Aspects of Chronic Airflow Obstruction*

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This report questions several commonly used definitions and commonly accepted concepts. It suggests that the term, “chronic airflow obstruction,” should replace the terms, “chronic obstructive pulmonary disease,” “chronic obstructive lung disease,” or “chronic airway obstruction,” because it is flow that is obstructed. It is suggested the term, “chronic mucous hypersecretion,” be used, rather than “chronic bronchitis,” and that the latter be avoided. Chronic bronchitis should not be equated with narrowing of the airway and emphysema with loss of elastic recoil. Chronic bronchitis, emphysema, and lesions of the small airways probably occur together more frequently than chance will allow because of a common etiologic agent, tobacco smoke. Chronic mucous hypersecretion without other airway or parenchymal lesions seldom produces airflow obstruction and does not impair prognosis significantly. Central airways are important in chronic airflow obstruction. It is time that someone found out what is happening in subjects with abnormal results on tests of the function of small airways. The definition of “destruction” as it occurs in emphysema is deceptive, and loss of recoil and emphysema may be separate conditions. The dysfunction that occurs in emphysematous lungs is due mainly to associated airway lesions and may perhaps be due in part to the site and nature of emphysematous lesions (as opposed to loss of elastic recoil).

It may seem that almost everything is known about chronic airflow obstruction and that all that remains is to determine the morphologic correlates and the epidemiologic significance of tests of the function of small airways. This is only partially true, and I would like to take this opportunity to point out that much is still unknown and that there is unnecessary confusion. I will question the number of concepts that have become conventional wisdom.

CNSLD, COPD, COLD or CAO?

More serious thought appears to have been directed at the terminology used in pulmonary disease than disease of most other organs, and recently a joint committee of the American College of Chest Physicians and the American Thoracic Society issued a report on pulmonary nomenclature.1 There is probably no more confusion or ambiguity at present in disease associated with airflow obstruction than in other disease, but the ambiguity that existed 20 years ago was a serious obstacle in understanding chronic airflow obstruction. It was primarily for this reason that a group of British physicians produced a set of definitions in 1959.2 These definitions and their application resulted in a much clearer understanding of those diseases associated with chronic airflow obstruction. Some of these definitions may have outlived their usefulness, and it is timely to reexamine some of them.

The original committee coined the term, “chronic non-specifc lung disease,” to encompass the conditions now usually termed “chronic bronchitis,” “emphysema,” and “asthma.” The originally coined term served little useful function, since it was a very cumbersome one and its positive definition was difficult. Because of this, it became common to use such terms as “chronic obstructive lung disease” (COLD), “chronic obstructive pulmonary disease” (COPD), or “chronic airway obstruction” (CAO). The joint committee of the American College of Chest Physicians and the American Thoracic Society recommended the use of the second term and defined “chronic obstructive pulmonary disease” as follows: “This term refers to diseases of uncertain etiology characterized by persistent slowing of airflow during expiration.”(485)

It takes temerity to disagree with an important and knowledgeable official committee, especially when the point at issue appears only to be the use of words. My objection is in part that the word, “disease,” may be used imprecisely, and Campbell3 has discussed this idea. More important, the term is unnecessarily complicated. The condition is defined as an alteration in function, in this instance a diminution in forced expiratory flow. Under these circumstances, it seems much more logical to use the term, “chronic airflow obstruction.” This term has much positive to recommend it. We know that the flow of air can be obstructed from the lung during expiration, both by loss of elastic recoil and by obstruction and narrowing of airways.4 Thus, air-
flow obstruction is a better term than airway obstruction, since airflow can be obstructed by loss of recoil, although there may be no organic airway obstruction.

Another serious criticism of the definition of the joint committee is that it uses diminished flow during forced expiration. It is now well recognized that there may be airflow obstruction when the expiratory flow rates are normal. The classic example is frequency dependence of compliance. There may be doubt about the precise meaning of the simpler tests of the function of small airways and the lesions that occur in them when they are abnormal, but most observers would agree that such tests represent good evidence of airflow obstruction.

There is a very important trap that must be avoided. Since diminution of (expiratory) airflow may be due to loss of elastic recoil or due to narrowing of the lumen of the airway, it is easy to reach the spurious conclusion that emphysema is the same as loss of recoil and that narrowing of the airway is the same as bronchitis. The former notion will be explored subsequently; the latter will be examined now.

**Chronic Bronchitis**

For generations, British physicians have used the term, "chronic bronchitis," synonymously with the syndrome of chronic airflow obstruction. Indeed, some still do. The Ciba group introduced the concept that chronic bronchitis was chronic mucous hypersecretion and described a precise definition of chronic production of phlegm that could be employed to recognize the occurrence of mucous hypersecretion. This definition has been used widely, and useful information about chronic production of phlegm has been obtained.

Unfortunately, the term, "chronic bronchitis," is still widely used to denote chronic airflow obstruction. More importantly, it seems that mucous hypersecretion is a relatively benign condition, and it may be little more than a marker of tobacco smoking. Smokers have abnormal results on tests of the function of small airways; it doesn't matter very much whether they have respiratory symptoms or not. The prognosis of patients with chronic airflow obstruction is determined by the degree to which expiratory flow is impaired. Whether the patients secrete too much mucus or not (and, perhaps, more surprising to some, whether or not they have repeated bronchopulmonary infections) does not further affect their outcome.

Thus, the term, "chronic bronchitis," can be used to describe some subjects with mucous hypersecretion who have no disturbance of function and who will never develop chronic airflow obstruction, as well as patients with mucous hypersecretion who are dying of airflow obstruction. The term, "chronic obstructive bronchitis," has been used to describe the latter group of patients, especially when clinically they were judged to have little or no emphysema; however, the implication exists that the observed airflow obstruction was due to excess intrabronchial mucus. Indeed, some studies purported to show a close correlation between morphologic abnormalities of bronchial mucous glands and the functional severity or type of chronic airflow obstruction. These observations have not been confirmed, and subsequent data obtained by one of the groups of observers did not substantiate their original observations.

This is not to say that excess mucous secretion or excess mucus within the airways never (or even seldom) produces airflow obstruction. There is evidence that mucous hypersecretion may be additive to functional abnormalities produced by emphysema or airway disease, and intuitively one would anticipate that this would be the case; however, it seems more likely that airflow obstruction in patients with mucous hypersecretion is due to associated emphysema and to narrowing and obliteration of peripheral airways. It is often tempting to use the term, "bronchitis," to describe the latter changes, and the temptation is one to which some authors and speakers (including myself) succumb from time to time.

Not only can the term, "chronic bronchitis," be unsatisfactory and ambiguous, but it also is unnecessary. Why not refer to chronic production of phlegm as chronic production of phlegm, and perhaps dignify this by the term, "chronic mucous hypersecretion"? This has the merits of simplicity and accuracy, and chronic production of phlegm remains a symptom, rather than becoming a "disease." The term, "chronic bronchitis," could be dropped altogether, and terms like "airway narrowing" and "airway obliteration" could be used when required. Accordingly, this will be the last time in this report that I use the term, "chronic bronchitis."

The main morphologic correlate of chronic mucous hypersecretion is enlargement of the tracheobronchial mucous glands, and this enlargement can be measured in a variety of ways. One of the simplest, and the one that correlates just as well with clinical symptoms as the more complex ones, is the ratio of bronchial glands to the thickness of the bronchial wall (the Reid index). Some years ago, we pointed out that the distribution curve of the Reid index in random necropsies was unimodal. The epidemiologic definition of chronic bronchitis as chronic production of phlegm implies that subjects either have the condition or they do not, and this.
concept is at variance with the morphologic findings of a continuous distribution curve for the size of mucous glands; however, it is apparent that the use of the criterion of chronic production of phlegm to recognize chronic hypersecretion of mucus is pragmatic. If we would measure the amount of mucus secreted into the airways, these measurements would probably be unimodally distributed. We would then have to choose an arbitrary level of mucous secretion above which the secretion would be regarded as abnormal. This is similar to measurements of blood pressure, and this concept is in keeping with the morphologic observations.

We recently examined the data and compared the Reid index in subjects with mucous hypersecretion to that in subjects without mucous hypersecretions, and this comparison expresses some of our original findings rather more clearly (Fig. 1). Not surprisingly, Figure 1 shows that each group has a unimodal distribution curve and that the values for the Reid index in the subjects with mucous hypersecretion are shifted to the right. Figure 1 also points out the limitation of the Reid index (and probably any other measurement of the size of mucous glands) in predicting the presence or absence of mucous hypersecretion. The Reid index is only effective at high and low values. Intermediate values, which constitute the majority of instances, predict the presence or absence of chronic mucous hypersecretion poorly.

**RELATION OF CHRONIC BRONCHITIS TO EMPHYSEMA**

Chronic production of phlegm is more frequent in patients with emphysema, and, conversely, emphysema is more common in patients with mucous hypersecretion than in those without. The size of mucous glands is increased in patients with emphysema in their lungs, and the average size of mucous glands increases in groups of lungs ranked by increasing amounts of emphysema; however, analysis of the data shows that the patients with the worst emphysema have mucous glands which are, on the average, smaller than the patients with slightly less severe emphysema. The exact significance of this is unclear, but it has been suggested that this represents a facet of atrophy of the bronchial walls which occurs in advanced emphysema and which is discussed further later.

Recently, the opportunity arose to reexamine the association between chronic mucous hypersecretion and emphysema in a large series of cases. This consists of all of the patients from McGill University whose lungs had been inflated post mortem and from whom a giant paper-mounted whole-lung section had been made. The amount of emphysema in the lungs was assessed using the panel grading method, and the lungs were placed in one of nine groups, depending on the amount of emphysema in the lungs. Group 1 consisted of patients with no emphysema, and succeeding groups had progressively more severe emphysema until group 9, which consisted of patients with very severe emphysema (an emphysema score of more than 65). The frequency of chronic mucous hypersecretion, as assessed from the patient's charts, is shown in Figure 2. This shows a steadily increasing frequency of chronic mucous hypersecretion as the amount of emphysema increases until group 7 is reached, in which there is a frequency of more than 80 percent.

What is the relationship between mucous hypersecretion and emphysema? It may seem logical to regard emphysema as a complication or consequence of chronic mucous hypersecretion, but the recent data from Fletcher's laboratory suggests that this is not the case. Subjects with mucous hypersecretion, matched for smoking habit, do not have greater deterioration of expiratory flow rates than patients without chronic mucous hypersecretion, suggesting, therefore, that emphysema does not regularly complicate chronic mucous hypersecretion.

Could emphysema precede, and perhaps produce, mucous hypersecretion? Figure 2 is consistent with

![Figure 1](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/20997/ on 06/06/2017)
hypersecretion
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to therapy, and thus
the role of the muscle of the airways in chronic airflow obstruction may be
important and should be investigated further. Increase in the muscle of the
airways is the characteristic morphologic finding in asthma, but there is controversy about the status
of muscle in the airways in patients with chronic mucous hypersecretion; some authors have
considered that the muscle of the airways was constantly increased in patients with chronic mucous
hypersecretion, whereas other authors have thought that the muscle of the airways was not increased.

We found increased muscle in those patients with chronic mucous hypersecretion who have
prominent attacks of wheezing or a partly reversible component of their chronic airflow
obstruction but not in other patients with chronic mucous hypersecretion. The major site of
obstruction in patients with chronic airflow obstruction is usually thought to lie in airways
less than 2 mm in internal diameter, but the data in this study were obtained from excised
lungs. Thus, the role of increased muscular tone in the airway of living lungs has not been
properly investigated.

Atrophy of bronchial cartilage is easily demonstrable in patients with emphysema, but the
meaning of the lesions is less certain. We have reviewed

cause of downstream closure of the airway during cough and diminished maximum airflow, so that
mucus could be trapped in the peripheral airways even if the amount of mucous secreted is
normal.

The simplest and most obvious explanation of the association of mucous hypersecretion and
emphysema is that they share a common etiologic agent, tobacco smoke. Different constituents of tobacco
smoke could produce each condition, or the same constituent could produce both. This suggestion
brings up any other possible relationships. Dysfunction of the small airways is related to cigarette
smoking, so that the dysfunction of the small airways observed in chronic mucous hypersecretion
may be directly due to the effect of tobacco smoke on the peripheral airways, rather than associated
with chronic mucous hypersecretion.

Central Airways in Chronic Airflow Obstruction

The present emphasis on tests designed to detect dysfunction in peripheral airways had led to neglect
of central airways. Recent work has indicated that downstream events during expiration have been
relatively ignored, and under certain circumstances the trachea may determine the maximum flow that
can be obtained from the lung. Disorders of the muscle of the airways may be important, especially
since these may be susceptible to therapy, and thus the role of the muscle of the airways in chronic airflow
obstruction may be important and should be investigated further. Increase in the muscle of the
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this, and we have also shown previously that patients with emphysema have excess mucus in their
peripheral airways, even if they did not have clinical evidence of chronic mucous hypersecretion. There is
much stronger evidence against this notion. If emphysema preceded chronic mucous hypersecretion,
then chronic mucous hypersecretion would be very uncommon in subjects under the age of 40 years,
since emphysema is rare before that age. The frequency of chronic mucous hypersecretion would
increase steadily with age, paralleling the increase in the frequency of emphysema. This does not happen;
chronic mucous hypersecretion is common before the age of 40 years in smokers, and its frequency
does not increase as much as the frequency and severity of emphysema does with age. Indeed, surveys
in North America indicate that the frequency of chronic mucous hypersecretion changes relatively
little after the age of 40 years. Also, if emphysema preceded mucous hypersecretion, then the latter
should be very commonly, or usually, associated with chronic airflow obstruction, but chronic airflow
obstruction is relatively uncommon in patients with chronic mucous hypersecretion under the age of 40
years and only becomes common in older subjects. The presence of excess mucus in the peripheral
airways of patients with emphysema but no mucous hypersecretion may indicate diminished clearance
of mucus, rather than hypersecretion. Diminished clearance of mucus could occur in emphysema be-

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the evidence\textsuperscript{12} which suggests that atrophy of bronchi- 
cchial cartilage occurs in regions that are not flow-lim- 
iting and that the portions of the airways that are 
hypercompliant and flow-limiting do not correspond 
to airways that have cartilaginous atrophy; however, 
there is radiographic evidence of narrowing of the 
airway at the site of atrophy of the airway in excised 
lungs, but these studies did not investigate whether 
limitation of flow occurred at these sites or not.\textsuperscript{28} 
Detailed studies of limitation of flow and of narrow-
ing of airways in living patients with chronic airflow 
obstruction have only been done in one laboratory. 
It is time that limitation of flow and collapse of the 
airway be examined further and that the role of the 
trachea in disease be examined more closely.

Several authors have suggested that enlargement 
of the bronchial glands may encroach on the lumen 
of the airway and produce airflow obstruction. It 
could also be that inflammation of the airways and 
edema in patients with chronic mucus hypersecret-
cation could further narrow the airways. At the present 
time, it does not seem likely that these are important 
mechanisms in chronic airflow obstruction. First, the 
increase in thickness of mucous glands is small in 
relation to the lumen of the airway. Secondly, edema 
and inflammation are not consistently found in asso-
iation with chronic mucous hypersecretion. More 
important evidence is that subsequent investigators 
have shown very little relationship between mea-
surements of the size of mucous glands and diminu-
tion of the results of tests of expiratory flow.\textsuperscript{12}

Disease of the Small Airways

We used the term, "disease of the small airways," to 
describe the lesions seen in airways smaller than 2 
mm in internal diameter in patients with chronic 
 airflow obstruction.\textsuperscript{22} The initial subjective 
 descriptions have been amplified, and the changes that have 
been documented include narrowing of the air-
ways, intraluminal mucous, and goblet cell 
metaplasia.\textsuperscript{11,24} In addition, there is destruction 
of peripheral airways in emphysema, although this is 
seldom severe.\textsuperscript{11} Goblet cell metaplasia is only 
obvious in patients with chronic clinical airflow ob-
struction and is not a consistent finding in patients 
with chronic mucous hypersecretion and no evi-
dence of chronic airflow obstruction.\textsuperscript{24}

While changes in the peripheral airways in pa-
tients with severe chronic airflow obstruction are 
obvious, quantitative measurements show rather less 
evidence of narrowing of the airways, loss of air-
ways, or mucous plugging than might be anticipated 
on the basis of functional data. On the average, 
peripheral airway resistance increased 18-fold in the 
lungs referred to previously,\textsuperscript{22} and the narrowing 
and loss of airways that have been observed are not 
adequate to account for this great increase in resis-
tance. Narrowing is more important than obliteration, 
because resistance is likely to increase to the 
forth power of the degree of narrowing, whereas 
resistance increases in direct proportion to the loss of 
airways.

A more important consideration is the great ir-
regularity and tortuosity of the peripheral airways in 
emphysema, factors which have been stressed re-
cently by Anderson's laboratory.\textsuperscript{28} These alterations 
are likely to produce a much greater alteration in 
airflow obstruction than would be predicted from 
measurements of the average diameter of the air-
ways. In addition, the distortion of the airways may 
convert flow in the airways from laminar flow to 
turbulent flow.

The term, "disease of the small airways," has taken 
on another meaning in the last few years, and it is 
now often used to indicate changes in structure and 
function in peripheral airways in patients with 
"early" chronic airflow obstruction, generally young 
smokers who have relatively normal results on tests 
of expiratory flow. It is astonishing to see the re-
sources being put into research and the technology 
of tests to determine the function of small airways 
when so little effort has been placed in determining 
the morphologic correlates of the lesions.

One can even question the wisdom of the choice 
of subjects used in such correlative studies that are 
in progress; in general, patients undergoing pneu-
monectomy and lobectomy are being studied. These 
patients are commonly in the sixth or seventh de-
decade of life, rather than being the younger patients 
that are of primary interest. Nearly all of the pa-
tients being studied have cancer of the lung, often 
involving major bronchi, which may affect the re-
sults of tests of pulmonary function. In many in-
stances, specimens from lobectomy, rather than 
pneumonectomy, are being examined; and extrap-
olating from a lobe to a lung, particularly in terms 
of emphysema, is fraught with hazard.

The most relevant data presently available are 
indirect and are those of Niewoehner et al,\textsuperscript{46} who 
examined the airway of young smokers dying of 
accidental death. They found that the most con-
sistent change was "respiratory bronchiolitis." The 
"term was used to refer to mild inflammation and 
edema of respiratory bronchioles, with the accumu-
lation of pigmented macrophages in the respiratory 
bronchioles and adjacent alveoli. Whether this lesion 
is responsible for producing dysfunction of the small 
airways in smokers is still not certain. The consistent 
ocurrence of this lesion in young smokers is in favor 
of the notion; however, resistance to flow in respira-

tory bronchioles is virtually zero at this point, and gas moves by diffusion, rather than convection. Thus, it is difficult to see how this lesion could cause chronic airflow obstruction, if our concepts of the quantitative anatomy of the lung and of gas exchange are correct.

**Emphysema**

Recent information should make us reexamine and question three aspects of emphysema. These are the definition of emphysema, the relationship between structure and function in emphysematous lungs, and the progress of emphysema once the initiating factor or factors are removed. These questions have arisen in large part from experimental models of emphysema using papain and elastase.

**Definition of Emphysema**

The usual definition of emphysema is “permanent, abnormal enlargement of any or all of the acinus, accompanied by destructive change,” and considerable emphasis usually has been placed on destruction. The definition is useful conceptually, since it separates simple overinflation (such as might occur, for example, in the contralateral lung following pneumonectomy) from the lesions in the lung of patients with dysfunction characteristic of emphysema. “Destruction” has never been defined. Destruction is often obvious, for even in relatively mild examples of emphysema, there is obvious loss of alveolar walls. It is usual to consider the earliest phase of destruction, and thus emphysema, to be present when there are abnormal “fenestrae” in alveolar walls. The fenestrae are distinguished from the normal interalveolar pores of Kohn in that fenestrae are larger and are not round or oval with smooth margins; rather, they are irregular in shape and have irregular margins, as though resulting from tears of the alveolar wall. The lesions described in elastase-induced emphysema suggest that it may be inadequate to consider the presence of fenestrae as being the earliest evidence of destruction in emphysema. Gross distortion of the architecture of the lung may be present (Fig 3), yet destruction may not be apparent, as defined by abnormal fenestrations of the alveolar wall.27

The changes observed in the lung are not those of simple overinflation. If this were the case, then linear dimensions in the lung would change to the cube root of the volume increase, and these changes would be very subtle quantitative ones. Instead, the changes are obvious, and they are qualitative ones. The architecture of the lung is distorted and abnormal. This change results in loss of alveolar surface area. With simple overinflation the alveolar surface area should increase to the two-thirds power of the increase in lung volume. Instead, alveolar surface area is lost, due to the rearrangement of the internal geometry of the lung.

These observations suggest that we should change our concepts of “destruction” and consider this to be present when the pulmonary architecture is clearly disarranged, and this should be a qualitative, rather than a quantitative, change. Of particular interest is the nature of this qualitative change in experimentally induced emphysema. These are changes in alveolar walls so that alveoli become shallower and their walls lower. Alveolar ducts and sacs become simpler.

This change bears a remarkable resemblance to the neonatal lung (Fig 4). Perhaps this is to be

![Figure 3. Hamster lungs are shown at various intervals after injection of elastase (A, two days; B, two weeks; C, two months; and D, one year). Note that there is progressive enlargement of air spaces, and at 12 months, several fenestrations can be seen (arrows) (scanning electron photomicrograph, original magnification X 17). (From Kuhn and Tavassoli27).](image)
expected. Elastic tissue (together with collagen and basement membrane to a lesser extent) appears to play a pivotal role in the alveolar multiplication that occurs after birth.\textsuperscript{28} This process results from the subdivision of the simple, peripheral primary saccules of the newborn by secondary septa. The latter characteristically have an elastic fiber with associated collagen fibers at their margins, and it has been postulated that this “fishnet” of elastic fibers forms the scaffolding on which alveolar walls are built. Elastase (but not collagenase) is known to produce emphysema experimentally, and papain produces emphysema by destroying elastic tissue and not collagen. Thus, with the loss of the support of the scaffold of elastic tissue, one might logically expect that under these circumstances the adult lung would revert to the appearance of a neonatal lung, rather than being surprised by the resemblance.

**Structure and Function in Emphysema**

As emphysema in the lung becomes more severe, symptoms of chronic airflow obstruction become progressively more frequent.\textsuperscript{8} Figure 5 shows the frequency of chronic airflow obstruction in nine groups of patients ranked according to the severity of emphysema in their lungs. About two-thirds of the patients with the severest grade of emphysema (grade 9) had severe chronic airflow obstruction. The status of the remaining one-third is uncertain. Figure 5 also shows the frequency of all degrees of chronic airflow obstruction. It would appear that mild grades of chronic airflow obstruction (the difference between severe chronic airflow obstruction and all chronic airflow obstruction) were uncom-

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**Figure 4.** Hamster lung three weeks after administration of elastase (A, top) resembles one-day-old mouse (B, center). Lung from six-day-old mouse (C, bottom) shows how secondary crests have subdivided the primary saccules into alveoli. This is for contrast to other figures. (scanning electron photomicrographs, original magnification × 200). (Part A is from Kuhn and Tavassoli\textsuperscript{27}).

**Figure 5.** Frequency of clinically detectable chronic airflow obstruction increases as amount of emphysema increases (emphysema severity groups 1 through 9). Majority of patients have severe airflow obstruction, mild airflow obstruction (difference between solid and broken lines) is substantially undetected. Patients with forced expiratory volume in first second (FEV\textsubscript{1}) of less than 80 percent of predicted or with maximum midexpiratory flow rate of less than 60 percent of predicted was placed in category of “all chronic airflow obstruction.” Patients were considered to have severe chronic airflow obstruction if they were thought to have died of chronic airflow obstruction on basis of clinical, functional, or autopsy findings, or if they died of other causes but had FEV\textsubscript{1} of less than 40 percent of predicted and maximum expiratory flow rate of less than 25 percent of predicted.

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**ASPECTS OF CHRONIC AIRFLOW OBSTRUCTION**

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mon and randomly distributed. More likely, this represents the poor recognition of mild grades of chronic airflow obstruction when routine spirometric studies are not performed and suggests that at least some degree of chronic airflow obstruction may be almost universal in patients with severe emphysema. The graph also suggests that routine spirometric studies would be a useful screening test on admission to the hospital, certainly more useful than a routine chest x-ray film.

Why were these patients with emphysema disabled? It is usual to ascribe the dysfunction associated with emphysema to loss of elastic recoil of the lung and to assume that the anatomic lesion (emphysema) is closely related (if not causative) to the functional abnormality (loss of recoil). This idea is at best an oversimplification. Much, if not most, of the disability that occurs with emphysema is due to associated airway lesions which are almost universally found in patients with severe emphysema and chronic airflow obstruction. Chronic mucous hypersecretion and a history of cigarette smoking are usual in patients with moderately severe and severe emphysema, so that all of the airways lesions of chronic mucous hypersecretion and cigarette smokers are commonly present in patients with emphysema.

Another way that emphysema may produce dysfunction is directly related to the nature of the emphysematous lesion. Panacinar emphysema produces destruction of the alveolar capillary bed. In centrilobular emphysema the emphysematous spaces may be situated in a critical position between mouth and alveolar wall. It has been suggested that the emphysematous spaces could constitute a large "in series" dead space that might be poorly perfused but well ventilated and that distal to it there might be well perfused but poorly ventilated pulmonary parenchyma. While theoretically an attractive idea, it seems likely that associated airway disease and loss of recoil may be more important in such lungs than the situation and nature of emphysematous spaces.

There is also the assumption that the amount of emphysema in the lung is closely related to the loss of elastic recoil. The available evidence indicates that the relationship between the two is not complete, and in some studies the relationship between pulmonary statics and emphysema has been no better, and sometimes worse, than other tests of pulmonary function, notably the diffusing capacity or transfer factor. Indeed, in some studies the relationship between flow rates and the amount of emphysema has been better than the studies comparing lung recoil and the amount of emphysema in the lung. The lack of a very close relationship between recoil and emphysema in the lung in these studies partly reflects the difficulties in collecting data. Many of the patients had other disease, primarily lung cancer, that might affect function. More important, the groups have been relatively homogeneous, so that correlation coefficients may show a spuriously low relationship, and true relationships between emphysema and recoil may be better than the present data indicate.

A more interesting hypothesis is that emphysema and recoil are not related as cause and effect but are related coincidentally, in perhaps the same way as chronic mucous hypersecretion and emphysema may be related; i.e., cigarette smoking could be etiologically responsible for pulmonary emphysema and also in some way alter the scleroprotein framework of the lung so that elastic recoil is diminished. There is some evidence for this notion. We have shown that the compliance of centrilobular emphysematous spaces is actually diminished compared to normal pulmonary tissue, although the compliance of the lung surrounding the centrilobular emphysematous spaces was increased in one instance. It is also true that lungs with trivial emphysema (to an extent that should not produce morphometric abnormalities) have an increased interalveolar distance but no loss of surface area. Since an increase in the distance between interalveolar walls without an increase in lung volume should reduce alveolar surface area, it follows that lung volume must have been increased in these cases. Thus, it is reasonable to surmise that elastic recoil was diminished in these patients with trivial emphysema so that distention at a standard transpulmonary pressure produced abnormally large lungs and an increased distance between interalveolar walls.

It is difficult to see how such trivial lesions could alter the compliance of the lung or alter the morphometric measurements. It seems more logical to consider that there is widespread submicroscopic damage to the scleroproteins of the lung, which resulted in loss of elastic recoil. Admittedly, the evidence is tenuous, but the important thing is that this hypothesis is testable. This can be done by measuring the elastic properties of excised human lungs and measuring the extent and severity of emphysema, as well as the average distance between interalveolar walls and the lung volumes. If emphysema and loss of elastic recoil are not closely related, then loss of elastic recoil should relate better to an increase in the distance between interalveolar walls and to an increase in predicted lung volume than to some measurement of the amount of emphysema in the lungs.

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How does emphysema develop? Besides stressing the significance of the pulmonary scleroproteins and the importance of inflammation and proteolysis in the pathogenesis of emphysema, the experiments using elastase have raised another important issue, which is the progression of emphysema. The steady deterioration of airflow with time in those who already have obstruction suggests that emphysema may be steadily progressive. Following administration of papain, the average distance between interalveolar walls progressively increases, and the emphysema gets progressively worse (for a year at least) (Fig 3). The inexorable course of severe chronic airflow obstruction is well known; cessation of smoking does not affect the steady deterioration. The state of affairs in less disabled subjects is less certain, and it is critical to determine at which stage deterioration in function can be arrested after stopping smoking. The progress of disease of the small airways appears to be not only capable of being arrested but the functional abnormalities may even return to normal; the question arises as to whether or not the same may be true for loss of elastic recoil.

References


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