Chronic Pulmonary Emphysema -Its Pathogenesis and Check Valve Mechanism-

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INTRODUCTION

There are many unsolved problems in chronic pulmonary emphysema. We believe that it is the most important to clarify the pathogenesis of this disease for early diagnosis, early treatment and prophylaxis. In this report, we try to make clear the pathogenesis and the check valve mechanism characteristic of this disease.

ETIOLOGY

The basic diseases subjected to this study, which were diagnosed carefully by the results of clinical and physical findings and lung function tests, were almost all bronchial asthma and chronic bronchitis (Table 1). According to the classification by Swineford,¹⁾ most of our bronchial asthma belong to infectious type. Atopic bronchial asthma hardly developed into chronic pulmonary emphysema in spite of the presence of the obstructive changes of air way; in other words, the participation of infection must be seriously considered.

TABLE I. Basic Diseases or Complications of 50 Patients
with Chronic Pulmonary Emphysema

Bronchial asthma	38%
atopic	2%
infectious	28%
mixed	8%
Chronic bronchitis	22%
Pneumoconiosis	12%
Bronchiectasis	10%
Pulmonary tuberculosis	6%
Unknown	12%

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Comparing our results with reports of Whitfield,²⁾ Scott *et al.*³⁾ and Spain *et al.*,⁴⁾ many cases were asthma and a few were bronchitis in our materials, but if infectious type of asthma is included in bronchitis, our results may coincide with theirs.

As for the age, chronic pulmonary emphysema due to asthma is mostly found in the fifties while the disease due to bronchitis is in the sixties; it is clear that the aging factor may play an important role. In the old age, pulmonary infection does not always bring about chronic pulmonary emphysema; disposition must be also considered.

As it is known that the chronic pulmonary emphysema is usually associated with the old persons who have been suffered from bronchial asthma or chronic bronchitis, it is important to understand the characteristic of the senile lung.

Structures of the lung and characteristics of the senile lung

The structure of the lung can be divided into respiratory area (air space) and non respiratory area (air way). The former is constituted by the respiratory bronchiolus, alveolar duct, alveolar sac and alveoli.

In the senile lung both hyperinflated and hypoinflated areas are observed (Fig. 1). The hyperinflated area includes the dilation of respiratory bronchioles and alveolar ducts, while hypoinflated area includes the constriction of alveoli (Fig. 2, 4); these findings are clearly observed in the serial section. We call this change type I of the senile change of the lung.

Histologically the emphysematous change in the senile lung can be divided into two types. One is considered to be derived from the type I of senile change; hyperinflated lung and the dilation of the respiratory bronchioles and alveolar ducts, are extremely progressed, and the alveoli, hypoinflated lung, are compressed just like septum as in Figs. 3, 4. This change was usually observed in cases aged the

Fig. 1. Senile changes of the lung.
Hyperinflated and hypoinflated areas are observed.

Fig. 2. Senile changes of the lung (air space) (Type I)

The hyperinflated area includes the dilation of the respiratory bronchioles and alveolar ducts, while the hypoinflated area consists of the constricted alveoli.

Fig. 3. Emphysematous change of the senile lung (Type II)

Above mentioned hyperinflated area is extremely progressed and the hypoinflated area is compressed just like septum.

eighth decade and we call it type II of senile change of the lung, which may be considered as end-results of the so-called senile process of the lung. Another type of the emphysematous change in the senile lung may be due to the existing infection. This emphysematous change is caused by a destruction of the respiratory bronchioles; here both type I and II coexisted. We call it type III of senile change of the lung (Fig. 4).

Adding to them, a slight increase of interstitial connective tissue is also observed in the senile lung, and in some cases atelectasis and fibrosis are usually complicated. Sometimes dust may be much accumulated to promote emphysematous change. In the bronchial wall, especially in the region from the bronchioles to the small bronchi, a dilation of them and hypersecretion are usually observed.

Fig. 4. Senile changes of the air space.

Comparison between the lung of chronic pulmonary emphysema and the senile lung

The lung of chronic pulmonary emphysema reveals more strongly infectious features in the air way and lung parenchyma than the senile lung does, and fibrotic changes are also marked, although they vary with each cases.

In the senile lung, the emphysematous change is diffuse and uniform and tends to appear in the upper lobe. On the contrary, in chronic pulmonary emphysema, it is not always limited in the upper lobe and emphysema shows various sizes and forms bullae especially in the subpleural space.

Histologically, the senile lung, even if it advances from the type I to the

Fig. 5. Emphysematous change in chronic pulmonary emphysema (Centrilobular emphysema stated by Gough)
Respiratory bronchioles are destructed.

Fig. 6. Emphysematous change in chronic pulmonary emphysema (Emphysematous space which is formed by the destruction of the respiratory bronchioles.)

Terminal bronchioles with scarred walls are observed in the emphysematous space.

type II, the structure of respiratory area is preserved comparatively well to appear emphysematous change as the whole, while in the lung of chronic pulmonary emphysema the structure of the respiratory area is almost destroyed. This destruction of the respiratory area (air space) usually seems to be derived from the destruction of respiratory bronchioles (Figs. 5, 6). In other words, the emphysematous changes which are equal to the centrilobular emphysema stated by Gough⁵⁾ are usually formed in the early stage; it may be the result from localized necrosis and scar accompanied with the destruction in this region: in the periphery of emphysematous space the structure of alveoli still remains normally.

We sometimes observe the emphysematous lung which resulted from the alveolar traction due to intra- and interalveolar scar formation, and resulted from the alveolar atrophy and traction due to interalveolitis and arteriolitis accompanied with vascular obstruction. Thus it is likely that dust accumulation promotes the formation of the emphysematous lung.

In chronic pulmonary emphysema, bronchiolitis and the scar formation of the bronchioli are usually found and rather dilation than contraction of the bronchioli, especially at the proximal portion of it, is commonly observed in the region adjacent to the emphysematous lung. The state of hypersecretion is almost equal to that of the senile lung.

The vascular changes are chiefly found in the pulmonary arterioles and small arteries, and sometimes reveal productive endoarteritis. The sclerotic changes of bronchial arteries usually corresponds to that of pulmonary arterial system. There is little remarkable difference between these changes in the emphysematous lung and senile lung.

Lung function in senile lung

In order to observe functionally the changes in senile lung, lung function studies are performed in 70 apparently healthy old persons of over 60 years old. In a few cases vital capacity considerably decreased but in almost all of them it was within normal range by predicted values of Ebina.⁶⁾ Residual volume ratio was almost over 35% (sometimes over 50%), $1^{\text{st}}\text{VC}/\text{VC} \times 100(\%)$ was almost over 70% (rarely below 70%), and the disturbance of intrapulmonary gas mixing was observed. The change in pulmonary visco-elasticity was uncommonly the same as that of chronic pulmonary emphysema. As shown in Fig. 7, static compliance rather tended to decrease, uncommon to increase, and viscous resistance was almost within normal range, but rarely increased remarkably in cases with chronic emphysema.

Fig. 7. Viscoelastic properties of the senile lung.

As the obstructive disturbance in ventilation is rarely found in the healthy senile lung, and this evidence is clearly differentiated from that of chronic pulmonary emphysema, it may be thought whether such an increase of residual volume ratio as reaches 50% is due to (1) change of visco-elasticity of the lung in quality, or due to (2) expiratory disturbance of the thorax. It has been considered that high residual volume ratio in the healthy senile lung was chiefly due to the disturbance of the movement of the thorax since the observations of Kountz and Alexander, because it could be hardly thought that the healthy senile lung might be the non-elastic and did not obey the Hook's law. Accordingly the obstructive disturbance in the senile lung can not always be judged by decrease of MBC.

The lung gradually becomes easy to extend with its growth till the age of about 15–20, and then its elasticity may be kept constant or the lung may rather become difficult to extend. As it is not proper to decide pulmonary elasticity only by the compliance, we must notice the intraesophageal pressure either at resting expiratory or maximum inspiratory level. Intraesophageal pressure in the senile lung varies, and it is very difficult to get a definite conclusion about it. In the average, however, in spite of an increase in functional residual capacity, intraesophageal pressure at resting expiratory level is almost equal to the young one's and intraesophageal pressure at maximum inspiratory level is rather lower. If the comparison between the two is given to draw the static compliance curve of the lungs, it may be presumed that the senile lung is easy to extend up pretty well to the resting expiratory level, so far as the senile lung is not extended forcibly.

Comparison between the lung function and pathological findings of the senile lung

Comparing the above-mentioned lung function with pathological findings, the changes in most of the senile lung may correspond to type I, and so-called senile emphysema may be compatible with type II in which only pulmonary elasticity decreases. However, histological change in the senile lung shows various findings accompanied by senility of the lung other than emphysematous change and impairment of the lung function. As no autopsy is performed in patients in whom lung function is measured during his life time, above results in lung function cannot be related to the structural changes of the senile lung subjected to this study. Theoretically, the development from type I and type II in the senile lung implies an advance to chronic pulmonary emphysema, but clinically or practically, without recurred pulmonary infection and its resultant various changes, this process is not induced probably. Clinically most of chronic pulmonary emphysema are suffering from pulmonary infection. Such a condition may be considered as one in which the extent and grade of type III of the senile lung are intensified.

Pathogenesis of chronic pulmonary emphysema

As for the essential factor of pathogenesis of chronic pulmonary emphysema, we wish to emphasize the importance of the abnormality of pulmonary elasticity due to the destruction of wall of the respiratory bronchioles caused by pulmonary infection. The scheme gives an explanation about the process of the destruction of the wall of the respiratory bronchiole to the emphysematous space. As each respiratory bronchiole is surrounded by its own alveolar sac, if the destruction is caused once in the wall of the respiratory bronchiole, a free communication is formed between the respiratory bronchiole and alveolar sac, and moreover, they become the one (Fig. 8).

Fig. 8. The process of the destruction of the respiratory bronchioles to the emphysematous space.

A.S.....alveolar sac
 A.D.....alveolar duct
 R.B.....respiratory bronchiolus

This change means the destruction of the myo-elastic system contributable to lung retraction. It may be also clear that a decrease of alveolar surface tension due to the diminution of alveolar surface, decreasing of pulmonary contraction, promotes emphysematous change.

We emphasize the great importance of chronic bronchitis, especially bronchiolitis, in regard to the occurrence of chronic pulmonary emphysema. Because chronic bronchitis, especially bronchiolitis is very apt to cause "acinous" lesion, so that it results in the destruction of the respiratory bronchiolus and alveolar duct.

As the thoracic cavity is always under negative pressure, when it is once damaged and the action of elastic tissue is decreased, pulmonary parenchyma is distended. Moreover, hyperinflation of the lung is stimulated by an increase of fluctuation of intrathoracic pressure due to obstructive impairment as asthma, cough by bronchial infection, hyperventilation due to exercise or pulmonary insufficiency, a loss of lung parenchyma and etc.

Cough mechanism

Christie regards the cough as a developmental factor of chronic pulmonary emphysema, while Gordon⁷⁾ opposes to this. Cough paroxysm has been considered to be divided into inspiratory, compressive and expulsive phase. The author has a little different opinion from these reports; the author has not infrequently observed inspiratory phenomenon in the early expulsive phase (Fig. 9), so that it may be presumed that cough may be rather inspiratory phenomenon than expiratory. The pressure and volume load which are put on the alveoli at the time of cough may be due to something so complicated as inspiration is mixed up with expiration; it is thought that actual damage of alveoli at cough

Fig. 9. Spirogram, pneumotachogram and intraesophageal pressure curve observed in cough.

would be more serious than that thought in the usual opinion.

Intrathoracic pressure becomes less negative accompanied by the weakening of pulmonary elasticity, when lung tension decreases. Adding to that, an increase of airway resistance and viscous resistance causes the expiratory ball-valving to develop pulmonary emphysema.

Collateral ventilation

McLean⁸⁾ emphasized the significance of collateral ventilation as a cause of air trapping in pulmonary emphysema. In our study of modified Van Allen's⁹⁾ method to record intrabronchial pressure by electromanometer, lobar bronchus or segmental bronchus was obstructed in manner of inspiratory or expiratory ball-valving and the air was flowed in and out the segmental or lobar bronchus in various flow rate by pump. In this experiment, it was showed that collateral ventilation was clearly demonstrated to occur between every segment but never between lobes. The existence of collateral ventilation is hardly recognizable in the pressure-volume diagram in the connection 4 of the experiment shown in Fig. 10. In the connection 5 at the inspiratory phase of the pressure-volume diagram, the beam of cathodray oscilloscope is observed to move to the left side following to the compliance of alveoli in one segment, and alveoli in another segment are gradually extended by the function of collateral ventilation, so that compliance is given as a sum of both segments (Fig. 11, a). This is similarly observed at the expiratory phase. As collateral ventilation 17cc are calculated roughly at inspiratory phase, while 14 cc at expiratory phase; it is equivalent to about 30% of tidal volume. According to the connection 3 and 5, the airflow in segmental bronchus on one side is observed at inspiratory phase (inspiratory spirogram); the air is rapidly inspirated; the inspiratory curve contains a straight

Fig. 10. The experiment of collateral ventilation.

a. Apparatus

The excised lung is suspended in the glass bottle and two segmental bronchi are taken up outside by the glass tube, and then connected to the body plethysmograph (about 500 L). The pressure in glass bottle is made negative and then the lung is inflated, when the pressure is measured by inductance electromanometer, and connected to X-axis of cathode ray oscilloscope. The volume flow from the lung is transformed to minute pressure change (about 1 mmH₂O) in body plethysmograph, and measured by electromanometer connected to Y-axis in cathode ray oscilloscope.

Fig. 10. The experiment of collateral ventilation.

b. Method

The figure shows the method of connection at the 3 way cook of glass bottle. In the connection 1, both right and left segmental bronchi are connected to the body plethysmograph, and ventilation is measured as the whole. In the connections 2 and 4, only one is connected and the other is left open, and in the experiments 3 and 5, only one is also connected and the other is closed. Each pressure-volume diagram in the 4 connections is shown in the figure below.

Fig. 11. Collateral ventilation.

a. Pressure-volume diagram

This figure shows the record according to the connection 4 shown in Fig. 3. In this figure collateral ventilation is measured 17 cc and 14 cc, and of course really more than those.

Fig. 11. Collateral ventilation.

b. Inspiratory spirogram

This figure shows the inspiratory volume change in the relation to the time. Spirogram of excised lung is given as a cathodray oscillogram (X-axis; time scale, and Y axis; pressure change in body plethysmograph (volume change)). Accompanied with the fast inspiration by pumping inspiratory spirogram is rising rapidly to a certain point, and the gradual change is followed by collateral ventilation. Collateral ventilation of 18cc was finished in 2 sec. in this case.

line together with a curved line; the curved line shows the airflow through collateral ventilation. In this experiment, ca. 18 cc of collateral ventilation are observed to have been fulfilled within 2 seconds.

The histological fact that atelectasis is not observed in the peripheral lung of the obliterated bronchioli due to plugging of secretion may suggest the existence of collateral ventilation. In the cases with these findings, hyperinflated area is usually remarkable, suggesting the occurrence of air-trapping.

Mechanical property of the lung in relation to pathogenesis of pulmonary emphysema

We believe that expiratory check valve is of a great importance as a factor to develop pulmonary emphysema and recently expiratory obstruction has been noticed as an interesting mechanical problem by physiologists.¹⁰⁾

Lung-thorax system may be regarded as a kind of pump; here the more the pressure increases, the more the flow rate usually increases. In the lung, at the inspiratory phase, intrapulmonary pressure is also in proportion to flow rate in the pressure-flow diagram recorded in pulmonary emphysema.

At the expiratory phase at first it does so, but flow rate is getting decreased as the expiration proceeds. The more the patient tries to expire, the more the expiration is difficult for him; it is the expiratory obstruction characteristic of chronic pulmonary emphysema.

In the elements of the pressure acting upon the wall of the airway, there are lung tension, alveolar pressure and intra-bronchial pressure; the balance between these pressures is determined by resistance of peripheral portion of airway, expiratory flow rate, pulmonary compliance, and lung volume.

Fig. 12. Relationship between viscoelastic properties of the lung and maximal expiratory flow rate.

The location in the X-Y co-ordinates is determined by both compliance and resistance of the patients, and the distance from this point to the curved surface is obtained to be maximal expiratory flow rate.

If lung volume is 5 L, the 3-dimensional relation between airway resistance and pulmonary compliance is given as the Fig. 12 with some assumption. The spherical surface shows maximal critical expiratory flow rate. From Fig. 12, it may be clear that maximal expiratory flow rate will be measured following the determination of airway resistance and pulmonary compliance. If we observe both healthy person and patient with chronic pulmonary emphysema in the coordinates of resistance and compliance (the author calls it the viscoelastic diagram), it is shown that in healthy person the maximal expiratory flow rate reaches over 10 L, while in chronic pulmonary emphysematous patient hardly does 5 L.

In the relation among lung volume, time constant and maximal critical expiratory flow rate, it is shown that in healthy subject the more the lung dilates, the more the lung tension increases, and the airway also dilates to make impossible to cause expiratory check valve. In the chronic pulmonary emphysema, however, time constant markedly increases, maximal expiratory flow rate scarcely reaches 2 or 3 L, even if the lung is hyperinflated.

The pressure to collapse the airway is greater in the proximal airway, but compliance of the proximal airway is too little to collapse the airway. Since in the peripheral portion of the airway, a diameter of the airway is maintained by the lung tension, airway is extremely narrowed only by the fact that the pressure on airway becomes almost equal to the lung tension.

The more in the periphery, airway obstruction is, the more this tendency is observed. It is, therefore, recognized that expiratory check valve is liable to occur in the peripheral portion of airway.

Check valve index

We call the ratio of expiratory 0.5"VC and inspiratory 0.5"VC check valve

Fig. 13. Diagram for diagnosis of chronic pulmonary emphysema.

index. When this index and $1''VC/VC \times 100(\%)$ are used together, we may diagnose emphysema more accurately. In the Figure 13, considering the relation between this index and $1''VC/VC \times 100(\%)$, it is known that the patients during asthmatic attack are diagnosed as chronic pulmonary emphysema if $1''VC/VC \times 100(\%)$ is used only a standard,¹¹⁾ while they are distinguished fairly sharply by the use of check valve index.

SUMMARY

The abnormalities of the lung structure and function in the senile and emphysema lung were studied, and the cardinal factors of the development from the senile lung to chronic obstructive emphysema were speculated as follows.

First, the chronic bronchitis which is the common disorder in senile lung, apt to develop bronchiolitis, with acinus inflammation in the acute exacerbation and causes the damage of the wall of respiratory bronchioli and alveolar ducts. Secondly, as the result, the pressure unbalance between the intrapulmonary pressure which tends to collapse airway, the elasticity which tends to distend airway and the intrabronchial pressure develops. These agents which disturb the pressure balance were studied theoretically and measured practically. Thirdly, the check valve phenomenon develops by the pressure unbalance. The vicious circle repeating check valve phenomenon accelerates the progression of the chronic pulmonary emphysema. The other agents; obstructive change, cough, exercise and hyperventilation also accelerate the development and progression of the chronic pulmonary emphysema. We believe the above theory is the most important factor in the pathogenesis of the chronic pulmonary emphysema.

The new index of check valve index (C.V.I.) was proposed in differentiating chronic pulmonary emphysema from bronchial asthma. Application of check valve index in conjunction with one second vital capacity per vital capacity ($1''VC/VC$) is available for diagnosis of chronic pulmonary emphysema.

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