole lung historadiogram revealed a diffuse loss of the finer vascular bed throughout the involved lung fields, (Fig. 19). On superimposition of the whole lung paper section, the vascular bed compromisation was clearly related to air membrane loss. Tri-dimensional viewing of the latex injected vasculature showed as a distinctive finding, the conversion of the normal capillary mesh (Fig. 20) through loss of fine intercommunicating capillaries, into a flow pathway of coarse parallel channels, (Fig. 21). In the late phases, there was a wide erasure of the entire capillary bed, (Fig. 22).

Communications between the lobular artery and the paralobular veins were demonstrated in 60 µ channels centrally situated in fibrous strands crossing the bullae. These channels were the end result of capillary disappearance, brought about by compression and atrophy of capillary beds by the enlarging alveolar wall fenestrations. With the elimination of the alveolar capill-
lary bed, the remnants of the terminal helical arteriolar bed passed directly into the paralobular venous system, (Fig. 14).

The trend of our current studies on the radioisotopic mensural technic of quantitating the vascular bed confirmed the previous observations on the progressive loss of the circulatory bed. Microscopic examination revealed a non-specific intimal fibrosis in the small pulmonary arterioles.

After defatting and anatomic dissection from the septum and left ventricle wall, the weight of the right ventricle in 60 cases of panlobular emphysema was determined. These right heart weights (“maximum permissible” normal weight, 49 gm.) were correlated with the anatomic extent of emphysema, determined by the grid method. In graph 1, the degree of emphysema (grade I less than 20 per cent, grade II, 20-40 per cent emphysema, 40-60 per cent in grade III, with the most severe grade IV being over 60 per cent) was correlated with right heart weights and revealed in the advanced stages of emphysema (40 per cent and above) a great numerical increase in hearts with right ventricular hypertrophy.

Figure 19: Whole lung historadiograms showing diffuse loss of arteriolar-capillary bed. Increased opacity of basilar segment due to septal pneumonia. Microtrast injection, paper macrosection, reduced one-third size. Inset shows wide loss of capillary bed and abnormal arteriolar channels, x8.
FIGURE 14: Arterial (yellow) venous (blue) communications across bullous space. Latex injection, stereoscopy, x25. **Figure 18a:** Pulmonary veins (blue) showing "spiders" and tortuous, abnormally distended channels. Vinylite corrosion cast, x10. **Figure 18b:** Pulmonary veins (blue) showing venous "arcades" and large draining segmental vessels. Vinylite corrosion cast, x2. **Figure 20:** Fine capillary mesh over air sac wall filled with blue gelatin. Its origin from coarse stream capillaries can be seen. Frozen section, 125μ, x40.
FIGURE 21: Conversion of delicate capillary mesh into coarse parallel pathways; red latex, stereoscopy, x25. FIGURE 22: Marked loss of capillary bed related to advanced fenestration in air sac walls. Latex injection, stereoscopy, x25. FIGURE 24a: Low power view of bronchial cartilage (metachromatically stained) showing peribronchial fibrosis (red). In this area abnormal proliferation and communications of the bronchial arteries (yellow) with the pulmonary arteries (white) are illustrated. Frozen section, 125L, Aldehyde-fuchsin stain, x20. FIGURE 24b: Admixture of yellow and white injectional masses indicate bronchopulmonary arteriolar communications, in a case of panlobular emphysema with extensive peribronchial fibrosis. Frozen section, 125L, x40.
PANLOBULAR EMPHYSEMA

Graph I: Incidence of right ventricular hypertrophy (RVH) in grades of panlobular emphysema.

Histomechanical Analysis by Spirometry

Postmortem inflationary and deflationary studies revealed a lag in the inspiratory phase and a profound delay in the deflationary phase, (Fig. 23a and b).

The flow rate for these panlobular emphysematous lungs averaged about half the speed of the flow rate recorded for normal lungs inflated to the same volume. The pressure exerted by the diseased lungs at maximum inflation was the same as normal, but resistance to flow was three to ten times that recorded for control lungs, (Graph II).

With the resistance (ml. H₂O/liter/sec.) calculated from the formula $R = P / F$, the degree of resistance being expressed on the abscissa and the estimation of macrosection emphysema recorded on the ordinate, the formulation in Graph II was obtained. From the graph, it is seen that the resistance to expiratory flow in panlobular emphysema increases with the advancement of the emphysema up to a resistance of 25 ml. H₂O/liter/sec.

Case Distribution

The distribution of cases and their ancillary pathologic conditions have been tabulated, (Table 1) in 102 examples of pulmonary emphysema. All these cases revealed by paper macrosection and confirmed by stereoscopy the common identifying features of panlobular emphysema. Due to the a posteriori value of these allied pathologic conditions, discussion of the airway restrictive factors underlying the disturbed res-

Graph II: Relationship between resistance, calculated from postmortem pressure and flow studies of panlobular emphysematous lungs, and degree of emphysema, estimated by macrosection method.
piratory dynamics in panlobular emphysema will be commented upon later.

<table>
<thead>
<tr>
<th>Associated Pathologic Conditions</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary kyphoscoliosis</td>
<td>7</td>
</tr>
<tr>
<td>&quot;Congenital&quot; infantile emphysema</td>
<td>5</td>
</tr>
<tr>
<td>Carcinoma of larynx</td>
<td>4</td>
</tr>
<tr>
<td>Localized major bronchial distortions</td>
<td>25</td>
</tr>
<tr>
<td>a) Hilar silicosis and tuberculosis</td>
<td>25</td>
</tr>
<tr>
<td>b) Bronchial root carcinoma</td>
<td>9</td>
</tr>
<tr>
<td>c) Lipid pneumonia</td>
<td>2</td>
</tr>
<tr>
<td>Chronic bronchitis with &quot;bronchiectasia&quot;</td>
<td>18</td>
</tr>
<tr>
<td>Chronic bronchitis (mild)</td>
<td>32</td>
</tr>
</tbody>
</table>

**Antemortem Pulmonary Function Analysis**

Twenty cases of generalized emphysema with chronic bronchitis studied during life by a battery of pulmonary function methods were found at necropsy to have widespread anatomic emphysema conforming to the panlobular pattern. To facilitate the discussion of correlating structural alterations with physiologic values, the pertinent pulmonary function values are summarized in Table 2.

<table>
<thead>
<tr>
<th>Function Studies</th>
<th>Per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total lung capacity</td>
<td>125-155 above normal</td>
</tr>
<tr>
<td>Maximum breathing capacity</td>
<td>Frequently 35-25 of normal</td>
</tr>
<tr>
<td>Residual volume/total lung capacity</td>
<td>Often 60 above normal</td>
</tr>
<tr>
<td>Alveolar nitrogen</td>
<td>2.5-3.5 (normal)</td>
</tr>
<tr>
<td>(after 7 minutes)</td>
<td>1-2.5 per cent)</td>
</tr>
<tr>
<td>Expiratory-Inspiratory vital capacity minus</td>
<td>25 air retention (normal 10 per cent)</td>
</tr>
<tr>
<td>Inspiratory-Expiratory vital capacity</td>
<td>85-90</td>
</tr>
<tr>
<td>Arterial oxygen saturation (without polycythemia)</td>
<td>75</td>
</tr>
<tr>
<td>Arterial oxygen saturation (with polycythemia)</td>
<td>75</td>
</tr>
</tbody>
</table>

**DISCUSSION**

The common usage of the term "obstructive hypertrophic" emphysema implies a single unified etiology and pathogenesis for the emphysema complex. Recent findings from ventilation/perfusion studies and anatomic evaluations based on whole lung patterns seriously challenge this unitarian concept and indicate that the emphysema complex probably possesses a multivalent causative and developmental background. Furthermore, with current morphologic technics utilized on a semi-quantitative basis, the pathologic events influencing the natural history of distinctive emphysematous processes can be reconstructed.

**A. Influence of Airway Disturbance**

The common basic feature of a widespread uniform emphysematous change lends credence to the view that major segmental bronchi, controlling air flow into or fluid clearance from many lung lobules, are implicated in the evolution of this form of pulmonary emphysema.

In primary kyphoscoliosis, Loeschcke emphasized that abnormal fixation of the thorax produced a uniform distensive type of generalized emphysema. The limited excursion of the chest and bronchial root distortions due to the gibbous thorax favors the development of pulmonary overdistension, but it is noteworthy that only moderate degrees of air sac dissolution are recorded. From stereoscopic observations, the air sac measurements indicate maximum distension with only modest numbers of Adriani-Macklin fenestrations. As the majority of the cases of panlobular overdistension occurring in kyphoscoliosis usually die from pulmonary heart disease due to vascular root distortion, it is apparent that an air membrane destroying factor as well as prolonged hyperinflation is essential if extensive air sac dissolution is to develop.

Although confined to a lobe or one lung, panlobular distension is the morphologic paradigm in infantile emphysema, with distension the prerequisite to destruction. In infantile overdistension, the basic disturbance is an interference with bronchial airway flow due to mural deficiencies with the result that major bronchi, owing to their flaccid state, completely collapse on expiration. The secondary lobules throughout the lung rapidly achieve adult size (120-160 μ), but apparently require at least five to six years of continued overdistension with the superimposition of other factors before polymorphic alveolar wall fenestrations and microcysts develop.

In hilar deformative lesions and occlusive laryngeal cancer, the airway restriction is probably due to a combination of air...
flow impediment and stagnation of bronchial fluids. It has been suggested that local nerve demyelination due to compression atrophy from the incarcerating effect of the hilar lesion develops. This pathologic denervation interferes with the mechanics of bronchial air flow and lung toilet. This latter factor favors the development of chronic bronchitis.

The controversial role of chronic bronchitis in the etiology of emphysema requires a separate analysis. Differing climatic conditions and environmental pollution implicate factors other than organismal infection in the destruction of aerating lung tissue. Topographic microdissection studies of the lung lobule suggest that chronic bronchitis, through bronchial hypersecretion, overpowers ciliary activity. This impairment of lung clearance sustains the erosive action of retained aerogenic agents or pollutants on the walls of air sacs. In cases with "mild chronic" bronchitis, functional closure of the bronchial airways during the dynamics of coughing, as Rayl has shown, may be dominant in the development of emphysema.

In the largest group of cases associated with varying degrees of chronic bronchitis, including the advanced stages with ectasis of the segmental bronchi, an intraluminal organic bronchiolar obstruction was not a constant anatomic feature. The airway obstruction is probably on a functional basis. During the expiratory phase of the respiratory cycle, air trapping may occur either due to structural malalignment of the bronchi, bronchial collapse from mural weakness or from extrabronchial compression by the surrounding parenchyma. Regardless of the method of the functional airway obstruction, both components, hyperinflation and interference with alveolar lung fluid clearance due to chronic bronchitis, are major factors concerned in the pathogenesis of emphysema.

B. Histomechanics and Pulmonary Resistance

The marked prolongation of the expiratory phase of respiration—a salient antemortem and postmortem feature of emphysema—indicates that in the isolated lung several intrinsic powers of contractibility may be concerned in lung retraction. The primary elastic components respond to the magnitude of the force applied, and a viscous system determines the response to a force exerted over a period of time. Although the pressure exerted on the lung was maintained, the flow rate was greatly impeded and a lengthy period of expiration was required before the postmortem residual volume was achieved. In these postmortem lungs in which bronchographic and dissection studies revealed little or no evidence of organic intraluminal obstruction, there was a progressive increase in resistance and prolonged retraction as revealed by spirometric tracings, (Fig. 23b). The investigations of McIlroy and Christie in studying viscosity of gases and bronchial

![Figure 23a: Postmortem spirogram of normal lung showing characteristic sharp deflationary curve (upper tracing) and rapid flow rate expressed by high peak (lower tracing).](http://journal.Publications.Chestnet.org/pdAccess.ashx?url=/data/journals/chest/21367/ on 06/24/2017)

![Figure 23b: Postmortem spirogram of panlobular emphysematous lung showing greatly prolonged expiratory cycle (upper tracing) and restricted flow expressed by small peak (lower tracing).](http://journal.Publications.Chestnet.org/pdAccess.ashx?url=/data/journals/chest/21367/ on 06/24/2017)
airway flow support our anatomic studies that the increase in viscous resistance in emphysema is not due to bronchial obstruction. The gradual increase in viscous tissue resistance bears a direct relationship to the progressive increment in residual volume, as reflected by the grid measurement technic in cases of panlobular emphysema. Due to the panlobular nature of the emphysematous alterations, which are generalized throughout the lung, both viscous and elastic contractile powers are progressively disturbed.

Recent investigations have confirmed the fundamental observations of von Neergaard that the major retractive force within the lung is not the elastica, but the intraluminal mucoprotein film covering the alveolar walls. With the advancement of emphysema, the omnipresent alveolar wall fenestrations increase in number and size, altering the parenchymal surface tension forces and increasing the intrapulmonary resistance to air flow.

C. Cardiopulmonary Pathodynamics

Although efforts to categorize the natural history of emphysema have been made earlier, these have rested solely on clinical impressions, or physiologic readings; a classification integrating antemortem pulmonary function with whole lung pathoanatomic studies has not been attempted previously.

The ventilatory disturbance in panlobular emphysema is accurately reflected by the greatly increased total lung capacity, (125-160 per cent above predicted normal) with the congruent values of residual volume being 60 per cent above normal. The degree of retention determined from alternating vital capacity studies of the expiratory-inspiratory cycle is an indicant of the extensive air entrapment originally expressed in the older specious terminology of "hypertrophic" emphysema. Although not of predictive diagnostic value, there is a severe deficit in maximum breathing capacity. These emphysematous patients were unable to raise their work effort to overcome the greatly increased pulmonic resistance. High nitrogen values, seen in cases of centrilobular emphysema, indicate the existence of numerous bullae which are poorly ventilated and empty slowly. The infrequency of sequestered bullous formations in panlobular emphysema is supported by the lowered nitrogen values recorded in this type of pulmonary overdistension.

Previous investigations concerning the lesser circulation in chronic pulmonary emphysema have stressed physiologic factors such as hypoxia due to vasospasm, carbon dioxide retention, hypoventilated lung fields, and the increased blood viscosity and hypervolemia of polycythemia as major factors responsible for pulmonary vascular resistance. With the structural alterations of the lung vasculature now analyzed on a whole lung purview, the basic role of the anatomic factors in the development of cor pulmonale in generalized panlobular emphysema can be highlighted.

Due to the diffuse nature of the emphysematous change, a critical compromisation of the total capillary bed appears to be the fundamental vascular disturbance. Riley has shown that the degree of destruction of the lung parenchyma is best measured by the diffusing capacity of the lung. Labelled gases, such as krypton and carbon monoxide, illustrate that perfusion and gaseous diffusion occur principally in the lower halves of the lung fields. It is in these areas that the earliest and greatest involvement of the capillary bed was found.

A dynamic factor undoubtedly contributing to the increased incidence of cor pulmonale is an intrapulmonic Valsalva phenomenon. Due to the marked degree of air trapping (Table 2) and the greatly prolonged expiratory phase, (Fig. 23b), the intra-alveolar pressure is markedly elevated with the result that the pulmonary capillary bed, already damaged through alveolar wall fenestration, is further compromised by the transmitted extramural pressure.

In panlobular emphysema, complicated by extensive fibrosis, e.g. pneumoconioses, numerous abnormal precapillary bronchial artery communications are readily demon-
strated at sites of peribronchial scarring, (Figs. 24a and b). These hemic shunts into the pulmonary artery are the major vascular factors responsible for pulmonary hypertension in this form of emphysema.  

In contradistinction, whole lung angiograms and vascular corrosion casts in pure panlobular emphysema without significant degrees of fibrosis revealed three common vascular lesions: (1) a generalized anatomic pruning in the number and reduction in the calibre of arterioles; (2) with atrophy of the stream-reticular bed, non-aerated blood is shunted from the pulmonary artery into paralobular veins across bullous areas, and (3) pulmonary vein aberrancies, apparently due to shunting of blood from right to left following valve decompensation in the bronchopulmonary-azygos system. The functional implication of these organic vascular lesions is increased intravascular pressure and arterial blood desaturation. The pressure on the pulmonary artery side is due to a universal reduction of the arteriolar bed and on the venous side to an incompetent parapulmonary circulation. The incompetency of the parapulmonary circulation and shunting across bullous fields are the major contributants to de-oxygenation of arterial blood in the advanced forms of pure panlobular emphysema.

The end sequel of this sustained intrapulmonic vascular pressure and venous admixture of blood in emphysema, with and without fibrosis, is the grave clinical finale of chronic hypoxia, right ventricular hypertrophy and pulmonary heart failure.

Conclusions

Based upon the structural concept of the secondary lobule of Miller, it is apparent that a common anatomic pattern of emphysema involving principally the terminal air ducts and sacs may be recognized on a localized or generalized basis. This form of emphysema we have labelled the panlobular type, as the entire secondary lobule of Miller shows overdistension and air sac rupture, and in advanced cases uniform bullous fields. An accompaniment of advancing degrees of emphysema is the presence of numerous alveolar fenestrations of major importance in the progression of this form of irreversible lung distension.

Panlobular emphysema is a morphologic denominator common to such heterogeneous conditions as primary kyphotic chest deformities, localized hilar scleroses or neoplastic states producing laryngeal or large bronchial airway deformities and congenital "lobar" emphysema. Less well-defined is the airway obstruction in chronic bronchitis and bronchiectasis observed in many cases of established panlobular emphysema. An additional emphysematous group without structural bronchial deformity was also found. These were usually associated with lesser degrees of emphysema.

Bronchial disturbances may produce not only an obstructive airway mechanism leading to air trapping, but indirectly influence surface tension phenomena within the lung or impair clearance of entrapped pollutants and in this way initiate erosion of the air sac membranes.

Hypertrophy of the right ventricle was a frequent companion of established cases of generalized panlobular emphysema. The air-to-blood exchanging surface—the pulmonary contribution to homeostasis—is progressively destroyed through alveolar sac dissolution with the concurrent loss of the perfusing lung bed being responsible for the common clinical manifestations of cor pulmonale. Other determinants involved in the development of cor pulmonale are pathologic bypasses from artery to vein, bronchopulmonary shunting particularly in emphysema with fibrosis and a decompensating portal azygos-pulmonary vein system. These morphologic findings reflect the primary importance of the pulmonary-cardiac disease in the natural history of this form of emphysema.

Conclusiones

Basándose en el concepto estructural del lóbulo secundario de Miller, es aparente que puede reconocerse un patrón anatómico común de enfisema comprometiendo principalmente los ductos terminales aéreos y los sacos alveolares ya sea...
localizada o generalizadamente. Esta forma de enfisema la llamamos tipo panlobular ya que el lóbulo secundario de Miller completo muestra sobredistensión y ruptura del saco aéreo y en casos avanzados, campos uniformes bulosos. Una cosa que acompaña a los grados avanzados de enfisema es la presencia de numerosas fenestraciones alveolares que son de importancia mayor en la evolución de esta forma de distensión e irreversible pulmonar.

El enfisema panlobular es denominador común morfológico a condiciones tan heterogéneas como las deformaciones xifípticas del Torax, las esclerosis hiliares localizadas o los estados neoplásicos que producen deformaciones laríngeas o grandes de las vías aéreas bronquiales y el enfisema “lobar” congénito.

Menos bien definida es la obstrucción de las vías aéreas en la bronquitis crónica y en la bronquietasia observadas en muchos casos de enfisema panlobular definido. Un grupo enfisematoso adicional sin deformación bronquial estructural también se encontró. Estos estuvieron asociados con grados menores de enfisema.

Los trastornos bronquiales pueden producir no solo un mecanismo obstructivo de las vías aéreas que conduce al atrapamiento de aire sino que indirectamente influyen sobre el fenómeno de tensión superficial dentro del pulmón o dificultan la expansión de los pulmones atrapados y de esta manera se inicia la erosión de las membranas de los sacos aéreos.

La hipertrofia del ventrículo derecho fué un acompañante frecuente de los casos establecidos de enfisema generalizado panlobular. El intercambio de aire-sangre en la superficie—que es la contribución pulmonar a la homeostasis—se destruye progresivamente por la lisis de los sacos alveolares con la consecuente pérdida del lecho pulmonar para la perfusión, lo que es causa de las manifestaciones clínicas del cor pulmonale. Otras determinantes del desarrollo del cor pulmonal son las intercomunicaciones patológicas entre arterias y venas, el “shunt” broncopulmonar, particularmente en enfisema con fibrosis y una descompensación entre la porto-azigos-vena pulmonar.

Estos hallazgos morfológicos reflejan la importancia primordial de la enfermedad cardio-pulmonar en la evolución de esta forma de enfisema.

Resumé
En se fondant sur le concept de structure du lobule secondaire de Miller, il apparaît qu'on peut reconnaitre les conditions anatomiques de l'emphysème banal atteignant principalement les conduits respiratoires terminaux, qu'il soit localisé ou généralisé. L'auteur a appelé cette forme d'emphysème le type “panlobulaire” puisque le lobule secondaire de Miller tout entier montre une distension et une rupture des sacs aériens, et dans ces cas avancés, des zones bulleuses uniformes. L'emphysème en s'accentuant s'accompagne de la présence de nombreuses fenestrations alvéolaires de grande importance dans l'évolution de cette forme de distension pulmonaire irreversible.

L'emphysème panlobulaire est un dénominateur morphologique commun à des états hétérogènes tels que les cyphoses thoraciques primaires, les scléroses hiliares localisées ou les états néoplasiques produisant des déformations des voies laryngées ou des gros conduits bronchiques, et l'emphysème “lobaire” congénital. Moins bien défini est l'obstruction aérienne dans la bronchite chronique et la bronchectasie, observée dans plusieurs cas d'emphysème panlobulaire établi. L'auteur trouve aussi un groupe supplémentaire d'emphysématous sans déformation de la structure bronchique. Ces cas furent habituellement associés à un emphysème de moindre degré.

Des perturbations bronchiques peuvent produire non seulement un mécanisme d'obstruction des conduits aériens, menant au “trapping” mais peuvent en outre influencer indirectement les phénomènes de tensions superficielles dans le poumon, ou troubler l'élimination des produits de pollution restés libres et dans ce sens commencer à érodé les membranes alvéolaires.

L'hypertrophie du ventricule droit fut un compagnon fréquent des cas certains d'emphysème panlobulaire généralisé. La surface d'échange air-sang est progressivement détruite par la dissolation du sac alvéolaire avec la perte simultanée du lit pulmonaire qui est responsable des manifestations cliniques communes du cœur pulmonaire. D'autres déterminants compris dans le développement du cœur pulmonaire sont les courts-circuits pathologiques de l'artère à la veine, le shunt bronchopulmonaire particulièrement dans l'emphysème avec fibrose, et la décompensation du système porte azigos-pulmonaire. Ces constatations morphologiques reflètent l'importance essentielle de l'affection cardio-pulmonaire dans l'histoire de cette forme d'emphysème.

References
259

Volume 41, No. 3
March, 1962

30 Unpublished observations.