

Incidence of emphysema at necropsy as assessed by point-counting

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The lungs from an unselected group of necropsies were fixed in inflation by boiling formaldehyde vapour, and the percentage of emphysema was determined by macroscopic point-counting. The emphysema was categorized into alveolar, centrilobular, bullous, and 'mixed'. The term 'mixed' emphysema was applied to cases which had a combination of two or all of the three forms.

Quantitative criteria were used in the diagnosis of emphysema. 'Significant' emphysema was defined as destruction of the lung parenchyma by 5% or more of centrilobular or 10% or more of alveolar or bullous emphysema.

Using these criteria, the overall incidence of emphysema in both sexes was 24%, the incidence in men being 35% and in women 9%. Alveolar emphysema was present in 25% of males and in 3% of females. The corresponding figures for centrilobular emphysema were 6% and 3%. Comparison of the present investigation with other studies suggests that there are geographical differences in the incidence of the alveolar and centrilobular forms of the disease.

It is virtually impossible to determine the incidence of pulmonary emphysema by clinical examination (Fletcher, 1952). This applies especially to the centrilobular variety. Even the diagnosis of emphysema at routine necropsy is unsatisfactory since in most cases the pathologist simply slices the unfixed lung to comment on the presence of the disease. This technique demonstrates severe panacinar emphysema with its grossly enlarged air spaces but not alveolar duct, and centrilobular emphysema where the air spaces are smaller. Consequently these varieties of the disease are underdiagnosed. Yet recognition of centrilobular emphysema may be of importance since some authors (Leopold and Gough, 1957; Hicken, Heath and Brewer, 1966) believe that it is more commonly associated with right ventricular hypertrophy than the alveolar duct or panacinar varieties.

The purpose of the present study was to determine the incidence of 'alveolar' (i.e., alveolar duct and panacinar), centrilobular, and bullous emphysema in a 'one-in-five' series of cases coming to necropsy. These terms have been defined previously (Hicken *et al.*, 1966). The term 'mixed' emphysema was introduced in the present study to denote cases where more than one type of emphysema was present.

MATERIALS AND METHODS

AREA OF INVESTIGATION All the patients studied died in the Queen Elizabeth Hospital, Birmingham, which is a teaching hospital serving the industrialized south-western area of the city. Many of the patients treated at the hospital come from predominantly rural areas of Herefordshire, Shropshire, and Worcestershire, and they will not have been exposed to the same level of atmospheric pollution as in the industrial Midlands. Thus the incidence of emphysema in this series is not representative of the city of Birmingham.

SAMPLING OF THE CASES The study extended for 15 months. Wherever possible one lung from every fifth necropsy was studied. If the lungs from the fifth case were needed for other purposes, the next necropsy was investigated, after which the sequence was resumed. In February and August of the first year no cases were examined but the month of February was represented in the second year. In most cases the left lung was studied but if it was bound down by dense adhesions or if it was pneumonic or infiltrated by tumour or accidentally torn, the right lung was examined. No specific respiratory or cardiac disease was excluded from the series.

It was important at the beginning of the study to know how many lungs would form a statistically acceptable sample of the population coming to necropsy. To determine the number of lungs that had

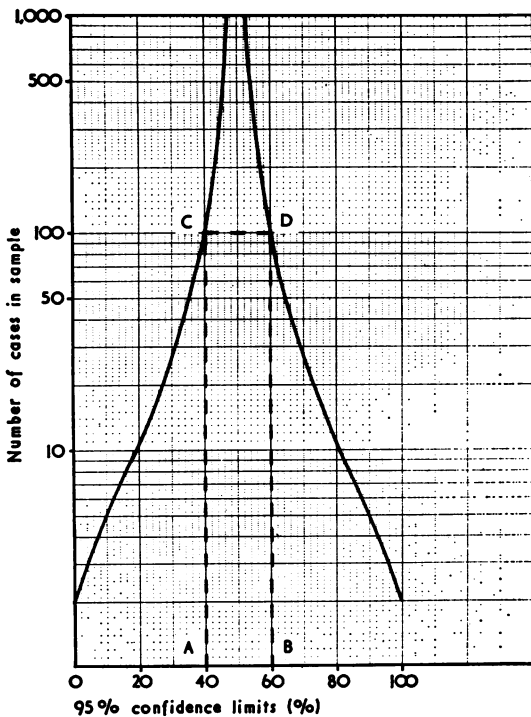


FIG. 1. Graph showing 95% confidence limits if the observed incidence of emphysema is 50%.

to be inflated, consideration was given to theoretical incidences of emphysema. The selected theoretical incidences were 10, 30, 50, 70, and 90%. The upper and lower 95% confidence limits were calculated for samples of 2, 4, 10, 20, 30, 40, 60, 80, 100 and 1,000 cases, using a modification of an equation derived by Mood (1950). At the beginning of the investigation a possible error of $\pm 10\%$ in the estimate of the true incidence was accepted. The results were plotted on five graphs, one of which (Fig. 1) is shown. In this graph the observed incidence of emphysema is 50% and if 100 cases are studied (shown by line CD) the lower 95% confidence limit is 40% (line CA) and the upper 95% confidence limit is 60% (line DB), an error of $\pm 10\%$. When the observed incidence is 10% or 90% only 60 cases have to be studied to ensure that the error is $\pm 10\%$.

When 83 cases had been studied the graphs were re-examined and it was felt that the extra work involved in inflating 17 lungs did not justify lowering the error from $\pm 10.5\%$ to 10% .

FIXATION OF LUNGS AND MACROSCOPIC POINT-COUNTING
The lungs were removed with meticulous care from the thoracic cavity so as to avoid making any holes or tears in the visceral pleura. Any holes were sealed by means of bulldog clips. The lungs were fixed in inflation in a Perspex box by the modification of the

formalin steam method of Weibel and Vidone (1961) described by Hicken *et al.* (1966). The fixed lung was cut into sagittal slices 1 cm thick.

The proportions of normal and emphysematous lung were determined by the method of macroscopic point-counting (Dunnill, 1962; Weibel, 1963).

QUANTITATIVE CRITERIA FOR DIAGNOSIS OF EMPHYSEMA

In the present study emphysema was diagnosed quantitatively. A few foci of dilated respiratory bronchioles or alveolar ducts cannot be accepted as a disease entity, especially as there is enlargement of the alveolar ducts and alveoli with age (Reid, 1967). 'Significant' centrilobular emphysema was diagnosed when 5% or more of the lung was involved by this form of the disease. 'Significant' alveolar or bullous emphysema was diagnosed when 10% or more of the lung parenchyma was involved by these forms of the disease. These figures are arbitrary but take into account that point-counting tends to underestimate the severity of the centrilobular as compared with the alveolar form of emphysema. If two or more forms of emphysema are present and together involve a total of 10% or more of the lung parenchyma, the case was diagnosed as 'significant' emphysema. Cases with less than 10% of alveolar or bullous emphysema and less than 5% centrilobular emphysema were recorded for the sake of comparison with data from other series. Such cases will be referred to as 'minimal alveolar', 'minimal centrilobular', and 'minimal bullous' emphysema.

The present study was carried out on the assumption that the percentage of emphysema in one lung is similar to that in the other. At the beginning of the investigation the validity of this assumption was tested using data obtained by Hicken (1966). This author studied 35 emphysematous patients in the same manner as in the present series. Emphysema was always present in both lungs and when the percentages of emphysema in the right and left lungs were compared statistically, there was little difference between the two ($t=0.039$, $P<0.975$, which is not significant). Thus one lung accurately reflects the percentage of emphysema in the opposite lung.

RESULTS

Eighty-three cases were studied with an age range of 26 to 86 years, the average age being 58.1 years. Of the 83 patients, 65 were aged 50 years or over. This series comprised 48 males and 35 females. Only 10 of the patients had died from pulmonary disease; in four of these, the clinical diagnosis was 'chronic bronchitis and emphysema'. The left lung was studied in 62 cases and the right lung in 21 cases.

The percentage and type of emphysema in each case are shown in Figure 2. Three cases of bullous emphysema are not shown in this figure. In one case with 3% bullous emphysema, it was the only form of emphysema present. In the other two

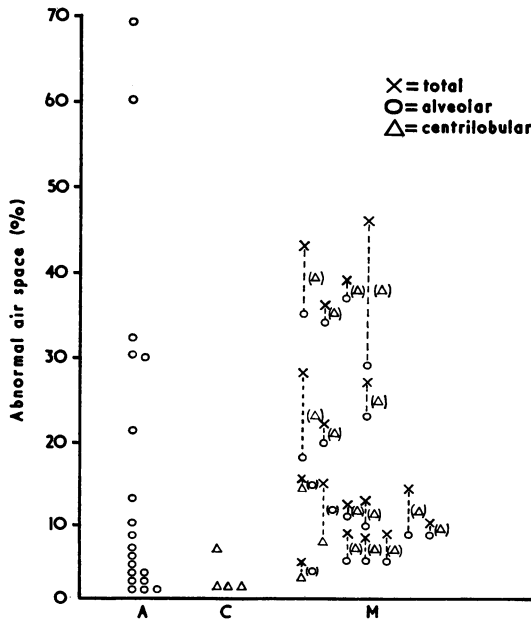


FIG. 2. Percentage of abnormal air spaces in the three types of emphysema: A=alveolar; C=centrilobular; M=mixed; X=total percentage of emphysema, the total being the percentage of the predominant form plus the second form which is indicated in brackets. Thus if the second form is centrilobular it is shown (Δ). The broken line indicates the percentage of the second form.

cases, each with 'minimal' bullous emphysema, alveolar emphysema was also present.

Emphysema (including 'minimal emphysema') was present in 41 cases (49%). Using Fig. 1 and the equation derived by Mood (1950), the upper and lower 95% confidence limits are respectively 59.9% and 38.9%. This is a difference of ±10.5%.

'Significant emphysema' was present in 24% of the cases, being found in 35% of the men and 9% of the women. These figures are shown in Table I, where they are compared with the percentage incidence of all cases, including cases with 'minimal emphysema'.

TABLE I
NECROPSY INCIDENCE OF EMPHYSEMA

Group	Emphysema including Minimal Degrees (%)	'Significant Emphysema' (%)
Total population ..	49	24
Males	67	35
Females	26	9

TABLE II

PERCENTAGE INCIDENCE OF ALVEOLAR, CENTRILOBULAR, AND MIXED EMPHYSEMA

Group	Alveolar		Centrilobular		Mixed	
	'Significant'	All Cases	'Significant'	All Cases	'Significant'	All Cases
Males	25.0	29.2	6.3	4.2	4.2	33.3
Females	2.9	11.4	2.9	5.7	2.9	5.7

INCIDENCE OF VARIOUS TYPES OF 'SIGNIFICANT EMPHYSEMA' Of all the male cases studied 25% had alveolar emphysema, 6.3% centrilobular emphysema, and 4.2% 'mixed' emphysema. In the females, alveolar, centrilobular, and mixed emphysema each accounted for 2.9% of the cases. These results are summarized in Table II.

In males with 'significant' alveolar emphysema, the percentage of lung tissue destroyed ranged from 12 to 68%, the corresponding figures for 'significant' centrilobular and mixed emphysema were 5 to 13% and 27 to 45%. The percentages of 'significant' alveolar, centrilobular, and mixed emphysema in the female cases were respectively 10, 6, and 42%.

There is a statistical difference in the incidence of emphysema in the male and female cases. This is shown by the chi-squared test where $\chi^2=5.1095$ and P is less than 0.05, which is significant.

DISCUSSION

Pulmonary emphysema is a common disease. If minimal degrees of abnormal air spaces in the lung are taken into account, half the population is affected and two-thirds of the men (Table I). When the stricter quantitative criteria used in this investigation are applied, a quarter of the population and a third of the men are still seen to have the disease. This is a high incidence when compared to another common disease like diabetes mellitus, which has an incidence of 9.3% in patients between the ages of 55 and 64 (Walker, 1959).

Alveolar emphysema is three times as common as the centrilobular form in the general population studied and four times as common in males (Table II). The reason for this difference in the incidence is difficult to explain. Centrilobular emphysema is not easily missed when the lungs are fixed in inflation by formalin steam because it has such a characteristic macroscopic picture (Hicken *et al.*, 1966). Confluent centrilobular emphysema can be distinguished from the panacinar form of the disease with care in most cases. Isolated foci of enlarged respiratory bronchioles were common and

if they were counted, the incidence of 'centrilobular emphysema' was spuriously raised to 52% in the males. In a selected series of cases, Hicken *et al.* (1966) also found that alveolar emphysema was commoner than centrilobular in the Birmingham area. This does not preclude the possibility that in other areas of Great Britain the incidences of the two main forms of emphysema are reversed. Thus in Merseyside there is some suggestion that the centrilobular form is commoner (Edwards, Heath, and Harris, 1971). Heard and Izukawa (1964) found that alveolar emphysema was commoner than centrilobular in London and Edinburgh (Heard, 1969). These authors used a grading system for measuring the severity of emphysema and one of their units is approximately equal to 5.5% of lung parenchyma destroyed. If cases with one unit or less of emphysema were excluded, the incidence of the alveolar form was 66% and the centrilobular form, 32%. These figures are comparable with those derived from the present series if cases with minimal amounts of abnormal air space are included (Table III).

It is difficult to compare the present results with those of previous workers because they do not give the percentage of alveolar and centrilobular emphysema in individual cases. A summary of the results of these authors is given in Table III. In

line 6a of this Table, cases with mixed emphysema have been counted twice, as both alveolar and centrilobular emphysema. This enables the present series to be compared more easily with the other studies. In three of the studies (Smith, 1965; Boushy, Greenberg, and Jenkins, 1968; Roberts and Scott, 1972), centrilobular emphysema was commoner than alveolar, whereas in the other two (Heard and Izukawa, 1964; Hayes, 1967) alveolar emphysema was predominant. Boushy *et al.* (1968) used the same method of fixation as in the present series but deliberately excluded alveolar duct emphysema, Smith, Hayes, and Roberts and Scott used the grading system devised by Heard and Izukawa.

Roberts and Scott (1972) found 'significant' centrilobular emphysema in 64% of cases, a higher figure than in the present study. The corresponding figure for panacinar emphysema was 40% but these authors regard more than 5% of panacinar emphysema as significant and thus the figure cannot be compared with 'significant' alveolar emphysema in the present series.

It is interesting that four investigations in different cities but using the same methods show a predominance of different types of emphysema. The reason for these conflicting results is not clear. One answer may be that insufficient cases have been studied for a disease as common as emphysema. Thus in the series quoted in Table III only 183 cases have been studied in the United Kingdom, 147 in the United States and Australia, and 643 in Jamaica. It is not possible to invoke differences in climate for the geographical differences in incidences noted above, since Hayes and Summerell (1969), in a study in Jamaica, found alveolar emphysema was commoner than centrilobular. This finding is in keeping with that of the present investigation yet the island has a climate that is warm for a large part of the year.

The present study also confirms that emphysema is commoner in men than in women. Only one-tenth of the women studied had pulmonary emphysema whereas one-third of the men had the disease. This sex difference has been noted before (Snider, Brody, and Doctor, 1962; Thurlbeck, 1963; Smith, 1965). The incidence of emphysema in male and female cases in the present and other series is summarized in Table III.

Although alveolar and centrilobular emphysema have been compared in numerical terms, care must be taken in the interpretation of the results. In centrilobular emphysema the abnormal air spaces are situated at a strategic point in the respiratory tree and may interfere with the movement of

TABLE III

COMPARISON OF PRESENT SERIES WITH PERCENTAGE INCIDENCE OF ALVEOLAR AND CENTRILOBULAR EMPHYSEMA AS FOUND IN OTHER CENTRES

Author(s)	City	Type of Emphysema			
		Centrilobular		Alveolar	
		Males	Females	Males	Females
1. Heard and Izukawa (1964)	London (U.K.)	40	—	80	—
2. Smith (1965)	Sydney (Australia)	73	23	33	16
3. Hayes (1967)	Kingston (Jamaica)	39.6	16.9	84.8	73.2
4. Boushy <i>et al.</i> (1968)	Houston (U.S.A.)	62.7	—	14.9	—
5. Roberts and Scott (1972)	Glasgow (U.K.)	72	—	50	—
6. Present series (a) All cases of emphysema including both minimal and mixed emphysema (b) 'Significant' emphysema (i.e. > 5% centrilobular and > 10% alveolar and/or bullous)	Birmingham (U.K.)	35.4	11.4	62.5	17.1
	Birmingham (U.K.)	6.3	2.9	25.0	2.9

oxygen into the alveoli and alveolar ducts, where most of the diffusion of this gas occurs. Thus a large number of centrilobular spaces, in total occupying a small volume, scattered throughout the lungs, is probably more important in terms of disturbance of function than a large percentage of alveolar emphysema confined to one lobe.

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