TERMINOLOGY, DEFINITIONS, AND CLASSIFICATION OF CHRONIC PULMONARY EMPHYSEMA AND RELATED CONDITIONS

A REPORT OF THE CONCLUSIONS OF A CIBA GUEST SYMPOSIUM

PURPOSE AND TERMS OF REFERENCE OF THE SYMPOSIUM

At present the word emphysema is used to indicate various morbid states of the lung differing widely in their pathology, symptomatology, and prognosis. This results in confusion and misunderstanding between investigators working in different centres and in different branches of medicine and thus retards advance in knowledge of a group of common and often serious disabling diseases.

The purpose of the symposium, the conclusions of which are reported here, was to see whether a group of British investigators could agree upon provisional definitions, classifications, and terminology, and suggest lines of investigation which might clarify obscurities which at present impede the formulation of a satisfactory system of classification.

Individual contributions to the symposium were presented informally and were not intended for publication. At the end of the meeting certain provisional conclusions and proposals were formulated. These were subsequently reconsidered, modified by a drafting committee, and finally approved (with minor reservations) by all the participants. The proposals are provisional and should not be regarded as committing any of the participants to any particular view. They are published in order to encourage people to use defined terms in making pathological, clinical, and functional assessments, to investigate the reproducibility of these assessments in the hands of the same and different observers, and to determine their significance and validity by comparing the results of the different types of assessment with one another. The participants thought this was necessary before any final definition or classification of emphysema itself or the conditions that may be associated with it could be elaborated. It is hoped that further investigations may be assisted by the suggestions put forward, and that in the light of this research what is found useful may become more widely used, and what is imperfect or incorrect may be revealed and corrected.

GENERAL PRINCIPLES OF DEFINITION IN RELATION TO EMPHYSEMA

A disease, as a general concept, may be defined as those abnormal phenomena observed in a group of organisms with disturbed function or structure, the group being defined in a stated way. There are four principal ways in which such a group may be defined: clinical, i.e., upon a simple descriptive basis; morbid anatomical; functional, or physiological; or aetiological.

The term emphysema indicates, and was originally applied by Laennec to, a morbid anatomical state. It is, therefore, appropriate to define it in anatomical terms. When this has been done it has not been found possible to correlate emphysema with any single uniform clinical, radiological, or functional syndrome. It is, therefore, necessary to attempt to define and designate in clinical, radiological, or functional terms syndromes which are thought to be associated with emphysema, and then to study the relation of these syndromes to various morbid anatomical changes. Only when this has been done will it be known whether it is possible to define combined clinico-pathological syndromes to which the word emphysema may justifiably be applied. Meanwhile it is suggested that only clinical and functional terms should be used to describe and define clinical and functional syndromes. The clinical use of the word emphysema should be regarded as presumptive and should only be applied to those cases in which, in the observer's opinion, the defined morbid anatomical changes of emphysema can confidently be asserted to be present. It should be noted that this procedure works well in the field.
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of cardiology, where the functional changes of circulatory failure are defined and classified separately from the morbid anatomical conditions that may cause them.

RECOMMENDATIONS FOR PATHOLOGICAL DEFINITION AND CLASSIFICATION OF EMPHYSEMA

Definition of Emphysema

"Emphysema is a condition of the lung characterized by increase beyond the normal in the size of air spaces distal to the terminal bronchiole either from dilatation or from destruction of their walls."

Emphysema can be diagnosed and classified consistently only on preparations from lungs distended and fixed before they are cut. The simplest technique is intrabronchial infusion of fixative. In some cases identification of the anatomical origin of enlarged spaces may require such techniques as the study of serial sections, or stereoscopic microscopy of lung slices.

It will be necessary to establish the normal range of sizes of air spaces according to age and sex by each technique of lung preparation in order to establish the upper limits of normal size. The term emphysema is restricted to dilatation of air spaces distal to the terminal bronchiole in order to differentiate emphysema from dilatation which includes structures proximal to the terminal bronchiole, as in various forms of honeycomb lung.

Classification of Emphysema

A classification is proposed upon a descriptive morbid anatomical basis, since too little is known about pathogenesis to justify a formal pathogenetic basis. The classification depends upon the distribution of changes within the acinus (defined here as the unit of broncho-pulmonary tissue distal to each terminal bronchiole), and upon the absence or presence of destruction of the walls of air spaces.

There is some difference of opinion as to which of these grounds for separation should be primary. The majority of pathologists at the symposium preferred to make the primary division according to distribution, since this was believed to indicate a difference of pathogenesis, and this is how the classification is first presented below.

An alternative arrangement is also given. This was preferred by one pathologist (L. McA.R.) and the majority of clinicians, because it may better match the clinical differentiation between potentially reversible and irreversible groups, and suggests an alternative pathogenesis. The actual types of emphysema which are to be distinguished are the same according to either arrangement.

1. Unselective distribution beyond the terminal bronchiole (panacinar emphysema).
   (a) Dilatation alone (e.g., compensatory emphysema and emphysema due to partial main bronchus obstruction).
   (b) Destruction of the walls of air spaces (panacinar destructive emphysema).

2. Selective distribution beyond the terminal bronchiole.
   (i) Predominantly affecting respiratory bronchioles.
      (a) Dilatation alone (e.g., focal emphysema due to dust).
      (b) Destruction of the walls of air spaces (centrilobular emphysema).
      (ii) Predominantly affecting alveolar ducts and sacs.
      (a) Dilatation alone.
      (b) Destruction.

3. Irregular distribution beyond the terminal bronchiole (irregular emphysema).

The following alternative arrangement of the classification was proposed.

1. Dilatation alone.
   (a) Unselective distribution (compensatory emphysema and emphysema due to partial main bronchus obstruction).
   (b) Selective distribution predominantly affecting respiratory bronchioles (e.g., focal emphysema due to dust).

2. Destruction of the walls of air spaces.
   (a) Unselective distribution (panacinar destructive emphysema).
   (b) Selective distribution predominantly affecting respiratory bronchioles (centrilobular emphysema).
   (c) Irregular distribution (irregular emphysema).

(Subgroups with selective distribution predominantly affecting alveolar ducts and sacs are omitted from this arrangement because those who favoured it did not recognize their existence. If later experience shows them to exist, they can be inserted in the appropriate positions under 1 (b) and 2 (b).)

It was difficult to decide on the most appropriate word to describe unselective distribution of emphysema within the acinus. The words "diffuse" and "generalized" have been used in this sense, but both were rejected because they could be taken to imply widespread distribution.

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throughout the lung. The word "panacinar" was introduced to replace these in so far as they refer to emphysema which involves all air spaces beyond the terminal bronchiole more or less uniformly.

The word "irregular" is introduced to describe the type of emphysema, commonly found in the neighbourhood of scars, in which dilatation and destruction of air spaces affects neither uniformly nor predominantly one section of the acini.

It is suggested that the word "widespread" should be used to indicate that emphysema of any type is widely distributed throughout the lung. Conversely the word "localized" should be used to indicate that emphysema of any type is confined to one or more segments or lobes of the lung.

Panacinar dilatation emphysema includes such conditions as emphysema compensatory to shrinkage of other parts of the lung, and emphysema due to partial obstruction of air flow anywhere from the larynx to the bronchioles. The adjective "obstructive" should not be used to qualify emphysema unless the presence of bronchial obstruction and its relation (aetiological and anatomical) to the emphysema can be demonstrated.

It was agreed that the use of the term "focal emphysema" to refer specifically to the changes due to focal deposition of dust was so well established that this name should be retained. This appears to represent the only recognized form of dilatation emphysema predominantly affecting the respiratory bronchioles. Similarly, the term "centrilobular emphysema" is well established and could continue to be used as a synonym for destruction emphysema predominantly affecting the more proximal parts of the acini.

The word "vesicular" was used by Laennec to distinguish the types of emphysema which we have defined from "interlobular" emphysema, which is now generally called "interstitial." If the word emphysema is used without qualification it should be assumed to refer to the vesicular, not to the interstitial, variety.

The words "bulla," "cyst," and "bleb" often appear to be used interchangeably, except that an air space lined by recognizable bronchial epithelium or by a fibrous wall is referred to as a cyst, and "bleb" indicates a collection of air between the layers of the visceral pleura. It is suggested that a bulla should be defined as an emphysematous space with a diameter of more than 1 cm. in the distended state. Bullae may accompany any sort of destruction emphysema and their presence should be separately noted.

The term "senile emphysema" does not appear to have been applied to any distinguishable type of disease. Its use is not recommended. When the normal range of size of air spaces in the lung at different ages has been established, the use of the term should be reconsidered.

**Grading of Severity of Emphysema**

It is necessary to have some means of grading the severity of emphysema for comparative studies and for correlation with clinical and physiological observations. In cases with widespread emphysema, the ideal method would be to take random samples of an agreed size from both lungs after distension and fixation and to grade the severity of the disease on the average of the findings in these samples. Since this is impracticable, it is proposed that the changes in each lobe should be graded from 0 to 3 (i.e., absent, mild, moderate, and severe). This grading should be based on an estimate of the average severity within each lobe. For simplicity, it is suggested that the right middle lobe should be included as part of the right upper lobe, thus making two lobes on each side for grading purposes. In cases of focal and centrilobular emphysema, assessments of the severity should be based chiefly on the amount of respiratory tissue affected by the emphysema. In mild cases less than 25%, in moderate cases 25% to 50%, and in severe cases more than 50% of the lung should be abnormal. Examples are given in the illustrations. In panacinar emphysema the size of the air spaces is the main consideration in grading, which should be done to conform as closely as possible with the examples shown in the illustrations. If desired, the overall severity can then be expressed as the sum of the grades in each lobe divided by four. The predominant type of emphysema in each lobe should be noted. The presence of bullae and other important broncho-pulmonary and vascular abnormalities should be separately recorded.

The illustrations of the different types of emphysema in different grades of severity given in Figs. 1 to 12 may assist in classification and grading. They have been produced by two methods. Figs. 1, 2, 7, 8, 9, and 10 are photographs of whole lung sections mounted on paper by the method of Gough and Wentworth (1949), and Figs. 3, 4, 5, 6, 11, and 12 are photographs of slices of lung distended and impregnated with barium sulphate by the method of Heard (1958). Figs. 1 and 2 show respectively the upper limit of
FIG. 1.—Panacinar emphysema. Upper limit of mild grade. From a man aged 40. Paper-mounted section. × 3.

FIG. 2.—Panacinar emphysema. Lower limit of severe grade. Paper-mounted section. × 3.
Fig. 3.—Normal lung (man of 69 years). Barium-sulphate-impregnated slice. ×20.

Fig. 4.—Panacinar emphysema (man of 72 years). Mild grade, dilatation only. Barium-sulphate-impregnated slice. ×20.
Fig. 5.—Panacinar emphysema. Moderate grade. Barium-sulphate-impregnated slice. ×20.

Fig. 6.—Panacinar emphysema. Severe grade. Barium-sulphate-impregnated slice. ×20.
Fig. 7.—Focal emphysema due to dust. Upper limit of mild grade. Paper-mounted section. × 3.

Fig. 8.—Focal emphysema due to dust. Lower limit of severe grade. Paper-mounted section. × 3.
Fig. 9.—Centrilobular emphysema. Upper limit of mild grade. Paper-mounted section. × 3.

Fig. 10.—Centrilobular emphysema. Lower limit of severe grade. Paper-mounted section. × 3.
Fig. 11.—Centrilobular emphysema. Upper limit of mild grade. Barium-sulphate-impregnated lung slice. ×3.

Fig. 12.—Centrilobular emphysema. Lower limit of severe grade. Lung slice. ×3.
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the mild grade and the lower limit of the severe grade of panacinar emphysema in paper-mounted sections. Fig. 3 is a normal lung, and Figs. 4, 5, and 6 lungs with mild, moderate, and severe panacinar emphysema prepared by barium sulphate impregnation. Figs. 7 and 8 show respectively the upper limit of the mild grade and the lower limit of the severe grade of focal emphysema in paper-mounted sections. Figs. 9 and 10, also prepared by this method, and Figs. 11 and 12, prepared by barium sulphate impregnation, show similar grades of centrilobular emphysema.

This method of grading will require studies of its reproducibility in the hands of different pathologists and of its validity in relation to clinical and functional studies before it can be accepted, but a start must be made towards a quantitative estimate of severity of emphysema and it is hoped that these proposals may provide such a starting point.

RECOMMENDATIONS FOR CLINICAL DEFINITIONS, CLASSIFICATION, AND CODING

At present the diagnoses "chronic bronchitis," "asthma," and "emphysema" are used without any general agreement about the clinical conditions to which they refer. Any one (or more) of these words may be used by different clinicians to describe the condition of the same patient. It appears that chronic bronchitis is often used in Great Britain to describe cases that would be called asthma or emphysema in the United States.

These conditions together constitute a group of chronic non-specific lung diseases (accepting the bronchial tree as part of the lung) with whose definition and classification we are here concerned.

The name "chronic non-specific lung disease" is suggested for the whole group. This cumbersome phrase will seldom be used in clinical practice, for patients will usually be allocated to one of the classes designated and defined below.

DEFINITION OF CHRONIC NON-SPECIFIC LUNG DISEASE

The group as a whole may be defined as comprising those subjects with one or more of the following: chronic cough with expectoration, and paroxysmal or persistent excessive breathlessness, which are not solely attributable to:

(a) Localized lung disease of any kind (e.g., tuberculosis, pneumonia, bronchiectasis, cystic disease).

(b) Generalized specific infective lung diseases (e.g., miliary tuberculosis).

(c) The pneumoconioses.

(d) Collagen diseases and the generalized pulmonary fibroses and granulomata.

(e) Primary cardiovascular-renal diseases.

(f) Diseases of the chest wall.

(g) Psychoneurosis.

Chronic non-specific lung disease may coexist with any of the diseases referred to above. For instance, in a case of healed tuberculosis or of simple pneumoconiosis, the symptoms may be due to chronic non-specific lung disease. In such cases, two independent diagnoses should be made. Psychoneurosis is excluded only if there is no somatic effect. Thus psychogenic asthma is included if there is narrowing of the airways.

CLASSIFICATION OF CHRONIC NON-SPECIFIC LUNG DISEASE

The purpose of proposing a classification of the various forms of chronic non-specific lung disease is to clarify the present confusion in the clinical use of the terms chronic bronchitis, asthma, and emphysema. It is proposed that patients be classified according to the three types of respiratory disorder commonly associated with these diagnostic labels:

1. Chronic or recurrent excessive secretion of bronchial mucus.

2. Intermittent obstruction to bronchial air flow.

3. Persistent obstruction to bronchial air flow.

The following main subdivisions (which may coexist) of chronic non-specific lung disease are proposed, and their correlation with current terminology is outlined in Table 1:

1. CHRONIC BRONCHITIS.—"Chronic bronchitis refers to the condition of subjects with chronic or recurrent excessive mucous secretion in the bronchial tree." The diagnostic criterion is clinical, and is chronic or recurrent cough with expectoration which is not attributable to conditions excluded from chronic non-specific lung disease.

2. Infection of the bronchi is frequently but not necessarily present.

3. Not infrequently subjects who produce sputum deny cough. Such subjects are included as having bronchitis. Subjects who habitually swallow sputum should also be included as having chronic bronchitis.

Opinion is divided concerning the significance of "dry" chronic bronchitis without hypersecretion, which is excluded by the proposed
most characteristic signs are rhonchi of sibilant character, but their presence or absence is not closely related to the severity of the obstruction.

(i) Intermittent or Reversible Obstructive Lung Disease: Asthma.—"Asthma refers to the condition of subjects with widespread narrowing of the bronchial airways, which changes its severity over short periods of time either spontaneously or under treatment, and is not due to cardiovascular disease.” The clinical characteristics are abnormal breathlessness, which may be paroxysmal or persistent, wheezing, and in most cases relief by bronchodilator drugs (including corticosteroids).

(ii) Irreversible or Persistent Obstructive Lung Disease.—Irreversible or persistent obstructive lung disease refers to the condition of subjects with widespread narrowing of the bronchial airways, which has been present for more than one year and which is unaffected by bronchodilator drugs (including corticosteroids).

DEGREES OF SEVERITY OF GENERALIZED OBSTRUCTIVE LUNG DISEASE

In subjects with generalized obstructive lung disease:

Lung impairment is present in those with objective evidence of obstruction to air flow but without symptoms.

Lung insufficiency is present in those with persistent abnormal breathlessness.

Lung failure is present in those whose arterial carbon dioxide exceeds, or the arterial oxygen (in the absence of a cardiac shunt) falls below, normal levels* when breathing air at normal atmospheric pressure. Lung failure may occur on exertion without failure at rest. The conditions under which failure occurs should be stated.

Many subjects, if not the majority, with chronic obstructive lung disease have some degree of reversible and some irreversible obstruction. The subdivision suggested is, however, useful clinically. It is suggested that patients should be described as having reversible obstruction or asthma alone if they are symptom-free in remission or under treatment.

Many patients with irreversible chronic obstructive lung disease and with lung insufficiency or failure are at present described as having emphysema. Some such patients have little or no emphysema on post-mortem examination. It is inappropriate to use the word emphysema as a clinical diagnosis only when combined clinical, radiological, and pathological evidence is such.

*Upper limit of normal for pCO₂ = 47 mm. Hg. Lower limit of oxygen saturation = 93% and of oxygen tension = 75 mm. Hg.
that the presence of anatomical emphysema can be confidently asserted. Only in such cases should the diagnosis be given as “chronic lung insufficiency or failure with emphysema.”

At present no proposals are made for sub-classification of the classes of chronic generalized non-specific lung disease, for there is as yet insufficient factual basis for such a classification. It is hoped that future systematic recording and coding of observations upon these cases may permit the development of a useful classification. Meanwhile the use of the main subdivisions in various combinations will enable certain generally recognized types of case to be more accurately and intelligibly distinguished than is possible with the present confused terminology. All the possible combinations of the proposed subdivisions of chronic non-specific lung disease are set out in the Table, where the diagnostic labels that are at present attached to them are compared with the terminology now proposed for each combination.

RECORDING OF CLINICAL AND RADIOLOGICAL OBSERVATIONS

For purposes of comparative studies in different centres, it would be useful to have some uniform method of recording and coding clinical and radiological observations in patients with chronic non-specific lung disease. A standard form for recording certain items of clinical and radiological information in a standardized manner was drafted at the symposium. Clinicians who intend to make comparable studies may like to use this form, duplicated copies of which can be obtained at a small charge from Dr. C. M. Fletcher, Postgraduate Medical School of London, Ducane Road, London, W.12.

THE USE OF LUNG FUNCTION TESTS IN THE STUDY OF CHRONIC NON-SPECIFIC LUNG DISEASE

DIVISIONS OF LUNG FUNCTION

Lung function can conveniently be considered in terms of an air pump, an interface, and a blood pump, or, in more conventional terms, ventilatory function, alveolar-capillary function, and pulmonary circulatory function.

DISTURBANCES OF LUNG FUNCTION IN CHRONIC NON-SPECIFIC LUNG DISEASE

In relation to the proposed clinical subdivisions of chronic non-specific lung disease, it appears that chronic bronchitis may be present without impairment of lung function. The chief impairment in reversible obstructive lung disease or asthma is increased resistance to air flow in the bronchial tree both on inspiration and expiration. In subjects with irreversible obstructive lung disease and with ventilatory insufficiency or failure any or all of the divisions of lung function may be impaired, and a wide variety of patterns of impairment have been described. In cases with severe emphysema there is usually a combination of increased resistance to air flow in the bronchial tree (usually greater on expiration than on inspiration), increase of residual volume, unevenness of ventilation and perfusion, and impairment of gas exchange resulting, when severe, in hypoxia and hypercapnia, and an increase in static compliance. With this combination of disturbances anatomical emphysema is usually thought to be present. Its anatomical type, extent, and severity cannot be determined by function studies, for at present not enough is known about the correlation between different patterns of functional disturbance and different pathological types of emphysema. It is not proposed, therefore, to suggest any diagnostic criteria or to put forward any system of classification based on disturbances of pulmonary function.

In the course of time, if clinical, functional, and pathological observations are made by standardized methods and recorded in a standardized fashion, it may prove possible to suggest diagnostic criteria for different forms of chronic non-specific lung disease with and without different kinds of emphysema.

MEASUREMENT OF IMPAIRED LUNG FUNCTION IN CHRONIC NON-SPECIFIC LUNG DISEASE

All three aspects of lung function must be considered in any patient. There has been a tendency to equate impairment of ventilatory function with impairment of lung function, because this function is usually impaired early in this group of diseases by obstruction to air flow and because its impairment is much easier to measure than impairment of function at the blood-gas interface or in the pulmonary circulation. The more elaborate methods required to test these latter functions are available in few centres. For correlation with morbid anatomy and description of functional syndromes, as complete an analysis as possible should be made in all cases. After careful consideration of all techniques of lung function assessment known to the participants in the conference, it was decided to recommend a group of essential tests which must be done at any centre concerned with advancing knowledge of the diagnosis and classification of chronic lung
diseases, and then to give a supplementary list of functions which should be tested out in the better-equipped centres and which are necessary for full evaluation. The list is not an exhaustive one, and tests additional to those listed may provide valuable additional and confirmatory information.

A. ESSENTIAL TESTS.—The group of tests considered to be essential comprises the following.

1. Ventilatory Function.—Single breath tests are recommended, measuring the one-second forced expiratory volume (F.E.V.1.) and vital capacity (F.V.C.) and also recording the ratio of the one to the other. These tests should be done before and after inhalation of a bronchodilator aerosol. It is suggested that adrenaline and atropine compound spray, 1% isoprenaline or 0.25% phenylephrine hydrochloride, should be used. It should be administered for two minutes, using a nebulizer whose effectiveness has been established. The Wright nebulizer (Aerosol Products (Colchester) Ltd., 87 Eccleston Square, London, S.W.1) has been found effective with a gas flow of 10 l./min. The test should be repeated one minute later.

2. Alveolar-capillary and Circulatory Function.—Some indication of impairment of these functions can be derived from (a) measurements of the ventilatory requirement on exercise, and (b) measurements at rest of arterial blood gases and pH, in addition to assessment of disturbance of the pulmonary circulation by clinical, radiological, and electrocardiographic studies.

(a) The type of exercise to be used will depend upon facilities. Its severity should be described. For estimation of the ventilatory cost of exertion, as opposed to a clinical estimate of exercise capacity, a standardized work level should be employed, using a step test, treadmill or bicycle ergometer adjusted so that at least three minutes of exercise is possible. The exercise ventilation and ventilatory cost of the exercise should be measured. It is desirable to measure changes in O₂ saturation during the exercise either by direct estimation on arterial blood or by oximeter. If neither method is available, it must be noted whether or not cyanosis develops or changes on exercise.

(b) Arterial blood gas and pH measurements at rest should be carried out with the subject breathing air and, if possible, when breathing 100% oxygen. Direct tension measurements of O₂ and CO₂ are greatly preferable. Alternative techniques are derivations of pCO₂ from arterial CO₂ content and pH, or from mixed venous pCO₂ estimated by rebreathing and estimation of oxygen saturation from Van Slyke analysis.

B. RECOMMENDED FUNCTION TESTS.—The supplementary list includes:

1. Subdivision of lung volume by open or closed circuit methods or by body plethysmograph.
2. Forced inspiratory spirogram for comparison with expiratory spirogram.
3. Unevenness of ventilation, from single breaths using a nitrogen or helium meter or by serial washout using open or closed circuit techniques.
4. Distribution of pulmonary ventilation and perfusion by the full technique of Riley or one of its simplified modifications or by expired gas analysis.
5. Measurement of compliance, airways resistance, and work of breathing by oesophageal pressure with spirometer and pneumotachygraph, by airways interrupter or by body plethysmograph.
6. Apparent diffusing capacity for oxygen or carbon monoxide, using either the steady state or the single breath technique.
7. Ventilatory response to oxygen inhalation by spirometry.

RECORDING, GRADING, AND CODING OF RESULTS.

Absolute values of the results of function tests should be recorded. It would be convenient to code them into slight, moderate, and severe deviations from normal. The degrees of disturbance revealed by different tests could then be tabulated in a simple fashion for correlation with pathological and clinical data similarly graded. When sufficient data on test results in normal individuals of specified age, sex, and size have been accumulated, it may be useful to express the results in particular patients as a percentage of the expected normal level. It is at present premature to propose any definite system of expressing or coding results. It is hoped that, so long as full anthropometric measurements and details of technique are provided, comparison between results obtained by different methods should be useful.

REFERENCES


APPENDIX

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