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EMPHYSEMA OF THE LUNGS*

BY

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PART I

Emphysema is a progressive and incapacitating disease, and, although its description is precise and dogmatic in most textbooks, the majority of cases diagnosed on the post-mortem table are not recognized during life, many experienced physicians admitting that they do not understand the diagnosis of emphysema, except in its later stages. Even the term "emphysema" is ambiguous: in these lectures it is used to mean chronic vesicular or hypertrophic emphysema of the lungs, it being understood that acute emphysema, senile emphysema, and localized emphysema are probably separate and distinct entities. I will discuss first the nature of the lesion as shown by observation of the living subject as well as by necropsy.

Nature and Extent of the Enlargement of the Lung

The most obvious changes are in the alveoli, the walls of which appear stretched, thin, and in many places ruptured, so that the septa between adjacent alveoli may be reduced to small projections. It has been claimed that the rupture of the alveolar wall begins at the so-called alveolar pores, but whether or not this is true seems to be of little significance. Of much greater importance is the effect of this destructive process on the air sacs of the lung and on the volume of the lung as a whole, and several changes have been described:

(a) The normal lung lobule or air sac consists of an alveolar duct opening into the atrium, around which are placed the alveoli, and in health there is a sudden transition from narrow alveolar duct to wide atrium, so that the inspired air may be thrown as a jet into the more remote parts of this terminal segment. These lobules have been studied in detail by means of serial sections and of specimens injected with celloidin, and in emphysema it has been shown that the lobule is distorted and sometimes distended (Beitzke, 1925; Kountz and Alexander, 1934). The alveolar duct is dilated and funnel-shaped, so that air is no longer thrown into the atrium as a jet. If it could be shown that this jet of air does in fact serve a useful purpose in ventilating the lobule, it would be reasonable to suppose that this function would be impaired in emphysema.

(b) As the alveolar walls become thin and disappear the air sacs may lose their honeycomb structure and so be deprived of their supporting framework; this is especially true on the surface of the lung, where large bullae may be formed. Provided that the airways to these lobules and bullae remain patent, one would expect that very little pressure would be required to deflate them, and once deflated very little traction would be required to distend them. In other words, it might reasonably be supposed that these flimsy lobules would be more distensible than those lobules which had not lost their supporting framework of alveolar septa.

(c) Another important sequel to this dilatation of the air sacs is the increase of the volume of the lungs as a whole, which is usually

obvious on the post-mortem table: the large fluffy lungs strongly suggest that during life there is an increase in the amount of air they contain. This amount can be measured, and early in the present century several investigators showed that there is usually an increase in the residual air in emphysema. But the residual air is the amount of air left after a forced expiration, and it is well known that patients with emphysema may have great difficulty in forcibly emptying their lungs. A more significant measurement is the amount of air in the lungs at the end of an ordinary quiet expiration; for this is their true air content during life, while the residual air is the result of respiratory gymnastics and may have no relation to the normal size of the lungs. In the accompanying Chart are shown the results of measurements of the lung volume and

Chart showing the lung volume and its subdivisions in emphysema. Cases are arranged from left to right in order of severity of dyspnoea.

its subdivisions in 8 patients suffering from emphysema; it is clear that the amount of air in the lungs was increased in all of them, although only very slightly in several. For instance, the increase was slight in the case of S. H., and yet he was an evident case of emphysema, with dyspnoea on the slightest exertion; while in C. N., a less severe case of emphysema, the volume of the lungs was greatly increased. In none of these cases was the increase ever as great as the volume of a normal lung in full inspiration. These findings have been confirmed by several investigators, and it is clear that in emphysema the lungs as a whole usually contain more air than they should, but this never amounts to more than the increase which occurs in the size of the lungs of a normal individual when he takes a breath of moderate depth. (Hurtado, Fray, and McCann, 1933; Christie, 1934; Anthony, 1936; Cournand, Lassen, and Richards, 1937.) There is certainly never evidence of true over-distension or overstretching of the lungs as a whole, and sometimes

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in even severe emphysema there is no enlargement, but this is uncommon. On the post-mortem table the lungs seem to be greatly enlarged mainly because they do not collapse, and the microscopical appearance of gross over-distension of the alveoli must be due chiefly to destruction of the alveolar walls and the fusion of air spaces.

We can conclude from these various observations that the emphysematous lung is deformed in at least three ways. First, many lobules or air sacs are misshapen and the alveolar ducts are dilated, so that air is no longer thrown into the atrium as a jet. Secondly, the septa between alveoli may disappear, so that the supporting framework of the air sac may be lost. These air sacs or bullae then become comparable to bags of tissue paper, which are easily compressed and easily dilated. Thirdly, the amount of air in the lungs is usually increased, but this increase is not proportionate to the severity of the disease, nor is the volume of the emphysematous lung at rest ever as great as the volume of a normal lung in full inspiration. Thus, whatever may be its microscopical appearance, the lung as a whole in emphysema is not overstretched or over-distended any more than a normal lung is over-distended or overstretched when a breath of moderate depth is taken.

Changes in the lumen of the bronchi and bronchioles also occur, but these are not constant. The terminal bronchioles as well as the alveolar ducts are usually dilated, and this may extend up to the smaller bronchi, producing a picture resembling cylindrical bronchiectasis. The state of the medium and larger bronchi is, however, very variable, and depends more on the degree of bronchitis than on the degree of emphysema, although some atrophy and dilatation are usual in severe cases.

Elasticity of the Lung

Changes in the elasticity of the emphysematous lung were first suggested by a Fellow of our College, William Watson, in 1795. When the thoracic cage is opened on the post-mortem table the lungs do not collapse, and this alone would appear to be proof that the normal elastic recoil of the lung had been lost. However, more detailed observations on the pulmonary elasticity made by measuring the force required to inflate and deflate the lung, have given conflicting results in emphysema (Tendeloo, 1925; Loeschke, 1928; Thies, 1932). Considerable changes in the elastic properties of the lung occur after death, and the significance of post-mortem measurements of elasticity has been seriously questioned. The fact that the lungs do not collapse when the thorax is opened has been said to mean only that they are overstretched in the same way as a spring may be overstretched and yet maintain much of its elasticity. Histological study of the lungs gets us no further, as there is the same disagreement among morbid anatomists as to whether the elastic fibres are destroyed or merely overstretched; nor do the morbid appearances indicate whether loss of elasticity is an early or a late manifestation of the disease. These points are not merely of academic interest, as, if it can be shown that loss of elasticity is early and complete, many of the changes in emphysema can be explained, and for this reason I have measured the elasticity of the lung during life in three cases of pulmonary emphysema. The method used has been described elsewhere and its accuracy has been confirmed (Christie and McIntosh, 1934; Paine, 1940a, 1940b). It is based on the simple observation that the intrapleural pressure is a direct measure of the tension or elastic recoil of the lung. In emphysema the intrapleural pressure is not always negative as it is in health; even at the end of a full inspiration the intrapleural pressure may be the same as that of the atmosphere, and it is not altered when the lung is collapsed by a pneumothorax. These phenomena can only mean that the elasticity of the lung in emphysema may be entirely lost at a comparatively early stage of the disease (Christie, 1934).

It is usually assumed that any loss of elasticity is secondary to over-distension—an assumption which is unsound, as the lungs as a whole are neither overstretched nor truly over-distended. It is not generally realized that the converse is more likely to be true: the enlargement of the air sacs and the fact that this enlargement is most conspicuous at the periphery of the lung can be fully explained as being the direct result of loss of elasticity. That this is so is apparent if it is remembered that, in health, distension of the lung is maintained by traction of the chest wall and diaphragm, and this traction is counterbalanced by the elastic pull of the lungs. It follows that if

these forces are abolished, as occurs when an artificial pneumothorax is given, expansion of the thoracic cage is to be expected, as well as collapse of the lung. That considerable expansion of the thoracic cage does in fact occur while an artificial pneumothorax is being given can be shown if the patient breathes from a recording spirometer; the air displaced into the spirometer is only about half of what is injected into the pleura, and the rest must have been utilized in expanding the thoracic cage (Christie and McIntosh, 1936). It is clear, therefore, both from first principles and from experiment, that loss of pulmonary elasticity in emphysema could be the direct cause of expansion of the thoracic cage.

Loss of elasticity could also explain the real over-distension of air sacs, with bulla formation which occurs on the surface of the lung. With loss of elasticity the expanding force is no longer equally distributed, and equal expansion in different parts of the lung should not be expected. In fact, the greatest expansion should occur where the force is applied, and this is at the surface of the lung. With each inspiration one would expect the superficial air sacs to be strained and stretched to a greater extent than the air sacs deep in the lung, and with this process going on for months and years, it is easy to understand the formation of bullae on the surface of the organ.

Pulmonary Circulation

Extensive changes are described in the pulmonary circulation. Many of the capillaries are torn and obliterated, and there is usually widespread atherosclerosis of the pulmonary vessels. A great deal has been said and written on the relationship of this vascular destruction to hypertrophy of the right ventricle, and, although this controversy may be of importance with regard to the aetiology of cor pulmonale, it seems to be of little significance in emphysema. All are agreed that the pulmonary vascular bed is diminished in emphysema and that the work of the right ventricle may be increased, but this does not mean that the total blood flow through the lung is diminished. If it were reduced the output of the left ventricle would also be reduced, and there is evidence, which I need not describe, that this does not occur until heart failure supervenes.

The lymphatic circulation in emphysema has received but scant attention. The peripheral lymphatics may show cellular infiltration, and the characteristic pigmentation of the lung probably reflects deficient lymphatic drainage.

Distribution of the Lesion

To the naked eye the lesion appears to be most pronounced on the surface of the lungs, especially along the margins, where large bullae may be apparent. Under the microscope, however, it is clear that the changes we have been discussing extend throughout the lung, although the dilatation of air sacs is most conspicuous at the periphery. Characteristic changes outside the lungs have been described. The visceral pleura is thin, flimsy, and atrophic. There is usually a moderate degree of kyphosis, involving all the thoracic vertebrae, which is in contrast to senile emphysema, in which the curvature is as a rule upper dorsal. The vertebral cartilage may be thin and compressed anteriorly, where there may be lipping of the vertebrae. Perhaps partly owing to this curvature, the ribs are widely spaced and run horizontally, and their cartilages frequently show ossification or become elongated and less elastic (Kountz and Alexander, 1934).

Haemo-respiratory Exchange

By far the most important disturbance of function in emphysema is an inability to ventilate the blood, and this is usually apparent many years before the patient reaches the pathologist. The simplest way to measure deficient ventilation in the lungs is to analyse the arterial blood, for this is what the lungs have ventilated. This has been done on many patients with emphysema (Meakins and Davies, 1925; Peters and van Slyke, 1931; Hurtado, Kaltreider, and McCann, 1935); in the accompanying Table are described the results of such an analysis in two of the patients whose pleural pressure had been measured and the elasticity of whose lungs was found to be destroyed, and in another even more severe case. These three

cases have been chosen as they represent moderate emphysema, severe emphysema, and emphysema in its terminal stages. The first (I. H.) had the obvious symptoms and signs of emphysema, but under conditions of rest there was no dyspnoea and no cyanosis. He could walk around the ward, but if hurried became dyspnoeic. His haemoglobin was normal in amount

The Arterial Blood in Emphysema. (For Methods used see Christie, 1934)

Case	Oxygen			Carbon Dioxide				Remarks
	Capacity	Content	Saturation	Content (Whole Blood)	Content (Plasma)	p. CO ₂ (calculated)	Alveolar p. CO ₂	
I. H.	Vols. % 19.4	Vols. % 17.5	% 90	Vols. % 51.4	Vols. % 62.6	mm. Hg 47	mm. Hg 39.3	
	21.0	19.4	92	47.2		44	38.5 45.4	
S. H.	26.4 28.6	21.6 22.4	82 78	53.1 51.1		83 73	71 68	Saturation 102% when breathing 100% oxygen
H. R.	20.9	15.1	72	74.5 74.1	101.7 88	93 90 84 91		{ Venous blood without stasis After venesection of 900 c.cm.

but only 90% saturated with oxygen, which suggests a slight impairment of oxygenation.

The second (S. H.) was a much more severe case of emphysema; he was short of breath on the slightest exertion, there was considerable cyanosis, and the changes in the arterial blood were more striking. The saturation of the blood with O₂ was only 80%, but this anoxaemia could be relieved by oxygen, which is characteristic of emphysema and is, of course, proof that the cause is some impairment of ventilation of the blood in the lungs. In an attempt to compensate for oxygen lack the amount of haemoglobin was increased; the oxygen-carrying power of the blood was 27 vols.%, which is equivalent to a Hb value of over 130% according to any of the ordinary standards. There was also a spectacular increase in the pressure of CO₂, both in the blood and in the alveolar air. This increase in CO₂ in the alveoli is, as I will stress later, characteristic of severe emphysema, and is proof that the cause of the accumulation of CO₂ in the blood is deficient ventilation, and not any barrier between the blood and the alveolar air.

The third case has been included because it represents the most marked disturbance of haemo-respiratory exchange in emphysema which, to the best of my knowledge, has ever been described. He was a typical case of advanced emphysema, and was critically ill, with severe heart failure. The oxygen saturation of his arterial blood was 72% and the pressure of CO₂ lay between 84 and 93 mm. Hg. Not only did he show a compensatory polycythaemia but also a compensatory increase in the bicarbonate reserve, without which he would have suffered a fatal acidosis. This combination is often found in severe cases of emphysema, and in my opinion is another illustration of how confusing is the practice of defining acidosis or acidaemia as a decrease in the alkali reserve or CO₂-combining power, and defining alkalosis or alkalaemia as an increase in the CO₂-combining power. In emphysema the alkali reserve or CO₂-combining power may be raised to over 110 vols.%, with a corresponding reduction in the plasma NaCl, and yet the patient, far from having an alkalosis, is hovering on the brink of acidosis. In the van Slyke classification of acid-base balance and its disturbances this condition would be called a compensated gaseous acidosis, which is obviously what it is in spite of the alkali reserve.

These are the important changes in the blood which occur in emphysema: in severe cases there is gross deficiency in both oxygen absorption and CO₂ elimination, and in the milder cases this deficiency is manifest only when the demands of metabolism are increased by exercise. The defect appears to lie in deficient ventilation of the alveoli rather than in any barrier between the alveolar air and the blood.

Cause of Impaired Haemo-respiratory Exchange

Many explanations of the impairment of aeration of the blood in emphysema have been given, but most of them are based only on conjecture and can be shown to be unsound:

(a) It has been suggested that the respiratory musculature is incapable of properly ventilating the lungs for the same reasons that the vital capacity and chest expansion are diminished; but the blame cannot be placed on the muscles of respiration, as the amount of air drawn into the lungs with each breath and during each minute is normal or even increased in emphysema. Diminution in vital capacity cannot therefore be the cause. The fault must lie in the lungs, as for some reason the air which is inspired does not properly ventilate the blood.

(b) It is obvious that the defect cannot be due to any barrier to the transfer of gases across the pulmonary epithelium, as if this were the cause CO₂ would increase in the blood but not in the alveoli. The fact that changes in the blood are associated with proportionate changes in the alveolar air rules out any suggested possibility of a barrier.

(c) An explanation which is commonly given is that with so many alveoli destroyed there is insufficient functioning lung. Many investigations of haemo-respiratory exchange have been made in patients with pneumothorax, pneumonectomy, and other conditions in which the amount of functioning lung is greatly reduced. Impairment of gaseous exchange, mainly affecting the absorption of oxygen, is found when the reduction in the volume of the lungs is so extreme that the tidal air or the amount of air breathed is diminished (Christie, 1936; Cournand and Berry, 1942). This is in contrast to emphysema, in which there is no diminution in the amount of air inspired and the elimination of CO₂ is impaired to the same extent as the absorption of O₂. "Diminution of the amount of functioning lung" or "diminution in the respiratory surface" cannot therefore explain the changes observed.

(d) Diminution in pulmonary blood-flow has been suggested as the cause. I have already stated that no such diminution occurs until heart failure supervenes. The amount of air entering the lungs is normal or even increased, so any diminution in pulmonary blood-flow would naturally lead to over-ventilation of the blood and not under-ventilation.

(e) A much more reasonable explanation, and one which is widely accepted on the Continent, is that the air sacs are not properly ventilated—partly because they are big, but mainly because the alveolar ducts are distorted (Beitzke, 1925; Kountz and Alexander, 1934). It is true that in emphysema the sudden transition from narrow alveolar duct to wide atrium is lost in many of the air sacs; and it is claimed that the air is no longer thrown in as a jet and the more distant alveoli are therefore not properly ventilated. This has been named the "stratification" theory, so called because it assumes a gradient of ventilation in the lobule, those parts next to the alveolar duct being over-ventilated and the parts further away being under-ventilated. This sounds reasonable, but the validity of this theory of stratification obviously depends on the assumption that in health there must be circulation of air in the air sacs and alveoli, and that diffusion alone is insufficient to maintain adequate exchange of gases in the lobules. The diffusion of gases is governed by well-defined laws, and it can be calculated that, even if the lobule is 1 cm. in diameter, diffusion alone would ensure the transport of gases across the alveolar space with a gradient of less than 1 mm. of Hg. The details of this calculation, together with other evidence which casts doubt on the stratification theory, have been published elsewhere, and it would appear that defective ventilation of the lobule cannot account for the extreme impairment of gaseous exchange observed in emphysema, in which the pressure of CO₂ may be raised by 30 or 40 mm. of Hg (Christie, 1939).

(f) Increase in the volume of the lungs has been suggested as the cause of impaired ventilation, on the assumption that it is more difficult to ventilate a large room than a small one. It is certainly true that in emphysema the amount of air remaining in the lungs at the end of an ordinary expiration is usually somewhat increased, and this explanation may therefore appear reasonable. Physiologists have paid but little attention to the significance of the amount of air in the lungs,

and I will not discuss the various factors involved. It can be said, however, without fear of contradiction, that, provided ventilation is distributed evenly throughout the lungs and alveoli, an increase in lung volume can in no way impair haemo-respiratory exchange. Increase in lung volume could only diminish the fluctuation in the concentration of alveolar gases which occurs during inspiration and expiration. The simile of the large and small room is fallacious, for if you have the same number of people in the small room as in the large room, and the same amount of air used for ventilation, there will be no significant difference in the atmosphere of the two rooms. In any case, increase in lung volume when it occurs is essentially due to increase in the size of individual lobules, and, as I have already stated, diffusion alone could maintain adequate gaseous exchange in a lobule much larger than the average size in emphysema.

(g) An increase in the respiratory dead space has been suggested as the cause of impaired haemo-respiratory exchange, but there is ample evidence that any increase in the anatomical dead space—i.e., the space occupied by the respiratory passages down to the bronchioles—is too small to be of practical significance (Hoover and Gammon, 1915). I will not enter into a discussion on the meaning of the physiological dead space. Most physiologists will agree that those who claim an increase in physiological dead space in emphysema are merely stating in a complicated way that the distribution of ventilation is unequal. In the normal individual the distribution of ventilation is remarkably even throughout the lungs, and consequently samples of alveolar air taken after expirations of varying depths are more or less uniform in composition. This is not the case in severe emphysema: the deeper the patient expires the higher is the CO_2 content and the lower is the O_2 content of the "alveolar air," and these patients show the apparent paradox that, although the amount of air inspired is normal or even increased, the alveoli are under-ventilated. That part of these lectures which deals with the analysis and interpretation of these observations is discussed elsewhere; the conclusion which has been drawn from them is that much of the inspired air is deflected to the enlarged air sacs and bullae, the walls of which are avascular and which are therefore not in contact with the pulmonary circulation. This wastage of ventilation on functionless air sacs cannot be defined as wastage due to increase in physiological dead space, as there is nothing physiological about an emphysematous bulla. Nor can it reasonably be called increase in anatomical dead space. If a definition is wanted I would prefer to give as the cause of impaired haemo-respiratory exchange in emphysema the formation of a pathological respiratory dead space, consisting of bullae and other air sacs which are not in contact with the pulmonary circulation. In very severe emphysema it is possible that all of the inspired air enters this pathological dead space, so that haemo-respiratory exchange would depend mainly on diffusion. In less severe cases it is probable that only some of the inspired air is wasted in this way.

Dyspnoea

The cause of dyspnoea in emphysema is clearly stimulation of the respiratory centre by the CO_2 retained in the blood. Under resting conditions the patient with emphysema either can just get rid of the CO_2 he is forming or, if not, he can compensate by increasing his alkali reserve; and in either case he is not dyspnoeic, because the acidity of his blood is normal. When he exercises, however, he cannot eliminate the extra CO_2 he forms; a gaseous acidosis occurs, and dyspnoea must result. In the absence of bronchospasm there is no orthopnoea, because there is no pulmonary congestion, which is the cause of true orthopnoea.

(Part II, concluding the lectures, will appear in next week's issue, with the list of references.)

The urgent need to prepare a new generation of Jewish physicians, especially in view of the tragic extermination of European Jewry, was urged by Prof. Bernhard Zondek of the Hebrew University when he recently opened the annual conference of the Palestine Jewish Medical Association. The conference was devoted mainly to discussing the problem of establishing a world-wide organization of Jewish physicians with its chair in Palestine. It is planned to issue an English edition of the Jewish medical journal *Harefuah* to be distributed among Jewish doctors throughout the world.

SUPERVISION OF PREGNANT WOMEN IN FACTORY EMPLOYMENT

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The employment of pregnant women has become of vital importance at the present time, and we think it will be of interest if we record our experience in a factory concerned with a specialized industry (light engineering) in which an ante-natal clinic has been established to supervise women employees. It is realized that the figures are small, but we feel that the time has come for a very careful investigation into all factors connected with pregnancy among industrial workers. To obtain sufficiently large figures from any one industry might take so long that much of the value of the ultimate findings would have lost their importance.

We have attended a total of 178 pregnant women, who have come from North-East London. Of these, 90 have been delivered in the first year—82 in hospital and 8 at home—and the greater number have been followed up after delivery to assess any ill effects. All were employed in such work as soldering, welding, assembling small machine parts, etc. Their heaviest jobs were operating capstan lathes and drills. Some of the workers are engaged in a specialized form of assembly in workshops where the temperature at any time is roughly 10° Fahrenheit higher than normal. A full-time factory medical officer is always at call for emergencies, and there is an adequate staff of State-registered nurses (a proportion of whom are certified midwives), who undertake to deal with normal emergencies of industrial medicine.

The Ante-natal Clinic

With the ever-increasing number of pregnancies being reported to the surgery nurses, it was decided—after consultation—that the most satisfactory arrangement would be to set up an ante-natal clinic within the factory. Women reported their pregnancy to the surgery nurses, to the medical officer, to the welfare department, or direct to the midwife in charge of the clinic. Arrangements were then made for their examination and confinement. If they wished to be confined at a hospital—and the larger proportion did—an appointment was made for them, and they were given a covering letter when they went to book at the out-patient department. Having booked a bed and made financial arrangements with the hospital almoner, the women then continued to receive routine examinations at the works ante-natal clinic until such time as they left their employment. One of us (Mr. J. V. O'Sullivan) visited the factory at fortnightly intervals in order to examine these cases. Later, the scheme was enlarged to include the treatment of gynaecological cases. Women from all the factory departments have taken advantage of the scheme, and they include clerical and canteen staffs and cleaners, as well as the factory bench operators referred to above.

Wherever it was deemed necessary, lighter work or shorter hours were advised, and the management put such medical suggestions into immediate practice. We consider this to be of great importance in the supervision of women's health in factories.

We first made a general rule that all patients should cease work at the fifth month of pregnancy, but as time went on we found that most of them wished to continue at their work in later pregnancy, and as they showed no evidence of fatigue or ill-health we permitted them to do so under the special supervision provided. It would appear that so little is the health of experienced workers affected by pregnancy that they continue to work on night shifts without any apparent strain.